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| • Calyculin A | • Nilotinib – New! |
| • Cyclopamine | • OSU-03012 – New! |
| • Cyclosporin A | • Paclitaxel (Taxol) |
| • Dasatinib – New! | • Rapamycin |
| • 17-DMAG | • Resiniferatoxin |
| • Erlotinib – New! | • Roscovitine |
| • Everolimus – New! | • Sorafenib – New! |
| • Equol | • 12 Soybean Isoflavones |
| • FK-506 | • SP600125 – New! |
| • Gefitinib – New! | • Staurosporine |
| • Geldanamycin | • Sunitinib – New! |
| • Gö 6976 | • Tyrphostin AG 1478 |
| • HA-1077 (Fasudil) | • Vandetanib – New! |
| • Imatinib – New! | • Vatalanib – New! |
| • Lapatinib – New! | |

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- Highest purities available

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Biological Activity Index

Adenylate Cyclase

Activators

F-9929 Forskolin	14
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Alcohol Dehydrogenase Inhibitors

D-2946 Daidzein	8
D-7878 Daidzin	8

Apoptosis Reagents

B-8500 Brefeldin A	5
C-8700 Cyclopamine	7

ATPase Inhibitors (See Also Ion channel Reagents – Ion Co-Transporters)

B-1080 Bafilomycin A1	2
T-3250 Thapsigargin	40

Calcineurin (See Protein Phosphatase 2B)

Calcium-Related Reagents

Calcium Releasers (from Intracellular Stores)

T-3250 Thapsigargin	40
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Ion Channel Activators

Calcium/Divalent Cation Channel Activators

I-6400 5'-Iodoresiniferatoxin	20
I-2000 6'-Iodoresiniferatoxin	20
P-6388 PPAHV (Phorbol 12-Phenylacetate 13-Acetate 20-Homovanillate)	33
R-6712 Resiniferatoxin	34
T-5096 Tinyatoxin	40

TRPV Cation Channel Activators (a.k.a. OTRPC,VR-OAC,TRP12, VRL-2)

P-1571 4 α -Phorbol 12,13-Diacetate	29
P-4678 4 α -Phorbol 12,13-Dibutyrate	29
P-2170 4 α -Phorbol 12,13-Didecanoate	30
P-8880 4 α -Phorbol 12-Myristate 13-Acetate	32

Ionophores, Calcium

I-5700 Ionomycin, Free Acid	21
I-6800 Ionomycin, Calcium Salt	21

Ion Transporter/Co-transporter Inhibitors (Ca²⁺)

T-3250 Thapsigargin	40
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Capsaicin-related Reagents

I-6400 5'-Iodoresiniferatoxin	20
I-2000 6'-Iodoresiniferatoxin	20
P-6388 PPAHV (Phorbol 12-Phenylacetate 13-Acetate 20-Homovanillate)	33
R-6712 Resiniferatoxin	34
T-5096 Tinyatoxin	40

cdc/cdk Kinases (See Cell Cycle Reagents)

Cell Cycle Reagents

Cyclin/cdc/cdk Kinases

Inhibitors

R-1234 Roscovitine	35
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CSBP Kinase (See MEK and MEK Kinases)

Cyclic Nucleotide Reagents (See individual entries, e.g. Adenylate Cyclase, Guanylate Cyclase, Phosphodiesterase, PKA, PKC, PKG)

Cyclin/cdc/cdk Kinases (See Cell Cycle Reagents)

EGF Receptor Kinase Inhibitors (See also Tyrosine Kinase Reagents)

T-7310 Tyrphostin AG 1478	41
T-3655 Tyrphostin AG 1478, Methanesulfonate Salt	41

Endoplasmic Reticulum Reagents

T-3250 Thapsigargin	40
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ERK Kinase (See MEK and MEK Kinases)

FLK-1 (See VEGF Receptor Kinase)

Golgi Reagents

B-8500 Brefeldin A 5

Heat Shock Protein Modulators

G-4500 Geldanamycin 15

Hedgehog Inhibitors

Smoothened (Smo) Inhibitors

C-8700 Cyclopamine 7

Histamine Secretagogues

T-3250 Thapsigargin 40

Immunosuppressants

C-6000 Cyclosporin A 7

E-4040 Everolimus 12

F-4900 FK-506 13

P-6040 Pimecrolimus 32

R-5000 Rapamycin 34

Ion-modulating Reagents

H⁺-ATPase Inhibitors

B-1080 Bafilomycin A1 2

Calcium Releasers (from Intracellular Stores)

T-3250 Thapsigargin 40

Ion Channel Activators

Calcium/Divalent Cation Channel Activators

I-2000 6'-Iodoresiniferatoxin 20

R-6712 Resiniferatoxin 34

T-5096 Tinyatoxin 40

TRPV Cation Channel Activators (a.k.a. OTRPCH, VR-OAC, TRP12, VRL-2)

P-1571 4 α -Phorbol 12,13-Diacetate 29

P-4678 4 α -Phorbol 12,13-Dibutyrate 29

P-2170 4 α -Phorbol 12,13-Didecanoate 30

P-8880 4 α -Phorbol 12-Myristate 13-Acetate 32

Ionophores, Calcium

I-5700 Ionomycin, Free Acid 21

I-6800 Ionomycin, Calcium Salt 21

Ion Transporter/Co-transporter Inhibitors (Ca²⁺)

T-3250 Thapsigargin 40

Isoflavones (See Soybean Isoflavones)

JAK-2 Kinase Inhibitors

T-9142 Tyrphostin AG 490 40

Kinase Inhibitors, Non-Selective

P-7600 PKC412 33

S-9300 Staurosporine 38

MAP Kinases (See MEK and MEK Kinases)

MEK and MEK Kinases

Inhibitors

D-2744 Doramapimod 10

P-4313 PD 98059 28

S-1700 SB 202190 36

S-3400 SB 203580 36

U-6770 U0126 42

Myosin Light Chain Kinase Reagents

Inhibitors

W-2990 Wortmannin 43

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I-6400 5'-Iodoresiniferatoxin 20

I-2000 6'-Iodoresiniferatoxin 20

P-6388 PPAHV (Phorbol 12-Phenylacetate 13-Acetate 20-Homovanillate) 33

R-6712 Resiniferatoxin 34

T-5096 Tinyatoxin 40

Nuclear Export Inhibitors

L-6100 Leptomycin B 22

p38 Kinase (See MEK and MEK Kinases)

p40 Kinase (See MEK and MEK Kinases)

Phosphatidylinositol 3-Kinase Inhibitors

L-7962 LY 294002 23

W-2990 Wortmannin 43

PI 3-Kinase (See Phosphatidylinositol 3-Kinase Inhibitors)

Proteasome Inhibitors

B-1408 Bortezomib 4

Protein Kinase A (PKA)

PKA Inhibitors

F-4660 Fasudil, Monohydrochloride Salt 12

H-5239 H-89, Dihydrochloride Salt 17

H-2330 HA-1077, Dihydrochloride Salt 17

S-9300 Staurosporine 38

Protein Kinase C (PKC)

PKC Activators

PKC-selective but not PKC Isotype-selective Activators

I-8560 Ingenol 19

M-2550 4-O-Methylphorbol 12-Myristate 13-Acetate 25

P-4227 Phorbol 13-Acetate 29

P-7350 Phorbol 13-Decanoate 29

P-5005 Phorbol 12,13-Diacetate 29

P-3106 Phorbol 12,13-Dibenzoate 29

P-4833 Phorbol 12,13-Dibutyrate 29

P-1925 Phorbol 12,13-Didecanoate 31

P-3814 Phorbol 12,13-Dihexanoate 31

P-1680 Phorbol 12-Myristate 13-Acetate 31

P-4462 Prostratin 33

R-8765 Resiniferonol 9,13,14-Orthophenylacetate 35

Negative Controls

P-1571 4 α -Phorbol 12,13-Diacetate 29

P-4678 4 α -Phorbol 12,13-Dibutyrate 29

P-2170 4 α -Phorbol 12,13-Didecanoate 30

P-8880 4 α -Phorbol 12-Myristate 13-Acetate 32

PKC Inhibitors

PKC-selective but not PKC Isotype-selective Inhibitors

C-3030 Chelerythrine Chloride 6

PKC Isotype-selective Inhibitors

G-6203 Gö 6976 17

R-9630 Rottlerin [See Important Note] 35

PKC Inhibitors not Selective for PKC or of Unknown Selectivity

H-5239 H-89, Dihydrochloride Salt 17

P-7600 PKC412 33

S-9300 Staurosporine 38

Protein Kinase G (PKG)

Inhibitors

F-4660	Fasudil, Monohydrochloride Salt	12
H-2330	HA-1077, Dihydrochloride Salt	17
S-9300	Staurosporine	38

Protein Kinase Inhibitors (see also individual enzymes)

C-3030	Chelerythrine Chloride	6
D-3307	Dasatinib	9
E-4007	Erlotinib, Hydrochloride Salt	11
F-4660	Fasudil, Monohydrochloride Salt	12
G-4408	Gefitinib	14
G-6055	Genistein	16
G-6203	Gö 6976	17
H-5239	H-89, Dihydrochloride Salt	17
H-2330	HA-1077, Dihydrochloride Salt	17
I-5508	Imatinib, Methanesulfonate Salt	18
L-4804	Lapatinib	22
L-7962	LY 294002	23
N-8207	Nilotinib	25
O-5679	OSU-03012, Hydrochloride Salt	27
P-4313	PD 98059	28
P-7600	PKC412	33
R-1234	Roscovitine	35
S-1700	SB 202190	36
S-3400	SB 203580	36
S-7979	SP600125	37
S-8502	Sorafenib, <i>p</i> -Toluenesulfonate Salt	36
S-9300	Staurosporine	38
S-8803	Sunitinib, Malate Salt	38
T-9142	Tyrphostin AG 490	40
T-7310	Tyrphostin AG 1478	41
T-3655	Tyrphostin AG 1478, Methanesulfonate Salt	41
T-2710	Tyrphostin SU 1498	42
U-6770	U0126	42
V-9402	Vandetanib	42
V-8303	Vatalanib, Dihydrochloride Salt	43
W-2990	Wortmannin	43

Protein Phosphatase 1 Reagents

Inhibitors

C-3987	Calyculin A	6
O-2220	Okadaic Acid, Free Acid	26
O-6410	Okadaic Acid, Ammonium Salt	26
O-7519	Okadaic Acid, Potassium Salt	27
O-5857	Okadaic Acid, Sodium Salt	27

Protein Phosphatase 2A Reagents

Inhibitors

C-3987	Calyculin A	6
O-2220	Okadaic Acid, Free Acid	26
O-6410	Okadaic Acid, Ammonium Salt	26
O-7519	Okadaic Acid, Potassium Salt	27
O-5857	Okadaic Acid, Sodium Salt	27

Protein Phosphatase 2B (Calcineurin) Reagents

Inhibitors

C-6000	Cyclosporin A	7
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Related Reagents

E-4040	Everolimus	12
F-4900	FK-506	13
P-6040	Pimecrolimus	32
R-5000	Rapamycin	34

Protein Trafficking Reagents

B-8500	Brefeldin A	5
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Rho-Associated Kinase II

Inhibitors

F-4660	Fasudil, Monohydrochloride Salt	12
H-2330	HA-1077, Dihydrochloride Salt	17

RK Kinase (See MEK and MEK Kinases)

Soybean Isoflavone-related Compounds

Soybean Constituents

A-6900	6"-O-Acetylaidzin	1
A-3000	6"-O-Acetylgenistin	2
A-7860	6"-O-Acetylglycitin	2
D-2946	Daidzein	8
D-7878	Daidzin	8
G-6055	Genistein	16
G-5200	Genistin	16
G-1152	Glycitein	16
G-2822	Glycitin	17
M-6730	6"-O-Malonyldaidzin	24
M-8090	6"-O-Malonylgenistin	24
M-4620	6"-O-Malonylglycitin	25

Soybean Isoflavone Metabolites

D-9200	(<i>R,S</i>)-2,3 Dihydrodaidzein	9
E-5880	(<i>R,S</i>)-Equol	11

TRPV Cation Channel Activators (a.k.a.

OTRTPCH,VR-OAC,TRP12, VRL-2)

P-1571	4 α -Phorbol 12,13-Diacetate	29
P-4678	4 α -Phorbol 12,13-Dibutyrate	29
P-2170	4 α -Phorbol 12,13-Didecanoate	30
P-8880	4 α -Phorbol 12-Myristate 13-Acetate	32

Tubulin Assembly/Stabilization Promoter

D-1000	Docetaxel	10
P-9600	Paclitaxel	28

VEGF Receptor Kinase Inhibitor

T-2710	Tyrphostin SU 1498	42
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Disposal Codes

A. Suspend or dissolve the compound with a flammable solvent and incinerate in a chemical incinerator with an afterburner and scrubber.

General Information and Conditions of Sale

To Order, Contact:

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Alphabetical Listing of Products and Prices

Novel Acetylated Forms of the Soybean Isoflavones

Only in recent years has it been recognized that large and variable portions of the total daidzein, genistein and glycitein found in certain soy products, especially those processed with heating, toasting and/or high pH, occur in the 6"-O-acetyl forms, not as the free glycosides or aglycones.

Because these compounds have only recently been found in soybean products, their specific biological, pharmacological and nutritional properties have not been extensively investigated. Given the increasing use of soy products and the many beneficial nutritional properties attributed to the isoflavone components of those soy products, it appears that further studies of the biological role of these novel soy isoflavones are of substantial scientific and medical importance.

LC Laboratories® offers the three acetylated isoflavones from soybeans: 6"-O-Acetyldaidzin (Cat. No. A-6900 on page 1), 6"-O-Acetylgenistin (Cat. No. A-3000 on page 2) and 6"-O-Acetylglycitin (Cat. No. A-7860 on page 2).

A-6880 17-AAG, >99%

[Telatinib] [17-(Allylamino)-17-demethoxygeldanamycin]
[17-(Allylamino)geldanamycin] [NSC-330507]
[Tanespimycin]

Size	US\$	€	£	¥
25 mg	98	81	54	11,800
100 mg	229	190	126	27,500
250 mg	445	369	245	53,400
1 g	988	820	543	118,600
2 g	1760	1461	968	211,200

M.W. 585.70 C₃₁H₄₃N₃O₈ [75747-14-7]

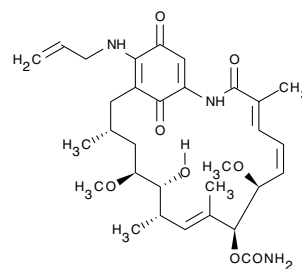
Warning: Toxic.

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO. **Disposal:** A

- Synthetic derivative of geldanamycin (Cat. No. G-4500 on page 15) demonstrating greater stability and lower *in vivo* toxicity than its parent compound. 17-AAG binds specifically to heat shock protein Hsp90 in a manner similar to geldanamycin, but the binding is weaker. Schulte, T.W. and Neckers, L.M. "The benzoquinone ansamycin 17-allylamino-17-demethoxygeldanamycin binds to Hsp90 and shares important biologic activities with geldanamycin." *Cancer Chemother. Pharmacol.* **42**: 273-279 (1998).
- Inhibits Akt activation and HER2 expression in tumor cells. Basso, A.D., *et al.* "Ansamycin antibiotics inhibit Akt activation and cyclin D expression in breast cancer cells that overexpress HER2." *Oncogene* **21**: 1159-1166 (2002).
- Exhibits 100-fold higher binding affinity for tumor-cell-derived Hsp90 over that derived from normal cells. Kamal, A., *et al.* "A high-affinity conformation of Hsp90 confers tumour selectivity on Hsp90 inhibitors." *Nature* **425**: 407-10 (2003).
- Sensitizes tumor cells to growth arrest and apoptosis induced by paclitaxel (Cat. No. P-9600 on p 28). Nguyen, D.M., *et al.* "Sequence-dependent enhancement of paclitaxel toxicity in non-small cell lung cancer by 17-allylamino 17-demethoxygeldanamycin." *J. Thorac. Cardiovasc. Surg.* **118**: 908-915 (1999) and Solit, D.B., *et al.* "Inhibition of heat shock protein 90 function down-regulates Akt kinase and sensitizes tumors to Taxol." *Cancer Res.* **63**: 2139-2144 (2003).
- Sensitizes colon cancer cells to cisplatin-induced cell death. Vasilevskaya, I.A., *et al.* "Quantitative effects on c-Jun N-terminal protein kinase signaling determine synergistic interaction of cisplatin and 17-allylamino-17-demethoxygeldanamycin in colon cancer cell lines." *Mol Pharmacol.* **65**: 235-243 (2004).
- Inhibits angiogenesis. Kaur, G, *et al.* "Antiangiogenic properties of 17-(dimethylaminoethylamino)-17-demethoxygeldanamycin: an

orally bioavailable heat shock protein 90 modulator." *Clin. Cancer Res.* **10**: 4813-4821 (2004).

- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



A-6900 6"-O-Acetyldaidzin, >98%

Size	US\$	€	£	¥
1 mg	66	55	36	7,900
5 mg	185	154	102	22,200
10 mg	315	261	173	37,800
25 mg	550	457	303	66,000

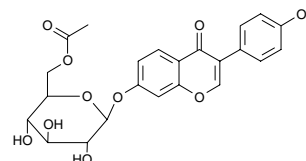
M.W. 458.42 C₂₃H₂₂O₁₀ [71385-83-6]

Storage: Store desiccated at or below -20 °C.

Solubility: Soluble in DMSO, methanol or ethanol.

Disposal: A

- Isoflavone derivative found in soy-based food products. Wang, H. and Murphy, P.A. "Isoflavone content in commercial soybean foods." *J. Agric. Food Chem.* **42**: 1666-1673 (1994).
- See the extensive comments before the listing for Genistein (Cat. No. G-6055 on page 16).
- STABILITY:** Very little information about the stability of this compound is available at present. In our experience, when stored in the dry state, frozen and desiccated, this compound has retained its original purity for several years. We have been informed that aqueous or alcoholic solutions can undergo substantial decomposition less than a day after being prepared, particularly if they are held at room temperature. We recommend that this product be stored in bulk in the dry state, with a desiccant, at the coldest available temperature. Small working quantities of solutions should be made up just prior to use.
- Aqueous solutions of this compound are somewhat unstable, particularly at room temperature; several percent decomposition can occur in 12-24 hours. For quantitative work, standard solutions should be made fresh daily.
- The 1 mg size (\pm ca. 2-3%) consists of a film adhering to the walls of the ampule and cannot be easily subdivided by weighing. The larger sizes contain a weighable powder.
- The 98% purity figure may include small amounts of acetyl monoesters other than the 6"-isomer.
- See also these related products:
 - D-2946 Daidzein, page 8.
 - D-7878 Daidzin, page 8.
 - M-6730 6"-O-Malonyldaidzin, page 24.
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



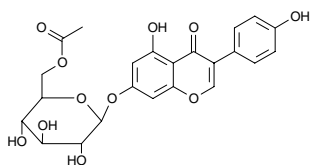
A-3000 6"-O-Acetylgenistin, >98%

Size	US\$	€	£	¥
1 mg	59	49	32	7,100
5 mg	168	139	92	20,200
10 mg	280	232	154	33,600
25 mg	525	436	289	63,000

M.W. 474.42 C₂₃H₂₂O₁₁ [73566-30-0]

Storage: Store desiccated at or below -20° C. **Solubility:** Soluble in DMSO, methanol or ethanol. **Disposal:** A

- Isoflavone derivative found in soy-based food products. Wang, H. and Murphy, P.A. "Isoflavone content in commercial soybean foods." *J. Agric. Food Chem.* **42**: 1666-1673 (1994).
- See the extensive comments before the listing for Genistein (Cat. No. G-6055 on page 16).
- **STABILITY:** Very little information about the stability of this compound is available at present. In our experience, when stored in the dry state, frozen and desiccated, this compound has retained its original purity for several years. We have been informed that aqueous or alcoholic solutions can undergo substantial decomposition less than a day after being prepared, particularly if they are held at room temperature. We recommend that this product be stored in bulk in the dry state, with a desiccant, at the coldest available temperature. Small working quantities of solutions should be made up just prior to use.
- Aqueous solutions of this compound are somewhat unstable, particularly at room temperature; several percent decomposition can occur in 12-24 hours. For quantitative work, standard solutions should be made fresh daily.
- The 1 mg size (\pm ca. 2-3%) consists of a film adhering to the walls of the ampule and cannot be easily subdivided by weighing. The larger sizes contain a weighable powder.
- See additional comments about acetyl isoflavones above the entry for 6"-O-Acetylaidzin (Cat. No. A-6900 on page 1).
- The 98% purity figure may include small amounts of acetyl monoesters other than the 6"-isomer.
- See also these related products:
 - G-6055 Genistein, page 16.
 - G-5200 Genistin, page 16.
 - M-8090 6"-O-Malonylgenistin, page 24.
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



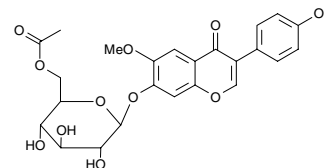
A-7860 6"-O-Acetylglycitin, >98%

Size	US\$	€	£	¥
1 mg	74	61	41	8,900
5 mg	195	162	107	23,400
10 mg	330	274	182	39,600
25 mg	585	486	322	70,200

M.W. 488.45 C₂₄H₂₄O₁₁

Storage: Store desiccated at or below -20° C. **Solubility:** Soluble in DMSO, methanol or ethanol. **Disposal:** A

- Isoflavone derivative found in soy-based food products. Wang, H. and Murphy, P.A. "Isoflavone content in commercial soybean foods." *J. Agric. Food Chem.* **42**: 1666-1673 (1994).
- See the extensive comments before the listing for Genistein (Cat. No. G-6055 on page 16).
- **STABILITY:** Very little information about the stability of this compound is available at present. In our experience, when stored in the dry state, frozen and desiccated, this compound has retained its original purity for several years. We have been informed that aqueous or alcoholic solutions can undergo substantial decomposition less than a day after being prepared, particularly if they are held at room temperature. We recommend that this product be stored in bulk in the dry state, with a desiccant, at the coldest available temperature. Small working quantities of solutions should be made up just prior to use.
- Aqueous solutions of this compound are somewhat unstable, particularly at room temperature; several percent decomposition can occur in 12-24 hours. For quantitative work, standard solutions should be made fresh daily.
- The 1 mg size (\pm ca. 2-3%) consists of a film adhering to the walls of the ampule and cannot be easily subdivided by weighing. The larger sizes contain a weighable powder.
- See additional comments about acetyl isoflavones above the entry for 6"-O-Acetylaidzin (Cat. No. A-6900 on p 1).
- The 98% purity figure may include small amounts of acetyl monoesters other than the 6"-isomer.
- See also these related products:
 - G-1152 Glycitein, page 16.
 - G-2822 Glycitin, page 17.
 - M-4620 6"-O-Malonylglycitin, page 25.
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



AG 1478 – see Tyrphostin AG 1478 (Cat. No. T-7310 on page 41).

AG 490 – see Tyrphostin AG 490 (Cat. No. T-9142 on page 40).

Alvespimycin – see 17-DMAG (Cat. No. D-3440 on page 10).

2'-Amino-3'-methoxyflavone – see PD 98059 (Cat. No. P-4313 on page 28).

AMN-107 – see Nilotinib (Cat. No. N-8207 on page 25).

AT-877 – see Fasudil, Monohydrochloride Salt (Cat. No. F-4660 on page 12) and HA-1077 (Cat. No. H-2330 on page 17).

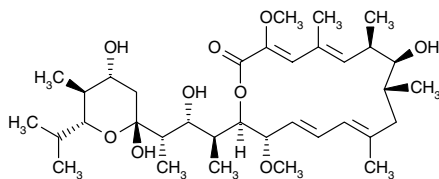
B-1080 Bafilomycin A1, >98%

Size	US\$	€	£	¥
1 mg	95	79	52	11,400
5 mg	355	295	195	42,600
10 mg	588	488	323	70,600

M.W. 622.84 C₃₅H₅₈O₉ [88899-55-2]

Storage: Store at or below -20° C. **Solubility:** Soluble in DMSO, ethanol or acetone. **Appearance:** Clear film. **Disposal:** A

- Specific, potent inhibitor of vacuolar ATPases. Bowman, E. *et al.* "Bafilomycins: A class of inhibitors of membrane ATPase from microorganisms, animal cells, and plant cells." *Proc. Natl. Acad. Sci. USA* **85**: 7972-7976 (1988).
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



B-2464 Bisindolylmaleimide I, >99%

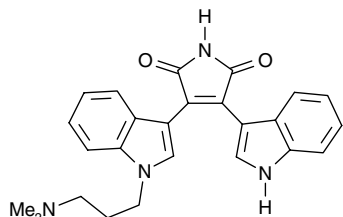
[GF 109203X] [Gö 6850]

Size	US\$	€	£	¥
5 mg	55	46	30	6,600
25 mg	198	164	109	23,800

M.W. 412.49 C₂₅H₂₄N₄O₂ [133052-90-1]

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO (1 mg/ml); store at -20 °C. **Appearance:** Orange solid. **Disposal:** A

- A very potent inhibitor of A-group PKCs (IC₅₀ = 8-20 nM); a less potent inhibitor of B-group PKCs (IC₅₀ = 210-700 nM); and a much less potent inhibitor of a C-group PKC (PKCζ, IC₅₀ = 5.8 μM). Martiny-Baron, G., *et al.* "Selective inhibition of protein kinase C isozymes by the indolocarbazole Gö 6976." *J. Biol. Chem.* **268**: 9194-9197 (1993). Please request Technical Note #2 for additional information on PKC nomenclature.
- Kinase inhibitor with improved selectivity for PKC over several serine/threonine and tyrosine kinases (PKA, IC₅₀ = 2 μM; phosphorylase kinase, IC₅₀ = 700 nM; EGFR-kinase, IC₅₀ >100 μM) as compared to staurosporine. Toullec, D., *et al.* "The bisindolylmaleimide GF 109203X is a potent and selective inhibitor of protein kinase C." *J. Biol. Chem.* **266**: 15771-15781 (1991).
- **CAUTIONARY NOTE:** BIM I shows a K_i = 14 nM on a cell-free, partially purified PKC mixture but potencies of 200-900 nM in cellular assays. Inhibition shows competitive kinetics versus ATP; since ATP levels are generally very high in cells, the potency of BIM I is substantially reduced in whole-cell assays.
- BIM I is one of the most widely used PKC inhibitors. See Bisindolylmaleimide I, Hydrochloride (Cat. No. B-6191 on page 3) for a water-soluble form of this compound.
- Please request Technical Note #9 for additional information.



B-6191 Bisindolylmaleimide I, Hydrochloride Salt, >99%

[GF 109203X, HCl Salt] [Gö 6850, HCl Salt]

Size	US\$	€	£	¥
5 mg	55	46	30	6,600
25 mg	198	164	109	23,800

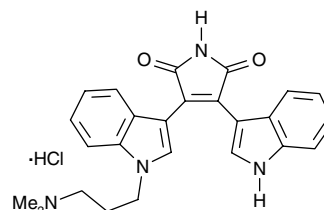
M.W. 448.95 C₂₅H₂₄N₄O₂•HCl [176504-36-2]

Storage: Store at or below -20 °C in the dark.

Solubility: Soluble in water, DMSO, or methanol.

Appearance: Reddish-orange solid. **Disposal:** A

- Water-soluble form of Bisindolylmaleimide I, Cat. No. B-2464. Kuchera, S. *et al.* "Anti-inflammatory properties of the protein kinase C inhibitor, 3-[1-[3-(dimethylamino)propyl]-1H-indol-3-yl]-4-(1H-indol-3-yl)-1H-pyrrole-2,5-dione monohydrochloride (GF109203X) in the PMA-mouse ear edema model." *Agents Actions* **39**: C169-C173 (1993).
- BIM I is a very potent inhibitor of A-group PKCs (IC₅₀ = 8-20 nM); a less potent inhibitor of B-group PKCs (IC₅₀ = 210-700 nM); and a much less potent inhibitor of a C-group PKC (PKCζ, IC₅₀ = 5.8 μM). Martiny-Baron, G., *et al.* "Selective inhibition of protein kinase C isozymes by the indolocarbazole Gö 6976." *J. Biol. Chem.* **268**: 9194-9197 (1993). Please request Technical Note #2 for additional information on PKC nomenclature.
- Kinase inhibitor with improved selectivity for PKC over several serine/threonine and tyrosine kinases (PKA, IC₅₀ = 2 μM; phosphorylase kinase, IC₅₀ = 700 nM; EGFR-kinase, IC₅₀ >100 μM) as compared to staurosporine. Toullec, D., *et al.* "The bisindolylmaleimide GF 109203X is a potent and selective inhibitor of protein kinase C." *J. Biol. Chem.* **266**: 15771-15781 (1991).
- **See the product description for Bisindolylmaleimide I (Cat. No. B-2464 on page 3) for a cautionary note regarding the effects of ATP concentrations on apparent inhibitory potencies.**
- Please request Technical Note #9 for additional information.



B-7334 Bisindolylmaleimide IX, Methanesulfonate Salt, >99%

[Ro 31-8220]

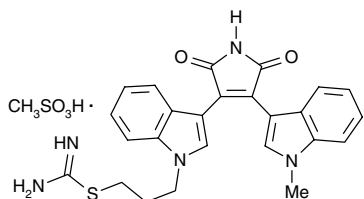
Size	US\$	€	£	¥
1 mg	38	32	21	4,600
5 mg	97	81	53	11,600
10 mg	135	112	74	16,200
25 mg	290	241	160	34,800

M.W. 553.66 C₂₅H₂₃N₅O₂S•CH₄O₃S [138489-18-6]

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO. **Disposal:** A

- Selective PKC inhibitor (IC₅₀ = 10 nM). IC₅₀ for the inhibition of PKA is 900 nM. Davis, P.D., *et al.* "Inhibitors of protein kinase C. 2. Substituted bisindolylmaleimides with improved potency and selectivity." *J. Med. Chem.* **35**: 994-1001 (1992).

- IC₅₀'s for the inhibition of the group A PKCs range from 5-27 nM and that for PKCε = 24 nM. Wilkinson, S.E., *et al.* "Isoenzyme specificity of bisindolylmaleimides, selective inhibitors of protein kinase C." *Biochem. J.* **294**: 335-337 (1993). Please request Technical Note #2 for additional information on PKC nomenclature.
- See the product description for Bisindolylmaleimide I (Cat. No. B-2464 on page 3) for a cautionary note regarding the effects of ATP concentrations on apparent inhibitory potencies.



B-7204 Bisindolylmaleimide X, Hydrochloride Salt,
>99%

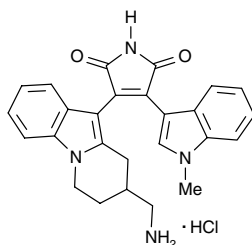
[Ro 31-8425]

Size	US\$	€	£	¥
1 mg	38	32	21	4,600
5 mg	129	107	71	15,500

M.W. 460.96 C₂₆H₂₄N₄O₂•HCl [131848-97-0]

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO. **Disposal:** A

- Potent inhibitor of PKC; IC₅₀ = 15 nM against rat brain PKC. IC₅₀'s for the inhibition of the group A PKCs range from 8-13 nM and that for PKCε = 39 nM. Wilkinson, S.E., *et al.* "Isoenzyme specificity of bisindolylmaleimides, selective inhibitors of protein kinase C." *Biochem. J.* **294**: 335-337 (1993). Please request Technical Note #2 for additional information on PKC nomenclature.
- Other kinases are inhibited at much higher concentrations, e.g., PKA (IC₅₀ = 2.8 μM), phosphorylase kinase (IC₅₀ = 1.3 μM) and myosin light chain kinase (IC₅₀ = 3.7 μM). Bit, R.A., *et al.* "Inhibitors of protein kinase C. 3. Potent and highly selective bisindolylmaleimides by conformational restriction." *J. Med. Chem.* **36**: 21-29 (1993).
- See the product description for Bisindolylmaleimide I (Cat. No. B-2464 on page 3) for a cautionary note regarding the effects of ATP concentrations on apparent inhibitory potencies.



B-8777 Bisindolylmaleimide XI, Hydrochloride Salt,
>99%

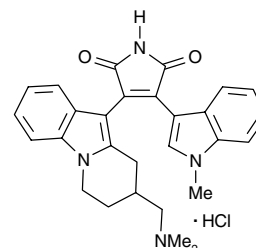
[Ro 32-0432]

Size	US\$	€	£	¥
1 mg	38	32	21	4,600
5 mg	129	107	71	15,500

M.W. 489.02 C₂₈H₂₈N₄O₂•HCl [151342-35-7]

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO. **Disposal:** A

- Orally active, potent and selective inhibitor of PKC; IC₅₀ = 21 nM for rat brain PKC. Slightly less potent for the inhibition of PKCε (IC₅₀ = 108 nM) than for the group A PKCs (IC₅₀ = 9-37 nM). Wilkinson, S.E., *et al.* "Isoenzyme specificity of bisindolylmaleimides, selective inhibitors of protein kinase C." *Biochem. J.* **294**: 335-337 (1993). Please request Technical Note #2.
- Other kinases are inhibited at much higher concentrations, e.g., PKA (IC₅₀ = 8.6 μM), phosphorylase kinase (IC₅₀ = 1.1 μM) and myosin light chain kinase (IC₅₀ = 17.8 μM). Bit, R.A., *et al.* "Inhibitors of protein kinase C. 3. Potent and highly selective bisindolylmaleimides by conformational restriction." *J. Med. Chem.* **36**: 21-29 (1993).
- See the product description for Bisindolylmaleimide I (Cat. No. B-2464 on page 3) for a cautionary note regarding the effects of ATP concentrations on apparent inhibitory potencies.



B-1408 Bortezomib, 97%

[Velcade] [MG-341] [PS-341]

Size	US\$	€	£	¥
2.5 mg	165	137	91	19,800
5 mg	290	241	160	34,800
25 mg	995	826	547	119,400

M.W. 384.24 C₁₉H₂₅BN₄O₄ [179324-69-7]

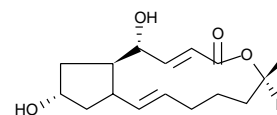
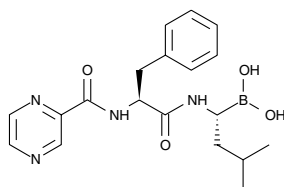
Storage: Store at or below -20 °C in the dark.

Solubility: Very soluble in DMSO or ethanol, up to about 200 mg/mL; poorly soluble in aqueous solution—maximum concentration recommended when diluting into aqueous media is 100-200 μM/L.

Disposal: A

- Bortezomib is a potent (K_i, 0.6 nM), specific and reversible proteasome inhibitor; it shows no significant inhibitory activity against other related or unrelated enzymes or receptors. Bouchard PR., *et al.*, "Nonclinical Discovery and Development of Bortezomib (PS-341, Velcade®), a Proteasome Inhibitor for the Treatment of Cancer." *55th Annual Meeting of the American College of Veterinary Pathologists (ACVP) & 39th Annual Meeting of the American Society of Clinical Pathology (ASVCP), ACVP and ASVCP (Eds.)*.
- In a study with the National Cancer Institute's panel of 60 human cell lines, bortezomib displayed a mean IC₅₀ of 7 nM as determined by SRB analysis. Adams, J., *et al.* "Proteasome inhibitors: a novel class of potent and effective antitumor agents." *Cancer Res.* **59**: 2615-2622 (1999).
- Bortezomib is active in preclinical models of human prostate cancer, but its effects on apoptosis *versus* angiogenesis are cell type dependent. Bortezomib caused comparable, concentration-dependent growth suppression in LNCaP-Pro5 and PC3M-Pro4 cells (IC₉₀ = 10 nM). Williams S., *et al.* "Differential effects of the proteasome inhibitor bortezomib on apoptosis and angiogenesis in human prostate tumor xenografts." *Mol. Cancer Ther.* **2**: 835-843 (2003).

- Bortezomib inhibits cell proliferation of H460 cells (Human non-small cell lung cancer cell lines) with an IC₅₀ of 0.1 μM. Ling Y., *et al.* "Mechanisms of Proteasome Inhibitor PS-341-induced G2-M-Phase Arrest and Apoptosis in Human Non-Small Cell Lung Cancer Cell Lines." *Clin. Cancer Res.* **9**: 1145-1154 (2003).
- Bortezomib is the active ingredient in the drug sold under the trade name Velcade®. This drug is approved to treat multiple myeloma.
- Sold for laboratory or manufacturing purposes only; not for human, veterinary, food, or household use.**
- This product is offered for R&D use in accordance with (i) 35 USC 271(e)+A13(1) in the U.S.; (ii) Section 69.1 of Japanese Patent Law in Japan; (iii) Section 11, No. 2 of the German Patent Act of 1981 in Germany; (iv) Section 60, Paragraph 5b of the U.K. Patents Act of 1977 in the U.K.; (v) Section 68B of the Patents Act of 1953 in New Zealand; (vi) such related legislation and/or case law as may be or become applicable in the aforementioned countries; and (vii) such similar laws and rules as may apply in various other countries.
- Not available in some countries; not available to some institutions; not available for some uses.



B-6697 Bryostatin 1, >99%

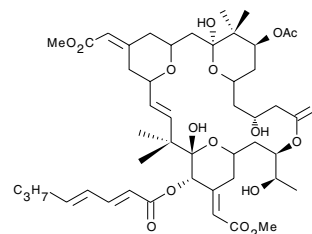
Size	US\$	€	£	¥
10 μg	61	51	34	7,300
25 μg	118	98	65	14,200
100 μg	298	247	164	35,800

M.W. 905.05 C₄₇H₆₈O₁₇ [83314-01-6]

Note: Binds to glass and plastic surfaces in aqueous solutions.

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO and ethanol. **Disposal:** A

- Bryostatin 1 binds to and activates protein kinase C, but its biological effects differ greatly from those induced by other protein kinase C activators. Bryostatin 1 fails to mimic many effects caused by PMA and actually blocks some PMA-induced responses in a variety of cells and tissues. Kraft, A.S. et al. "Bryostatin, an activator of the calcium phospholipid-dependent protein kinase, blocks phorbol ester-induced differentiation of human promyelocytic leukemia cell HL-60." *Proc. Natl. Acad. Sci. USA* **83**: 1334-1338 (1986); Sako, T. et al. "Partial parallelism and partial blockade by bryostatin 1 of effects of phorbol ester tumor promoters on primary mouse epidermal cells." *Cancer Res.* **47**: 5445-5450 (1987). Dell'Aquila, M.L. et al. "Inhibition by bryostatin 1 of the phorbol ester-induced blockage of differentiation in hexamethylene bisacetamide-treated Friend erythroleukemia cells." *Cancer Res.* **47**: 6006-6009 (1987). Hess, A.D. et al. "Activation of human T lymphocytes by bryostatin." *J. Immunol.* **141**: 3263-3269 (1988).
- The true affinity of bryostatin 1 for the PDBu binding site on PKC appears to be in the low picomolar range or lower. de Vries, D.J. et al. "Demonstration of sub-nanomolar affinity of bryostatin 1 for the phorbol ester receptor in rat brain." *Biochem. Pharmacol.* **37**: 4069-4073 (1988).
- Please request Technical Note #1 for extensive technical information.
- Please note: The correct molecular weight for bryostatin 1 is 905.04. Perhaps the M.W. 887 error found in other catalogs arises because the original publication describing bryostatin 1 mentions a mass spectrum peak at 887, but apparently that peak resulted from the loss of one water molecule during the mass spectral process.
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



B-8500 Brefeldin A, >99%

[Decumbin] [Ascotoxin] [Cyanein] [BFA]

Size	US\$	€	£	¥
10 mg	45	37	25	5,400
25 mg	99	82	54	11,900
50 mg	165	137	91	19,800
100 mg	295	245	162	35,400
300 mg	698	579	384	83,800

M.W. 280.36 C₁₆H₂₄O₄ [20350-15-6]
 RTECS: GY8410000 M.I. 11: 1363

Warning: Toxic

Storage: Store at or below -20 °C in the dark.

Solubility: Soluble in DMSO. **Disposal:** A

- Specifically and reversibly blocks translocation of proteins from the endoplasmic reticulum to the Golgi apparatus. Misumi, Y., *et al.* "Novel blockade by brefeldin A of intracellular transport of secretory proteins in cultured rat hepatocytes." *J. Biol. Chem.* **261**: 11398-11403 (1986).
- Brefeldin A has been shown to induce apoptosis in human tumor cells via a process requiring caspase activation. Guo, H., *et al.* "Brefeldin A-mediated apoptosis requires the activation of caspases and is inhibited by Bcl-2." *Exp. Cell Res.* **245**: 57-68 (1998).
- Brefeldin A has been identified as an activator of the sphingomyelin signal transduction cycle. Linardic, C. M., *et al.* "Activation of the sphingomyelin cycle by brefeldin A: effects of brefeldin A on differentiation and implications for a role for ceramide in regulation of protein trafficking." *Cell Growth Differ.* **7**: 765-774 (1996). Alessenko A. V. "The role of sphingomyelin cycle metabolites in transduction of signals of cell proliferation, differentiation and death." *Membr. Cell Biol.* **13**: 303-320(2000).
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.

B-3517 Bryostatin 2, >99%

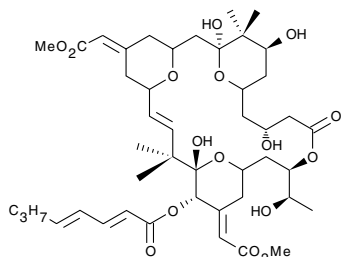
Size	US\$	€	£	¥
10 µg	83	69	46	10,000
25 µg	159	132	87	19,100
100 µg	375	311	206	45,000

M.W. 863.01 C₄₅H₆₆O₁₆ [87745-28-6]

Note: Binds to glass and plastic surfaces in aqueous solutions.

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO and ethanol. **Disposal:** A

- Protein kinase C activator exhibiting a K_i value 1 order of magnitude higher than bryostatin 1. Inhibits DNA synthesis at 100 nM in SH-SY5Y human neuroblastoma cells. Jalava, A.M., *et al.* "Effects of bryostatins 1 and 2 on morphological and functional differentiation of SH-SY5Y human neuroblastoma cells." *Cancer Res.* **50**: 3422-3428 (1990).
- Has somewhat different effect on various cells and tissues than bryostatin 1. See Technical Note #1 for more technical information.
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



"C-kinase..." entries appear under "Protein Kinase C..."

"Calcium/phospholipid-dependent Protein Kinase..." entries appear under "Protein Kinase C..."

C-3987 Calyculin A, >98%

Size	US\$	€	£	¥
50 µg	118	98	65	14,200
100 µg	192	159	106	23,000
300 µg	518	430	285	62,200
1 mg	1490	1237	820	178,800

M.W. 1009.18 C₅₀H₈₁N₄O₁₅P [101932-71-2]

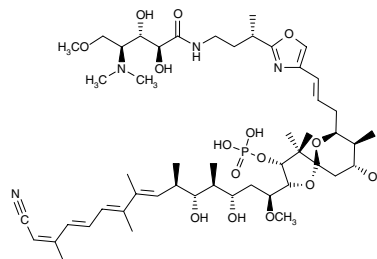
SPECIAL HAZARD: TUMOR PROMOTER. Gloves and mask should be worn when using this compound. Care must be taken to prevent contact through all routes of exposure.

NOTE: Do not expose to sunlight or fluorescent lights for extended periods.

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO or ethanol; insoluble in water. **Disposal:** A

- Very potent inhibitor (K_i = ca. 0.1 nM) with high specificity for the PP-1 and PP-2 classes of protein serine/threonine phosphatase. Ishihara, H. *et al. Biochem. Biophys. Res. Comm.* **159**: 871-877 (1989).
- Potent non-phorbol type tumor promoter. Suganuma, M. *et al. Cancer Res.* **50**: 3521-3525 (1990).
- Please request Technical Note #19 for additional information.

- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



"Ca²⁺/phospholipid-dependent Protein Kinase..." entries appear under "Protein Kinase C..."

CCI-779 – see Temsirolimus (Cat. No. T-8040 on page 39).

Certican – see Everolimus (Cat. No. E-4040 on page 12).

CGP-57148B – see Imatinib, Methanesulfonate Salt (Cat. No. I-5508 on page 18).

C-3030 Chelerythrine Chloride, >99%

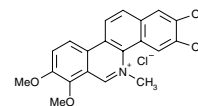
Size	US\$	€	£	¥
5 mg	35	29	19	4,200
10 mg	61	51	34	7,300
25 mg	127	105	70	15,200
100 mg	395	328	217	47,400

M.W. 383.83 C₂₁H₁₈NO₄Cl [3895-92-9]
M.I. **12**: 2093

Storage: Store at or below -20 °C. **Solubility:** Soluble in water (5 mg/ml) or DMSO (>10 mg/ml).

Appearance: Yellow to orange solid. **Disposal:** A

- Selective protein kinase C inhibitor; IC₅₀ is 0.66 µM for PKC. Herbert, J.M. *et al. Biochem. Biophys. Res. Comm.* **172**: 993-999 (1990).
- Inhibitor of BclXL function. *J. Biol. Chem.* **278**: 20453-20456 (2003)
- Free of biologically active impurities, such as sanguinarine, sometimes present at high levels in less expensive products from other suppliers.
- Rather insoluble in aqueous media that contain substantial saline concentrations.
- Please request Technical Note #8 for additional information.
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



Cocarcinogen A1 – see Phorbol 12-Myristate 13-Acetate (Cat. No. P-1680 on page 31).

Colforsin – see Forskolin (Cat. No. F-9929 on page 14).

CP-358774 – see Erlotinib, Hydrochloride Salt (Cat. No. E-4007 on page 11).

C-3669 Croton Oil

Size	US\$	€	£	¥
25 mL	39	32	21	4,700
100 mL	107	89	59	12,800
1 L	470	390	258	56,400

[8001-28-3] M.I. 12: 2665

SPECIAL HAZARD: TUMOR PROMOTER. Gloves and mask should be worn when using this compound. Care must be taken to prevent contact through all routes of exposure. **WARNING:** Highly irritant to skin and mucous membranes.

Storage: Store at or below room temperature.

Solubility: Soluble in DMSO, ethanol or acetone.

Disposal: A

- Natural source of phorbol and phorbol esters. Formerly used in folk medicine as a counterirritant. Occasionally used as a standard inflammatory agent in mouse ear testing of anti-inflammatory drugs and drug candidates.
- This is the seed oil of the shrub *Croton tiglium* Linnaeus. This seed oil was used in the past as an ingredient in "liniment of croton oil".
- Powerful skin irritant and vesicant; violent purgative if ingested. Avoid all contact with this substance by any route.
- Not to be confused with "crotonal", a very different substance whose proper name is crotonaldehyde. The term "crotonal" has also been used to mean a solution of crotonaldehyde in kerosene.
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.

C-8700 Cyclopamine, >99%

[11-Deoxyjervine]

Size	US\$	€	£	¥
10 mg	72	60	40	8,600
25 mg	149	124	82	17,900
100 mg	565	469	311	67,800
300 mg	1425	1183	784	171,000

M.W. 411.63 C₂₇H₄₁NO₂ [4449-51-8]
RTECS GY0750000

SPECIAL HAZARD: TERATOGEN. Gloves and mask should be worn when using this compound. Care must be taken to prevent contact through all routes of exposure. Women of childbearing age should be extremely careful in handling cyclopamine!

Storage: Store at or below -20 °C. **Solubility:** See Below. **Disposal:** A

- Cyclopamine blocks activation of the Hedgehog response pathway associated with mutations that either activate the proto-oncogene *Smoothened* (Smo) or inactivate the tumour suppressor *Patched* (Ptch) both of which encode multipass transmembrane proteins. Furthermore, it has been demonstrated that the inhibitory effect of cyclopamine results from its direct binding to the Smo heptahelical protein bundle. Taipale, J., *et al.* "Effects of oncogenic mutations in *Smoothened* and *Patched* can be reversed by cyclopamine." *Nature* **406**: 944-945 (2000). Chen, J.K., *et al.* "Inhibition of Hedgehog signaling by direct binding of cyclopamine to *Smoothened*." *Genes & Dev.* **16**: 2743-2748 (2002)
- Induces chick embryo malformations associated with the interruption of Sonic hedgehog (Shh)-mediated dorsoventral patterning. Incardona, J.P., *et al.* "The teratogenic *Veratrum* alkaloid cyclopamine inhibits sonic hedgehog signal transduction." *Development.* **125**: 3553-3562 (1998).
- Displays anti-tumor properties. It has been shown to induce apoptosis in both colorectal adenoma- and carcinoma-derived cell lines and in skin basal cell carcinomas. Qualtrough, D., *et al.*

Hedgehog signalling in colorectal tumour cells: induction of apoptosis with cyclopamine treatment." *Int J Cancer.* **110**: 831-837 (2004). Tabs, S., and Avci, O." Induction of the differentiation and apoptosis of tumor cells *in vivo* with efficiency and selectivity." *Eur J Dermatol.* **14**: 96-102 (2004).

- Pregnant cattle, goats, or sheep who graze on the corn lily plant *Veratrum californicum* at the 14th day of gestation (for sheep) can give birth to deformed offspring with a characteristic single eye in the middle of the forehead. [For example, view www.cybergoat.com/cyclopiacyclopiac.htm]

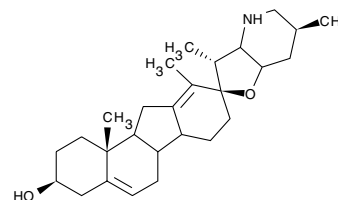
This type of birth defect recalls one of the most unforgettable images in all of mythology, namely Homer's Cyclops (for which cyclopamine was named). If plants containing cyclopamine or a similar compound existed in the Mediterranean area in ancient times, it would then seem likely that the Cyclops was not merely a product of Homer's imagination but rather was based on known, naturally-occurring birth defects in animals. Alternatively, this type of birth defect might arise from spontaneous mutation, as may have been the case for the kitten recently reported: www.samtsai.com/p131.

- CYCLOPAMINE SOLUBILITY:** Ethanol is the best cyclopamine solvent for biological use. A 2% solution (20 mg/mL) can be prepared by warming the cyclopamine in ethanol to 50-60 °C; boiling is not necessary. Upon cooling, the cyclopamine remains in solution at room temperature, even if left for several days. However, storage at -20 °C is recommended, and at this temperature the cyclopamine will crystallize out of solution. Upon thawing, the mixture will need to be heated again to redissolve the cyclopamine.

Methanol and DMSO can also be used as cyclopamine solvents, but solubility in methanol is only about 0.7% (7 mg/mL) at best, and solubility in DMSO is about 0.4% (4 mg/mL). Substantial heating is again needed to achieve solution with methanol or DMSO, but once the cyclopamine is dissolved it will remain in solution if kept at room temperature. Storage in either solvent at the recommended -20 °C will also cause crystallization, as noted above for ethanol, and reheating is necessary after thawing in order to achieve full dissolution.

Methanol is less desirable than the other two solvents because it is the most volatile; merely standing open in air will lead to slow volume loss and consequent artefactual increase in concentration of the solution. DMSO is the least volatile solvent and is preferred if a stock solution need only be 4 mg/mL or less. Ethanol is a compromise between volatility and achievable concentration.

- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



C-6000 Cyclosporin A, >99%

[Cyclosporine] [Antibiotic S 7481F1] [Ciclosporin A] [Ramihyphin A] [CsA]

Size	US\$	€	£	¥
1 g	69	57	38	8,300
5 g	147	122	81	17,600
10 g	249	207	137	29,900
25 g	471	391	259	56,500

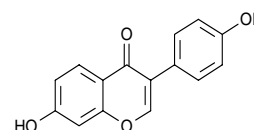
M.W. 1202.63 C₆₂H₁₁₁N₁₁O₁₂ [59865-13-3]
RTECS GZ4120000 M.I. 12: 2821

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO or ethanol (1 ml of ethanol will dissolve 160 mg). **Disposal:** A

- Cyclic hydrophobic oligopeptide isolated from the filamentous fungi, *Tolyposcladium inflatum*, with potent immunosuppressant properties. "Identification of immunosuppressant-induced apoptosis in a murine B-cell line and its prevention by bcl-x but not bcl-2." *Proc. Natl. Acad. Sci. USA* **91**: 7350-7354 (1994).
- The complex of cyclosporin A with the protein cyclophilin inhibits T-cell receptor signal transduction pathway via the inhibition of calcineurin (protein phosphatase 2B) with nanomolar affinity ($K_1 = 270$ nM). Etzkorn, F.A., *et al.* Cyclophilin residues that affect noncompetitive inhibition of the protein serine phosphatase activity of calcineurin by the cyclophilin-cyclosporin A complex." *Biochemistry* **33**: 2380-2388 (1994). Liu, J. "FK-506 and cyclosporin: molecular probes for studying intracellular signal transduction." *Trends Pharmacol. Sci.* **14**: 182-188 (1993).
- Inhibits interleukin-1 α -, lipopolysaccharide-, and TNF- α -nitric oxide synthesis induction. Fast, D.J., *et al.* "Cyclosporin A inhibits nitric oxide production by L929 cells in response to tumor necrosis factor and interferon-gamma." *J. Interferon Res.* **13**: 235-240 (1993). Marumo, T., *et al.* "Cyclosporin A inhibits nitric oxide synthase induction in vascular smooth muscle cells." *Hypertension* **25**: 764-768 (1995). Hattori, Y., and Naranishi, N. "Effects of cyclosporin A and FK-506 on nitric oxide and tetrahydrobiopterin synthesis in bacterial lipopolysaccharide-treated J774 macrophages." *Cell Immunol.* **165**: 7-11 (1995).
- See also our other standard immunosuppressant products:
 - Rapamycin (Cat. No. R-5000 on page 34)
 - FK-506 (F-4900 on page 13)
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO; very poorly soluble in other solvents. **Disposal:** A

- Negative control for genistein. Akiyama, T. *et al.* *J. Biol. Chem.* **262**: 5592-5595 (1987). Wijetunge, S. *et al.* *Biochem. Biophys. Res. Comm.* **189**: 1620-1623 (1992).
- Please request Technical Note #22 for additional information.
- Daidzein is also a cytostatic agent capable of arresting the cell cycle at G₁.
- Weak inhibitor of hamster mitochondrial alcohol dehydrogenase. Keung, W.M., Klyosov, A.A. and Vallee, B.L. *Proc. Natl. Acad. Sci. USA* **94**: 1675-1679 (1997).
- Isoflavone derivative found in soy-based food products. Wang, H. and Murphy, P.A. "Isoflavone content in commercial soybean foods." *J. Agric. Food Chem.* **42**: 1666-1673 (1994).
- See the extensive comments before the listing for Genistein (Cat. No. G-6055 on page 16).
- See also these related products:
 - 6"-O-Acetyldaidzin (Cat. No. A-6900 on page 1).
 - Daidzin (Cat. No. D-7878 on page 8).
 - (R,S)-Dihydrodaidzein (Cat. No. D-9200 on page 9).
 - (R,S)-Equol (Cat. No. E-5880 on page 11).
 - 6"-O-Malonyldaidzin (Cat. No. M-6730 on page 24).
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



D-7878 Daidzin, >99%

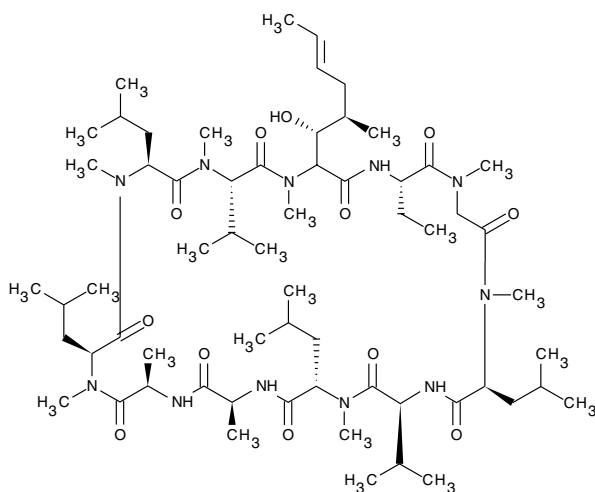
[4',7-Dihydroxyisoflavone, 7-O- β -D-glucopyranoside]

Size	US\$	€	£	¥
25 mg	39	32	21	4,700
100 mg	100	83	55	12,000
300 mg	225	187	124	27,000
1 g	370	307	204	44,400

M.W. 416.38 C₂₁H₂₀O₉ [552-66-9]
 RTECS: DJ3094000 M.I. 12: 2868

Storage: Store desiccated at or below -20 °C. **Solubility:** Soluble in DMSO. **Disposal:** A

- Isoflavone derivative found in soy-based food products. Wang, H. and Murphy, P.A. "Isoflavone content in commercial soybean foods." *J. Agric. Food Chem.* **42**: 1666-1673 (1994).
- See the extensive comments before the listing for Genistein (Cat. No. G-6055 on page 16).
- Inhibits ethanol intake of Syrian golden hamsters and rats, and inhibits human mitochondrial alcohol dehydrogenase (ADH) but not hamster cytosolic ADH; further evidence suggests that the mechanism for reducing alcohol consumption is different from ADH inhibition typical of antabuse-type drugs. Keung, W.M., *et al.*, *Proc. Natl. Acad. Sci. USA* **94**: 1675-1679 (1997).
- See also these related products:
 - 6"-O-Acetyldaidzin (Cat. No. A-6900 on page 1).
 - Daidzein (Cat. No. D-2946 on page 8).
 - 6"-O-Malonyldaidzin (Cat. No. M-6730 on page 24).
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.

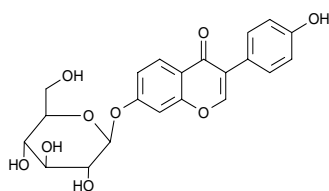


D-2946 Daidzein, >99%

[4',7-Dihydroxyisoflavone]

Size	US\$	€	£	¥
1 g	59	49	32	7,100
10 g	245	203	135	29,400
25 g	490	407	270	58,800
100 g	1330	1104	732	159,600

M.W. 254.24 C₁₅H₁₀O₄ [486-66-8]
 RTECS: DJ3100040 M.I. 12: 2868



D-3307 Dasatinib, >99%
[BMS-354825] [Sprycel®]

	Size	US\$	€	£	¥
NEW!	100 mg	263	218	145	31,600
	300 mg	515	427	283	61,800
	1 g	985	818	542	118,200

M.W. 488.02 C₂₂H₂₆ClN₇O₂S

Storage: Store at or below -20 °C in the dark.

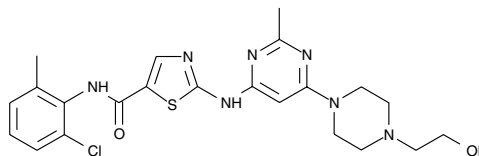
Solubility: Very soluble in DMSO, up to about 200 mg/mL; very poorly soluble in water or ethanol.

Disposal: A

- Small molecule inhibitor of both the SRC and BCR/ABL tyrosine kinases with IC₅₀'s for the isolated kinases of 0.55 and 3.0 nM, respectively. Lombardo LJ, *et al.* "Discovery of N-(2-chloro-6-methylphenyl)-2-(6-(4-(2-hydroxyethyl)-piperazin-1-yl)-2-methylpyrimidin-4-ylamino) thiazole-5-carboxamide (BMS-354825), a dual Src/Abl kinase inhibitor with potent antitumor activity in pre-clinical assays." *J. Med. Chem.* **47**: 6658-6661 (2004).
- Dasatinib also inhibits Lyn (IC₅₀ = 8.5 nM) and Src (IC₅₀ = 3.0 nM) kinase activities *in vitro* using 0.1 mg/mL poly (Glu4-Tyr) as the substrate. Nam S., *et al.* "Action of the Src Family Kinase Inhibitor, Dasatinib (BMS-354825), on Human Prostate Cancer Cells." *Cancer Res.* **65**: 9185-9189 (2005).
- Dasatinib exhibits greater potency than imatinib mesylate and inhibits the majority of kinase mutations in imatinib-resistant chronic myeloid leukemia. Copland M., *et al.* "Dasatinib (BMS-354825) targets an earlier progenitor population than imatinib in primary CML but does not eliminate the quiescent fraction." *Blood* **107**: 4532-4539 (2006).
- Responses were seen in patients with all BCR/ABL genotypes, with the exception of T315I mutation, which confers resistance to both dasatinib and imatinib *in vitro*. O'Hare T., *et al.* "In vitro Activity of Bcr-Abl Inhibitors AMN107 and BMS-354825 against Clinically Relevant Imatinib-Resistant Abl Kinase Domain Mutants." *Cancer Res.* **65**: 4500-4505 (2005).
- Dasatinib and nilotinib are respectively 325-fold (IC₅₀: 0.6 versus 280 nM) and 20-fold (IC₅₀: 15 versus 280 nM) more potent than imatinib against cells expressing wild-type Bcr-Abl. Similar improvements are maintained for all imatinib-resistant mutants tested, with the exception of T315I. Thus, both inhibitors hold promise for treating imatinib-refractory CML. O'Hare T., *et al.* "In vitro activity of Bcr-Abl inhibitors AMN107 and BMS-354825 against clinically relevant imatinib-resistant Abl kinase domain mutants." *Cancer Res.* **65**: 4500-4505 (2005).
- Dasatinib is the active ingredient in the drug sold under the trade name Sprycel®. This drug is currently approved for use in patients with chronic myelogenous leukemia and Philadelphia chromosome-positive acute lymphoblastic leukemia. It is also being assessed for use in metastatic melanoma.
- **Sold for laboratory or manufacturing purposes only; not for human, veterinary, food, or household use.**
- This product is offered for R&D use in accordance with (i) 35 USC 271(e)+A13(1) in the U.S.; (ii) Section 69.1 of Japanese Patent Law in Japan; (iii) Section 11, No. 2 of the German Patent Act of 1981 in Germany; (iv) Section 60, Paragraph 5b of the U.K. Patents Act of 1977 in the U.K.; (v) Section 68B of the Patents Act of 1953 in New Zealand; (vi) such related legislation and/or case law as

may be or become applicable in the aforementioned countries; and (vii) such similar laws and rules as may apply in various other countries.

- Not available in some countries; not available to some institutions; not available for some uses.



12-Deoxyphorbol 13-Acetate – see Prostratin
(Cat. No. P-4462 on page 33).

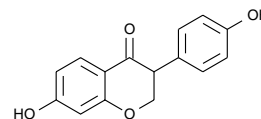
D-9200 (R,S)-2,3-Dihydrodaidzein, >99%

	Size	US\$	€	£	¥
	50 mg	73	61	40	8,800
	100 mg	129	107	71	15,500
	500 mg	495	411	272	59,400

M.W. 256.26 C₁₅H₁₂O₄

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO, methanol or ethanol. **Disposal:** A

- Human urinary metabolite of daidzein. Heinonen, S. *et al.*, "Identification of isoflavone metabolites dihydrodaidzein, dihydrogenistein, 6'-OH-O-dma, and *cis*-4-OH-equol in human urine by gas chromatography-mass spectrometry using authentic reference compounds." *Anal. Biochem.* **274**: 211-219 (1999).
- This product is a racemic mixture of the *R*- and *S*-enantiomers. As of this writing, we are not aware of any studies establishing the stereochemistry of the human urinary metabolite form of dihydrodaidzein. This is an important point; the natural metabolite is likely to be a single stereoisomer with different biological properties from the racemic mixture.
- The Heinonen *et al.* article makes many references to the "enol tautomer" of dihydrodaidzein. Although it is not always obvious from the wording in their descriptions, a careful reading indicates that all references in this article to the "enol tautomer" of dihydrodaidzein refer to a *silylated* derivative of this compound. The trimethylsilyl ether of the enol is indeed an isolatable compound, whereas the free, unsilylated enol form is in dynamic equilibrium with the keto form and cannot be isolated separately.
- **We have found that dihydrodaidzein is somewhat unstable in air; it partially oxidizes to form daidzein if left at room temperature for a few days, even if kept in the dark as a dry powder. Storage in solid form at -20 °C under nitrogen is recommended. Solutions are expected to be even more susceptible to oxidation than the solid, so they should be freshly prepared and used as quickly as possible.**
- **NOTE: Although there are one or two exceptions, we generally do not carry products that are unstable and not easily maintained at 98-99+ % purity under ordinary handling conditions. At present, dihydrodaidzein is not in stock, and we are working to solve production problems for this compound related to its stability.**
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



17-(Dimethylaminoethylamino)-17-demethoxygeldanamycin – see 17-DMAG (Cat. No. D-3440 on page 10).

D-3440 17-DMAG, Hydrochloride Salt, >99%

[17-(Dimethylaminoethylamino)-17-demethoxygeldanamycin] [NSC-707545] [Alvespimycin]

Size	US\$	€	£	¥
25 mg	98	81	54	11,800
100 mg	229	190	126	27,500
250 mg	445	369	245	53,400
1 g	988	820	543	118,600
2 g	1760	1461	968	211,200

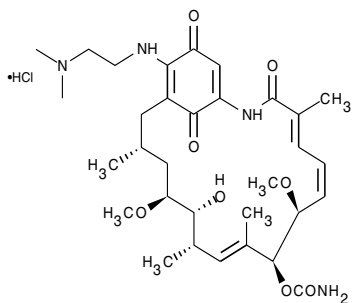
M.W. 653.22 C₃₂H₄₈N₄O₈•HCl [150270-08-9]

Warning: Toxic.

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO; Soluble up to about 2 mg/mL in water.

Disposal: A

- Synthetic derivative of geldanamycin (Cat. No. G-4500 on page 15) and water-soluble analog of 17-AAG (Cat. No. A-6880 on page 1) demonstrating stability and low *in vivo* toxicity similar to 17-AAG, but undergoes limited metabolism compared to 17-AAG. Egorin, M.J., *et al.* "Pharmacokinetics, tissue distribution, and metabolism of 17-(dimethylaminoethylamino)-17-demethoxygeldanamycin (NSC 707545) in CD2F1 mice and Fischer 344 rats." *Cancer Chemother. Pharmacol.* **49**: 7-19 (2002).
- Binds specifically to heat shock protein Hsp90 in a manner similar to geldanamycin. Tian, Z.Q., *et al.* "Synthesis and biological activities of novel 17-aminogeldanamycin derivatives." *Bioorg. Med. Chem.* **12**: 5317-5329 (2004).
- Inhibits angiogenesis. Kaur, G., *et al.* "Antiangiogenic properties of 17-(dimethylaminoethylamino)-17-demethoxygeldanamycin: an orally bioavailable heat shock protein 90 modulator." *Clin. Cancer Res.* **10**: 4813-4821 (2004).
- Enhances the radiation-induced cell cycle arrest of human solid tumor cell lines both *in vitro* and *in vivo*. Bull, E.E., *et al.* "Enhanced tumor cell radiosensitivity and abrogation of G2 and S phase arrest by the Hsp90 inhibitor 17-(dimethylaminoethylamino)-17-demethoxygeldanamycin." *Clin. Cancer Res.* **10**: 8077-8084 (2004).
- Exhibits potent anti-tumor activity against MDA-MB-231 breast carcinoma cells and HL60-TB leukemia cells both of which are relatively insensitive to 17-AAG. Hollingshead, M., *et al.* "In vivo antitumor efficacy of 17-DMAG (17-dimethylaminoethylamino-17-demethoxygeldanamycin hydrochloride), a water-soluble geldanamycin derivative." *Cancer Chemother. Pharmacol.* **56**: 115-125 (2005).
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



dPAC – see Prostratin (Cat. No. P-4462 on page 33).

D-1000 Docetaxel, >99%

[Taxotere] [RP 56976]

Size	US\$	€	£	¥
25 mg	97	81	53	11,600
100 mg	255	212	140	30,600
500 mg	670	556	369	80,400
1 g	990	822	545	118,800
2 g	1670	1386	919	200,400

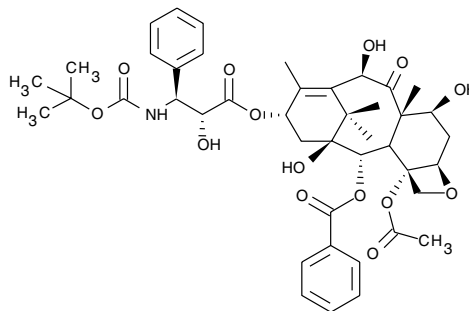
M.W. 807.89 C₄₃H₅₃NO₁₄ [114977-28-5]

M.I. 13: 3431

Storage: Store at or below -20 °C.

Solubility: Soluble in DMSO (up to about 200 mg/mL) or ethanol (up to about 100 mg/mL). **Disposal:** A

- Docetaxel, a semisynthetic analog of paclitaxel, shares the latter's mechanism of action: the promotion of microtubule assembly and inhibition of microtubule disassembly. This anti-mitotic behavior results in apoptosis of human leukemia HL-60 cells arrested at the M phase in the cell cycle. Pazdur, R., *et al.* "The taxoids: paclitaxel (Taxol) and docetaxel (Taxotere)." *Cancer Treat Rev.* **19**: 351-386 (1993). Hagsisawa, S., *et al.* "Docetaxel-induced apoptosis in the mitotic phase: electron microscopic and cytochemical studies of human leukemia cells." *Med Electron Microsc.* **32**: 167-174 (1999).
- Docetaxel has exhibited significant antitumor activity against prostate cancer, metastatic breast cancer, gastric cancer, and others. Pienta, K.J. "Preclinical mechanisms of action of docetaxel and docetaxel combinations in prostate cancer." *Semin Oncol.* **4**: 3-7 (2001). Yoshida, K., *et al.* "Phase I study of combination therapy with S-1 and docetaxel (TXT) for advanced or recurrent gastric cancer." *Anticancer Res.* **24**: 1843-1851 (2004). Taberero, J., *et al.* "A multicentre, randomised phase II study of weekly or 3-weekly docetaxel in patients with metastatic breast cancer." *Ann Oncol.* **15**: 1358-1365 (2004).
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



D-2744 Doramapimod, >98%

[BIRB 796]

Size	US\$	€	£	¥
5 mg	81	67	45	9,700
25 mg	275	228	151	33,000
100 mg	820	681	451	98,400

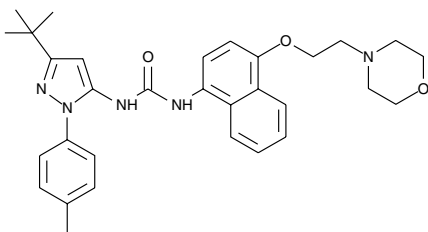
M.W. 527.67 C₃₁H₃₇N₅O₃ [285983-48-4]

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO. **Disposal:** A

- Doramapimod is a protein kinase inhibitor with a >330-fold selectivity for p38 MAPK compared with 12 other protein kinases. In contrast to other p38 MAPK inhibitors (e.g., SB203580),

doramapimod prevents both the kinetic activity and phosphorylation of p38 MAPK by binding to the ATP pocket as well as to a novel allosteric binding site on p38 MAPK. Branger, J., *et al.* "Anti-Inflammatory Effects of a p38 Mitogen-Activated Protein Kinase Inhibitor During Human Endotoxemia." *J. Immunol.* **168**: 4070-4077 (2002).

- Inhibits ABL(T315I). Doramapimod blocked proliferation of cells expressing BCR-ABL(T315I), with an IC₅₀ of 2-3 μM; this is more potent than for cells expressing BCR-ABL with no resistance mutation (IC₅₀ > 10 μM). Doramapimod prevented BCR-ABL(T315I) autophosphorylation in Ba/F3 cells (IC₅₀ = 1-2 μM). By comparison, imatinib did not inhibit BCR-ABL(T315I) in this assay, even at 10 μM. Carter, T.A., *et al.* "Inhibition of drug-resistant mutants of ABL, KIT, and EGF receptor kinases." *Proc. Natl. Acad. Sci. USA* **102**: 11011-11016 (2005).
- The p38 inhibitor doramapimod binds tightly (Kd = 40 nM) to ABL(T315I) and inhibits the BMS-354825- and imatinib-resistant ABL(T315I) kinase. Fabian, M.A., *et al.* "A small molecule-kinase interaction map for clinical kinase inhibitors." *Nat. Biotechnol.* **23**: 329-336 (2005).
- Doramapimod has high picomolar affinity (Kd = 100 pM) for p38 MAP kinase and low nanomolar inhibitory activity (IC₅₀ = 18 nM) against TNFα in THP-1 cell culture. The association of a fluorescent analog of doramapimod to p38 MAP kinase is slow and the dissociation is even slower. The high overall binding affinity of doramapimod is due to a reduction in the dissociation rate constant. The apparent IC₅₀ value decreases as the preincubation time increases. The time-dependence of apparent inhibitory potency and the fluorescent binding assays confirm the slow binding behavior of doramapimod, which is apparently required for the conformational change of the binding site. Pargellis, C., *et al.* "Inhibition of p38 MAP kinase by utilizing a novel allosteric binding site." *Nat. Struct. Biol.* **9**: 268-272 (2002).
- A 600-mg dose of doramapimod in humans strongly inhibited LPS-induced coagulation activation, as determined by plasma concentrations of the prothrombin fragment F1 + 2. Doramapimod also dose-dependently decreased the activation and subsequent inhibition of the fibrinolytic system (plasminogen activator inhibitor type 1, plasma tissue-type plasminogen activator, and plasmin-α2-antiplasmin complexes) and endothelial cell activation (von Willebrand factor and plasma soluble E-selectin). Branger, J., *et al.* "Inhibition of coagulation, fibrinolysis, and endothelial cell activation by a p38 mitogen-activated protein kinase inhibitor during human endotoxemia." *Blood* **101**: 4446-4448 (2003).
- Doramapimod inhibits the protein kinases p38_α and p38_β and is undergoing clinical trials for the treatment of inflammatory diseases.
- **Sold for laboratory or manufacturing purposes only; not for human, veterinary, food, or household use.**
- This product is offered for R&D use in accordance with (i) 35 USC 271(e)+A13(1) in the U.S.; (ii) Section 69.1 of Japanese Patent Law in Japan; (iii) Section 11, No. 2 of the German Patent Act of 1981 in Germany; (iv) Section 60, Paragraph 5b of the U.K. Patents Act of 1977 in the U.K.; (v) Section 68B of the Patents Act of 1953 in New Zealand; (vi) such related legislation and/or case law as may be or become applicable in the aforementioned countries; and (vii) such similar laws and rules as may apply in various other countries.
- Not available in some countries; not available to some institutions; not available for some uses.



Elidel – see Pimecrolimus (Cat. No. P-6040 on page 32).

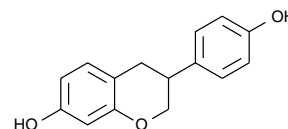
E-5880 (R,S)-Equol, >99%

Size	US\$	€	£	¥
100 mg	78	65	43	9,400
500 mg	285	237	157	34,200
1 g	470	390	259	56,400
5 g	1230	1021	677	147,600

M.W. 242.27 C₁₅H₁₄O₃ [531-95-3]
M.I. **13**: 3673

Storage: Store at or below -20°C. **Solubility:** Soluble in DMSO, methanol, or ethanol. **Disposal:** A

- Urinary metabolite of daidzein, produced by humans and horses. Heinonen, S. *et al.* "Identification of isoflavone metabolites dihydrodaidzein, dihydrogenistein, 6'-OH-dma, and *cis*-4-OH-equol in human urine by gas chromatography-mass spectrometry using authentic reference compounds." *Anal. Biochem.* **274**: 211-219 (1999).
- This product is a racemic mixture of the *R*- and *S*-enantiomers. However, the naturally-occurring form or equol from horse urine consists of a single stereoisomer. While the *chemical* properties of the single isomer form are essentially identical to those of the racemic mixture (except for rotation of plane polarized light, melting point, etc.), the *biological* properties of the single-isomer, naturally-occurring form are quite likely to be somewhat different from those of the racemic mixture. In the future, LC Labs will offer, at attractive prices, the pure single-isomer form of equol corresponding to the naturally occurring urinary metabolite.
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



Eritel – see Fasudil, Monohydrochloride Salt (Cat. No. F-4660 on page 12) and HA-1077 (Cat. No. H-2330 on page 17).

E-4007 Erlotinib, Hydrochloride Salt, >99%

[CP-358774] [OSI-774] [Tarceva]

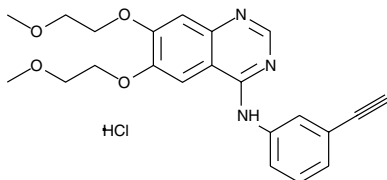
	Size	US\$	€	£	¥
NEW!	300 mg	185	154	102	22,200
	1 g	480	398	264	57,600
	2 g	845	701	465	101,400

M.W. 429.90 C₂₂H₂₃N₃O₄ •HCl [183319-69-9]

Storage: Store at or below -20 °C in the dark.
Solubility: Slightly soluble in DMSO with heating; not soluble in water or ethanol. **Disposal:** A

- Erlotinib specifically targets the epidermal growth factor receptor tyrosine kinase, which is highly expressed and occasionally mutated in various forms of cancer. It binds reversibly to the adenine triphosphate binding site of the receptor. Raymond E., *et al.* "Epidermal growth factor receptor tyrosine kinase as a target for anticancer therapy." *Drugs* **60 Suppl 1**: 15-23, discussion 41-42 (2000).
- Erlotinib is a directly acting inhibitor of human EGFR tyrosine kinase with an IC₅₀ of 2 nM and reduces EGFR autophosphorylation in intact tumor cells with an IC₅₀ of 20 nM. Moyer J.D., *et al.* "Induction of Apoptosis and Cell Cycle Arrest by erlotinib, an Inhibitor of Epidermal Growth Factor Receptor Tyrosine Kinase." *Cancer Res.* **57**: 4838-4848 (1997).

- Erlotinib has recently been shown to be a potent inhibitor of JAK2-V617F activity. JAK2-V617F is a mutant of tyrosine kinase JAK2 and is found in most patients with polycythemia vera (PV) and a substantial proportion of patients with idiopathic myelofibrosis or essential thrombocythemia. The study suggests that erlotinib may be used for treatment of JAK2-V617F-positive PV and other myeloproliferative disorders. Li Z., *et al.* "Erlotinib effectively inhibits JAK2V617F activity and polycythemia vera cell growth." *J. Biol. Chem.* **282**: 3428–3432 (2007).
- Found to be a potent inhibitor of EGFR kinase ($K_i = 0.7$ nM), but much weaker for ErbB-2 kinase ($K_i = 1$ μ M) and ErbB-4 kinase ($K_i = 1.5$ μ M). Wood E.R., *et al.* "A Unique Structure for Epidermal Growth Factor Receptor Bound to GW572016 (Lapatinib), Relationships among Protein Conformation, Inhibitor Off-Rate, and Receptor Activity in Tumor Cells." *Cancer Res.* **64**: 6652-6659 (2004).
- Erlotinib is the active ingredient in the drug sold under the trade name Tarceva®. This drug is currently approved for use in patients with non-small cell lung cancer, pancreatic cancer and several other types of cancer.
- **Sold for laboratory or manufacturing purposes only; not for human, veterinary, food, or household use.**
- This product is offered for R&D use in accordance with (i) 35 USC 271(e)+A13(1) in the U.S.; (ii) Section 69.1 of Japanese Patent Law in Japan; (iii) Section 11, No. 2 of the German Patent Act of 1981 in Germany; (iv) Section 60, Paragraph 5b of the U.K. Patents Act of 1977 in the U.K.; (v) Section 68B of the Patents Act of 1953 in New Zealand; (vi) such related legislation and/or case law as may be or become applicable in the aforementioned countries; and (vii) such similar laws and rules as may apply in various other countries.
- Not available in some countries; not available to some institutions; not available for some uses.



E-4040 Everolimus, >98%

[SDZ-RAD] [Certican] [RAD001]
[40-O-(2-hydroxyethyl)-rapamycin]

Size	US\$	€	£	¥
5 mg	99	82	54	11,900
25 mg	245	203	135	29400
100 mg	680	564	374	81,600

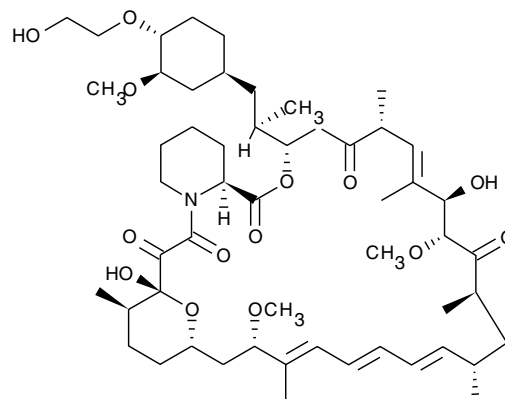
M.W. 958.24 $C_{53}H_{83}NO_{14}$ [159351-69-6]

Storage: Store at or below -20 °C in the dark.

Solubility: Soluble in DMSO and ethanol, up to about 25 mg/mL. **Disposal:** A

- Everolimus is an immunosuppressant analog of rapamycin that blocks growth factor-mediated proliferation of haematopoietic and nonhaematopoietic cells. Chapman T.M. And Perry C.M. "Everolimus." *Drugs* **64**: 861-872 (2004); discussion 873-874.
- Everolimus displays a potent inhibitory effect on posttransplant lymphoproliferative disorder (PTLD) -derived cells *in vitro* and *in vivo*, in a dose range that can prevent allograft rejection, and may prove effective in both the prevention and treatment of PTLDS in transplant patients. Majewski M., *et al.* "Immunosuppressive TOR kinase inhibitor everolimus (RAD) suppresses growth of cells derived from posttransplant lymphoproliferative disorder at allograft-protecting doses." *Transplantation* **75**: 1710-1717 (2003).

- Oral everolimus suppresses in-stent neointimal growth in the rabbit iliac artery. At a dose of 1.5 mg/kg given 1 day before stenting followed by 0.75 mg/kg per day for 28 days, everolimus was well tolerated and was associated with significant neointimal healing. Farb A., *et al.* "Oral Everolimus Inhibits In-Stent Neointimal Growth." *Circulation* **106**: 2379-2384 (2002).
- Everolimus is the active ingredient in the drug sold under the trade name Certican and in the drug-eluting stent sold under the trade name Xience V. The drug is approved for prophylaxis of organ rejection in patients who have received a kidney or heart transplant, and the stent is approved for use in patients undergoing angioplasty.
- **Sold for laboratory or manufacturing purposes only; not for human, veterinary, food, or household use.**
- This product is offered for R&D use in accordance with (i) 35 USC 271(e)+A13(1) in the U.S.; (ii) Section 69.1 of Japanese Patent Law in Japan; (iii) Section 11, No. 2 of the German Patent Act of 1981 in Germany; (iv) Section 60, Paragraph 5b of the U.K. Patents Act of 1977 in the U.K.; (v) Section 68B of the Patents Act of 1953 in New Zealand; (vi) such related legislation and/or case law as may be or become applicable in the aforementioned countries; and (vii) such similar laws and rules as may apply in various other countries.
- Not available in some countries; not available to some institutions; not available for some uses.



F-4660 Fasudil Monohydrochloride Salt, >99%

[1-(5-Isoquinolinesulfonyl)homopiperazine] [Erit] [AT-877]

Size	US\$	€	£	¥
100 mg	83	69	46	10,000
500 mg	345	286	190	41,400
1 g	598	496	329	71,800
2 g	995	826	547	119,400

M.W. 327.84
[105628-07-7]
M.I. 14: 3942

$C_{14}H_{17}N_3O_2S \cdot HCl$
RTECS: HM4031166

Storage: Store at or below -20 °C. **Solubility:** Very soluble in water, up to 200 mg/mL or more; soluble in DMSO up to about 95 mg/mL; not soluble in ethanol; addition of an aqueous solution of this monohydrochloride salt into a buffer solution may significantly alter its solubility. **Disposal:** A

- **Nomenclature.** Two names have been widely used for this compound, "HA-1077" and "Fasudil", and these names have been variously and inconsistently applied to the free base, the monohydrochloride salt and the dihydrochloride salt forms. For



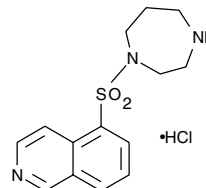
many years LC Labs has sold the dihydrochloride salt under the name HA-1077, Dihydrochloride Salt (Cat. No. H-2330 on page 17). For historical reasons and for continuity, we have elected to continue using the HA-1077 name for our dihydrochloride salt product, even though we recently introduced the monohydrochloride salt form under the name Fasudil, Monohydrochloride Salt (Cat. No. F-4660 as described in this listing).

- The monohydrochloride salt is the form used to prepare formulations of this drug for clinical use. Note that the solubility properties of the mono- and di-HCl salts are different.
- Kinase inhibitor; has antivasospastic properties.
 - Asano, T., *et al.* "Vasodilator actions of HA1077 *in vitro* and *in vivo* putatively mediated by the inhibition of protein kinases." *Br. J. Pharmacol.* **98**: 1091-1100 (1989).
 - Sasaki, Y. and Sasaki, Y. "Inhibition of myosin light chain phosphorylation in cultured smooth muscle cells by HA1077, a new type of vasodilator." *Biochem. Biophys. Res. Commun.* **171**: 1182-1187 (1990).
 - Seto, M., *et al.* "Effects of HA 1077, a protein kinase inhibitor, on myosin phosphorylation and tension in smooth muscle." *Eur. J. Pharmacol.* **195**: 267-272 (1991).
 - Shibuya, O., *et al.* The effects of an intracellular calcium antagonist HA 1077 on delayed cerebral vasospasm in dogs. *Acta Neurochir.* **90**: 53 (1988).
 - Shirotni, M. *et al.* "A new type of vasodilator, HA 1077, an isoquinoline derivative, inhibits proliferation of bovine vascular smooth muscle cells in culture." *J. Pharmacol. Exp. Ther.* **259**: 738-744 (1991).
 - Swärd, K. *et al.* "Inhibition of Rho-associated kinase blocks agonist-induced Ca²⁺ sensitization of myosin phosphorylation and force in guinea-pig ileum." *J. Physiol.* **522**: 33-49 (2000).
 - Davies, S.P. *et al.* "Specificity and mechanism of action of some commonly used protein kinase inhibitors." *Biochem. J.* **351**: 95-105 (2000).
- Potencies for inhibition of various kinases by Fasudil:

Enzyme	IC50	Ki	Reference
Rho-associated Kinase II	1.9 µM		Davies, S.P. <i>et al.</i>
Protein Kinase C-Related Kinase 2	4 µM		Davies, S.P. <i>et al.</i>
Mitogen- and Stress-Activated Protein Kinase 1	5 µM		Davies, S.P. <i>et al.</i>
Mitogen Activated Protein Kinase-Activated Protein Kinase 1b	5 µM		Davies, S.P. <i>et al.</i>
Rho-associated Kinase	10.7 µM		Swärd, K. <i>et al.</i>
Myosin Light Chain Kinase	95.2 µM		Swärd, K. <i>et al.</i>
Protein Kinase C	425 µM		Swärd, K. <i>et al.</i>
Cyclic AMP-Dependent Protein Kinase		1.6 µM	Asano, T. <i>et al.</i>
Cyclic GMP-Dependent Protein Kinase		1.6 µM	Asano, T. <i>et al.</i>
Myosin Light Chain Kinase		36 µM	Asano, T. <i>et al.</i>

- This monohydrochloride salt form is the active ingredient in drug formulations marketed in Japan to treat cerebral vasospasm following surgery for subarachnoid hemorrhage and associated cerebral ischemic symptoms. Zhao, J. *et al.* "Effect of Fasudil Hydrochloride, a Protein Kinase Inhibitor, on Cerebral Vasospasm and Delayed Cerebral Ischemic Symptoms After Aneurysmal Subarachnoid Hemorrhage." *Neurologia Medico-Chirurgica* **46**: 421-428 (2006). Also, the monohydrochloride form has been or presently is in human clinical trials for treatment of acute cerebral thrombosis, subarachnoid hemorrhage, and angina pectoris.

- Regarding CAS Numbers: the Chemical Abstracts Service (CAS) has assigned the number 103745-39-7 to the free base form of this compound (a form that LC Labs does not sell). CAS has also assigned a different number, 105628-07-7, to the monohydrochloride salt form described on this page. CAS apparently has not assigned a separate number to the dihydrochloride salt, so for our dihydrochloride salt product, HA-1077 Dihydrochloride Salt (Cat. No. H-2330 on page 17), we have used the number that CAS has assigned to the free base.
- Sold for laboratory or manufacturing purposes only; not for human, veterinary, food, or household use.**



FHPI – see SB 202190 (Cat. No. S-1700 on page 36).

F-4900 FK-506, >98%

[Tacrolimus] [Prograf]

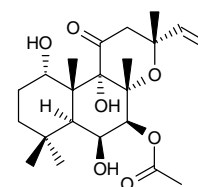
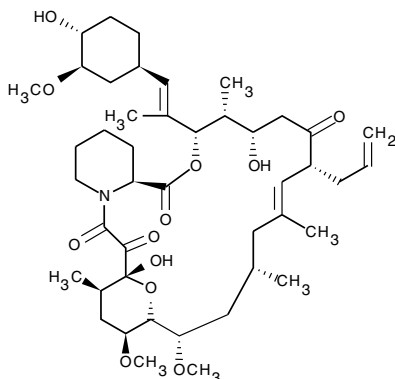
Size	US\$	€	£	¥
10 mg	45	37	25	5,400
25 mg	89	74	49	10,700
100 mg	290	241	160	34,800
200 mg	465	386	256	55,800
500 mg	695	577	382	83,400

M.W. 804.03 C₄₄H₆₉NO₁₂ [104987-11-3]
RTECS: KD4200000 M.I. **13**: 9117

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO or methanol. **Disposal:** A

- Ascomycin level is less than 0.5%.
- Available in gram to kilogram quantities—request a bulk quote.
- FK-506 is a potent immunosuppressant and *in vitro* T cell proliferation blocker. It has been shown to disrupt calcineurin (also known as phosphatase 2B)-mediated signal transduction in T lymphocytes. The compound interacts with its FK-506-binding protein-12 (FKBP-12). The resulting complex, in turn, interferes with calcineurin substrate interaction. Dumont, F.J. "FK-506, an immunosuppressant targeting calcineurin function." *Curr. Med. Chem.* **7**: 731-748 (2000).
- FK-506 inhibits FKBP activity resulting in an increase in the release of sarcoplasmic reticulum-derived calcium. FK-506 also appears to inhibit Na(+)-Ca²⁺ exchange. Prolonged exposure of *Xenopus* A6 cells to FK-506 significantly inhibits aldosterone-stimulated Na⁺ transport and Na(+)-K(+)-ATPase activity. Unlike rapamycin, which also binds to FK-506-binding protein-12, FKBP12 with or without bound FK-506 has no effect on rat brain PKC activity *in vitro*. McCall, E. "Effects of FK-506 on contraction and Ca²⁺ transients in rat cardiac myocytes." *Circ. Res.* **79**: 1110-1121 (1996). Rokaw, M.D., *et al.* "FK-506 and rapamycin but not cyclosporin inhibit aldosterone-stimulated sodium transport in A6 cells." *Am. J. Physiol.* **271**: C194-202 (1996). Rokaw, M.D., *et al.* "Rapamycin inhibits protein kinase C activity and stimulates Na⁺ transport in A6 cells." *J. Biol. Chem.* **271**: 32468-32473 (1996).
- Not available in some countries; not available to some institutions; not available for some uses.
- See also our other standard immunosuppressant products:
 - Rapamycin (Cat No. R-5000 on page 34)

- Cyclosporin (Cat No. C-6000 on page 7)
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



F-9929 Forskolin, >99%

[Colforsin]

Size	US\$	€	£	¥
50 mg	77	64	42	9,200
100 mg	132	110	73	15,800
300 mg	325	270	179	39,000
1 g	660	548	363	79,200

M.W. 410.51 C₂₂H₃₄O₇ [66575-29-9]
 RTECS: QL6150000 M.I. 12: 2539

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO (5 mg/ml) or ethanol (6 mg/ml). **Disposal:** A

- Forskolin is a naturally occurring diterpene from the Indian plant, *Coleus forskohlii*, that works as an activator of adenylate cyclase resulting in an increase in the intracellular concentration of cAMP. Laurenza, A., *et al.* "Forskolin: a specific stimulator of adenylate cyclase or a diterpene with multiple sites of action?" *Trends Pharm. Sci.* **10**: 442-447 (1989). Barber, R. and Goka, T.J. "Adenylate cyclase activity as a function of forskolin concentration." *J. Cyclic Nucleotide Protein Phosphor. Res.* **10**: 23-29 (1985).
- Forskolin acts as a smooth muscle relaxant and vasodilator in a concentration-dependent manner that affects both cytoplasmic calcium levels and contractile element calcium sensitivity. Abe, A. and Karaki, H.J. "Effect of forskolin on cytosolic Ca²⁺ level and contraction in vascular smooth muscle." *J. Pharmacol. Exp. Ther.* **249**: 895-900 (1989).
- Forskolin is an inhibitor of mammalian glucose transporters and of a bacterial galactose-H⁺ transporter, GalP. Joost, H.G. and Steinfelder, H.J. "Forskolin inhibits insulin-stimulated glucose transport in rat adipose cells by a direct interaction with the glucose transporter." *Mol. Pharmacol.* **31**: 279 (1987). Martin, G.E., *et al.* "Forskolin specifically inhibits the bacterial galactose-H⁺ transport protein, GalP." *J. Biol. Chem.* **269**: 24870-24877 (1994).
- Forskolin blocks PKC-activated ERK1 and ERK2 tyrosine phosphorylation and inhibits PKC-stimulated MAPK and Raf-1 activities in mouse bone-forming cells (MC3T3-E1 osteoblasts). Siddhanti, S.R., *et al.* "Forskolin inhibits protein kinase C-induced mitogen activated protein kinase activity in MC3T3-E1 osteoblasts." *Endocrinology.* **136**: 4834-4841 (1995).
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.

G-4408 Gefitinib, >99%

[ZD-1839] [Iressa]

	Size	US\$	€	£	¥
NEW!	300 mg	125	104	69	15,000
	1 g	245	203	135	29,400
	2 g	385	320	212	46,200
	5 g	695	577	382	83,400

M.W. 446.91 C₂₂H₂₄ClFN₄O₃ [184475-35-2]

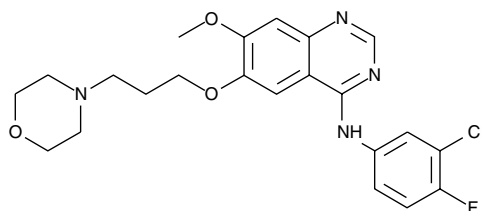
Storage: Store at or below -20 °C in the dark.

Solubility: Soluble in DMSO, up to about 100 mg/mL; very poorly soluble in water or ethanol. **Disposal:** A

- Gefitinib inhibits EGFR tyrosine kinase by binding to the adenosine triphosphate (ATP)-binding site of the enzyme. Thus the function of the EGFR tyrosine kinase in activating the Ras signal transduction cascade is inhibited, and malignant cell growth is inhibited. Research on gefitinib-sensitive non-small cell lung cancers has shown that a mutation in the EGFR tyrosine kinase domain is responsible for activating anti-apoptotic pathways. These mutations tend to confer increased sensitivity to tyrosine kinase inhibitors such as gefitinib and erlotinib. Of the types of non-small cell lung cancer histologies, adenocarcinoma is the type that most often harbors these mutations. These mutations are more commonly seen in Asians, women, and non-smokers (who also tend to more often have adenocarcinoma). Pao W., *et al.* "EGF receptor gene mutations are common in lung cancers from "never smokers" and are associated with sensitivity of tumors to gefitinib and erlotinib." *Proc. Natl. Acad. Sci. USA* **101**: 13306-13311 (2004). Sordella R., *et al.* "Gefitinib-sensitizing EGFR mutations in lung cancer activate anti-apoptotic pathways." *Science* **305**: 1163-1167 (2004).
- The IC₅₀ values for gefitinib for inhibiting HT-29 and LoVo cell growth were 23.6->100 μM and 7.3-48.5 μM, respectively, when the exposure times are from 18 hours to 3 days. A time-dependent reduction in IC₅₀ was observed for gefitinib, with the IC₅₀ after 3 days of exposure being 4-8 times lower than after 18 hours of exposure. Azzariti A., *et al.* "Prolonged exposure of colon cancer cells to the epidermal growth factor receptor inhibitor gefitinib (Iressa™) and to the antiangiogenic agent ZD6474: Cytotoxic and biomolecular effects." *World J. Gastroenterol.* **12**: 5140-5147 (2006).
- Found to be a potent inhibitor of EGFR kinase (K_i = 0.40 nM), but much weaker against ErbB-2 kinase (K_i = 870 nM) and ErbB-4 kinase (K_i = 1.1 μM). Wood E.R., *et al.* "A Unique Structure for Epidermal Growth Factor Receptor Bound to GW572016 (Lapatinib), Relationships among Protein Conformation, Inhibitor Off-Rate, and Receptor Activity in Tumor Cells." *Cancer Res.* **64**: 6652-6659 (2004).
- Selectivity was demonstrated by the >100-fold difference in IC₅₀ for cells grown in the presence (IC₅₀ = 0.054 μM) or absence (IC₅₀ = 8.8 μM) of EGF. Similarly, gefitinib selectively inhibited EGF-stimulated growth of HUVECs compared with FGF- or VEGF-stimulated growth. Enzyme kinetic studies to determine the characteristics of gefitinib inhibition of EGFR TK, in which peptide substrate concentration was fixed at 2 mM (~6-fold higher than the K_m) and the ATP concentration was varied, showed that gefitinib is a competitive inhibitor with respect to ATP (K_i = 2.1 nM). Similarly, when the ATP concentration was fixed at 50 μM (~6-fold higher than the K_m) and peptide concentration was varied, gefitinib

showed noncompetitive kinetics ($K_i = 15.0$ nM). Wakeling A.E., *et al.* "ZD1839 (Iressa), An Orally Active Inhibitor of Epidermal Growth Factor Signaling with Potential for Cancer Therapy." *Cancer Res.* **62**: 5749-5754 (2002).

- Gefitinib is the active ingredient in the drug sold under the trade name Iressa. Gefitinib is currently indicated for the treatment of locally advanced or metastatic non-small cell lung cancer in patients who have previously received chemotherapy. While gefitinib, as of this writing, has yet to be proven effective in other cancers, there may be potential for its use in the treatment of other cancers where EGFR overexpression is involved.
- **Sold for laboratory or manufacturing purposes only; not for human, veterinary, food, or household use.**
- This product is offered for R&D use in accordance with (i) 35 USC 271(e)+A13(1) in the U.S.; (ii) Section 69.1 of Japanese Patent Law in Japan; (iii) Section 11, No. 2 of the German Patent Act of 1981 in Germany; (iv) Section 60, Paragraph 5b of the U.K. Patents Act of 1977 in the U.K.; (v) Section 68B of the Patents Act of 1953 in New Zealand; (vi) such related legislation and/or case law as may be or become applicable in the aforementioned countries; and (vii) such similar laws and rules as may apply in various other countries.
- Not available in some countries; not available to some institutions; not available for some uses.



G-4500 Geldanamycin, >99%

[NSC 122750]

Size	US\$	€	£	¥
25 mg	98	81	54	11,800
100 mg	229	190	126	27,500
250 mg	445	369	245	53,400
1 g	988	820	543	118,600
2 g	1760	1461	968	211,200

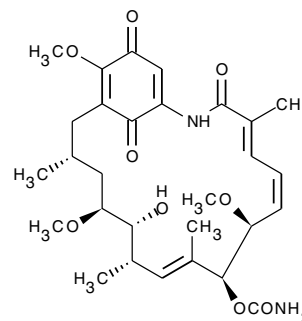
M.W. 560.64 $C_{29}H_{40}N_2O_9$ [30562-34-6]

RTECS: LX8920000

Warning: Toxic.

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO. **Disposal:** A

- Binds specifically to heat shock protein Hsp90 and its GP96 homologue; inhibits protein maturation. Whitesell, L. and Cook, P. "Stable and specific binding of heat shock protein 90 by geldanamycin disrupts glucocorticoid receptor function in intact cells." *Mol. Endocr.* **10**: 705-712 (1996).
- Geldanamycin is somewhat sensitive to water; when dissolved in DMSO, it may react with moisture or other impurities in the DMSO. A very similar, but more stable, geldanamycin analog is 17-allylaminogeldanamycin (17-AAG, Cat. No. A-6880 on page 1).
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



A Major Advance in Soybean Isoflavone Research: The Soybean Isoflavone Family Now Numbers Twelve Members!

The presence in soybeans of genistein and its glucoside, genistin, has been recognized for many decades. For much of that time it was believed that the primary form of this isoflavone in unprocessed soybeans was the glucoside form, genistin. Similarly, daidzin and its aglycone daidzein have long been known as soy constituents.

There is now a large literature describing the biological properties of genistein in particular, because of its activity as a tyrosine kinase inhibitor, as a possible anti-oxidant and as a potential anti-cancer compound, among other notable discoveries. Over the years much has also been published regarding the interesting and potentially useful activities of daidzein and daidzin.

More recently, another glucoside/aglycone pair, namely glycitin and glycitein respectively, were identified in soy extracts. Because of the relatively low levels of glycitin and glycitein in soy products and attendant lack of affordable material for experimental use, their biological properties have remained largely a mystery in spite of their potential importance.

LC Laboratories® is pleased to make available all six of these glucosides and aglycones at reasonable prices.

The story does not stop here, however. Research in the last few years has turned up the surprising fact that a large, and often the predominant, fraction of the isoflavones found in soybeans occurs not as the glucoside forms but rather as their 6''-O-malonyl esters. Chemically, these compounds consist of the glucoside form esterified with a single malonate half-ester, located at the primary (6'') hydroxy group of the sugar moiety.

This remarkable development has introduced major new uncertainties as to the pharmacologically active components of soy products. Moreover, further complicating matters, the malonyl esters are thermally and chemically unstable and are easily converted during soy product processing to either the free glucoside form or to yet another type of isoflavone derivative, namely the 6''-O-acetyl esters, which are much more stable.

As a result, the isoflavone fractions of soy products typically contain, in varying proportions, the entire twelve-compound isoflavone ensemble – the malonyl glucosides of genistein, daidzein and glycitein; their acetyl glucosides, their free glucosides and the free aglycones. Wang and Murphy [*J. Agric. Food Chem.* **42**: 1666-1673 (1994)] have published an analytical method for the simultaneous analysis of all twelve compounds and extensive data on their levels in a wide variety of soy-based products.

With these new developments, soy isoflavone research is entering a new era, and LC Laboratories® is pleased to be able to offer all twelve members of this biologically, nutritionally and medically important family of compounds. (Please see individual catalog entries; bulk quantities are available for all twelve products.)

G-6055 Genistein, >99%

[4',5,7-Trihydroxyisoflavone]

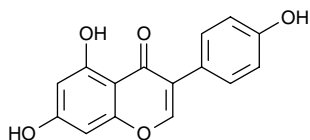
Size	US\$	€	£	¥
1 g	59	49	32	7,100
10 g	245	203	135	29,400
25 g	490	407	270	58,800
100 g	1330	1104	732	159,600

M.W. 270.24 C₁₅H₁₀O₅ [446-72-0]
 RTECS: NR2392000 M.I. 12: 4395

Storage: Store at or below -20°C.

Solubility: Soluble in DMSO. **Disposal:** A

- Tyrosine kinase inhibitor. Akiyama, T. *et al. J. Biol. Chem.* **262**: 5592-5595 (1987).
- See the extensive comments before the listing for Genistein (Cat. No. G-6055 on page 16).
- Please request Technical Note #22 for additional information.
- Isoflavone derivative found in soy-based food products. Wang, H. and Murphy, P.A. "Isoflavone content in commercial soybean foods." *J. Agric. Food Chem.* **42**: 1666-1673 (1994).
- See also these related products:
 - 6"-O-Acetyldaidzin (Cat. No. A-6900 on page 1).
 - 6"-O-Acetylgenistin (Cat. No. A-3000 on page 2).
 - 6"-O-Acetylglycitin (Cat. No. A-7860 on page 2).
 - Daidzein (Cat. No. D-2946 on page 8).
 - Daidzin (Cat. No. D-7878 on page 8).
 - (R,S)-Dihydrodaidzein (Cat. No. D-9200 on page 9).
 - (R,S)-Equol (Cat. No. E-5880 on page 11).
 - Genistin (Cat. No. G-5200 on page 16).
 - Glycitein (Cat. No. G-1152 on page 16).
 - Glycitin (Cat. No. G-2822 on page 17).
 - 6"-O-Malonyldaidzin (Cat. No. M-6730 on page 24).
 - 6"-O-Malonylgenistin (Cat. No. M-8090 on page 24).
 - 6"-O-Malonylglycitin (Cat. No. M-4620 on page 25).
- A catalog containing just these 14 products can be viewed and printed from our website, www.lclabs.com.
- Shipping charges for the 100 g size are slightly higher than our normal rates.
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



G-5200 Genistin, >99%

[Genistein, 7-O-β-D-glucopyranoside]

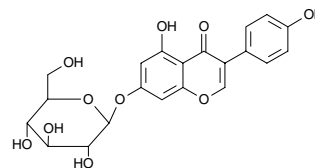
Size	US\$	€	£	¥
25 mg	85	71	47	10,200
100 mg	225	187	124	27,000
300 mg	465	386	256	55,800
1 g	790	656	435	94,800

M.W. 432.38 C₂₁H₂₀O₁₀ [529-59-9]
 RTECS: DJ3093000 M.I. 12: 4395

Storage: Store desiccated at or below

-20°C. **Solubility:** Soluble in DMSO. **Disposal:** A

- Isoflavone derivative found in soy-based food products. Wang, H. and Murphy, P.A. "Isoflavone content in commercial soybean foods." *J. Agric. Food Chem.* **42**: 1666-1673 (1994).
- See the extensive comments before the listing for Genistein (Cat. No. G-6055 on page 16).
- See also these related products:
 - 6"-O-Acetylgenistin (Cat. No. A-3000 on page 2).
 - Genistein (Cat. No. G-6055 on page 16).
 - 6"-O-Malonylgenistin (Cat. No. M-8090 on page 24).
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



Gleevec – see Imatinib, Methanesulfonate Salt (Cat. No. I-5508 on page 18).

Glivec – see Imatinib, Methanesulfonate Salt (Cat. No. I-5508 on page 18).

G-1152 Glycitein, >99%

[4',7-Dihydroxy-6-methoxyisoflavone]

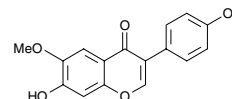
Size	US\$	€	£	¥
5 mg	65	54	36	7,800
10 mg	99	82	54	11,900
25 mg	210	174	116	25,200
100 mg	680	564	374	81,600

M.W. 284.27 C₁₆H₁₂O₅ [40957-83-3]

Storage: Store at or below -20°C. **Solubility:** Very insoluble (less than 100 mg/ml) in methanol, ethanol, or water; soluble in DMSO. **Disposal:** A

NOTE: This highly purified glycitein is very insoluble in aqueous alcohol or aqueous acetonitrile; with heating, a solution of 100 µg/mL can be made, but upon cooling most of the glycitein crystallizes out, leaving approximately 10 µg/mL or less in solution.

- Isoflavone derivative found in soy-based food products. Wang, H. and Murphy, P.A. "Isoflavone content in commercial soybean foods." *J. Agric. Food Chem.* **42**: 1666-1673 (1994).
- See the extensive comments before the entry for Genistein (Cat. No. G-6055 on page 16).
- LC Laboratories® is pleased to be the first source of glycitein at prices low enough for routine study of this important dietary soy constituent.
- See also these related products:
 - 6"-O-Acetylglycitin (Cat. No. A-7860 on page 2).
 - Glycitin (Cat. No. G-2822 on page 17).
 - 6"-O-Malonylglycitin (Cat. No. M-4620 on page 25).
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



G-2822 Glycitin, >99%

[Glycitein, 7-O-β-D-glucopyranoside]

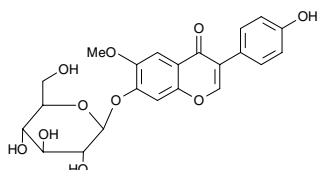
Size	US\$	€	£	¥
5 mg	59	49	32	7,100
10 mg	88	73	48	10,600
25 mg	185	154	102	22,200
100 mg	590	490	324	70,800

M.W. 446.41 C₂₂H₂₂O₁₀ [40246-10-4]

Storage: Store desiccated at or below -20 °C.

Solubility: Soluble in DMSO; poorly insoluble on other solvents. **Disposal:** A

- Isoflavone derivative found in soy-based food products. Wang, H. and Murphy, P.A. "Isoflavone content in commercial soybean foods." *J. Agric. Food Chem.* **42**: 1666-1673 (1994).
- See the extensive comments before the listing for Genistein (Cat. No. G-6055 on page 16).
- LC Laboratories® is pleased to be the first source of glycitin at prices low enough for routine study of this important dietary soy constituent.
- See also these related products:
 - 6"-O-Acetylglycitin (Cat. No. A-7860 on page 2).
 - Glycitein (Cat. No. G-1152 on page 16).
 - 6"-O-Malonylglycitiin (Cat. No. M-4620 on page 25).
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



Go 6976 – see Gö 6976 (Cat. No. G-6203 on page 17).

G-6203 Gö 6976, >99%

[PD 406976] [Go 6976]

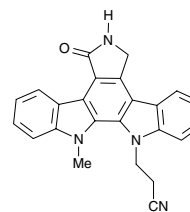
Size	US\$	€	£	¥
1 mg	83	69	46	10,000
5 mg	345	286	190	41,400

M.W. 378.43 C₂₄H₁₈N₄O [136194-77-9]

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO. **Appearance:** Off-white to yellow solid.

Disposal: A

- Novel, very potent PKC inhibitor with high selectivity for the A-group of PKC isotypes (α, β and γ), with IC₅₀ values in the 2-10 nM range. Little or no inhibition of the B- and C-groups of PKC isotypes, even at much higher concentrations. Kleinschroth, J., Hartenstein, J., Rudolph, C. and Schächtele, C. "Non-glycosidic/non-aminoalkyl-substituted indolocarbazoles as inhibitors of protein kinase C." *Bioorg. Med. Chem. Lett.* **3**: 1959-1964 (1993). Martiny-Baron, G., Kazanietz, M.G., Mischak, H., Blumberg, P., Kochs, G., Hug, H., Marme, D. and Schächtele, C. "Selective inhibition of protein kinase C isozymes by the indolo-carbazole Gö 6976." *J. Biol. Chem.* **268**: 9194-9197 (1993).
- Please request Technical Note #2 for additional information about the nomenclature of PKC isotypes.
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



H-2339 H-89, Dihydrochloride Salt, >99%

[N-[2-(p-Bromocinnamylamino)ethyl]-5-isoquinolinesulfonamide, Di-HCl Salt]

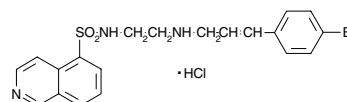
Size	US\$	€	£	¥
10 mg	57	47	31	6,800
25 mg	119	99	65	14,300
100 mg	399	331	219	47,900
300 mg	975	809	536	117,000

M.W. 519.29 C₂₀H₂₀BrN₃O₂S•2HCl [127243-85-0]

Storage: Store desiccated at or below -20 °C.

Solubility: Soluble in DMSO, water (up to 25 mg/mL) or ethanol. **Disposal:** A

- Potent and selective inhibitor of PKA, with an IC₅₀ of about 50 nM. Chijiwa, T., *et al.* "Inhibition of forskolin-induced neurite outgrowth and protein phosphorylation by a newly synthesized selective inhibitor of cyclic AMP-dependent protein kinase, N-[2-(p-bromocinnamylamino)ethyl]-5-isoquinolinesulfonamide (H-89), of PC12D pheochromocytoma cells." *J. Biol. Chem.* **265**: 5267-5272 (1990).
- Also inhibits PKG and the μ isotype of PKC (at about 500 nM). In contrast, most other PKC isotypes are much more weakly inhibited, with IC₅₀'s in the 32 μM range. Johannes, F.-J., Prestle, J., Dieterich, S., Oberhagemann, P., Link, G. and Pfizenmaier, K. "Characterization of activators and inhibitors of protein kinase C_μ." *Eur. J. Biochem.* **227**: 303-307 (1995).
- Please request Technical Note #24 for additional information.
- **Sold for laboratory or manufacturing purposes only; not for human, veterinary, food, or household use.**



H-2330 HA-1077, Dihydrochloride Salt, >99%

[1-(5-Isoquinolinesulfonyl)homopiperazine] [Eril] [AT-877]

Size	US\$	€	£	¥
100 mg	83	69	46	10,000
500 mg	345	286	190	41,400
1 g	598	496	329	71,800
2 g	995	826	547	119,400

M.W. 364.30
[103745-39-7]
M.I. 14: 3942

C₁₄H₁₇N₃O₂S•2HCl
RTECS: HM4031166

Storage: Store at or below -20 °C. **Solubility:** Very soluble in water, up to 200 mg/mL or more; soluble in DMSO up to about 10 mg/mL; not soluble in ethanol; addition of an aqueous solution of this dihydrochloride salt into a buffer solution may significantly alter its solubility. **Disposal:** A

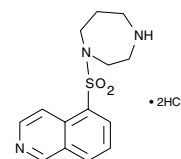
- **Nomenclature.** Two names have been widely used for this compound, "HA-1077" and "Fasudil", and these names have been variously and inconsistently applied to the free base, the monohydrochloride salt and the dihydrochloride salt forms. For many years LC Labs has sold the dihydrochloride salt under the name HA-1077, Dihydrochloride Salt, as described in this listing. For historical reasons and for continuity, we have elected to maintain the HA-1077 name for our dihydrochloride salt product, even though we recently introduced the monohydrochloride salt form under the name Fasudil, Monohydrochloride Salt (Cat. No. F-4660 on page 12).
- The monohydrochloride salt is the form used to prepare formulations of this drug for clinical use. Note that the solubility properties of the mono- and di-HCl salts are different.
- Kinase inhibitor; has antivasospastic properties:
 - Asano, T., *et al.* "Vasodilator actions of HA1077 *in vitro* and *in vivo* putatively mediated by the inhibition of protein kinases." *Br. J. Pharmacol.* **98**: 1091-1100 (1989).
 - Sasaki, Y. and Sasaki, Y. "Inhibition of myosin light chain phosphorylation in cultured smooth muscle cells by HA1077, a new type of vasodilator." *Biochem. Biophys. Res. Commun.* **171**: 1182-1187 (1990).
 - Seto, M., *et al.* "Effects of HA 1077, a protein kinase inhibitor, on myosin phosphorylation and tension in smooth muscle." *Eur. J. Pharmacol.* **195**: 267-272 (1991).
 - Shibuya, O., *et al.* The effects of an intracellular calcium antagonist HA 1077 on delayed cerebral vasospasm in dogs. *Acta Neurochir.* **90**: 53 (1988).
 - Shirovani, M. *et al.* "A new type of vasodilator, HA 1077, an isoquinoline derivative, inhibits proliferation of bovine vascular smooth muscle cells in culture." *J. Pharmacol. Exp. Ther.* **259**: 738-744 (1991).
 - Swärd, K. *et al.* "Inhibition of Rho-associated kinase blocks agonist-induced Ca²⁺ sensitization of myosin phosphorylation and force in guinea-pig ileum." *J. Physiol.* **522**: 33-49 (2000).
 - Davies, S.P. *et al.* "Specificity and mechanism of action of some commonly used protein kinase inhibitors." *Biochem. J.* **351**: 95-105 (2000).
- Potencies for inhibition of various kinases by HA-1077:

Enzyme	IC50	Ki	Reference
Rho-associated Kinase II	1.9 µM		Davies, S.P. <i>et al.</i>
Protein Kinase C-Related Kinase 2	4 µM		Davies, S.P. <i>et al.</i>
Mitogen- and Stress-Activated Protein Kinase 1	5 µM		Davies, S.P. <i>et al.</i>
Mitogen Activated Protein Kinase-Activated Protein Kinase 1b	5 µM		Davies, S.P. <i>et al.</i>
Rho-associated Kinase	10.7 µM		Swärd, K. <i>et al.</i>
Myosin Light Chain Kinase	95.2 µM		Swärd, K. <i>et al.</i>
Protein Kinase C	425 µM		Swärd, K. <i>et al.</i>
Cyclic AMP-Dependent Protein Kinase		1.6 µM	Asano, T. <i>et al.</i>
Cyclic GMP-Dependent Protein Kinase		1.6 µM	Asano, T. <i>et al.</i>
Myosin Light Chain Kinase		36 µM	Asano, T. <i>et al.</i>

- The monohydrochloride salt form of this compound, Fasudil, Monohydrochloride Salt (Cat. No. F-4660 on page 12), is marketed in Japan to treat cerebral vasospasm following surgery for subarachnoid hemorrhage and associated cerebral ischemic symptoms. Zhao, J. *et al.* "Effect of Fasudil Hydrochloride, a

Protein Kinase Inhibitor, on Cerebral Vasospasm and Delayed Cerebral Ischemic Symptoms After Aneurysmal Subarachnoid Hemorrhage." *Neurologia Medico-Chirurgica* **46**: 421-428 (2006). The same monohydrochloride form has been or presently is in human clinical trials for treatment of acute cerebral thrombosis, subarachnoid hemorrhage and angina pectoris.

- Regarding CAS Numbers: the Chemical Abstracts Service (CAS) has assigned the number 103745-39-7 to the free base form of this compound (a form that LC Labs does not sell). CAS has also assigned a different number, 105628-07-7, to the monohydrochloride salt form, which LC Labs sells under the name Fasudil, Monohydrochloride Salt (Cat. No. F-4660 on page 12). CAS apparently has not assigned a separate number to the dihydrochloride, so for our dihydrochloride salt product described in this listing, we have used the number that CAS has assigned to the free base.
- Sold for laboratory or manufacturing purposes only; not for human, veterinary, food, or household use.



40-O-(2-hydroxyethyl)-rapamycin – see Everolimus (Cat. No. E-4040 on page 12).

Imatinib Mesylate – see Imatinib, Methanesulfonate Salt (Cat. No. I-5508 on page 18).

I-5508 Imatinib, Methanesulfonate Salt, >99%

[Imatinib Mesylate] [Gleevec] [Glivec]
[CGP-57148B] [STI-571]

	Size	US\$	€	£	¥
NEW!	100 mg	67	56	37	8,000
	500 mg	168	139	92	20,200
	1 g	265	220	146	31,800
	2 g	415	344	228	49,800
	5 g	748	621	411	89,800

M.W. 589.72 C₂₉H₃₁N₇O • CH₄SO₃
[220127-57-1]

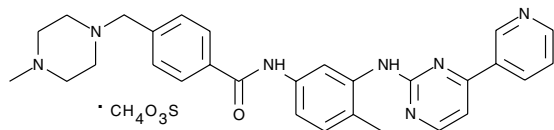
Storage: Store at or below -20 °C in the dark.

Solubility: Very soluble in water (up to about 200 mg/mL) and DMSO (up to about 100 mg/mL); very poorly soluble in ethanol. **Disposal:** A

- Imatinib is a member of a new class of agents that act by inhibiting particular tyrosine kinase enzymes instead of non-specifically inhibiting rapidly dividing cells. Imatinib is used to decrease *bcr-abl* tyrosine kinase activity, upon which some types of tumor cells depend for growth. Imatinib works by binding to the ATP binding site of *bcr-abl* and competitively inhibiting the enzyme activity of the protein. Imatinib is selective for *bcr-abl*, though it also inhibits other enzymes (c-kit and PDGF-R). Deininger M. and Druker B.J. "Specific Targeted Therapy of Chronic Myelogenous Leukemia with Imatinib." *Pharmacol. Rev.* **55**: 401-423 (2003).
- Inhibition of the *bcr-abl* tyrosine kinase also stimulates its entry into the nucleus, where it is unable to perform any of its normal anti-apoptotic functions. Vigneri P. and Wang J.Y. "Induction of apoptosis in chronic myelogenous leukemia cells through nuclear entrapment of BCR-ABL tyrosine kinase." *Nat. Med.* **7**: 228-234 (2001).
- Imatinib inhibits EOL-1 cell viability (IC₅₀ = 0.5 nM), phosphorylation of a fusion protein (IC₅₀ = 30 nM), and viability of BaF3 cells expressing Rhe-PDGFRα in the absence of IL-3 (IC₅₀ = 0.17 nM). Griffin J.H., *et al.* "Discovery of a fusion kinase in

EOL-1 cells and idiopathic hypereosinophilic syndrome." *Proc. Natl. Acad. Sci. USA* **100**: 7830-7835 (2003).

- Inhibition of CSF-1R by imatinib is competitive with ATP, with a K_i value of 120 nM. Guo J., *et al.* "Inhibition of phosphorylation of the colony-stimulating factor-1 receptor (c-Fms) tyrosine kinase in transfected cells by ABT-869 and other tyrosine kinase inhibitors." *Mol. Cancer Ther.* **5**: 1007-1013 (2006).
- The IC_{50} values for imatinib inhibition of KBM5 and KBM7 cell growth were 0.48 and 0.24 μ M, respectively, while the IC_{50} values for imatinib in KBM5-STI571^{R1.0} and KBM7-STI571^{R1.0} cells were 6.40 and 3.30 μ M, respectively. The calculated resistance indexes of 13.3 for KBM5-STI571^{R1.0} cells and 13.8 for KBM7-STI571^{R1.0} confirmed comparable degrees of imatinib resistance. Golemovic M., *et al.* "AMN107, a Novel Aminopyrimidine Inhibitor of Bcr-Abl, Has *In vitro* Activity against Imatinib-Resistant Chronic Myeloid Leukemia." *Clin. Cancer Res.* **11**: 4941-4947 (2005).
- Imatinib is the active ingredient in the drug sold under the trade name Gleevec® in USA or Glivec in Europe and Australia. This drug is currently approved for use in patients with chronic myelogenous leukemia, gastrointestinal stromal tumors and a number of other malignancies.
- Sold for laboratory or manufacturing purposes only; not for human, veterinary, food, or household use.**
- This product is offered for R&D use in accordance with (i) 35 USC 271(e)+A13(1) in the U.S.; (ii) Section 69.1 of Japanese Patent Law in Japan; (iii) Section 11, No. 2 of the German Patent Act of 1981 in Germany; (iv) Section 60, Paragraph 5b of the U.K. Patents Act of 1977 in the U.K.; (v) Section 68B of the Patents Act of 1953 in New Zealand; (vi) such related legislation and/or case law as may be or become applicable in the aforementioned countries; and (vii) such similar laws and rules as may apply in various other countries.
- Not available in some countries; not available to some institutions; not available for some uses.



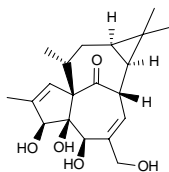
I-8560 Ingenol, >99%

Size	US\$	€	£	¥
1 mg	35	29	19	4,200
5 mg	164	136	90	19,700

M.W. 348.44 C₂₀H₂₈O₅ [30220-46-3]

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO or ethanol. **Disposal:** A

- Extremely weak PKC activator ($K_i = 30 \mu$ M). Hasler, C.M., *et al.* "Specific binding to protein kinase C by ingenol and its induction of biological responses." *Cancer Res.* **52**: 202-208 (1992).
- Starting material for synthesis of ingenol derivatives.
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



I-5900 Ingenol 3-Angelate, >99%

[PEP005] [3-Inganyl Angelate] [Inganyl 3-Angelate]

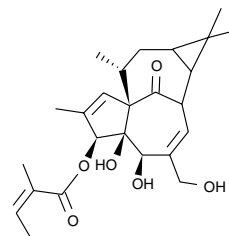
Size	US\$	€	£	¥
1 mg	119	99	65	14,300

M.W. 430.54 C₂₅H₃₄O₆

SPECIAL HAZARD: TUMOR PROMOTER. Gloves and mask should be worn when using this compound. Care must be taken to prevent contact through all routes of exposure.

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO or ethanol. **Disposal:** A

- Protein kinase C activator; anti-cancer drug.
- Treatment with acids or bases or heating may cause rearrangement of the angeloyl group to the 5- or 20- positions, leading to a significant decrease in potency.
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



I-9000 Ingenol 3-Angelate 20-Acetate, >99%

[Inganyl 3-Angelate 20-Acetate]
[3-Inganyl Angelate 20-Acetate]

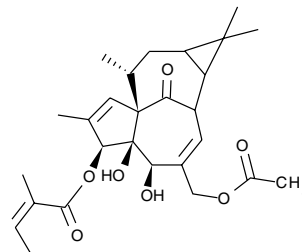
Size	US\$	€	£	¥
1 mg	133	110	73	16,000

M.W. 472.58 C₂₇H₃₆O₇

SPECIAL HAZARD: TUMOR PROMOTER. Gloves and mask should be worn when using this compound. Care must be taken to prevent contact through all routes of exposure.

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO or ethanol. **Disposal:** A

- Protein Kinase C activator; anti-cancer drug.
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



I-6400 5'-Iodoresiniferatoxin, >99%

[5'-IRTX]

Size	US\$	€	£	¥
1 mg	78	65	43	9,400
5 mg	270	224	149	32,400

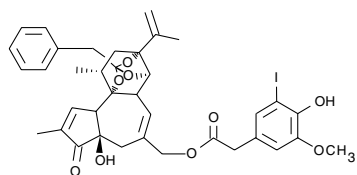
M.W. 754.62

C₃₇H₃₉IO₉

Storage: Store at or below -20 °C in the dark.

Solubility: Soluble in DMSO or ethanol. **Disposal:** A **LIGHT-SENSITIVE!**

- 5'-IRTX is an important new compound that appears to be a very potent vanilloid receptor antagonist. 5'-IRTX binds to the VR1 receptor with high affinity (K_d = 4.3 nM) but does not induce RTX- or capsaicin-like effects in *Xenopus laevis* oocytes expressing VR1. 5'-IRTX completely blocked capsaicin-induced currents in these cells, with an IC₅₀ of 3.9 nM. *In vivo*, intrathecal 5'-IRTX was 3.5-fold more potent than morphine in blocking a pain response induced in the mouse paw by injected capsaicin. In this assay capsaizepine was inactive at 3 mg/mouse, a 113-fold higher dose than the 5'-IRTX ED₅₀. 5'-IRTX's potency as a vanilloid antagonist is some 40-fold higher than that of capsazepine, a weak vanilloid antagonist having other, unrelated biological activities. Wahl, P. *et al.* "Iodo-resiniferatoxin, a new potent vanilloid receptor antagonist." *Mol. Pharm.* **59**: 9-15 (2001).
- 5'-IRTX has also been shown to be a pure antagonist in HEK cells expressing the human VR1, with an IC₅₀ of 27 nM. McDonnell, M.E. *et al.*, "Synthesis and *in vitro* evaluation of a novel iodinated resiniferatoxin derivative that is an agonist at the human vanilloid VR1 receptor." *Bioorg. Med. Chem. Lett.* **12**: 1189-1192 (2002).
- NOTE:** The structure shown in Fig. 1 of Wahl *et al.* is incorrect; the iodine atom should be next to the free OH-group on the homovanillic acid moiety, as depicted below.
- Comments on nomenclature for this class of compounds can be found in the product listing for 6'-Iodoresiniferatoxin (Cat No. I-2000 on page 20).
- Please inquire for bulk quantities of 5'-IRTX at substantial discounts.
- Anti-inflammatory uses and pharmaceutical formulations containing this compound are covered by U.S. patent 5,643,948, and such formulations and their use in medicine are covered by European patent EP 0455271, DE P375210808, FR 0455271, GB 0455271 and SW 0455271, all assigned to PKC Pharmaceuticals, Inc., the parent company of LC Laboratories.
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



I-2000 6'-Iodoresiniferatoxin, >99%

[6'-IRTX]

Size	US\$	€	£	¥
1 mg	78	65	43	9,400
5 mg	270	224	149	32,400

M.W. 754.62

C₃₇H₃₉IO₉

Storage: Store at or below -20 °C in the dark.

Solubility: Soluble in DMSO or ethanol. **Disposal:** A **LIGHT-SENSITIVE!**

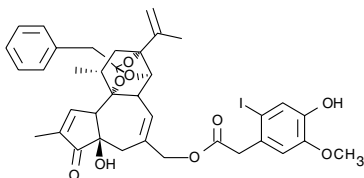
- Novel, high-affinity partial agonist at the human vanilloid VR1 receptor; K_i = 0.71 nM. In a functional assay measuring induction of increases in intracellular calcium in HEK cells stably expressing hVR1, 6'-IRTX was only able to induce a 50% response relative to capsaicin. The EC₅₀ for 6'-IRTX in these cells was 130 nM. In contrast to the result in cells expressing human VR1, 6'-IRTX was a full agonist, or very nearly so (92 ± 6% of the capsaicin response), in HEK cells expressing the rat VR1 ortholog. McDonnell, M.E. *et al.*, "Synthesis and *in vitro* evaluation of a novel iodinated resiniferatoxin derivative that is an agonist at the human vanilloid VR1 receptor." *Bioorg. Med. Chem. Lett.* **12**: 1189-1192 (2002). [N.B. In light of the data for effects on hVR1 in the article, the title should say "partial agonist" – ed.]
- Thus, 6'-IRTX shows activity intermediate between the full hVR1 agonist resiniferatoxin (Cat. No. R-6712 on page 34) and the hVR1 silent antagonist 5'-IRTX (Cat. No. I-6400 on page 20).
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.
- NOTE:** The McDonnell *et al.* article contains a number of errors, some trivial, some quite significant:
 - The structure depicted in Fig. 2 for 5'-IRTX is not correct; the iodine atom should be next to the free hydroxy group on the homovanillic acid moiety. The same error occurs in the original article describing 5'-IRTX [Wahl, P. *et al.*, *Mol. Pharm.* **59**: 9-15 (2001)].
 - The order of substituent citation for the substituted phenylacetic acid cited in the second sentence of the abstract should be "... 4-hydroxy-2-iodo-5-methoxy..." (aromatic ring substituents are listed in alphabetical order). Likewise, the order of substituents for one of the reactants in reference 8 should be "... 4-acetoxy-2-iodo-5-methoxyphenylacetic acid ..."
 - In reference 9, which is actually a synthetic chemical procedure, the substituent position numbering and order of substituent naming are incorrect for the starting material cited in the first sentence; the correct description is "... 4-acetoxy-2-iodo-5-methoxy ..."
 - The substituent numbering of the positions of the homovanillic acid ester moiety for compound 4 in Scheme 1 is inconsistent with the position numbering in Fig. 1, the latter being the numbering system routinely used in the vanilloid field for resiniferatoxin derivatives. (See "Nomenclature", below.)
 - In the second-to-last paragraph on page 1190, right column, the substituent position numbering and order of substituent naming for the compound from Wahl *et al.* referred to in the first sentence should be "... 4-hydroxy-5-iodo-3-methoxy ...".
- Nomenclature** The convention in the vanilloid field is to name and number resiniferatoxin (RTX) derivatives as substituted RTX's (this is explained further below). In this numbering convention, all the position numbers of the diterpene and homovanillic moieties remain unchanged when new substituents are introduced. The diterpene moiety is taken to be the parent structure, and its carbon atoms are numbered 1-20. The carbon atoms of the homovanillic benzene ring are numbered with primes, 1'-6'. Thus, introduction of an iodine atom next to the free OH-group of RTX results in "5'-IRTX", and introducing an iodine atom at the less-crowded of the two positions next to the carbon atom-bearing side chain, *i.e.*, not next to the methoxy group, produces "6'-IRTX". It is important to note that introduction of an iodine into that same position in free homovanillic acid itself, as a separate entity not connected to a diterpene parent, would result of renumbering of the benzene ring positions. But because the numbering of the RTX positions does not change when substituents are introduced, 6'-IRTX is the correct name for this compound. An alternate way of naming RTX derivatives, used in several places in the McDonnell *et al.* paper, is technically acceptable but is not consistent with conventions in the vanilloid field and might cause extensive confusion to non-chemists. This alternate naming scheme treats the compounds in question as 20-esters of the parent diterpene, resiniferonol 9,13,14-orthophenylacetate. Thus, McDonnell *et al.* use "... 9,13,14-orthophenylacetylresiniferonol-20-(4-hydroxy-2-iodo-5-methoxyphenylacetate ...)" at the top of

page 1190 as the name for 6'-IRTX. By this naming scheme, the homovanillic acid positions are numbered as if the homovanillic acid were a separate compound, in which the iodo group would properly be at position 2, rather than as part of an RTX molecule with invariant numbering.

Strictly speaking, according to IUPAC rules, none of these naming and numbering schemes is remotely close to being correct.

However, the numbering scheme taking the diterpene to be the parent entity, with invariant position numbering, has now been used for many decades in the RTX and phorbol ester fields, in a literature now numbering many thousands of articles. Thus it appears that this system would constitute the least confusing approach to designating new RTX derivatives and related compounds.

- Please inquire for bulk quantities of 6'-IRTX at substantial discounts.
- Anti-inflammatory uses and pharmaceutical formulations containing this compound are covered by U.S. patent 5,643,948, and such formulations and their use in medicine are covered by European patent EP 0455271, DE P375210808, FR 0455271, GB 0455271 and SW 0455271, all assigned to PKC Pharmaceuticals, Inc., the parent company of LC Laboratories.



I-6800 Ionomycin, Calcium Salt, >99%

Size	US\$	€	£	¥
5 mg	79	66	43	9,500
10 mg	138	115	76	16,600
25 mg	275	228	151	33,000

M.W. 747.08 C₄₁H₇₀O₉•Ca [56092-82-1]
RTECS: NO0650000

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO. **Disposal:** A

- Antibiotic that acts as a potent and selective calcium ionophore; more effective than A23187. Ionomycin binds Ca²⁺ in the 7.0-9.5 pH range with the resulting complex exhibiting intense UV absorption. Liu, C. M., *et al.* "Characterization of ionomycin as a calcium ionophore." *J. Biol. Chem.* **253**: 5892-5894 (1978). Kauffman R. F., *et al.* "Cation transport and specificity of ionomycin. Comparison with ionophore A23187 in rat liver mitochondria." *J. Biol. Chem.* **255**: 2735-2739 (1980).
- Ionomycin induces apoptosis in immature B cell lines, for example, in Burkitt lymphoma cells, and in cultured embryonic rat cortical neurons. More mature B cell lines do not undergo apoptosis, but are arrested in the G1 phase of the cell cycle. Takei, N., *et al.* "Ca²⁺ ionophore-induced apoptosis on cultured embryonic rat cortical neurons." *Brain Res.* **652**: 65-70 (1994). Aagaard-Tillery, K.M., *et al.* "Differential activation of a calcium-dependent endonuclease in human B lymphocytes. Role in ionomycin-induced apoptosis." *J. Immunol.* **155**: 3297-3307 (1995).
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.

I-5700 Ionomycin, Free Acid, >99%

Size	US\$	€	£	¥
1 mg	29	24	16	3,500
5 mg	130	108	72	15,600
10 mg	225	187	124	27,000
25 mg	445	369	245	53,400

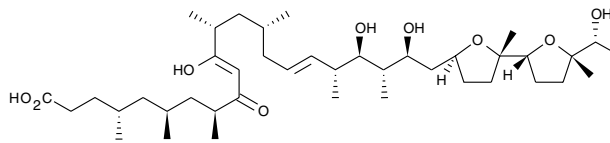
M.W. 709.02 C₄₁H₇₂O₉ [56092-81-0]
RTECS: NO0600000

Warning: Toxic.

Storage: Store at or below -20 °C.

Solubility: Soluble in DMSO. **Disposal:** A

- Antibiotic that acts as a potent and selective calcium ionophore; more effective than A23187. Ionomycin binds Ca²⁺ in the 7.0-9.5 pH range with the resulting complex exhibiting intense UV absorption. Liu, C. M., *et al.* "Characterization of ionomycin as a calcium ionophore." *J. Biol. Chem.* **253**: 5892-5894 (1978). Kauffman R. F., *et al.* "Cation transport and specificity of ionomycin. Comparison with ionophore A23187 in rat liver mitochondria." *J. Biol. Chem.* **255**: 2735-2739 (1980).
- Ionomycin induces apoptosis in immature B cell lines, for example, in Burkitt lymphoma cells, and in cultured embryonic rat cortical neurons. More mature B cell lines do not undergo apoptosis, but are arrested in the G1 phase of the cell cycle. Takei, N., *et al.* "Ca²⁺ ionophore-induced apoptosis on cultured embryonic rat cortical neurons." *Brain Res.* **652**: 65-70 (1994). Aagaard-Tillery, K.M., *et al.* "Differential activation of a calcium-dependent endonuclease in human B lymphocytes. Role in ionomycin-induced apoptosis." *J. Immunol.* **155**: 3297-3307 (1995).
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



Iressa – see Gefitinib (Cat. No. G-4408 on page 14).

1-(5-Isoquinolinesulfonyl)homopiperazine – see Fasudil, Monohydrochloride Salt (Cat. No. F-4660 on page 12) and HA-1077 (Cat. No. H-2330 on page 17).

K-9609 K252c, >99%

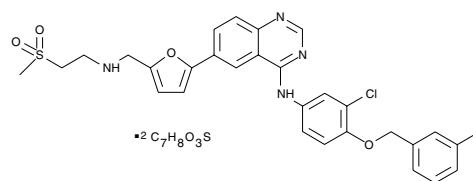
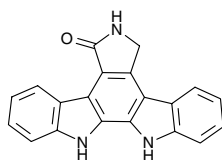
[Staurosporine Aglycone]

Size	US\$	€	£	¥
1 mg	47	39	26	5,600
5 mg	169	140	93	20,300

M.W. 311.34 C₂₀H₁₃N₃O [85753-43-1]

Storage: Store at or below -20 °C. **Solubility:** Soluble DMSO. **Appearance:** Off-white solid. **Disposal:** A

- Inhibits PKC with IC₅₀ of 2.5 μM and PKA at about 10-fold higher concentrations. Kleinschroth, J., *et al.* "Non-glycosidic/non-aminoalkyl-substituted indolocarbazoles as inhibitors of protein kinase C." *Bioorg. Med. Chem. Lett.* **3**: 1959-1964 (1993).
- We are pleased to offer this product now at >99% rather than the previous 95% purity.



L-4804 Lapatinib Di-p-Toluenesulfonate Salt, >98%

[Tykerb] [GW-572016] [Tyverb]

	Size	US\$	€	£	¥
NEW!	25 mg	268	222	147	32,200
	100 mg	570	473	314	68,400
	300 mg	998	828	549	119,800

M.W. 581.07 C₂₉H₂₆ClFN₄O₄S [388082-78-8]

Storage: Store at or below -20 °C in the dark.

Solubility: Slightly soluble in DMSO. **Disposal:** A

- Lapatinib is an epidermal growth factor receptor (EGFR) and HER2/neu (ErbB-2) dual tyrosine kinase inhibitor. It binds to the intracellular phosphorylation domain to prevent receptor autophosphorylation upon ligand binding. The exact site of binding has currently not been confirmed (EGFR and ErbB2 have a number of intracellular phosphorylation sites). It appears to arrest the development of breast cancer in some patients with metastatic, treatment-refractory disease. Burris H.A. III "Dual Kinase Inhibition in the Treatment of Breast Cancer: Initial Experience with the EGFR/ErbB-2 Inhibitor Lapatinib." *Oncologist* **9**: 10-15 (2004).
- Potent inhibitor of EGFR kinase (K_i = 3 nM), ErbB-2 kinase (K_i = 13 nM), ErbB-4 kinase (K_i = 347 nM). Wood E.R., *et al.* "A Unique Structure for Epidermal Growth Factor Receptor Bound to GW572016 (Lapatinib), Relationships among Protein Conformation, Inhibitor Off-Rate, and Receptor Activity in Tumor Cells." *Cancer Res.* **64**: 6652-6659 (2004).
- Lapatinib can restore tamoxifen sensitivity in ER-positive, tamoxifen-resistant breast cancer models. Chu I., *et al.* "The Dual ErbB1/ErbB2 Inhibitor, Lapatinib (GW572016), Cooperates with Tamoxifen to Inhibit Both Cell Proliferation- and Estrogen-Dependent Gene Expression in Antiestrogen-Resistant Breast Cancer." *Cancer Res.* **65**: 18-25 (2005).
- Lapatinib is the active ingredient in the drug sold under the trade names Tykerb® in the US and Tyverb in Europe. This drug is currently approved for use in patients with advanced metastatic breast cancer in conjunction with the chemotherapy drug Xeloda.
- The CAS number for the free base of Lapatinib is [231277-92-2].
- Sold for laboratory or manufacturing purposes only; not for human, veterinary, food, or household use.**
- This product is offered for R&D use in accordance with (i) 35 USC 271(e)+A13(1) in the U.S.; (ii) Section 69.1 of Japanese Patent Law in Japan; (iii) Section 11, No. 2 of the German Patent Act of 1981 in Germany; (iv) Section 60, Paragraph 5b of the U.K. Patents Act of 1977 in the U.K.; (v) Section 68B of the Patents Act of 1953 in New Zealand; (vi) such related legislation and/or case law as may be or become applicable in the aforementioned countries; and (vii) such similar laws and rules as may apply in various other countries.
- Not available in some countries; not available to some institutions; not available for some uses.

L-6100 Leptomycin B, >99%

[LMB] [Elactocin] [CI-940] [CL-1957A]

[NSC-364372] [PD-114720]

(SOLUTION IN ABSOLUTE ETHANOL)

	Size	US\$	€	£	¥
	100 µg	69	57	38	8,300
	500 µg	275	228	151	33,000
	1 mg	395	328	217	47,400

M.W. 540.74 C₃₃H₄₈O₆ [87081-35-4]

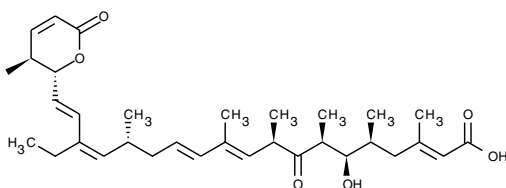
Storage: Store tightly sealed at or below -20 °C in the dark. **Solubility:** Soluble in methanol or ethanol.

Disposal: A

- Leptomycin B (LepB) is a potent, specific inhibitor of nuclear export signal (NES)-dependent protein export from the nucleus. Fukuda, M., *et al.* "CRM1 is responsible for intracellular transport mediated by the nuclear export signal." *Nature* **390**: 308-311 (1997).
- The effect of LepB on the CRM1 (exportin 1) NES receptor results from selective alkylation by LepB of a single cysteine residue. Kudo, N., *et al.* "Leptomycin B inactivates CRM1/exportin 1 by covalent modification at a cysteine residue in the central conserved region." *Proc. Natl. Acad. Sci. USA* **96**: 9112-9117 (1999).
- LepB inhibits the nucleo-cytoplasmic translocation of the HIV Rev protein at nanomolar concentrations. Wolff, B., *et al.* "Leptomycin B is an inhibitor of nuclear export: inhibition of nucleo-cytoplasmic translocation of the human immunodeficiency virus type 1 (HIV-1) Rev protein and Rev-dependent mRNA." *Chem Biol.* **4**: 139-147 (1997).
- LepB also exhibits potent antitumor activity *in vitro* and *in vivo*, and possesses potent antimycotic and antibiotic activity. Tunac, J.B., *et al.* "Novel antitumor antibiotics, CI-940 (PD 114,720) and PD 114,721. Taxonomy, fermentation and biological activity." *J. Antibiot.* **38**: 460-465 (1985).
- POTENCY: LepB typically exhibits IC₅₀ values in the 1 nM range, depending on the species, cell type, and phenomenon under study.
- Our LepB is supplied in serum bottles with teflon-lined closures containing a solution in absolute ethanol (a better solvent than methanol/water; see "Solvent" below).
 - The 100 µg size is supplied as 185 µL of a 1 mM solution (540 µg/mL)
 - The 500 µg size is supplied as 925 µL of a 1 mM solution (540 µg/mL)
 - The 1 mg size is supplied as 1.85 mL of a 1 mM solution (540 µg/mL)
- TISSUE CULTURE TESTED:** Our LepB is tested for inhibition of COS cell growth, to be sure that it is active and its potency is equal, within experimental error, to LepB products offered by other vendors.
- Larger quantities and higher concentrations are available—please request a quotation.
- SOLVENT: Ethanol is a better solvent for LepB than methanol for at least three reasons. First, published information indicates that LepB is more stable in ethanol (purity unchanged after 5 months at room temperature: *US patent* 4,771,070) than in methanol/water 70/30 (freezer temperatures required for storage for more than a few days: Sigma newsletter *LifeScience* **2**, April 2001, page 11).

Second, ethanol has a significantly higher boiling point than methanol, so ethanol solutions are expected to be less susceptible to changes in concentration due to solvent evaporation. Third, LepB is a relatively hydrophobic compound, and may have a tendency to stick to plastic. Being a much stronger organic solvent than methanol/water, ethanol reduces the potential loss of LepB when handled in plastic. NOTE: LepB is also reported to be unstable in DMSO, so the latter solvent should not be used for dilutions.

- **DILUTING LepB SOLUTIONS:** Dilutions of LepB for dose response studies should be made in an organic solvent, preferably ethanol, with only the final dilution being made into culture medium.
- **STABILITY WARNING: LepB in any quantity is unstable when dried down into a film. Thus, under no circumstances should the solvent be removed from solutions of LepB, because rapid decomposition may result.**
- **STABILITY TESTING:** To test LepB stability in ethanol, we tested LepB dilutions under two different temperature conditions. One set of samples was maintained at freezer temperatures after purification and dilution, and then sent in ice to an academic laboratory in Texas. A second set of samples was heated in an oven to 60 °C for two hours, then shipped to the same Texas lab, in the middle of August, without ice or refrigeration, and the samples were assayed for inhibition of COS cell growth. No significant differences were found between the two temperature conditions. In another test, we refluxed a sample of our LepB in ethanol (b.p. 78.5 °C) for an hour; at the end of this period, HPLC analysis showed that decomposition products amounted to less than 1%.
- **SHIPPING CONDITIONS:** We ship our LepB product at ambient temperature, without ice. All the information we have indicates that LepB is stable for at least many days, if not months, under ambient conditions. Thus, the extra cost of ice shipments does not appear to be justified. However, for maximum long-term stability, LepB solutions should always be stored at -20 °C or colder.
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



L-6307 Lestaurtinib, >98%

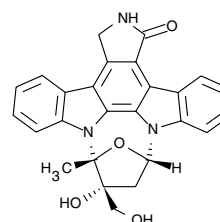
Size	US\$	€	£	¥
1 mg	115	95	63	13,800
5 mg	295	245	162	35,400
25 mg	780	647	429	93,600

M.W. 439.47 C₂₆H₂₁N₃O₄ [111358-88-4]

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO. **Disposal:** A

- Lestaurtinib is a potent inhibitor of several tyrosine kinases, such as FLT-3 and TrkA, that are associated with cancer growth and progression. Schmidt-Arras, D., *et al.* "FLT-3 receptor tyrosine kinase as a drug target in leukemia." *Curr. Pharm. Des.* **10**: 1867-1883 (2004).
- Lestaurtinib inhibited tumor growth when administered at 10 mg/kg s.c. b.i.d. 5 days a week for 21-28 days in Panc-1, AsPc-1, BxPc-3, Colo 357, and MiaPaCa2 s.c. xenografts in athymic nude mice. Reductions in tumor growth volume were 50-70%. Miknyoczki, S.J., *et al.* "The Trk tyrosine kinase inhibitor CEP-701 (KT-5555) exhibits significant antitumor efficacy in preclinical xenograft models of human pancreatic ductal adenocarcinoma." *Clin. Cancer Res.* **5**: 2205-2212 (1999).

- Lestaurtinib inhibited RET and RET phosphorylation in medullary thyroid carcinoma (MTC) cells. It also blocked the growth of these MTC cells in culture and tumor growth in MTC cell xenografts. Strock, C.J., *et al.* "CEP-701 and CEP-751 Inhibit Constitutively Activated RET Tyrosine Kinase Activity and Block Medullary Thyroid Carcinoma Cell Growth." *Cancer Res.* **63**: 5559-5563 (2003).
- FLT3 inhibition by lestaurtinib is associated with its clinical activity in AML patients harboring FLT3-activating mutations. Smith, B.D., *et al.* "Single-agent CEP-701, a novel FLT-3 inhibitor, shows biologic and clinical activity in patients with relapsed or refractory acute myeloid leukemia." *Blood* **103**: 3669-3676 (2004).
- Lestaurtinib is a FLT3 inhibitor that is both potent (IC₅₀ of 2 nM) and selective (no activity on the other members of the type III RTK family at >500 nM). Levis, M. and Small, D. "Novel FLT3 tyrosine kinase inhibitors." *Expert Opin. Investig. Drugs* **12**: 1951-1962 (2003).
- In TF-1/ITD cells, lestaurtinib potently inhibited the phosphorylation of FLT3/ITD (IC₅₀ < 5 nM). Lestaurtinib inhibited the proliferation of TF-1/ITD cells (IC₅₀ ≈ 10 nM), but showed very little effect at 10 nM on TF-1 cells. Chen, P., *et al.* "FLT3/ITD Mutation Signaling Includes Suppression of SHP-1." *J. Biol. Chem.* **280**: 5361-5369 (2005).
- **Sold for laboratory or manufacturing purposes only; not for human, veterinary, food, or household use.**
- This product is offered for R&D use in accordance with (i) 35 USC 271(e)+A13(1) in the U.S.; (ii) Section 69.1 of Japanese Patent Law in Japan; (iii) Section 11, No. 2 of the German Patent Act of 1981 in Germany; (iv) Section 60, Paragraph 5b of the U.K. Patents Act of 1977 in the U.K.; (v) Section 68B of the Patents Act of 1953 in New Zealand; (vi) such related legislation and/or case law as may be or become applicable in the aforementioned countries; and (vii) such similar laws and rules as may apply in various other countries.
- Not available in some countries; not available to some institutions; not available for some uses.



L-7962 LY 294002, >99%

[2-(4-Morpholino)-8-phenyl-4H-1-benzopyran-4-one]

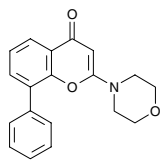
Size	US\$	€	£	¥
5 mg	38	32	21	4,600
25 mg	158	131	87	19,000
100 mg	525	436	289	63,000
300 mg	1230	1021	677	147,600

M.W. 307.35 C₁₉H₁₇NO₃ [154447-36-6]

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO (up to about 40 mg/mL) or ethanol.

Appearance: Off-white to cream solid. **Disposal:** A

- Specific inhibitor of phosphatidylinositol 3-kinase. Vlahos, C.J. *et al.* *J. Biol. Chem.* **269**: 5241-5248 (1994).
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



Novel Malonyl Forms of the Soybean Isoflavones

Only in recent years has it been recognized that large and often predominant fractions of the daidzein, genistein and glycitein in unprocessed or mildly processed soybean products occur in the 6''-O-malonyl forms, not as the free glycosides or aglycones.

Because these compounds have only recently been found in soybean products, their specific biological, pharmacological and nutritional properties are essentially unknown at the present time. Given the increasing use of soy products and the many beneficial nutritional properties attributed to the isoflavone components of those products, it appears that further studies of the biological role of these novel soy isoflavones are of substantial scientific and medical importance.

LC Laboratories® now offers the three malonyl isoflavones from soybeans: 6''-O-Malonyldaidzin (Cat. No. M-6730 on page 24), 6''-O-Malonylgenistin (Cat. No. M-8090 on page 24) and 6''-O-Malonylglycitein (Cat. No. M-4620 on p 25).

M-6730 6''-O-Malonyldaidzin, >98%

Size	US\$	€	£	¥
1 mg	59	49	32	7,100
5 mg	165	137	91	19,800
10 mg	270	224	149	32,400
25 mg	490	407	270	58,800

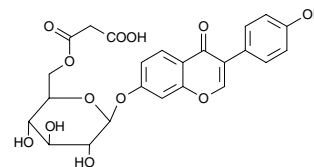
M.W. 502.43 C₂₄H₂₂O₁₂

Storage: Store desiccated at or below -20 °C.

Solubility: Soluble in DMSO, methanol, ethanol, or mixtures of acetonitrile/water. **Disposal:** A

- Isoflavone derivative found in soy-based food products. Wang, H. and Murphy, P.A. "Isoflavone content in commercial soybean foods." *J. Agric. Food Chem.* **42**: 1666-1673 (1994).
- See the extensive comments before the listing for Genistein (Cat. No. G-6055 on page 16).
- Typical purity at time of shipment is >99%; this figure may include small amounts of monomalonyl hemiesters other than the 6''-isomer.
- The 1 mg size (accuracy is ± ca. 2-3%) consists of a film adhering to the walls of the ampule and cannot be easily subdivided by weighing. The larger sizes contain a weighable powder.
- **STABILITY:** Very little information about the stability of this compound is available at present. In our experience, when stored in the dry state, frozen and desiccated, this compound has retained its original purity for several years. Our manufacturing process results in a highly crystalline, stable form of this product; *thus, it does not need to be shipped on ice.* Our thermal stability tests show that heating our dry product at 85 °C for 10 hours causes only ca. 1% decomposition. However, we have been informed that aqueous or alcoholic solutions at various pH's can undergo substantial decomposition less than a day after being prepared, particularly when held at room temperature. We recommend that this product be stored in bulk in the dry state, very tightly sealed, thoroughly desiccated, at the coldest available temperature. Small working quantities of solutions should be made freshly each day, just prior to use, and should be discarded at the end of the day. Thaw containers to room temperature prior to opening, and minimize exposure to air during handling to keep moisture levels low.
- See additional comments about malonyl isoflavones directly above this product entry.

- **SHIPMENT:** Shipped at ambient temperature.
- See also these related products:
 - 6''-O-Acetyldaidzin (Cat No. A-6900 on page 1).
 - Daidzein (Cat No. D-2946 on page 8).
 - Daidzin (Cat No. D-7878 on page 8).
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



M-8090 6''-O-Malonylgenistin, >98%

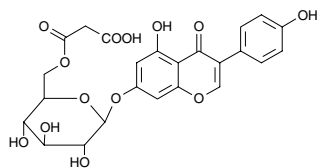
Size	US\$	€	£	¥
1 mg	53	44	29	6,400
5 mg	149	124	82	17,900
10 mg	255	212	140	30,600
25 mg	465	386	256	55,800

M.W. 518.43 C₂₄H₂₂O₁₃

Storage: Store desiccated at or below -20 °C.

Solubility: Soluble in DMSO, methanol, ethanol, or mixtures of acetonitrile/water. **Disposal:** A

- Isoflavone derivative found in soy-based food products. Wang, H. and Murphy, P.A. "Isoflavone content in commercial soybean foods." *J. Agric. Food Chem.* **42**: 1666-1673 (1994).
- See the extensive comments before the listing for Genistein (Cat. No. G-6055 on page 16).
- See additional comments about malonyl isoflavones above the entry for 6''-O-Malonyldaidzin (Cat. No. M-6730 on page 24).
- Typical purity at time of shipment is >99%; this figure may include small amounts of monomalonyl hemiesters other than the 6''-isomer.
- The 1 mg size (accuracy is ± ca. 2-3%) consists of a film adhering to the walls of the ampule and cannot be easily subdivided by weighing. The larger sizes contain a weighable powder.
- **STABILITY:** Very little information about the stability of this compound is available at present. In our experience, when stored in the dry state, frozen and desiccated, this compound has retained its original purity for several years. Our manufacturing process results in a highly crystalline, stable form of this product; *thus, it does not need to be shipped on ice.* Our thermal stability tests show that heating our dry product at 85 °C for 10 hours causes only ca. 1% decomposition. However, we have been informed that aqueous or alcoholic solutions at various pH's can undergo substantial decomposition less than a day after being prepared, particularly when held at room temperature. We recommend that this product be stored in bulk in the dry state, very tightly sealed, thoroughly desiccated, at the coldest available temperature. Small working quantities of solutions should be made freshly each day, just prior to use, and should be discarded at the end of the day. Thaw containers to room temperature prior to opening, and minimize exposure to air during handling to keep moisture levels low.
- **SHIPMENT:** Shipped at ambient temperature.
- See also these related products:
 - 6''-O-Acetylgenistin (Cat No. A-3000 on page 2).
 - Genistein (Cat No. G-6055 on page 16).
 - Genistin (Cat. No. G-5200 on page 16).
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



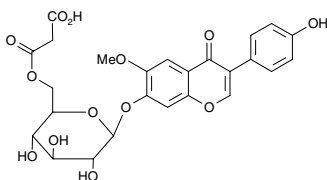
M-4620 6''-O-Malonylglycitin, >98%

Size	US\$	€	£	¥
1 mg	65	54	36	7,800
5 mg	178	148	98	21,400
10 mg	310	257	171	37,200
25 mg	510	423	281	61,200

M.W. 532.46 C₂₅H₂₄O₁₃

Storage: Store desiccated at or below -20 °C. **Solubility:** Soluble in DMSO, methanol, ethanol, or mixtures of acetonitrile/water. **Disposal:** A

- Isoflavone derivative found in soy-based food products. Wang, H. and Murphy, P.A. "Isoflavone content in commercial soybean foods." *J. Agric. Food Chem.* **42**: 1666-1673 (1994).
- See the extensive comments before the listing for Genistein (Cat. No. G-6055 on page 16).
- See additional comments about malonyl isoflavones above the entry for 6''-O-Malonyldaidzin (Cat. No. M-6730 on page 24).
- Typical purity at time of shipment is >99%; this figure may include small amounts of monomalonyl hemiesters other than the 6''-isomer.
- The 1 mg size (accuracy is ± ca. 2-3%) consists of a film adhering to the walls of the ampule and cannot be easily subdivided by weighing. The larger sizes contain a weighable powder.
- **STABILITY:** Very little information about the stability of this compound is available at present. In our experience, when stored in the dry state, frozen and desiccated, this compound has retained its original purity for several years. Our manufacturing process results in a highly crystalline, stable form of this product; *thus, it does not need to be shipped on ice.* Our thermal stability tests show that heating our dry product at 85 °C for 10 hours causes only ca. 1% decomposition. However, we have been informed that aqueous or alcoholic solutions at various pH's can undergo substantial decomposition less than a day after being prepared, particularly when held at room temperature. We recommend that this product be stored in bulk in the dry state, very tightly sealed, thoroughly desiccated, at the coldest available temperature. Small working quantities of solutions should be made freshly each day, just prior to use, and should be discarded at the end of the day. Thaw containers to room temperature prior to opening, and minimize exposure to air during handling to keep moisture levels low.
- **SHIPMENT:** Shipped at ambient temperature.
- See also these related products:
 - 6''-O-Acetylglycitin (Cat. No. A-7860 on page 2).
 - Glycitein (Cat. No. G-1152 on page 16).
 - Glycitin (Cat. No. G-2822 on page 17).
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



M-2550 4-O-Methylphorbol 12-Myristate 13-Acetate, >99%

[MPMA]

Size	US\$	€	£	¥
1 mg	62	51	34	7,400
5 mg	179	149	98	21,500

M.W. 630.86 C₃₇H₅₈O₈ [57716-89-9]

CAUTION: Weak tumor promoter.

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO, ethanol, or acetone. **Disposal:** A

MG-341 – see Bortezomib (Cat. No. B-1408 on page 4).

MPMA – see 4-O-Methylphorbol 12-Myristate 13-Acetate (Cat. No. M-2550 on page 25).

N-8207 Nilotinib, >99%

[AMN-107] [Tasigna]

Size	US\$	€	£	¥
25 mg	228	189	125	27,400
100 mg	740	614	407	88,800

M.W. 529.53 C₂₈H₂₂F₃N₇O [641571-10-0]

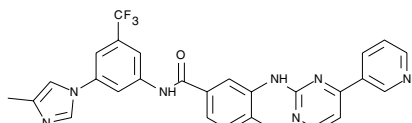
Storage: Store at or below -20 °C in the dark.

Solubility: Soluble in DMSO (up to about 50 mg/mL); not soluble in ethanol or water. **Disposal:** A

- Nilotinib, a novel, selective *BCR-ABL* inhibitor, fits into the ATP-binding site of the *BCR-ABL* protein with higher affinity than imatinib. In addition to being more potent than imatinib (IC₅₀ < 30 nM) against wild-type *BCR-ABL*, nilotinib is also significantly active against 32/33 imatinib-resistant *BCR-ABL* mutants. Weisberg E., *et al.* "AMN107 (nilotinib): a novel and selective inhibitor of *BCR-ABL*." *Br. J. Cancer* **94**: 1765-1769 (2006).
- Nilotinib inhibited the proliferation of haematopoietic cells expressing the mutations in Ph⁺ chronic myelogenous leukemia (CML) and acute lymphoblastic leukaemia with IC₅₀'s of ~ 12 nM, thus being more potent than imatinib. Nilotinib was also effective against several imatinib-resistant *Bcr-Abl* mutants, but not T3151. Weisberg E., *et al.* "Characterization of AMN-107, a selective inhibitor of native and mutant *Bcr-Abl*." *Cancer Cell.* **7**: 129-141 (2005).
- Nilotinib and dasatinib are respectively 20-fold (IC₅₀: 15 nM *versus* 280 nM) and 325-fold (IC₅₀: 0.6 nM *versus* 280 nM) more potent than imatinib against cells expressing wild-type *Bcr-Abl*. Similar improvements are maintained for all imatinib-resistant mutants tested, with the exception of T3151. Thus, both inhibitors hold promise for treating imatinib-refractory CML. O'Hare T., *et al.* "In vitro activity of *Bcr-Abl* inhibitors AMN107 and BMS-354825 against clinically relevant imatinib-resistant *Abl* kinase domain mutants." *Cancer Res.* **65**: 4500-4505 (2005).
- The effects of nilotinib were compared with those of imatinib on imatinib-sensitive (KBM5 and KBM7) and imatinib-resistant CML cell lines (KBM5-STI571R1.0 and KBM7-STI571R1.0). Compared with the antiproliferative activity of imatinib, nilotinib was 43 times more potent in KBM5 (IC₅₀ of 11 nM *versus* 480 nM) and 60 times more potent in KBM7 (IC₅₀ of 4 nM *versus* 259 nM) cells. IC₅₀'s for nilotinib and imatinib were 2.4 μM and 6.4 μM, respectively, in KBM5-STI571R1.0, and 97 nM and 2.5 μM, respectively, in KBM7-STI571R1.0 cells. Golemovic M., *et al.* "AMN107, a Novel Aminopyrimidine Inhibitor of *Bcr-Abl*, Has *In vitro* Activity against Imatinib-Resistant Chronic Myeloid Leukemia." *Clin. Cancer Res.* **11**: 4941-4947 (2005).
- Nilotinib was as potent as imatinib in inducing apoptosis and inhibiting proliferation of EOL-1 cells, with IC₅₀ values of 0.54 and

0.20 nM, respectively. Verstovsek S., *et al.* "Activity of AMN107, a novel aminopyrimidine tyrosine kinase inhibitor, against human FIP1L1-PDGFR-alpha-expressing cells." *Leuk. Res.* **30**: 1499-1505 (2006).

- Nilotinib is a tyrosine kinase inhibitor under investigation as a possible treatment for chronic myelogenous leukemia (CML). In June 2006, a Phase I clinical trial found nilotinib to have relatively favorable safety profile and to show activity in cases of CML resistant to treatment with imatinib (Gleevec®).
- Nilotinib is the active ingredient in the drug sold under the trade name Tasigna®. This drug is currently approved for use in patients with Philadelphia Chromosome-positive chronic myeloid leukemia.
- **Sold for laboratory or manufacturing purposes only; not for human, veterinary, food, or household use.**
- This product is offered for R&D use in accordance with (i) 35 USC 271(e)+A13(1) in the U.S.; (ii) Section 69.1 of Japanese Patent Law in Japan; (iii) Section 11, No. 2 of the German Patent Act of 1981 in Germany; (iv) Section 60, Paragraph 5b of the U.K. Patents Act of 1977 in the U.K.; (v) Section 68B of the Patents Act of 1953 in New Zealand; (vi) such related legislation and/or case law as may be or become applicable in the aforementioned countries; and (vii) such similar laws and rules as may apply in various other countries.
- Not available in some countries; not available to some institutions; not available for some uses.



NSC-707545 – see 17-DMAG (Cat. No. D-3440 on page 10).

NSC 122750 – see Geldanamycin (Cat. No. G-4500 on page 15).

O-2220 Okadaic Acid, >98%

Size	US\$	€	£	¥
50 µg	48	40	26	5,800
100 µg	85	71	47	10,200
300 µg	228	189	125	27,400
1 mg	690	573	380	82,800

M.W. 805.02 C₄₄H₆₈O₁₃ [78111-17-8]
 RTECS: AA8227800 M.I. 12: 6958

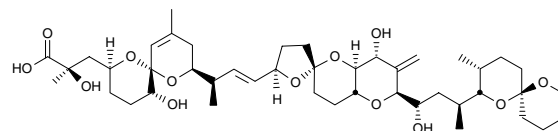
WARNING: Highly irritant to skin and mucous membranes. SPECIAL HAZARD: TUMOR PROMOTER. Gloves and mask should be worn when using this compound. Care must be taken to prevent contact through all routes of exposure.

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO or ethanol. **Disposal:** A

- Potent inhibitor of protein phosphatases, especially the PP-1 and PP-2A classes, in numerous cell types. Cohen, P. *et al. Trends Biochem. Sci.* **15**: 98-102 (1990).
- Non-phorbol type tumor promoter. Suganuma, M. *et al. Proc. Natl. Acad. Sci. USA* **85**: 1768-1771 (1988).
- Please request Technical Note #18 for additional information.
- **Important Notes on Stability:**

1. We believe this product and the three okadaic acid salts below, as shipped from our inventory, are the purest and most stable okadaic acid products available anywhere. In contrast, material from other vendors is often degraded and quite impure. Long-term stability of our four okadaic acid products in their unopened ampules is excellent (one year or more).

2. All four okadaic acid products must first be dissolved in an organic solvent to prepare stock solutions. The okadaic acid molecule is large and somewhat hydrophobic, and material cannot be reliably dissolved out of the ampule with purely aqueous solutions. We understand that some practitioners use mixed aqueous/organic solvents to dissolve material out of the ampules, but we have not tested the efficacy of this approach ourselves.
 3. Solutions of the free acid form of okadaic acid in organic solvents are distinctly less stable, even in the freezer, than those made from the three salt forms listed below.
 4. Once diluted into aqueous media (and assuming equal starting purities), the information available to us indicates that all four forms of okadaic acid show comparable stability.
 5. The biological activity of all four products is identical for the okadaic acid portion, but obviously the counter-ions themselves may affect ion-sensitive experimental systems.
 6. In summary: ignoring the counter-ions, all four forms of okadaic acid are biologically equivalent and equally useful if made up as a stock solution in an organic solvent and used within a few days. If freezer storage of an organic solvent-based stock solution of okadaic acid is anticipated to extend beyond a week or so, we recommend a salt form rather than the free acid.
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



O-6410 Okadaic Acid, Ammonium Salt, >98%

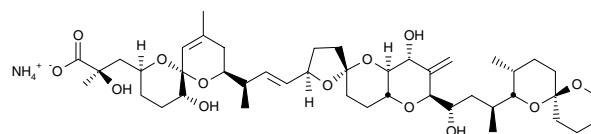
Size	US\$	€	£	¥
50 µg	48	40	26	5,800
100 µg	85	71	47	10,200
300 µg	228	189	125	27,400
1 mg	690	573	380	82,800

M.W. 822.05 C₄₄H₆₇O₁₃•NH₄ [155716-06-6]

WARNING: Highly irritant to skin and mucous membranes. SPECIAL HAZARD: TUMOR PROMOTER. Gloves and mask should be worn when using this compound. Care must be taken to prevent contact through all routes of exposure.

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO or ethanol. **Disposal:** A

- Salt form of okadaic acid, with somewhat greater stability than the free acid when stored in organic solvents. **See notes on stability in the entry for okadaic acid free acid (Cat. No. O-2220 on page 26).**
- Please request Technical Note #18 for additional information.
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



O-7519 Okadaic Acid, Potassium Salt, >98%

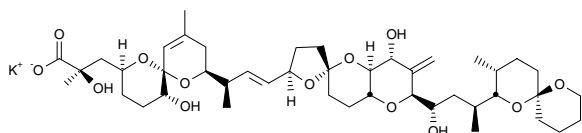
Size	US\$	€	£	¥
50 µg	48	40	26	5,800
100 µg	85	71	47	10,200
300 µg	228	189	125	27,400
1 mg	690	573	380	82,800

M.W. 843.11 C₄₄H₆₇O₁₃•K [155751-72-7]

WARNING: Highly irritant to skin and mucous membranes. SPECIAL HAZARD: TUMOR PROMOTER. Gloves and mask should be worn when using this compound. Care must be taken to prevent contact through all routes of exposure.

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO or ethanol. **Disposal:** A

- Salt form of okadaic acid, with somewhat greater stability than the free acid when stored in organic solvents. See notes on stability in the entry for okadaic acid free acid (Cat. No. O-2220 on page 26).
- Please request Technical Note #18 for additional information.
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



O-5857 Okadaic Acid, Sodium Salt, >98%

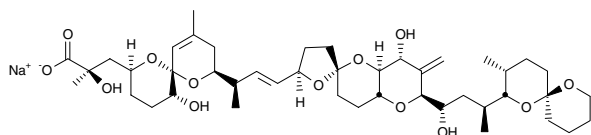
Size	US\$	€	£	¥
50 µg	48	40	26	5,800
100 µg	85	71	47	10,200
300 µg	228	189	125	27,400
1 mg	690	573	380	82,800

M.W. 827.00 C₄₄H₆₇O₁₃•Na [209266-80-8]

WARNING: Highly irritant to skin and mucous membranes. SPECIAL HAZARD: TUMOR PROMOTER. Gloves and mask should be worn when using this compound. Care must be taken to prevent contact through all routes of exposure.

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO or ethanol. **Disposal:** A

- Salt form of okadaic acid, with somewhat greater stability than the free acid when stored in organic solvents. See notes on stability in the entry for okadaic acid free acid (Cat. No. O-2220 on page 26).
- Please request Technical Note #18 for additional information.
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



OSI-774 – see Erlotinib, Hydrochloride Salt (Cat. No. E-4007 on page 11).

O-5679 OSU-03012, Hydrochloride Salt, >98%

Size	US\$	€	£	¥
5 mg	88	73	48	10,600
25 mg	265	220	146	31,800
100 mg	745	618	410	89,400

NEW!

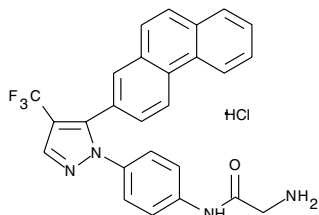
M.W. 496.92 C₂₆H₁₉F₃N₄O •HCl [742112-33-0]

Storage: Store at or below -20 °C in the dark. **Solubility:** Soluble in DMSO. **Disposal:** A

- Inhibitor of phosphoinositide-dependent kinase-1. OSU-03012, Hydrochloride Salt inhibited both recombinant 3-phosphoinositide-dependent kinase-1 activity and PC-3 cell viability with similar IC₅₀ values of ~5 µM. Exposure of PC-3 cells to OSU-03012, Hydrochloride Salt led to Akt dephosphorylation and inhibition of p70 S6 kinase activity. Moreover, overexpression of constitutively active forms of PDK-1 and Akt partially protected against OSU-03012-induced apoptosis. Screening in a panel of 60 cell lines and more extensive testing in PC-3 cells indicated that the mean concentration for total growth inhibition by OSU-03012, Hydrochloride Salt was approximately 3 µM. Zhu J., *et al.* "From the Cyclooxygenase-2 Inhibitor Celecoxib to a Novel Class of 3-Phosphoinositide-Dependent Protein Kinase-1 Inhibitors." *Cancer Res.* **64**: 4309-4318 (2004).
- OSU-03012, Hydrochloride Salt showed no increased resistance in the mutant cells Ba/F3p210^{E255K} and Ba/F3p210^{T315I}, with an IC₅₀ of 5 µM irrespective of mutations. Nevertheless, in the presence of OSU-03012, Hydrochloride Salt the susceptibility of these mutant cells to imatinib-induced apoptosis was significantly enhanced. Together these data provide a novel therapeutic strategy to overcome imatinib mesylate resistance, especially with the Abl mutant T315I. Tseng P.H., *et al.* "Synergistic interactions between imatinib mesylate and the novel phosphoinositide-dependent kinase-1 inhibitor OSU-03012, Hydrochloride Salt in overcoming imatinib mesylate resistance." *Blood* **105**: 4021-4027 (2005).
- The dose of OSU-03012, Hydrochloride Salt to induce 50% chronic lymphocytic leukemia cell death (LC₅₀) at 24 hours was 7.1 µM. Additionally, OSU-03012, Hydrochloride Salt mediates apoptosis by activation of the intrinsic, mitochondrial pathway of apoptosis but also activates alternative cell death pathways that are caspase independent. Johnson A.J., *et al.* "A novel celecoxib derivative, OSU-03012, Hydrochloride Salt, induces cytotoxicity in primary CLL cells and transformed B-cell lymphoma cell line via a caspase- and Bcl-2-independent mechanism." *Blood* **105**: 2504-2509 (2005).
- OSU-03012, Hydrochloride Salt inhibited phosphorylated Akt (P-Akt) and its downstream signalling through 4E binding protein and glycogen synthase kinase at concentrations well below that of celecoxib. Disruption of P-Akt was followed by induction of apoptosis and more than 90% cell death. Kucab J.E., *et al.* "Celecoxib analogues disrupt Akt signaling, which is commonly activated in primary breast tumours." *Breast Cancer Res.* **7**: R796-R807 (2005).
- OSU-03012, Hydrochloride Salt caused a dose-dependent induction of cell death that was not altered by p53 mutation or expression of ERBB1 vIII. OSU-03012, Hydrochloride Salt promotes glioma cell killing that is dependent on endoplasmic reticulum stress, lysosomal dysfunction, and BID-dependent release of AIF from mitochondria, and whose lethality is enhanced by irradiation or by inhibition of protective signaling pathways. Yacoub A., *et al.* "OSU-03012 promotes caspase-independent but PERK-, cathepsin B-, BID-, and AIF-dependent killing of transformed cells." *Mol. Pharmacol.* **70**: 589-603 (2006).
- Sold for laboratory or manufacturing purposes only; not for human, veterinary, food, or household use.**
- This product is offered for R&D use in accordance with (i) 35 USC 271(e)+A13(1) in the U.S.; (ii) Section 69.1 of Japanese Patent Law in Japan; (iii) Section 11, No. 2 of the German Patent Act of

1981 in Germany; (iv) Section 60, Paragraph 5b of the U.K. Patents Act of 1977 in the U.K.; (v) Section 68B of the Patents Act of 1953 in New Zealand; (vi) such related legislation and/or case law as may be or become applicable in the aforementioned countries; and (vii) such similar laws and rules as may apply in various other countries.

- Not available in some countries; not available to some institutions; not available for some uses.



P-9600 Paclitaxel, >99.5%

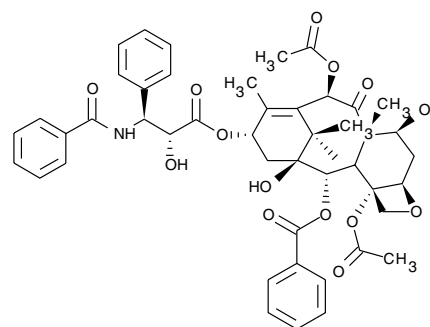
[Taxol]

Size	US\$	€	£	¥
25 mg	45	37	25	5,400
100 mg	133	110	73	16,000
500 mg	292	242	161	35,000
1 g	540	448	297	64,800
2 g	864	717	475	103,700
5 g	1870	1552	1029	224,400

M.W. 853.92 C₄₇H₅₁NO₁₄ [33069-62-4]
M.I. 12: 7117

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO (up to about 200 mg/mL) or ethanol (up to about 40 mg/mL). **Disposal:** A

- Antitumor and antileukemic agent isolated from the bark of the yew tree, *Taxus brevifolia*. Wani, M.C., *et al.* "Plant antitumor agents. VI. The isolation and structure of taxol, a novel antileukemic and antitumor agent from *Taxus brevifolia*." *J. of Amer. Chem. Soc.* **93**: 2325-2327 (1971). McGuire, W.P., *et al.* "Taxol: a unique antineoplastic agent with significant activity in advanced ovarian epithelial neoplasms." *Ann. Int. Med.* **111**: 273-279 (1989).
- Binds to β-tubulin and promotes the assembly of microtubules that resist depolymerization preventing normal cell division. Rowinsky, E.K., *et al.* "Taxol: a novel investigational antimicrotubule agent." *J. Natl. Cancer Inst.* **82**: 1247-1259 (1990). Parekh, H. and Simpkins, H. "The transport and binding of taxol." *Gen. Pharmacol.* **29**: 167-172 (1997). Jordan, A., *et al.* "Tubulin as a target for anticancer drugs: agents which interact with the mitotic spindle investigational antimicrotubule agent." *Med. Res. Rev.* **18**: 259-296 (1998).
- Induces apoptosis through a JNK-dependent pathway in the early phase followed by a JNK-independent pathway that results in Bcl-2 phosphorylation. Wang, T.H., *et al.* "Microtubule dysfunction induced by paclitaxel initiates apoptosis through both c-Jun N-terminal kinase (JNK)-dependent and -independent pathways in ovarian cancer cells." *J. Biol. Chem.* **274**: 8208-8216 (1999). Shil, A.A., *et al.* Differential regulation of mitogen-activated protein kinases by microtubule-binding agents in human breast cancer cells. *Oncogene* **18**: 377-384 (1999). Srivastava, R.K. *et al.* Involvement of microtubules in the regulation of Bcl2 phosphorylation and apoptosis through cyclic AMP-dependent protein kinase. *Mol. Cell. Biol.* **18**: 3509-3517 (1998). Torres, K., and Horwitz, S.B., Mechanisms of Taxol-induced cell death are concentration dependent. *Cancer Res.* **58**: 3620-3626 (1998).
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



P-4313 PD 98059, >99%

[2'-Amino-3'-methoxyflavone]

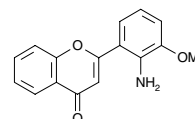
Size	US\$	€	£	¥
5 mg	27	22	15	3,200
10 mg	48	40	26	5,800
25 mg	105	87	58	12,600
50 mg	190	158	105	22,800
100 mg	345	286	190	41,400

M.W. 267.28 C₁₆H₁₃NO₃ [167869-21-8]

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO. **Appearance:** Pale-yellow powder.

Disposal: A

- Potent, selective and cell-permeable inhibitor of MAP kinase (also known as MAPK/ERK kinase or MEK kinase). Inhibits phosphorylation of MAP kinase by MAP kinase kinase. PD 98059 does not inhibit MAP kinase itself. IC₅₀ values for PD 98059-induced effects are in the 1-20 μM range for many assays; it is somewhat weaker in inhibiting cell growth in monolayers or agar for some cell lines. Dudley, D.T. *et al. Proc. Natl. Acad. Sci. USA* **92**: 7686-7689 (1995). Pang, L. *et al. J. Biol. Chem.* **270**: 13585-13588 (1995). Waters, S.B. *et al. J. Biol. Chem.* **270**: 20883-20886 (1995). Langlois, W.J. *et al. J. Biol. Chem.* **270**: 25320-25323 (1995). Alessi, D.R. *et al. J. Biol. Chem.* **270**: 27489-27494 (1995).
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



PDBu – see Phorbol 12,13-Dibutyrate
(Cat. No. P-4833 on page 29).

4α-PDD – see 4α-Phorbol 12,13-Didecanoate
(Cat. No. P-2170 on page 30).

P-1010 Phorbol, >99%

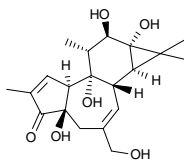
Size	US\$	€	£	¥
1 mg	17	14	9	2,000
5 mg	33	27	18	4,000

M.W. 364.44 C₂₀H₂₈O₆ [17673-25-5]
RTECS: GZ0600000 M.I. 12: 7487

Storage: Store at or below -20 °C. **Solubility:** Soluble in ethanol, DMSO or water.

Disposal: A

- Unsubstituted parent diterpene from which phorbol esters are derived; biologically inactive in most assays.
- Please request Technical Note #30 for a note on nomenclature.
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



P-4227 Phorbol 13-Acetate, >99%

Size	US\$	€	£	¥
1 mg	28	23	15	3,400
5 mg	77	64	42	9,200

M.W. 406.48 C₂₂H₃₀O₇ [32752-29-7]

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO or ethanol. **Disposal:** A

P-7350 Phorbol 13-Decanoate, >99%

Size	US\$	€	£	¥
1 mg	33	27	18	4,000
5 mg	125	104	69	15,000

M.W. 518.69 C₃₀H₄₆O₇ [123597-59-1]

WARNING: Highly irritant to skin and mucous membranes. **SPECIAL HAZARD:** TUMOR PROMOTER. Gloves and mask should be worn when using this compound. Care must be taken to prevent contact through all routes of exposure.

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO or ethanol. **Disposal:** A

P-1571 4α-Phorbol 12,13-Diacetate, >99%

[4α-PDA]

Size	US\$	€	£	¥
1 mg	28	23	15	3,400
5 mg	77	64	42	9,200

M.W. 448.51 C₂₄H₃₂O₈ [56144-62-8]

Storage: Store at or below -20 °C in the dark. **Solubility:** Soluble in DMSO or ethanol. **Disposal:** A

P-5005 Phorbol 12,13-Diacetate, >99%

[PDA]

Size	US\$	€	£	¥
1 mg	15	12	8	1,800
5 mg	42	35	23	5,000

M.W. 448.51 C₂₄H₃₂O₈ [24928-15-2]
RTECS: GZ0651000

WARNING: Highly irritant to skin and mucous membranes.

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO or ethanol. **Disposal:** A

P-3106 Phorbol 12,13-Dibenzoate, >99%

[PDBz]

Size	US\$	€	£	¥
1 mg	28	23	15	3,400
5 mg	77	64	42	9,200

M.W. 572.66 C₃₄H₃₆O₈ [25405-85-0]

WARNING: Highly irritant to skin and mucous membranes. **SPECIAL HAZARD:** TUMOR PROMOTER. Gloves and mask should be worn when using this compound. Care must be taken to prevent contact through all routes of exposure.

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO or ethanol. **Disposal:** A

P-4678 4α-Phorbol 12,13-Dibutyrate, >99%

[4α-PDBu]

Size	US\$	€	£	¥
1 mg	28	23	15	3,400
5 mg	77	64	42	9,200

M.W. 504.62 C₂₈H₄₀O₈ [93781-54-5]

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO or ethanol. **Disposal:** A

P-4833 Phorbol 12,13-Dibutyrate, >99%

[PDBu]

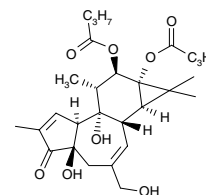
Size	US\$	€	£	¥
1 mg	16	13	9	1,900
5 mg	42	35	23	5,000
10 mg	74	61	41	8,900

M.W. 504.62 C₂₈H₄₀O₈ [37558-16-0]
RTECS: EK7767000

WARNING: Highly irritant to skin and mucous membranes. **SPECIAL HAZARD:** TUMOR PROMOTER. Gloves and mask should be worn when using this compound. Care must be taken to prevent contact through all routes of exposure.

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO or ethanol. **Disposal:** A

- Widely used PKC activator; less potent than PMA, but also less hydrophobic, making it easier to wash out of cells in tissue culture.
- This was the ligand used, in radioactive form, in the discovery of the phorbol ester receptor. Driedger, P.E. and Blumberg, P.M. *Proc. Natl. Acad. Sci. USA* **77**: 567-571 (1980).
- Tritium-labeled PDBu, [³H]PDBu, is available from several suppliers of radiochemicals.
- Please request Technical Note #14 for additional information.
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



P-2170 4 α -Phorbol 12,13-Didecanoate, >99%[4 α -PDD]

Size	US\$	€	£	¥
1 mg	29	24	16	3,500
5 mg	99	82	54	11,900
10 mg	179	149	98	21,500
25 mg	390	324	215	46,800

M.W. 672.94 C₄₀H₆₄O₈ [27536-56-7]**Storage:** Store at or below -20 °C. **Solubility:** Soluble in DMSO or ethanol. **Disposal:** A

- Please request Technical Note #13 for additional information.
- NOTE:** This product is not Phorbol 12,13-Didecanoate.
- 4 α -PDD Activation of TRPV4 Channels** Long thought to be a biologically inactive or extremely weak phorbol ester analog (*i.e.*, an ED₅₀ >25 μ M for binding to protein kinase C compared to ~1 nM potency for PMA), 4 α -PDD has now been shown to be a reasonably potent activator of two TRPV4 channels, namely human VRL-2 and murine TRP12 channels [H. Watanabe *et al.*, *J. Biol. Chem.* **277**: 13569-13577 (2002)]. The ED₅₀ of 4 α -PDD for activation of the TRP12 channel was ~400 nM, and ~185 nM for increasing internal calcium levels in 1321N1 astrocytoma cells expressing human VRL-2. This work extends earlier results showing non-phorbol-ester-like effects of 4 α -PDD [H. Reeve *et al.*, *Pflugers Arch. Eur. J. Physiol.* **429**: 729-737 (1995)] and 4 α -phorbol 12,13-dibutyrate (4 α -PDBu) [D. Doerner *et al.*, *J. Neurosci.* **10**: 1699-1706 (1990)] on calcium currents.

Because 4 α -PDD has few, if any, recognized biological effects at sub-micromolar concentrations other than these effects on TRPV4 channels, Watanabe *et al.* certainly seem justified in stating that “4 α -PDD can be used as a robust and reliable tool to study several features of TRPV channels and to probe functional effects of the activation of this channel in *in vivo* systems”. That said, it is also important to note that absolute selectivity of 4 α -PDD for activating TRPV4 channels may not yet have been thoroughly tested. Though 4 α -PDD has been shown over the years to have little or no effect in a fairly wide range of biological assays, it might prove to have other, as-yet-unidentified activities if subjected to more extensive testing against various targets.

[As an aside, we point out that reference #25 in the Watanabe article, cited in support of the inactivity of 4 α -PDD on PKC, appears not to contain any mention at all of 4 α -PDD or other 4 α -phorbol esters.]

[Also, see below for an important note about nomenclature. Technically, 4 α -PDD is not a phorbol ester, it is a 4 α -phorbol ester — a small but important distinction — and must always be specified as such to avoid confusion with the dramatically different properties of the phorbol esters.]

Surprisingly (in view of historical structure-activity data), PMA (phorbol 12-myristate 13-acetate), the classical nanomolar-potency PKC activator, was shown by Watanabe, *et al.* to be 10- to 50-fold weaker than 4 α -PDD for activation of the TRPV4 channels. If both PMA and 4 α -PDD were targeting a PKC-related protein, via a mechanism fundamentally similar to that of classical PKC activation by phorbol esters, PMA would be expected to be many orders of magnitude more potent than 4 α -PDD. Watanabe *et al.* tested a wide range of PMA and 4 α -PDD concentrations, and there appears to be no doubt that the relative potencies expected for PMA and 4 α -PDD for classical PKC-related effects are strikingly reversed for the TRPV4 channel activation phenomenon. Furthermore, in some assays PMA was merely a “partial agonist”, showing only 50-65% of the response elicited by 4 α -PDD.

The PMA/4 α -PDD potency inversion in turn strongly suggests that 4 α -PDD must be acting via a mechanism distinct from the classical interaction of a phorbol 12,13-diester with a phorbol ester/diacylglycerol-type receptor target, such as those found on the PKC family of proteins. Given the long history and, until now, largely settled picture of the biological properties of phorbol and 4 α -

phorbol esters, this question of mechanism is of high interest, and the answer(s) might turn out to have a wide impact on several areas of pharmacology.

Watanabe *et al.* favor direct binding of 4 α -PDD to the TRPV4 channels as the specific pharmacological mechanism underlying the effects they observed. However, as of this writing (April 2003) no evidence for direct binding of PMA or 4 α -PDD to TRPV4 channels appears to be available. Lacking such evidence, the target question remains open, and serious consideration must also be given to other, indirect potential mechanisms.

PMA and 4 α -PDD have close structural similarity, and the family of highly specific phorbol ester receptors, of known amino acid sequence pattern, have been extensively characterized. Thus, in the absence of evidence to the contrary, “the usual suspect” for a target mediating the effects of 4 α -PDD on TRPV4 would be a site similar to the well-known family of phorbol ester receptors, perhaps with some crucial amino acid residue differences that result in reversal of the usual comparative potencies of phorbol *vs.* 4 α -phorbol esters for a given effect. Such a target might occur either on a PKC-type protein or on some other, perhaps non-kinase, protein bearing a phorbol-type receptor. Furthermore, the well-established ability of PKC to phosphorylate and modulate a number of ion channels supports suspicions that a phorbol ester-like compound such as 4 α -PDD might be acting through a PKC-like entity to activate TRPV4 channels.

It appears that Watanabe *et al.* did not test the effects of any PKC inhibitors in their experimental systems. If several kinase inhibitors known to be reasonably specific for PKC were to be tested and shown not to inhibit the 4 α -PDD effects on TRPV4 channels, this would further support the direct binding hypothesis. In this context it is important to note that some PKC isotypes are affected only weakly or not at all by common PKC inhibitors; such inhibitors are imperfect pharmacological tools. Also, even if inhibitor studies were to reasonably rule out the PKC family as a target site, there remain several other classes of cellular proteins that are not PKC's but nonetheless have functioning, high-affinity phorbol ester receptors. These other phorbol ester receptor-bearing proteins could also be candidates for the actual target of 4 α -PDD in the present case.

Clearly, if the amino acid sequences of the TRPV4 channels contain a region homologous to phorbol ester receptors, that would strongly support a direct binding mechanism for the effects of 4 α -PDD on these channels. For lack of space and time, our discussion here does not include any comparative sequence information about this obvious question. If other investigators do make such comparisons and find an absence of the well-known phorbol ester receptor-like sequences in the TRPV4 channel family, such a result would then require that either a completely new sequence motif for binding 4 α -phorbol-type compounds be present in TRPV4 channels, or that the mechanism of action of 4 α -PDD on these channels be indirect.

With respect to the details of an indirect mechanism for the effects of 4 α -PDD on TRPV4 channels, it is not difficult to imagine how 4 α -PDD might interact with a PKC or similar phorbol ester receptor in a manner sufficiently different from that of the classical PMA-PKC interaction to elicit a profile of biological activities distinct from that of PMA, such as reported now in the TRPV4 studies of Watanabe *et al.* Considerable evidence already exists indicating that even subtly different phorbol ester analogs can all bind to PKC family members but at the same time can differ from one another in terms of the cellular location to which the resulting binding complex is directed. This topological control might be functioning in the case of 4 α -PDD, wherein both PMA and 4 α -PDD might bind to a PKC family member or other phorbol-receptor-containing protein but tend to direct the resulting complexes to different cellular locations, adjacent to, *e.g.*, different kinase substrates or scaffold proteins.

There remains also the question of possible non-specific effects of 4 α -PDD as an explanation for its effects on TRPV4 channels. 4 α -PDD is a non-ionic, detergent-like molecule having a polar head group and a long hydrophobic tail, and it might be expected to perturb membranes and ion channels in a non-specific manner.

Ironically, 4 α -phorbol esters such as 4 α -PDD have themselves long been used as "inactive negative controls" for potential detergent-like or other non-specific effects of the PKC-activating phorbol esters. Hence, in the present case, one needs "a control for the control", *i.e.*, an analog of 4 α -PDD having similar hydrophobicity and detergent-like structure but which is inactive on all potentially relevant targets such as TRPV4 channels, PKC family members and other proteins bearing phorbol ester receptors. In pursuit of more details about the interaction of 4 α -PDD with its biological target, one might hope to employ a ligand-protein binding interaction using a labeled 4 α -PDD in a receptor binding protocol. Unfortunately, this may prove to be quite difficult in the case of 4 α -PDD because (i) it is not terribly potent (only about 400 nM, compared to *ca.* 1 nM potencies for phorbol ester binding to PKC), and (ii) it is highly hydrophobic. The latter property is especially problematic because the typical phorbol ester/receptor complex requires the presence of quite a bit of phospholipid, to which large of amounts of 4 α -PDD would be expected to bind nonspecifically. Taken together, this all suggests that the active 4 α -PDD/receptor complex involved in the present case, whether PKC-related or not, might not be measurable because of an overwhelming level of non-specific binding of labeled 4 α -PDD. This would obscure any specific binding in a typical preparation containing membrane lipids.

From the point of view of structure-activity relations, to date (April, 2003) it appears that, among 4 α -phorbols, only the effects of 4 α -PDD on TRPV4 channels have been reported. LC Laboratories also offers other 4 α -phorbol diesters of varying hydrophobicity; these presumably can be used for structure-activity studies of the TRPV4 activation effect. For example, we offer 4 α -PMA (Cat. No. P-8880, page 32) which is less hydrophobic than 4 α -PDD.

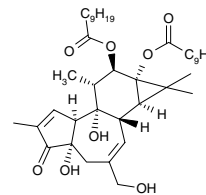
Analogues of 4 α -PDD have considerable potential utility. The high hydrophobicity (high lipid partition coefficient) of 4 α -PDD makes it quite soluble in cellular membrane compartments, and it is reliably presumed to be difficult to wash this compound out of membrane preparations or cell cultures. 4 α -PMA or 4 α -PDBu may prove to be less potent than 4 α -PDD, but if they retain sufficient potency *vis-a-vis* 4 α -PDD, they might be preferable as research tools because of their enhanced potential to equilibrate among aqueous and lipid cellular compartments and to be washed out of experimental preparations.

In the past, in addition to 4 α -PMA, we have also made some other 4 α -phorbol diesters, such as 4 α -PDBu and 4 α -phorbol 12,13-diacetate, a compound of very low hydrophobicity. These other 4 α -phorbol derivatives are not currently listed as LC Labs products but are available by special request. We are also pleased to offer all of our 4 α -phorbol products in bulk quantities at substantial discounts.

- **Chemical Structures.** The primary structural difference between 4 α -PDD and the highly potent phorbol ester-type PKC activators is the configuration at C4. In the highly active phorbol ester family, the hydroxy group at C4 is in the β configuration, *i.e.*, rising *up* out of the two-dimensional structure as viewed on paper or a computer monitor. The 4 α -phorbol esters such as 4 α -PDD, 4 α -PMA and 4 α -PDBu have the 4-OH group oriented *down* below the paper or computer screen's two-dimensional plane.
- **Nomenclature.** Unless "4 α " is specified, all "phorbol" compounds are automatically defined, by operation of standard chemical nomenclature conventions, as having the 4 β -configuration, as part of the meaning of the word "phorbol". This is much like the word "cholesterol", which automatically means that its hydroxy group at carbon 3 is in the β configuration; there is no need to specify "3 β -cholesterol", whereas a cholesterol derivative with a 3 α hydroxy group would require a "3 α -cholesterol" specification.

To avoid confusion in this field, it is useful to note that, technically, 4 α -PDD is not a "phorbol ester", it is a "4 α -phorbol ester", and the structural differences, though minor overall, are quite significant biologically. Given the extreme differences in their biological properties, both on PKC and TRPV4 channel-based phenomena, efforts to maintain distinctive names for members of these two biologically quite distinct classes of compounds appear to be well justified.

- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



P-1925 Phorbol 12,13-Didecanoate, >99%
[PDD]

Size	US\$	€	£	¥
1 mg	15	12	8	1,800
5 mg	49	41	27	5,900

M.W. 672.94 C₄₀H₆₄O₈ [24928-17-4]
RTECS: GZ0653000

WARNING: Highly irritant to skin and mucous membranes. **SPECIAL HAZARD:** TUMOR PROMOTER. Gloves and mask should be worn when using this compound. Care must be taken to prevent contact through all routes of exposure.

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO or ethanol. **Disposal:** A

- Very potent and hydrophobic PKC activator; potent tumor promoter.
- Please request Technical Note #14 for additional information.

P-3814 Phorbol 12,13-Dihexanoate, >99%
[PDH]

Size	US\$	€	£	¥
1 mg	37	31	20	4,400
5 mg	98	81	54	11,800

M.W. 560.73 C₃₂H₄₈O₈ [37558-17-1]

WARNING: Highly irritant to skin and mucous membranes. **SPECIAL HAZARD:** TUMOR PROMOTER. Gloves and mask should be worn when using this compound. Care must be taken to prevent contact through all routes of exposure.

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO or ethanol. **Disposal:** A

P-1680 Phorbol 12-Myristate 13-Acetate, >99.5%
[PMA] [TPA] [Cocarcinogen A1]
[12-O-Tetradecanoyl-phorbol 13-Acetate]

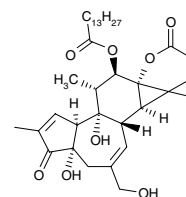
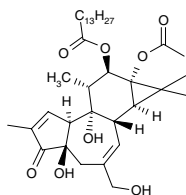
Size	US\$	€	£	¥
1 mg	11	9	6	1,300
5 mg	45	37	25	5,400
10 mg	79	66	43	9,500
25 mg	172	143	95	20,600

M.W. 616.84 C₃₆H₅₆O₈ [16561-29-8]
RTECS: QH4377000 M.I. 12: 7487

WARNING: Highly irritant to skin and mucous membranes. **SPECIAL HAZARD:** TUMOR PROMOTER. Gloves and mask should be worn when using this compound. Care must be taken to prevent contact through all routes of exposure.

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO or ethanol. **Disposal:** A

- This is the most commonly used phorbol ester. It binds to and activates protein kinase C, causes an extremely wide range of effects in cells and tissues, and is a very potent mouse skin tumor promoter. Blumberg, P.M. *CRC Crit. Rev. Toxicol.* **8**: 153-197 and 199-234 (1980).
- Although PMA is quite toxic, it has shown anti-leukemic and anti-neutopenic activity in humans. Han, Z.T. *et al. Proc. Natl. Acad. Sci. USA* **95**: 5357-5361 (1998) and *Proc. Natl. Acad. Sci. USA* **95**: 5362-5365 (1998).
- Please request Technical Note #14 for additional information.
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



P-6040 Pimecrolimus, >98%

[Elidel] [SDZ-ASM-981]

(PLEASE INQUIRE ABOUT AVAILABILITY)

Size	US\$	€	£	¥
5 mg	99	82	54	11,900
25 mg	245	203	135	29,400
100 mg	680	564	374	81,600

M.W. 810.47 C₄₃H₆₈O₁₁ [137071-32-0]
M.I. **14**: 7429

Storage: Store at or below -20 °C in the dark.

Solubility: Soluble in DMSO and ethanol, up to about 25 mg/mL. **Disposal:** A

- Pimecrolimus, a rapamycin (sirolimus) derivative, is a cell-selective inhibitor of inflammatory cytokines specifically developed for the treatment of inflammatory skin diseases, such as atopic dermatitis, allergic contact dermatitis, irritant contact dermatitis, and plaque-type psoriasis. It inhibits the production of inflammatory cytokines in T cells and mast cells and prevents the release of preformed inflammatory mediators from mast cells. Stuetz A., *et al.* "Pimecrolimus (Elidel, SDZ ASM 981)—preclinical pharmacologic profile and skin selectivity." *Semin. Cutan. Med. Surg.* **20**: 233-241 (2001).
- In 13 of 26 (50%) lesions of vitiligo, repigmentation was noted after a 6 month treatment of 1% pimecrolimus with a median percentage of repigmentation of 72.9% (interquartile range: 30.5-98.3%). Duration of vitiligo and total affected body surface area tended to be inversely correlated with the success rate of treatment. Boone B., *et al.* "Topical pimecrolimus in the treatment of vitiligo." *Eur. J. Dermatol.* **17**: 55-61 (2007).
- Pimecrolimus is active against mild to moderate atopic dermatitis in adults and children aged ≥ 2 years. Pimecrolimus improved the signs and symptoms of atopic dermatitis and delayed time to a major flare. Hebert A.A. "Review of pimecrolimus cream 1% for the treatment of mild to moderate atopic dermatitis." *Clin. Ther.* **28**: 1972-1982 (2006).
- Pimecrolimus is the active ingredient in the drug sold under the trade name Elidel®. This drug is an immunomodulating agent used in the treatment of atopic dermatitis (eczema).
- **Sold for laboratory or manufacturing purposes only; not for human, veterinary, food, or household use.**
- This product is offered for R&D use in accordance with (i) 35 USC 271(e)+A13(1) in the U.S.; (ii) Section 69.1 of Japanese Patent Law in Japan; (iii) Section 11, No. 2 of the German Patent Act of 1981 in Germany; (iv) Section 60, Paragraph 5b of the U.K. Patents Act of 1977 in the U.K.; (v) Section 68B of the Patents Act of 1953 in New Zealand; (vi) such related legislation and/or case law as

P-8880 4α-Phorbol 12-Myristate 13-Acetate, >99%

[4α-PMA] [4α-TPA]

[4α-12-O-Tetradecanoylphorbol 13-Acetate]

Size	US\$	€	£	¥
1 mg	36	30	20	4,300
5 mg	129	107	71	15,500
10 mg	225	187	124	27,000
25 mg	495	411	272	59,400

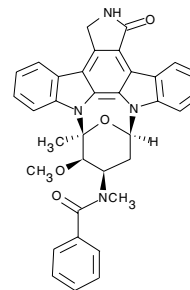
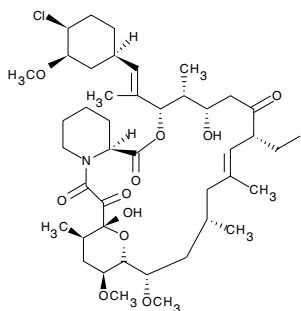
M.W. 616.84 C₃₆H₅₆O₈ [63597-44-4]

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO or ethanol. **Disposal:** A

- Negative control for studies with PMA (Cat. No. P-1680, page 31). Van Duuren, B.L. *et al. Cancer Res.* **39**: 2644-2646 (1979).
- Please request Technical Note #13 for additional information.
- **4α-Phorbol Ester Activation of TRPV4 Channels** Though long thought to be a biologically inactive or extremely weak phorbol ester analog (*i.e.*, an ED₅₀ >25 μM for binding to protein kinase C), 4α-PMA may prove to be a reasonably potent activator of TRPV4 channels, with utility for structure-activity studies of this phenomenon. The supposition of agonist activity for 4α-PMA on TRPV4 channels is based on the potent agonist response elicited by the very similar compound, 4α-PDD, in systems containing human VRL-2 and murine TRP12 channels [H. Watanabe *et al.*, *J. Biol. Chem.* **277**: 13569-13577 (2002)]. **See the entry for 4α-PDD, Cat. No. P-2170, page 30, for a more extensive description.**
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.
- **Chemical Structures.** The primary structural difference between 4α-PDD and the highly potent phorbol ester-type PKC activators is the configuration at C4. In the highly active phorbol ester family, the hydroxy group at C4 is in the β configuration, *i.e.*, rising up out of the two-dimensional structure as viewed on paper or a computer monitor. The 4α-phorbol esters such as 4α-PDD, 4α-PMA and 4α-PDBu have the 4-OH group oriented down below the paper or computer screen's two-dimensional plane.
- **Nomenclature.** Unless "4α" is specified, all "phorbol" compounds are automatically defined, by operation of standard chemical nomenclature conventions, as having the 4β-configuration, as part of the meaning of the word "phorbol". This is much like the word "cholesterol", which automatically means that its hydroxy group at carbon 3 is in the β configuration; there is no need to specify "3β-

may be or become applicable in the aforementioned countries; and (vii) such similar laws and rules as may apply in various other countries.

- Not available in some countries; not available to some institutions; not available for some uses.



P-7600 PKC412, >99%

[CGP41251] [4'-N-Benzoyl Staurosporine]
[Midostaurin]

Size	US\$	€	£	¥
1 mg	67	56	37	8,000
5 mg	255	212	140	30,600
10 mg	380	315	209	45,600
25 mg	595	494	327	71,400
100 mg	1480	1228	814	177,600

M.W. 570.65 C₃₅H₃₀N₄O₄

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO. **Disposal:** A

- The staurosporine analog, PKC412, inhibits a variety of serine/threonine and tyrosine kinases including PKC (IC₅₀ 50 nM), cyclic AMP-dependent protein kinase (IC₅₀ 2.4 μM), S6 kinase (IC₅₀ 5.0 μM), and EGFR (epidermal growth factor receptor) tyrosine-kinase activity (IC₅₀ 3.0 μM). Meyer, T., *et al.* "A derivative of staurosporine (CGP 41 251) shows selectivity for protein kinase C inhibition and *in vitro* anti-proliferative as well as *in vivo* anti-tumor activity." *Int. J. Cancer* **43**: 851-856 (1989).
- PKC412 inhibits autophosphorylation of platelet-derived growth factor (PDGF) receptor in BALB/c 3T3 cells at submicromolar concentrations. Andrejauskas-Buchdunger, E. and Regenass, U. "Differential inhibition of the epidermal growth factor-, platelet-derived growth factor-, and protein kinase C-mediated signal transduction pathways by the staurosporine derivative CGP 41251." *Cancer Research*, **52**: 5353-5358 (1992).
- PKC412 strongly blocks the proliferation of ras-transformed pancreatic cancer cells (TUC-3) by causing apoptosis and induction of phenotypic reversion. Way, D., *et al.* "A protein kinase C inhibitor induces phenotypic reversion of ras-transformed pancreatic cancer cells and cooperatively blocks tumor cell proliferation with an anti-ras peptide." *Cancer Chemother. Pharmacol.* **49**: 429-437 (2002).
- PKC412 suppresses Akt activity by blocking serine phosphorylation in the kinase activation loop and induces apoptosis in myeloma cell lines. Bahlis, N.J., *et al.* "N-Benzoylstaurosporine (PKC412) inhibits Akt kinase inducing apoptosis in multiple myeloma cells." *Leuk. Lymphoma* **46**: 899-908 (2005).
- PKC412 selectively inhibits T lymphocyte production of TNF-α; (tumor necrosis factor - alpha) with an IC₅₀ of 0.5 μM. Si, M.S., *et al.* "Effects of the kinase inhibitor CGP41251 (PKC 412) on lymphocyte activation and TNF-alpha production." *Int. Immunopharmacol.* **5**: 1141-11419 (2005).
- Not available in some countries; not available to some institutions; may not be sold for some uses.

- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.

PMA – see Phorbol 12-Myristate 13-Acetate, Cat. No. P-1680, page 31.

4α-PMA – see 4α-Phorbol 12-Myristate 13-Acetate, Cat. No. P-8880, page 32.

P-6388 PPAHV, >99%

[Phorbol 12-Phenylacetate 13-Acetate 20-Homovanillate]

Size	US\$	€	£	¥
1 mg	38	32	21	4,600
5 mg	162	134	89	19,400

M.W. 688.77 C₃₉H₄₄O₁₁ [175796-50-6]

WARNING: May be irritant to skin and mucous membranes. **SPECIAL HAZARD:** possible tumor promoter. Gloves and mask should be worn when using this compound. Care must be taken to prevent contact through all routes of exposure.

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO or ethanol. **Disposal:** A

P-4462 Prostratin, >99%

[12-Deoxyphorbol 13-Acetate] [dPAC]

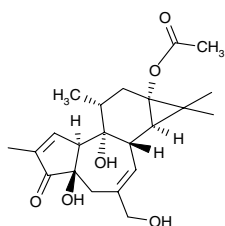
Size	US\$	€	£	¥
1 mg	52	43	29	6,200
5 mg	190	158	105	22,800

M.W. 390.48 C₂₂H₃₀O₆ [60857-08-1]

WARNING: Highly irritant to skin and mucous membranes.

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO or ethanol. **Disposal:** A

- Isolated from strathmore weed (*Pimelia prostrata* Wild), a New Zealand plant toxic to livestock. Cashmore, A.R. *et al.* *Tetrahedron Lett.* **20**: 1737-1738 (1976).
- Weak mouse ear irritant, but lethal to mice at 1 μg per mouse. Zayed, S. *et al.* *Experientia* **33**: 1554-1555 (1977).
- Please request Technical Note #5 for additional information.
- This product was previously sold under Cat-No. D-4462 and the name "12-Deoxyphorbol 13-Acetate".
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



PS-341 – See Bortezomib (Cat. No. B-1408 on page 4).

RAD001 – see Everolimus (Cat. No. E-4040 on page 12).

Rapamune – see Rapamycin (Cat. No. R-5000 on page 34).

R-5000 Rapamycin, >99%

[RAPA] [Rapamune] [Sirolimus] [AY-22989]
[NSC-226080]

Size	US\$	€	£	¥
25 mg	59	49	32	7,100
100 mg	199	165	109	23,900
200 mg	339	281	186	40,700
500 mg	592	491	326	71,000
1 g	987	819	543	118,400
2 g	1590	1320	875	190,800

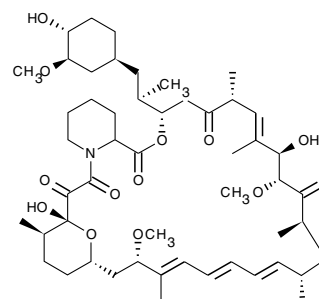
M.W. 914.19 C₅₁H₇₉NO₁₃ [53123-88-9]
RTECS: VE6250000 M.I.12:8288

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO or ethanol (up to about 50 mg/mL for either solvent). **Disposal:** A

- Available in gram to kilogram quantities—request a bulk quote.
- Immunosuppressant, related to FK-506, but without calcineurin inhibitory activity even when complexed to FK-506 binding protein. Selectively blocks signalling that leads to p70 S6 kinase activation (IC₅₀ = 50 pM). “Failure of rapamycin to block proliferation once resting cells have entered the cell cycle despite inactivation of p70 S6 kinase.” Terada, N. *et al.*, *J. Biol. Chem.* **268**: 12062 (1993). “Dissociation of pp70 ribosomal protein S6 kinase from insulin-stimulated glucose transport in 3T3-L1 adipocytes.” D.C. Fingar *et al.*, *J. Biol. Chem.* **268**: 3005 (1993). “Rapamycin-induced inhibition of the 70-kilodalton S6 protein kinase.” Price, D.J. *et al.*, *Science* **257**: 973 (1992). “Rapamycin-FKBP specifically blocks growth-dependent activation of and signalling by the 70 kd S6 protein kinases.” J. Chung *et al.*, *Cell* **69**: 1227 (1992).
- Lymphokine-induced cell proliferation at the G1 phase is inhibited and apoptosis in a murine B cell line is induced by rapamycin. Rapamycin arrests the *Saccharomyces cerevisiae* cell cycle irreversibly in the G1 phase. “Rapamycin-induced inhibition of p34cdc2 kinase activation is associated with G1/S-phase growth arrest in T lymphocytes.” W.G. Morice *et al.*, *J. Biol. Chem.* **268**: 3734 (1993). “Inhibition of T and B lymphocyte proliferation by rapamycin.” J.E. Kay *et al.*, *Immunology* **72**: 544 (1991). “Targets for cell cycle arrest by the immunosuppressant rapamycin in yeast.” J. Heitman *et al.*, *Science* **253**: 905 (1991).
- Due to a different mechanism of action from cyclosporin and FK-506, rapamycin may prove to be important in organ transplant patient therapy. Fewer side effects than the standard anti-rejection treatments have been observed. Proliferation of activated T cells, but not apoptosis, is blocked by rapamycin. The induction of apoptosis of rejection-causing T cells reduces the tendency towards transplant rejection. “The future role of target of rapamycin inhibitors in renal transplantation.” C. Schwarz and R. Oberbauer *Curr Opin Urol.* **12**: 109 (2002). “Requirement for T-

cell apoptosis in the induction of peripheral transplantation tolerance.” A.D. Wells *et al.*, *Nat Med.* **5**: 1303 (1999). “Blocking both signal 1 and signal 2 of T-cell activation prevents apoptosis of alloreactive T cells and induction of peripheral allograft tolerance.” Y. Li *et al.* *Nat Med.* **5**: 1298 (1999).

- **Formulations of *in vivo* administration.** Researchers wishing to administer rapamycin *in vivo* may find the following references useful, particularly as a source of information about formulations of rapamycin in various vehicles that have been used for *i.p.*, *i.m.* and *i.v.* administration:
 1. *Circulation* **99**: E1080-E1087 (1999). Carboxymethylcellulose, polysorbate 80; *i.m.*
 2. *Proc. Natl. Acad. Sci. USA* **96**: 8657-8662 (1999). Dimethylacetamide, PEG 400, polyoxyethylene sorbitan monooleate; *i.p.*
 3. *Am. J. Physiol. Endocrin. Metab.* **279**: E1080-E1087 (2000). 5% DMSO, *i.v.*
 4. *Blood* **100**: 1084-1087 (2002). PEG 300, polysorbate and ethanol; *i.p.*
 5. *Cancer Res.* **62**: 7291-7297 (2002). Ethanol, Tween 80; *i.p.*
- See also our other standard immunosuppressant products:
 - C-6000 Cyclosporin, page 7
 - F-4900 FK-506, page 13
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



R-6712 Resiniferatoxin, >99%

[RTX]

Size	US\$	€	£	¥
1 mg	34	28	19	4,100
5 mg	138	115	76	16,600
10 mg	255	212	140	30,600
25 mg	525	436	289	63,000

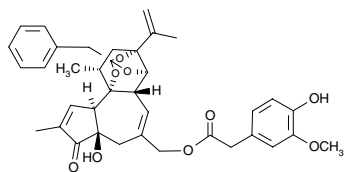
M.W. 628.72 C₃₇H₄₀O₉ [57444-62-9]

WARNING: Highly irritant to skin and mucous membranes. SPECIAL HAZARD: POTENT NEUROTOXIN. Gloves and mask should be worn when using this compound. Care must be taken to avoid contact via all routes of exposure.

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO or ethanol. **Disposal:** A

- Extremely potent analog of capsaicin, the major active principle of common red pepper. Szallasi, A. and Blumberg, P.M. *Neuroscience* **30**: 515-520 (1989).
- Please request Technical Note #28 for additional information.
- Anti-inflammatory uses and pharmaceutical formulations containing this compound are covered by U.S. patent 5,643,948, and such formulations and their use in medicine are covered by European patent EP 0455271, DE P375210808, FR 0455271, GB 0455271 and SW 0455271, all assigned to PKC Pharmaceuticals, Inc., the parent company of LC Laboratories.

- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



R-8765 Resiniferonol 9,13,14-Orthophenylacetate, >99%

[ROPA]

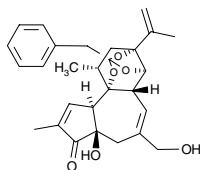
Size	US\$	€	£	¥
1 mg	39	32	21	4,700
5 mg	127	105	70	15,200
10 mg	239	198	131	28,700
25 mg	515	427	283	61,800
100 mg	1525	1266	839	183,000

M.W. 464.56 C₂₈H₃₂O₆ [57852-42-3]

WARNING: Highly irritant to skin and mucous membranes. SPECIAL HAZARD: TUMOR PROMOTER. Gloves and mask should be worn when using this compound. Care must be taken to prevent contact through all routes of exposure.

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO or ethanol. **Disposal:** A

- 20-Deacylated derivative of resiniferatoxin and tinyatoxin. Not active as a capsaicin analog.
- Binds to and activates protein kinase C, with high potency.
- Useful as starting material for synthesis of resiniferatoxin analogs.
- Please request Technical Note #28 for additional information.
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



ROPA – see Resiniferonol 9,13,14-Orthophenylacetate (Cat. No. R-8765, page 35).

R-1234 Roscovitine, >99%

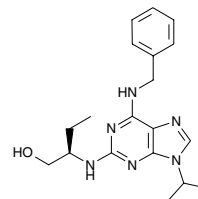
[CYC202] [Seliciclib]

Size	US\$	€	£	¥
5 mg	48	40	26	5,800
10 mg	82	68	45	9,800
25 mg	167	139	92	20,000
100 mg	499	414	274	59,900
300 mg	1095	909	602	131,400

M.W. 354.46 C₁₉H₂₆N₆O [186692-46-6]

Storage: Store at or below -20 °C. **Solubility:** Prepare initial stock solutions in DMSO (soluble at 200 mg/mL) or ethanol (soluble at 200 mg/mL) for *in vitro* use; solubility in water is low. **Appearance:** White to off-white powder; mp 106-107 °C. **Disposal:** A

- Analog of olomoucine, but more potent as an inhibitor of p34^{cdc2} (IC₅₀ = 0.2 μM). Also inhibits p33^{cdc2} and p33^{cdk5}. Havlicek, L. *et al. J. Med. Chem.* **40**: 408-412 (1997).
- Not available in some countries; not available to some institutions; may not be sold for some uses.
- Note:** The word "roscovitine" inherently means the R-Isomer.
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



R-9630 Rottlerin, >98%

[Mallotoxin]

(THIS PRODUCT AND ITS SUPPORT HAVE BEEN DISCONTINUED FOR THE REASONS NOTED BELOW)

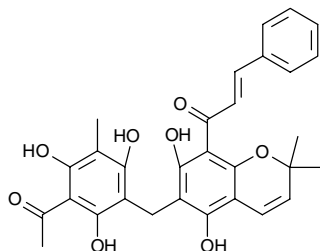
M.W. 516.55 C₃₀H₂₈O₈ [82-08-6]
RTECS: AM6913800

Rottlerin has been referred to as a specific inhibitor of PKCδ, but this appears to be incorrect for the following reasons:

- An excellent and very thorough review of the numerous and confounding biological activities of rottlerin is now available: Soltoff, Stephen P. "Rottlerin: an inappropriate and ineffective inhibitor of PKCδ." *Trends Pharm. Sci.* **28**: 453-458 (2007). This review makes it clear that, unfortunately, there may now be hundreds of published articles that contain erroneous, rottlerin-based conclusions about PKCδ functions.
- Initially, rottlerin was reported to inhibit PKCδ (IC₅₀ = 3-6 μM) 5- to 10-fold more potently than PKCα or PKCβ and 13- to 33-fold more potently than PKCε, ζ, or η. It also inhibited CAM kinase III at 3-6 μM, was inactive against SRC kinase, and was a weak inhibitor of PKA and casein kinase II. *Biochem. Biophys. Res. Comm.* **199**: 93-98 (1994).
- At best, these potency differences of 5- to 13- fold are quite modest, pharmacologically speaking, and in practice would require careful manipulation of concentrations to produce meaningful differentiation of PKC isotype effects.
- Much more serious problems with rottlerin have come to light. In an extensive study of protein kinases and inhibitors, rottlerin failed to show any PKC inhibitory activity at all against the α and δ PKC isotypes, even at 20 μM and very low ATP concentrations and under a variety of conditions. It was, however, a potent inhibitor of MAPK-activated protein kinase 2, p38-regulated/activated kinase, protein kinase A, and glycogen synthase kinase 3-beta. *Biochem. J.* **351**: 95-105 (2000). Thus, rottlerin does not appear to have any utility as a PKCδ-selective tool.
- Furthermore, rottlerin has been shown to be an uncoupler of mitochondrial oxidative phosphorylation. *J. Biol. Chem.* **276**: 37986-37992 (2001) and *Endocrinology* **143**: 3884-3896 (2002). This effect results in additional non-specific, confounding activities for rottlerin: *Cancer Res.* **63**: 5118-5125 (2003).
- LC Labs has tested the purity of rottlerin obtained from the same source used in the BBRC article cited above, and many substantial impurities were found. Our highly purified product was free of these impurities, and we believe the rottlerin used in the *Biochem. J.* study is traceable to LC Labs. Thus, the original inhibitory activity of rottlerin for PKCδ may have been due to an impurity not present in the later study.
- There are now many published studies that cite the effects of rottlerin as a basis for conclusions about the cellular roles of PKCδ.

These conclusions now appear to be incorrect. We would appreciate receiving from our readers any information that might shed more light on this topic, so that we can inform other researchers of the latest findings regarding rottlerin's actual biological properties.

- In the past, we produced rottlerin by purifying it from raw material from a source in Europe, but that source no longer sells crude rottlerin. Given the highly questionable utility of rottlerin as a kinase inhibitor, we decided not to pursue alternative sources of raw materials. Therefore, we have now discontinued all sales of rottlerin.



RTX – see Resiniferatoxin (Cat. No. R-6712 on page 34).

S-1700 SB 202190, >99%

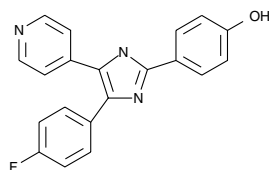
[4-(4-Fluorophenyl)-2-(4-hydroxyphenyl)-5-(4-pyridyl)1H-imidazole] [FHPI]

Size	US\$	€	£	¥
5 mg	38	32	21	4,600
10 mg	66	55	36	7,900
25 mg	139	115	76	16,700
100 mg	415	344	228	49,800

M.W. 331.35 C₂₀H₁₄FN₃O [152121-30-7]

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO. **Disposal:** A

- SB 202190, a pyridinyl imidazole, inhibits p38 kinase activity *in vivo* through competition with ATP. Young, P.R., *et al.* "Pyridinyl Imidazole Inhibitors of p38 Mitogen-activated Protein Kinase Bind in the ATP Site." *J. Biol. Chem.* **272**: 12116-12121 (1997).
- Induces apoptosis through activation of cysteine protease (CPP32)-like caspases. Nemoto, S., *et al.* "Induction of apoptosis by SB 202190 through inhibition of p38beta mitogen-activated protein kinase." *J Biol Chem.* **273**: 16415-16420 (1998).
- Blocks both lipopolysaccharide (LPS)-induced gene expression and nitric oxide (NO)-induced stabilization of interleukin (IL)-8 mRNA in monocytes. Manthey, C.L., *et al.* "SB 202190, a selective inhibitor of p38 mitogen-activated protein kinase, is a powerful regulator of LPS-induced mRNAs in monocytes." *J Leukoc Biol.* **64**: 409-417 (1998). Ma, P., *et al.* "Nitric oxide post-transcriptionally up-regulates LPS-induced IL-8 expression through p38 MAPK activation." *J Leukoc Biol.* **76**: 278-287 (2004).
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



S-3400 SB 203580, >99%

[4-(4'-Fluorophenyl)-2-(4'-methylsulfinylphenyl)-5-(4'-pyridyl)imidazole]

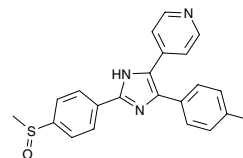
Size	US\$	€	£	¥
5 mg	49	41	27	5,900
10 mg	77	64	42	9,200
25 mg	143	119	79	17,200
100 mg	499	414	274	59,900
250 mg	1125	934	619	135,000

M.W. 377.44 C₂₁H₁₆FN₃OS [152121-47-6]

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO. **Appearance:** white to off-white solid.

Disposal: A

- Important, highly specific new inhibitor of the kinase known variously as p38, p40, CSBP or RK. This kinase is a homolog of MAP kinase. Gallagher, T. F. *et al.* "2,4,5-Triarylimidazole inhibitors of IL-1 biosynthesis." *Bioorg. Med. Chem. Lett.* **5**: 1171-1176 (1995); Cuenda, A. *et al.* "SB203580 is a specific inhibitor of MAP kinase homologue which is stimulated by cellular stresses and interleukin-1." *FEBS Lett.* **364**: 229-233 (1995); Hazzalin, C.A. *et al.* "Effects of the inhibition of p38/RK MAP kinase on induction of five *fos* and *jun* genes by diverse stimuli." *Oncogene* **15**: 2321-2331 (1997).
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



SDZ-ASM-981 – see Pimecrolimus (Cat. No. P-6040 on page 32).

SDZ-RAD – see Everolimus (Cat. No. E-4040 on page 12).

Sirolimus – see Rapamycin (Cat. No. R-5000 on page 34).

S-8502 Sorafenib p-Toluenesulfonate Salt, >99%

[Sorafenib Tosylate] [Nexavar] [Bay 43-9006]

Size	US\$	€	£	¥
100 mg	98	81	54	11,800
300 mg	225	187	124	27,000
1 g	465	386	256	55,800

M.W. 637.04 C₂₁H₁₆ClF₃N₄O₃ • C₇H₈O₃S [475207-59-1] M.I. **14**: 8720

Storage: Store at or below -20 °C in the dark.

Solubility: Very soluble in DMSO, up to about 200 mg/mL; very poorly soluble in water or ethanol. **Disposal:** A

- Sorafenib (Bay 43-9006) is a novel bi-aryl urea compound that inhibits the ERK pathway and angiogenesis by targeting the receptor tyrosine kinases VEGFR-2 and PDGFR-β and their associated signaling cascades. Although sorafenib was initially developed as a Raf kinase inhibitor (IC₅₀, 6 nM), it has since been shown to have activity against many receptor tyrosine kinases involved in tumorigenesis and angiogenesis including FGFR-1, wt BRAF and V599E mutant BRAF, as well as members of the so-called "split kinase" family: VEGFR-2, VEGFR-3, PDGFR-β, c-KIT, and Flt3. However, sorafenib is not active against erbB1, erbB2, ERK-1, MEK-1, EGFR, HER-2, IGFR-1, c-MET, c-yes,

PKB, PKA, cdk1/cyclinB, PKC α , PKC γ , and pim-1. In cellular mechanistic assays, sorafenib reduced basal phosphorylation of the ERK pathway in a panel of breast, melanoma, pancreatic, and colon tumor cell lines. Wilhelm S.M., *et al.* "BAY 43-9006 Exhibits Broad Spectrum Oral Antitumor Activity and Targets the RAF/MEK/ERK Pathway and Receptor Tyrosine Kinases Involved in Tumor Progression and Angiogenesis." *Cancer Res.* **64**: 7099-7109 (2004).

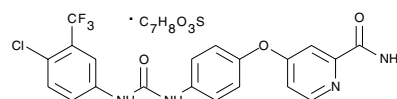
Biochemical Assays*	IC ₅₀ (nM) \pm SD
Raf-1**	6 \pm 3
BRAF wild-type	22 \pm 6
V599E BRAF mutant	38 \pm 9
VEGFR-2	90 \pm 15
mVEGFR-2 (flk-ss1)	15 \pm 6
mVEGR-3	20 \pm 6
mPDGFR- β	57 \pm 20
Flt-3	58 \pm 20
c-KIT	68 \pm 21
FGFR-1	580 \pm 100
ERK-1, MEK-1, EGFR, HER-2, IGFR-1, c-met, PKB, PKA, cdk1/cyclinB, PKC γ , PKC α , pim-1	>10,000
Cellular Mechanism Assays	IC ₅₀ (nM) \pm SD
MDA MB 231 MEK phosphorylation (human breast)	40 \pm 20
MDA MB 231 ERK 1/2 phosphorylation (human breast)	90 \pm 26
BxPC-3 ERK 1/2 phosphorylation (human pancreatic)	1,200 \pm 165
LOX ERK 1/2 phosphorylation (human melanoma)	880 \pm 90
VEGFR-2 phosphorylation (human, NIH 3T3 cells)	30 \pm 21
VEGF-ERK 1/2 phosphorylation (human, HUVEC)	60 \pm 26
PDGFR- β phosphorylation (human HAoSMC)	80 \pm 40
mVEGFR-3 phosphorylation (mouse, HEK-293 cells)	100 \pm 80
Flt-3 phosphorylation (human ITD, HEK-293 cells)	20 \pm 10
Cellular Proliferation Assays	IC ₅₀ (nM) \pm SD
MDA MB 231 (10% FCS)	2,600 \pm 810
PDGF-BB HAoSMC	280 \pm 140

* Kinase assays were carried out at ATP concentrations at or below K_m (1-10 μ M).

** Lck activated NH₂-terminal-truncated Raf-1

- Sorafenib is less potent in an enzyme assay (IC₅₀ = 107 nM) than in a cellular system (IC₅₀ = 20 nM). Guo J., *et al.* "Inhibition of phosphorylation of the colony-stimulating factor-1 receptor (c-Fms) tyrosine kinase in transfected cells by ABT-869 and other tyrosine kinase inhibitors." *Mol. Cancer Ther.* **5**: 1007-1013 (2006).
- Sorafenib potently inhibited activation of the MAPK pathway and ERK phosphorylation in human cancer cell lines, irrespective of whether they harbored *K-ras* mutations, *V599E-B-Raf*, or both. Wilhelm S., *et al.* "The novel Raf inhibitor Bay 43-9006 blocks signaling and proliferation in *BRAF* mutant and wildtype melanoma and colorectal tumor cell lines." [Abstract]. *Proc. Am. Assoc. Cancer Res.* **44**: 106609 (2003).

- Sorafenib inhibited various nonkinase targets, including adenosine A3, dopamine D1, and muscarine M3 receptors, albeit at much higher (micromolar) concentrations than kinase targets. Carter C., *et al.* "Investigators Brochure Bay 43-9006/ Raf Kinase Inhibitor." *Version No. 5. West Haven, CT, Bayer Pharmaceuticals Corporation, 2004.*
- Sorafenib tosylate is the active ingredient in the drug sold under the trade name Nexavar®. This drug is currently approved for use in patients with advanced renal cell cancer.
- Sold for laboratory or manufacturing purposes only; not for human, veterinary, food, or household use.**
- This product is offered for R&D use in accordance with (i) 35 USC 271(e)+A13(1) in the U.S.; (ii) Section 69.1 of Japanese Patent Law in Japan; (iii) Section 11, No. 2 of the German Patent Act of 1981 in Germany; (iv) Section 60, Paragraph 5b of the U.K. Patents Act of 1977 in the U.K.; (v) Section 68B of the Patents Act of 1953 in New Zealand; (vi) such related legislation and/or case law as may be or become applicable in the aforementioned countries; and (vii) such similar laws and rules as may apply in various other countries.
- Not available in some countries; not available to some institutions; not available for some uses.



S-7979 SP600125, >99%

	Size	US\$	€	£	¥
NEW!	300 mg	125	104	69	15,000
	1 g	298	247	164	35,800
	2 g	475	394	261	57,000
	5 g	865	718	476	103,800

M.W. 220.23 C₁₄H₈N₂O [129-56-6]
RTECS: CB4585000

Storage: Store at or below -20 °C in the dark.

Solubility: Prepare initial stock solutions in DMSO (soluble at 200 mg/mL) for *in vitro* use; solubility in ethanol or water is low. **Disposal:** A

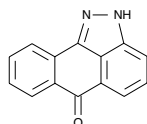
- A novel, potent and selective JNK-1,-2, and -3 inhibitor (K_i = 0.19 μ M). SP600125 is a reversible ATP-competitive inhibitor with >20-fold selectivity vs. a range of kinases and enzymes tested. In cells, SP600125 dose dependently inhibited the phosphorylation of c-Jun, the expression of inflammatory genes *COX-2*, *IL-2*, *IFN- γ* , *TNF- α* , and prevented the activation and differentiation of primary human CD4 cell cultures. In animal studies, SP600125 blocked bacterial lipopolysaccharide-induced expression of tumor necrosis factor- and inhibited anti-CD3-induced apoptosis of CD4⁺ CD8⁺ thymocytes. Bennett, B.L., *et al.* "SP600125, an anthrapyrazolone inhibitor of Jun N-terminal kinase." *Proc. Natl. Acad. Sci. USA* **98**: 13681-13686 (2001).
- SP600125 completely blocked IL-1-induced accumulation of phospho-Jun and induction of c-Jun transcription in synovocytes. This article also reported the inhibitory activity of SP600125 on various enzymes:

Enzyme	IC ₅₀ (μ M)
JNK1	0.11
JNK2	0.11
JNK3	0.15
ERK2	>30
p38 β	>30
I κ B kinase-2	>30
Acetylcholine esterase	>10
Cyclooxygenase-2	>10

5' -lipoxygenase	>10
PDE I, III, IV, V	>10
PDE IV	7
Inos	>10
Phospholipase A2	>10
Adenylate cyclase	>10
Guanylate cyclase	>10
ATPase (Na/K)	>10
Protein kinase C	>10
HIV-1 protease	>10
Monoamine oxidase	>10
Tyrosine hydrolase	>10
Elastase	>10
Cathepsin B, G	>10
EGF tyrosine kinase	>10
Cathepsin B, G	>10

Han Z., *et al.* "c-Jun N-terminal kinase is required for metalloproteinase expression and joint destruction in inflammatory arthritis." *J. Clin. Invest.* **108**: 73-81 (2001).

- Inhibiting JNK with SP600125 reduced the levels of c-Jun phosphorylation, protected dopaminergic neurons from apoptosis, and partly restored the level of dopamine in MPTP-induced PD in C57BL/6N mice. Wang W., *et al.* "SP600125, a new JNK inhibitor, protects dopaminergic neurons in the MPTP model of Parkinson's disease." *Neurosci. Res.* **48**: 195-202 (2004).
- Sold for laboratory or manufacturing purposes only; not for human, veterinary, food, or household use.**
- This product is offered for R&D use in accordance with (i) 35 USC 271(e)+A13(1) in the U.S.; (ii) Section 69.1 of Japanese Patent Law in Japan; (iii) Section 11, No. 2 of the German Patent Act of 1981 in Germany; (iv) Section 60, Paragraph 5b of the U.K. Patents Act of 1977 in the U.K.; (v) Section 68B of the Patents Act of 1953 in New Zealand; (vi) such related legislation and/or case law as may be or become applicable in the aforementioned countries; and (vii) such similar laws and rules as may apply in various other countries.
- Not available in some countries; not available to some institutions; not available for some uses.



S-9300 Staurosporine, >99%
[Antibiotic AM-2282]

Size	US\$	€	£	¥
1 mg	69	57	38	8,300
5 mg	199	165	109	23,900
10 mg	340	282	187	40,800
25 mg	490	407	270	58,800
100 mg	1370	1137	754	164,400

M.W. 466.54 C₂₈H₂₆N₄O₃ [62996-74-1]
RTECS: KD5084000

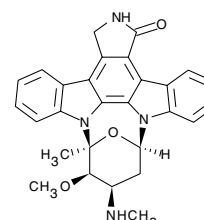
Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO; insoluble in water. **Disposal:** A

- Staurosporine is a potent inhibitor of many, many kinases including protein kinase C (IC₅₀ = 0.7 nM), protein kinase A (IC₅₀ = 7 nM), protein kinase G (IC₅₀ = 8.5 nM), and other kinases at sub-nanomolar potencies. Staurosporine is NOT a selective inhibitor of PKC, contrary to widespread erroneous citations in the literature. Matsumoto, H., *et al.* "Staurosporine, a protein kinase C inhibitor, interferes with proliferation of arterial smooth muscle cells."

Biochem. Biophys. Res. Commun. **158**: 105-109 (1989). Tamaoki, T., *et al.*

"Staurosporine, a potent inhibitor of phospholipid/Ca⁺⁺ dependent protein kinase." *Biochem. Biophys. Res. Commun.* **135**: 397-402 (1986).

- Staurosporine induces apoptosis in human neuroblastoma cell lines and chick embryonic neurons. Boix, J., *et al.* "Characterization of the cell death process induced by staurosporine in human neuroblastoma cell lines." *Neuropharmacology* **36**: 811-821 (1997). Wiesner, D.A. and Dawson, G., "Staurosporine induces programmed cell death in embryonic neurons and activation of the ceramide pathway." *J. Neurochem.* **66**: 1418-1425 (1996).
- Please request Technical Note #24 for additional information.
- We don't want to waste much ink disparaging our competitors, but we can't help noting that many vendors sell staurosporine, at purities lower than ours, for audacious prices of \$300-600 per mg (!).
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



STI-571 – see Imatinib, Methanesulfonate Salt
(Cat. No. I-5508 on page 18).

SU 1498 – see Tyrphostin SU 1498 (Cat. No. T-2710 on page 42).

SU-11248 – see Sunitinib, Malate Salt
(Cat. No. S-8803 on page 38).

S-8803 Sunitinib, Malate Salt, >99%
[Sunitinib Maleate] [SU-11248] [Sutent]

	Size	US\$	€	£	¥
NEW!	300 mg	149	124	82	17,900
	1 g	375	311	206	45,000
	2 g	685	569	377	82,200

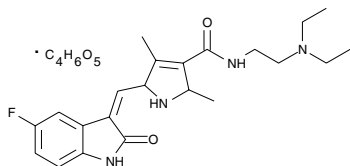
M.W. 532.57 C₂₂H₂₇N₄O₂ • C₄H₆O₅
[341031-54-7] M.I. 14: 9000

Storage: Store at or below -20 °C in the dark.
Solubility: Soluble in DMSO, up to about 40 mg/mL; very poorly soluble in water or ethanol. **Disposal:** A

- Sunitinib and its active metabolite (SU012662) are selective inhibitors of multiple receptor tyrosine kinases, including platelet-derived growth factor receptor and vascular endothelial growth factor receptor, that are associated with tumor growth and angiogenesis. Deeks E.D. and Keating G.M. "Sunitinib." *Drugs* **66**: 2255-2266 (2006).
- Sunitinib is a potent inhibitor of colony-stimulating factor -1 receptor kinase in an enzyme assay (IC₅₀ = 7 nM) and inhibits receptor phosphorylation in a cellular assay (IC₅₀ = 61 nM). Guo J., *et al.* "Inhibition of phosphorylation of the colony-stimulating factor-1 receptor (c-Fms) tyrosine kinase in transfected cells by ABT-869 and other tyrosine kinase inhibitors." *Mol. Cancer Ther.* **5**: 1007-1013 (2006).
- Sunitinib reduced stem cell factor (SCF)-induced phosphotyrosine levels on KIT in a dose-dependent manner, with an IC₅₀ value between 1 and 10 nM. Sunitinib also inhibited SCF-stimulated

ERK1/2 phosphorylation in a dose-dependent manner, with an IC₅₀ value consistent with that for inhibition of KIT phosphotyrosine levels. Sunitinib also inhibited SCF-stimulated proliferation in NCI-H526 cells with an IC₅₀ value of 2 nM. Abrams T.J., *et al.* "SU11248 Inhibits KIT and Platelet-derived Growth Factor Receptor β in Preclinical Models of Human Small Cell Lung Cancer." *Mol. Cancer Ther.* 2: 471-478 (2003).

- Sunitinib inhibited FLT3-ITD phosphorylation in a dose-dependent manner with an IC₅₀ of 50 nM following a 2-hour treatment. For the FLT3-ITD cell line MV-4-11, sunitinib dramatically inhibited cellular proliferation in a dose-dependent manner with an IC₅₀ of 1 to 10 nM. O'Farrell A., *et al.* "SU11248 is a novel FLT3 tyrosine kinase inhibitor with potent activity *in vitro* and *in vivo*." *Blood* 101: 3597-3605 (2003).
- Sunitinib is the active ingredient in the drug sold under the trade name Sutent. This drug is a small molecule receptor tyrosine kinase inhibitor that is approved for the treatment of patients having gastrointestinal stromal tumors (GIST) or renal cell carcinoma (RCC).
- Sold for laboratory or manufacturing purposes only; not for human, veterinary, food, or household use.**
- This product is offered for R&D use in accordance with (i) 35 USC 271(e)+A13(1) in the U.S.; (ii) Section 69.1 of Japanese Patent Law in Japan; (iii) Section 11, No. 2 of the German Patent Act of 1981 in Germany; (iv) Section 60, Paragraph 5b of the U.K. Patents Act of 1977 in the U.K.; (v) Section 68B of the Patents Act of 1953 in New Zealand; (vi) such related legislation and/or case law as may be or become applicable in the aforementioned countries; and (vii) such similar laws and rules as may apply in various other countries.
- Not available in some countries; not available to some institutions; not available for some uses.



Sunitinib Maleate – see Sunitinib, Malate Salt (Cat. No. S-8803 on page 38).

Sutent – see Sunitinib, Malate Salt (Cat. No. S-8803 on page 38).

Tacrolimus – see FK-506 (Cat. No. F-4900 on page 13).

Tarceva – see Erlotinib, Hydrochloride Salt (Cat. No. E-4007 on page 11).

Tasigna – see Nilotinib (Cat. No. N-8207 on page 25).

Taxol – see Paclitaxel (Cat. No. P-9600 on page 28).

Telatinib – see 17-AAG (Cat. No. A-6880 on page 1).

T-8040 Temsirolimus, >98%

[CCI-779] [Torisel]

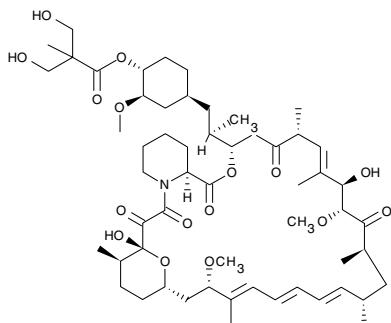
(PLEASE INQUIRE ABOUT AVAILABILITY)

Size	US\$	€	£	¥
5 mg	160	133	88	19,200
25 mg	355	295	195	42,600
100 mg	725	602	399	87,000

M.W. 1030.30 C₅₆H₈₇NO₁₆ [162635-04-3]
M.I. 14: 9142

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO. **Disposal:** A

- Temsirolimus, a rapamycin (sirolimus) derivative, also known as CCI-779, is an mTOR inhibitor with anti-cancer activity. Wan, X., *et al.* "CCI-779 Inhibits Rhabdomyosarcoma Xenograft Growth by an Antiangiogenic Mechanism Linked to the Targeting of mTOR/Hif-1α/VEGF Signaling." *Neoplasia* 8: 394-401 (2006).
- Antiangiogenic effects may contribute to the antitumor activity of temsirolimus observed in breast cancer. Del Bufalo, D., *et al.* "Antiangiogenic potential of the Mammalian target of rapamycin inhibitor temsirolimus." *Cancer Res.* 66: 5549-5554 (2006).
- Temsirolimus showed synergistic *in vivo* antimyeloma effects in combination with dexamethasone in a xenograft model. Yan, H., *et al.* "Mechanism by Which Mammalian Target of Rapamycin Inhibitors Sensitize Multiple Myeloma Cells to Dexamethasone-Induced Apoptosis." *Cancer Res.* 66: 2305-2313 (2006).
- In lymphoblasts from adult patients with acute lymphoblastic leukemia (ALL), cells treated with sirolimus showed an increase in apoptotic cells and a dramatic decrease in cell proliferation compared to untreated cells. Mice bearing NOD/SCID xenografts treated with temsirolimus showed a decrease in splenomegaly and in peripheral-blood blasts. On the other hand, untreated mice continued to show expansion of human ALL. Temsirolimus also down-regulated the mTOR signaling intermediate phospho-S6 in xenografted human ALL. Teachey, D.T., *et al.* "The mTOR inhibitor CCI-779 induces apoptosis and inhibits growth in preclinical models of primary adult human ALL." *Blood* 107: 1149-1155 (2006).
- Temsirolimus is able to reverse cisplatin resistance in small cell lung cancer cell lines selected for cisplatin resistance and in cell lines derived from patients who failed cisplatin therapy. Wu, C., *et al.* "Overcoming cisplatin resistance by mTOR inhibitor in lung cancer." *Mol. Cancer* 4: 25-34 (2005).
- Temsirolimus is the active ingredient in the drug sold under the trade name Torisel®. This drug is currently approved for use in patients with advanced renal (kidney) cell carcinoma.
- Sold for laboratory or manufacturing purposes only; not for human, veterinary, food, or household use.**
- This product is offered for R&D use in accordance with (i) 35 USC 271(e)+A13(1) in the U.S.; (ii) Section 69.1 of Japanese Patent Law in Japan; (iii) Section 11, No. 2 of the German Patent Act of 1981 in Germany; (iv) Section 60, Paragraph 5b of the U.K. Patents Act of 1977 in the U.K.; (v) Section 68B of the Patents Act of 1953 in New Zealand; (vi) such related legislation and/or case law as may be or become applicable in the aforementioned countries; and (vii) such similar laws and rules as may apply in various other countries.
- Not available in some countries; not available to some institutions; not available for some uses.



12-O-Tetradecanoylphorbol 13-Acetate – see Phorbol 12-Myristate 13-Acetate (Cat. No. P-1680 on page 31).

4α-12-O-Tetradecanoylphorbol 13-Acetate – see 4α-Phorbol 12-Myristate 13-Acetate (Cat. No. P-8880 on page 32).

T-3250 Thapsigargin, >99%

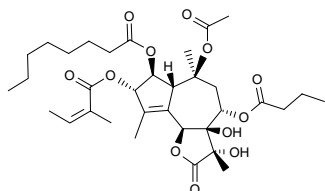
Size	US\$	€	£	¥
1 mg	32	27	18	3,800
5 mg	139	115	76	16,700
10 mg	245	203	135	29,400
25 mg	495	411	272	59,400

M.W. 650.76 C₃₄H₅₀O₁₂ [67526-95-8]

WARNING: Irritant to skin and mucous membranes. **SPECIAL HAZARD:** TUMOR PROMOTER. Wear gloves and mask when using this compound. Care must be taken to prevent contact through all routes of exposure.

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO or ethanol. **Disposal:** A

- Potent, cell permeable IP₃-independent intracellular calcium releaser. Takemura, H. *et al. J. Biol. Chem.* **264**: 12266-12271 (1989).
- Inhibits microsomal Ca²⁺-ATPase. Thastrup, O. *et al. Agents Actions* **27**: 17-23 (1989).
- Rat mast cell histamine secretagogue. Rasmussen, U.S.B. *et al. Acta Pharm. Suecica* **15**: 133-140 (1978). Patkar, S.A. *et al. Agents Actions* **9**: 53-57 (1979).
- Mouse skin tumor promoter with potency somewhat weaker than teleocidin or PMA, but does not bind to protein kinase C or induce ornithine decarboxylase activity. Hakii, H. *et al. J. Cancer Res. Clin. Oncol.* **111**: 177-181 (1986).
- Stimulates arachidonic acid metabolism in macrophages. Ohuchi, K. *et al. J. Cancer Res. Clin. Oncol.* **113**: 319-324 (1987).
- Please request Technical Note #15.
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



T-5096 Tinyatoxin, >99%

[TNX] [TYX]

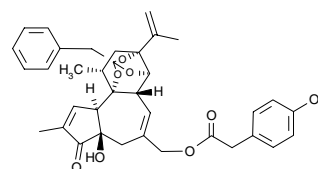
Size	US\$	€	£	¥
1 mg	59	49	32	7,100
5 mg	239	198	131	28,700

M.W. 598.69 C₃₆H₃₈O₈ [58821-95-7]

WARNING: Irritant to skin and mucous membranes.

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO or ethanol. **Disposal:** A

- Analog of resiniferatoxin (RTX), Cat. No. R-6712, page 34; 6-fold weaker than RTX in mouse ear erythema tests.
- Tinyatoxin inhibits specific [³H]RTX binding with a K_d of 0.8 nM, about three-fold weaker than for resiniferatoxin. Szallasi, A. and Blumberg, P.M. *Brain Res.* **547**: 335-338 (1991).
- Please request Technical Note #28 for additional information.
- Anti-inflammatory uses and pharmaceutical formulations containing this compound are covered by U.S. patent 5,643,948, and such formulations and their use in medicine are covered by European patent EP 0455271, DE P375210808, FR 0455271, GB 0455271 and SW 0455271, all assigned to PKC Pharmaceuticals, Inc., the parent company of LC Laboratories.
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



TNX – see Tinyatoxin (Cat. No. T-5096 on page 40).

Torisel – see Temsirolimus (Cat. No. T-8040 on page 39).

TPA – see Phorbol 12-Myristate 13-Acetate (Cat. No. P-1680 on page 31).

4α-TPA – see 4α-Phorbol 12-Myristate 13-Acetate (Cat. No. P-8880 on page 32).

4',5',7-Trihydroxyisoflavone – see Genistein (Cat. No. G-6055 on page 16).

T-9142 Tyrphostin AG 490, >99%

[AG 490] [Tyrphostin B42]

Size	US\$	€	£	¥
25 mg	69	57	38	8,300
100 mg	215	178	118	25,800
300 mg	485	403	267	58,200

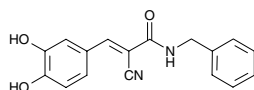
M.W. 294.31 C₁₇H₁₄N₂O₃ [134036-52-5]

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO. **Appearance:** Cream solid. **Disposal:** A

- Specific and potent JAK-2 protein tyrosine kinase inhibitor. Also inhibits EGF receptor autophosphorylation, with an IC₅₀ of 100 nM. Inhibits DNA synthesis and cell growth; induces apoptosis. Levitzki, A. "Tyrphostins—potential antiproliferative agents and novel molecular tools." *Biochem. Pharmacol.* **40**: 913-918 (1990). Gazit, A., *et al.* "Tyrphostins. 2. Heterocyclic and alpha-substituted benzylidenemalononitrile tyrphostins as potent inhibitors of EGF

receptor and ErbB2/neu tyrosine kinases." *J. Med. Chem.* **34**: 1896-1907 (1991).

- Inhibits the growth of leukemic cells *in vitro* and *in vivo*. Blocks STAT3 constitutive activation and inhibits both interleukin 2(IL2)-induced and spontaneous growth of Mycosis fungoides (MF), a cutaneous T cell lymphoma. Growth of human ovarian and breast cancer cell lines was shown to be significantly suppressed by AG 490 via JAK/STAT3 pathway inhibition. Meydan, N., *et al.* "Inhibition of acute lymphoblastic leukaemia by a Jak-2 inhibitor." *Nature* **379**: 645-648 (1996). Nielsen M., *et al.* "Constitutive activation of a slowly migrating isoform of Stat3 in mycosis fungoides: tyrphostin AG490 inhibits Stat3 activation and growth of mycosis fungoides tumor cell lines." *Proc Natl Acad Sci USA*. **94**: 6764-6769 (1997). Eriksen, K.W., *et al.* "Constitutive STAT3-activation in Sezary syndrome: tyrphostin AG490 inhibits STAT3-activation, interleukin-2 receptor expression and growth of leukemic Sezary cells." *Leukemia* **15**: 787-793 (2001). Burke W.M., *et al.* "Inhibition of constitutively active Stat3 suppresses growth of human ovarian and breast cancer cells." *Oncogene* **20**: 7925-7934 (2001). Levitzki, A. "Tyrosine kinases as targets for cancer therapy." *Eur J Cancer* **38 Suppl 5**: S11-S18 (2002). Burdelya L., *et al.* "Combination therapy with AG-490 and interleukin 12 achieves greater antitumor effects than either agent alone." *Mol Cancer Ther* **11**: 893-899 (2002).
- AG 490 is a JAK3/STAT, JAK3/AP-1, and JAK3/MAPK signaling pathway inhibitor and also blocks JAK3 autophosphorylation. Kirken, R.A., *et al.* "Tyrphostin AG-490 inhibits cytokine-mediated JAK3/STAT5a/b signal transduction and cellular proliferation of antigen-activated human T cells." *J. Leukoc. Biol.* **65**: 891-899 (1999). Wang, L.H., *et al.* "JAK3, STAT, and MAPK signaling pathways as novel molecular targets for the tyrphostin AG-490 regulation of IL-2-mediated T cell response." *J. Immunol.* **162**: 3897-3904 (1999). De Vos, J., *et al.* "JAK2 tyrosine kinase inhibitor tyrphostin AG490 downregulates the mitogen-activated protein kinase (MAPK) and signal transducer and activator of transcription (STAT) pathways and induces apoptosis in myeloma cells." *Br. J. Haematol.* **109**: 823-828 (2000).
- Previously sold as "Tyrphostin B42"; the catalog number has not changed.
- Please request Technical Note #22 for additional information.
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



T-7310 Tyrphostin AG 1478, >99%
[AG 1478] [4-(3'-Chloroanilino)-6,7-dimethoxyquinazoline]

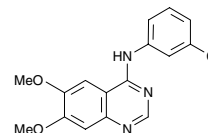
Size	US\$	€	£	¥
25 mg	49	41	27	5,900
100 mg	150	25	83	18,000
500 mg	590	490	325	70,800
1 g	985	818	542	118,200

M.W. 315.76 C₁₆H₁₄ClN₃O₂ [175178-82-2]

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO, to about 60 mg/ml. **Appearance:** White solid. **Disposal:** A

- Very potent EGF receptor kinase (tyrosine kinase) inhibitor (IC₅₀ = 3 nM). Very weak on PDGF receptor and HER2-NEU kinases (IC₅₀ >100 µM). Oshero, N. and Levitski, A. "Epidermal-growth-factor-dependent activation of the src-family kinases." *Eur. J. Biochem.* **225**: 1047-1053 (1994). Levitski, A. and Gazit, A. "Tyrosine kinase inhibition: an approach to drug development." *Science* **267**: 1782-1788 (1995).

- Reversibly inhibits (IC₅₀ = 9.8 µM) the rat brain Kv1.5 potassium channel *in vitro* in a non-protein-tyrosine-kinase-mediated manner. Choi, B.H., *et al.* "Direct inhibition of the cloned Kv1.5 channel by AG-1478, a tyrosine kinase inhibitor." *Am. J. Physiol. Cell Physiol.* **282**: C1461-C1468 (2002).
- This product is the free base, which is best dissolved in DMSO. Please note that we also offer the methanesulfonate ("mesylate") salt as Tyrphostin AG 1478, Methanesulfonate Salt (Cat. No. T-3655, p. 41) which is easily dissolved in aqueous Captisol (β-cyclodextrin hepta-sulfobutyl ether).
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



T-3655 Tyrphostin AG 1478, Methanesulfonate Salt, >99%
[AG 1478]

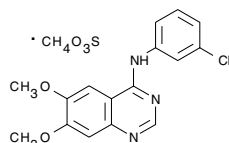
Size	US\$	€	£	¥
25 mg	49	41	27	5,900
100 mg	150	45	83	18,000
500 mg	590	490	325	70,800
1 g	985	818	542	118,200

M.W. 411.87
[175178-82-2]

C₁₆H₁₄ClN₃O₂•CH₄O₃S

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO, to more than 50 mg/ml. **Appearance:** White solid. **Disposal:** A

- Very potent EGF receptor kinase (tyrosine kinase) inhibitor (IC₅₀ = 3 nM). Very weak on PDGF receptor and HER2-NEU kinases (IC₅₀ >100 µM). Oshero, N. and Levitski, A. "Epidermal-growth-factor-dependent activation of the src-family kinases." *Eur. J. Biochem.* **225**: 1047-1053 (1994). Levitski, A. and Gazit, A. "Tyrosine kinase inhibition: an approach to drug development." *Science* **267**: 1782-1788 (1995).
- Reversibly inhibits (IC₅₀ = 9.8 µM) the rat brain Kv1.5 potassium channel *in vitro* in a non-protein-tyrosine-kinase-mediated manner. Choi, B.H., *et al.* "Direct inhibition of the cloned Kv1.5 channel by AG-1478, a tyrosine kinase inhibitor." *Am. J. Physiol. Cell Physiol.* **282**: C1461-C1468 (2002).
- Formulations for *in vivo* use.** This product, the methanesulfonate (mesylate) salt of Tyrphostin AG 1478, can be conveniently formulated as a water-soluble complex with Captisol (β-cyclodextrin hepta-sulfobutyl ether). Captisol is available from Cydex (Lenexa, Kansas). Further details about Captisol solutions of Tyrphostin AG 1478 mesylate can be found in:
 - Proc. Natl. Acad. Sci. USA* **100**: 15871-15876 (2003) Various concentrations of AG 1478 mesylate were dissolved in 100 mM Captisol for administration to mice via s.c., and i.p. injections.
 - Biochem. Pharmacol.* **71**: 1422-1434 (2006) AG 1478 mesylate in Captisol was administered to mice by s.c. injection and to rats by i.v. injection.
 - Anal. Biochem.* **42**: 292-299 (2005) These workers used 49 mM AG 1478 mesylate and 49 mM Captisol in aqueous solution to study the *in vitro* association of this drug with albumin.
 - Clin. Cancer Res.* **11**: 7080s-7086s (2005) Here, AG 1478 mesylate at 4 mg/mL was dissolved in 100 mM Captisol and administered to nude mice by i.p. injection.
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



Tyrphostin B42 – see Tyrphostin AG 490
(Cat. No. T-9142 on page 40).

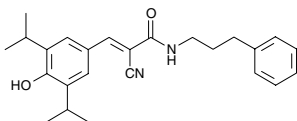
T-2710 Tyrphostin SU 1498, >99%
[SU 1498]

Size	US\$	€	£	¥
5 mg	59	49	32	7,100
25 mg	199	165	109	23,900
100 mg	575	477	316	69,000

M.W. 390.53 C₂₅H₃₀N₂O₂

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO. **Appearance:** Pale yellow solid. **Disposal:** A

- Potent and selective inhibitor of the VEGF receptor kinase, Flk-1 (IC₅₀ = 700 nM). Very weak inhibitor of PDGFR-kinase, EGFR-kinase and HER-2 kinase. Strawn, L.M. *et al.* "Flk-1 as a target for tumor growth inhibition." *Cancer Res.* **56**: 3540-3545 (1996).
- Vascular endothelial growth factor (VEGF) has been shown to play a role in angiogenesis. SU 1498 inhibits vascular permeability as well as angiogenesis in cellular and animal studies.
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



TYX – see Tinyatoxin (Cat. No. T-5096 on page 40).

U-6770 U0126, >99%

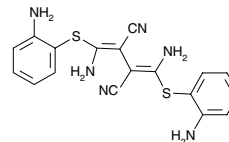
Size	US\$	€	£	¥
5 mg	49	41	27	5,900
25 mg	163	135	90	19,600
100 mg	490	407	270	58,800
300 mg	990	822	545	118,800
1 g	1850	1536	1018	222,000

M.W. 380.50 C₁₈H₁₆N₆S₂ [109511-58-2]

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO. **Appearance:** White solid. **Disposal:** A

- Selective inhibitor of the mitogen-activated protein kinase kinases, MEK-1 and MEK-2, with 100-fold higher potency than PD 98059, but is, at most, a weak inhibitor of PKC, Raf, ERK, JNK, MEKK, MKK-3, MKK-4/SEK, MKK-6, Abl, Cdk2 and Cdk4. U0126 is an inhibitor of AP-1 transactivation in cell-based reporter assays. Favata, M.F. *et al.* "Identification of a novel inhibitor of mitogen-activated protein kinase kinase." *J. Biol. Chem.* **273**: 18623-18632 (1998); DeSilva, D.R. *et al.* "Inhibition of mitogen-activated protein kinase kinase blocks T cell proliferation but does not induce or prevent anergy." *J. Immunol.* **160**: 4175-4181 (1998); Scherle, P.A. *et al.* "Inhibition of MAP kinase kinase prevents cytokine and prostaglandin E2 production in lipopolysaccharide-stimulated monocytes." *J. Immunol.* **161**: 5681-5686 (1998).

- Our U0126 is highly purified. In crystalline form and in aprotic solvents it is a single chemical entity. However, it appears that, in solution in protic solvents, U0126 exists as a mixture of isomers. This phenomenon does not affect overall biological activity. Note that DMSO normally contains water so that it behaves, in this case, as a protic solvent. (PKC Pharmaceuticals, Inc., unpublished results.)
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



V-9402 Vandetanib, >98%
[Zactima] [ZD6474]

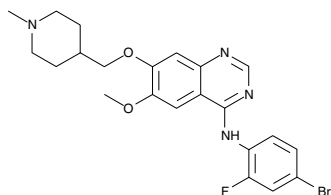
	Size	US\$	€	£	¥
NEW!	5 mg	99	82	54	11,900
	25 mg	245	203	135	29,400
	100 mg	680	564	374	81,600

M.W. 475.37 C₂₂H₂₄BrFN₄O₂ [443913-73-3]

Storage: Store at or below -20 °C in the dark. **Solubility:** Soluble in DMSO. **Appearance:** White solid. **Disposal:** A

- Vandetanib inhibits VEGFR-dependent tumor angiogenesis and EGFR- and RET-dependent tumor cell proliferation and survival. Herbst R.S., *et al.* "Vandetanib (ZD6474): an orally available receptor tyrosine kinase inhibitor that selectively targets pathways critical for tumor growth and angiogenesis." *Expert Opin. Investig. Drugs* **16**: 239-249 (2007).
- The IC₅₀ values for vandetanib in HT-29 and LoVo cells are 10-80 μM and 3.5-16 μM, respectively, when the exposure times are from 18 hours to 3 days. Azzariti A., *et al.* "Prolonged exposure of colon cancer cells to the epidermal growth factor receptor inhibitor gefitinib (Iressa™) and to the antiangiogenic agent ZD6474: Cytotoxic and biomolecular effects." *World J. Gastroenterol.* **12**: 5140-5147 (2006).
- Vandetanib is a potent, *p.o.* active, low molecular weight inhibitor of kinase insert domain-containing receptor [KDR/vascular endothelial growth factor receptor (VEGFR) 2] tyrosine kinase activity (IC₅₀ = 40 nM). This compound has some additional activity against the tyrosine kinase activity of fms-like tyrosine kinase 4 (VEGFR3; IC₅₀ = 110 nM) and epidermal growth factor receptor (EGFR/HER1; IC₅₀ = 500 nM) but demonstrates selectivity relating to a range of other tyrosine and serine-threonine kinases. The activity of vandetanib against KDR tyrosine kinase may explain its potent inhibition of vascular endothelial growth factor A-stimulated human umbilical vein endothelial cell proliferation *in vitro* (IC₅₀ = 60 nM). Wedge S.R., *et al.* "ZD6474 Inhibits Vascular Endothelial Growth Factor Signaling, Angiogenesis, and Tumor Growth following Oral Administration." *Cancer Res.* **62**: 4645-4655 (2002).
- A dose-dependent inhibition of EGFR tyrosine kinase activity was observed after treatment with vandetanib (IC₅₀ of ~0.25 μM). Vandetanib also inhibited colony formation of seven cancer cell lines in soft agar with IC₅₀'s ranging between 0.5 and 1 μM. Ciardiello F., *et al.* "Antitumor Effects of ZD6474, a Small Molecule Vascular Endothelial Growth Factor Receptor Tyrosine Kinase Inhibitor, with Additional Activity against Epidermal Growth Factor Receptor Tyrosine Kinase." *Clin. Cancer Res.* **9**: 1546-1556 (2003).
- Vandetanib is the active ingredient in the drug sold under the trade name Zactima® and is approved for treatment of patients with follicular, medullary, anaplastic, and locally advanced and metastatic papillary thyroid cancer.

- Sold for laboratory or manufacturing purposes only; not for human, veterinary, food, or household use.
- This product is offered for R&D use in accordance with (i) 35 USC 271(e)+A13(1) in the U.S.; (ii) Section 69.1 of Japanese Patent Law in Japan; (iii) Section 11, No. 2 of the German Patent Act of 1981 in Germany; (iv) Section 60, Paragraph 5b of the U.K. Patents Act of 1977 in the U.K.; (v) Section 68B of the Patents Act of 1953 in New Zealand; (vi) such related legislation and/or case law as may be or become applicable in the aforementioned countries; and (vii) such similar laws and rules as may apply in various other countries.
- Not available in some countries; not available to some institutions; not available for some uses.



V-8303 Vatalanib, Dihydrochloride Salt, >99%
[CGP-79787] [PTK 787] [ZK 222584]

	Size	US\$	€	£	¥
NEW!	100 mg	192	159	106	23,000
	300 mg	315	261	173	37,800
	1 g	795	660	437	95,400

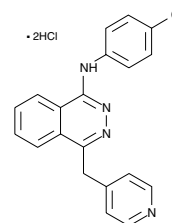
M.W. 419.74 $C_{20}H_{15}ClN_4 \cdot 2HCl$
 [212141-54-3] M.I. 14: 9939

Storage: Store at or below -20 °C in the dark.
Solubility: Soluble in water, up to about 100 mg/mL; very poorly soluble in ethanol; slightly soluble in DMSO, up to about 10-20 mg/mL after heating. **Disposal:** A

- Vatalanib is a potent, orally active, selective inhibitor of the VEGFR tyrosine kinases VEGFR-1 (Flt-1) and VEGFR-2 (FLK-1/KDR), with slightly higher potency against the latter. At higher concentrations, other tyrosine kinases are also inhibited, including PDGFR-β, c-KIT, and c-FMS. In contrast, vatalanib is not active against the EGFR, fibroblast growth factor receptor-1, c-MET, and TIE-2 or intracellular kinases such as c-SRC, c-ABL, and protein kinase C-α. Lin B., *et al.* "The vascular endothelial growth factor receptor tyrosine kinase inhibitor PTK787/ZK222584 inhibits growth and migration of multiple myeloma cells in the bone marrow microenvironment." *Cancer Res.* **62:** 5019-5026 (2002). Rini B.I. and Small E.J. "Biology and clinical development of vascular endothelial growth factor-targeted therapy in renal cell carcinoma." *J. Clin. Oncol.* **23:** 1028-1043 (2005).
- Vatalanib is taken up by cells to reach its intracellular target, as shown by its effects on receptor phosphorylation tested in cell-based assays. Measurement of VEGF-induced autophosphorylation of KDR in a double antibody chemiluminescence assay, using either HUVECs or CHO cells transfected with the KDR receptor, showed that vatalanib inhibits VEGF-induced phosphorylation with an IC₅₀ of 17 nM and 34 nM for HUVECs and CHO cells, respectively. Vatalanib inhibited thymidine incorporation induced by VEGF in HUVECs with an IC₅₀ of 7.1 nM. In concentrations up to 1 μM, neither vatalanib nor SU5416 inhibited the response to bFGF or serum. In a cell migration assay, vatalanib inhibited VEGF-induced HUVEC migration dose dependently (IC₅₀ = 58 nM). Vatalanib inhibited tumor cell proliferation (IC₅₀'s of 17 μM and 18 μM for A431 and DU145 cells, respectively) and sprout formation in rat aortas (IC₅₀ = 675 nM). Wood J.M., *et al.* "PTK787/ZK 222584, a Novel and Potent Inhibitor of Vascular Endothelial Growth Factor Receptor Tyrosine Kinases, Impairs Vascular Endothelial Growth Factor-

induced Responses and Tumor Growth after Oral Administration." *Cancer Res.* **60:** 2178-2189 (2000).

- Sold for laboratory or manufacturing purposes only; not for human, veterinary, food, or household use.
- This product is offered for R&D use in accordance with (i) 35 USC 271(e)+A13(1) in the U.S.; (ii) Section 69.1 of Japanese Patent Law in Japan; (iii) Section 11, No. 2 of the German Patent Act of 1981 in Germany; (iv) Section 60, Paragraph 5b of the U.K. Patents Act of 1977 in the U.K.; (v) Section 68B of the Patents Act of 1953 in New Zealand; (vi) such related legislation and/or case law as may be or become applicable in the aforementioned countries; and (vii) such similar laws and rules as may apply in various other countries.
- Not available in some countries; not available to some institutions; not available for some uses.



Velcade – See Bortezomib (Cat. No. B-1408 on page 4).

W-2990 Wortmannin, >98%
[KY 12420]

	Size	US\$	€	£	¥
	5 mg	59	49	32	7,100
	10 mg	94	78	52	11,300
	25 mg	199	165	109	23,900
	100 mg	690	573	380	82,800

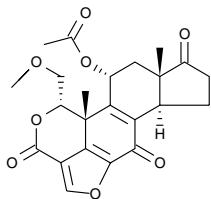
M.W. 428.44 $C_{23}H_{24}O_8$ [19545-26-7]
 RTECS CB9641000 M.I. 12: 10188

Storage: Store at or below 4 °C. **Solubility:** Soluble in DMSO or ethanol. **Disposal:** A

- Isolated from the filamentous fungus, *Penicillium funiculosum*, wortmannin is a potent, irreversible, and specific inhibitor of phosphatidylinositol 3-kinase (PI3-K) with an IC₅₀ of 2-5 nM. Arcaro, A., and Wymann, M.P. "Wortmannin is a potent phosphatidylinositol 3-kinase inhibitor: the role of phosphatidylinositol 3,4,5-trisphosphate in neutrophil responses." *Biochem. J.* **296:** 297-301 (1993). Wymann, M.P., and Arcaro, A. "Platelet-derived growth factor-induced phosphatidylinositol 3-kinase activation mediates actin rearrangements in fibroblasts." *Biochem. J.* **298:** 517-520 (1994). Powis, G., *et al.* "Wortmannin, a potent and selective inhibitor of phosphatidylinositol-3-kinase." *Cancer Res.* **54:** 2419-2423 (1994). Wymann, M.P., *et al.* "Wortmannin inactivates phosphoinositide 3-kinase by covalent modification of Lys-802, a residue involved in the phosphate transfer reaction." *Mol. Cell Biol.* **16:** 1722-1733 (1996).
- Inhibitor of both myosin light chain kinase (IC₅₀ = 200 nM) and phosphatidylinositol 4-kinase at concentrations approximately 100-fold higher than the that required for PI3-K inhibition. Nakanishi, S., *et al.* "Wortmannin, a microbial product inhibitor of myosin light chain kinase." *J. Biol. Chem.* **267:** 2157-2163 (1992).
- Enhances radiation- or serum withdrawal-induced apoptosis through the inhibition of PI3-K/Akt signal transduction cascade and blocks the antiapoptotic effect of cytokines. Krasilnikov, M., *et al.* "Contribution of phosphatidylinositol 3-kinase to radiation resistance in human melanoma cells." *Mol. Carcinog.* **24:** 64-69 (1999). Allen, M.P., *et al.* "Growth arrest-specific gene 6/adhesion related kinase signaling promotes gonadotropin-releasing hormone

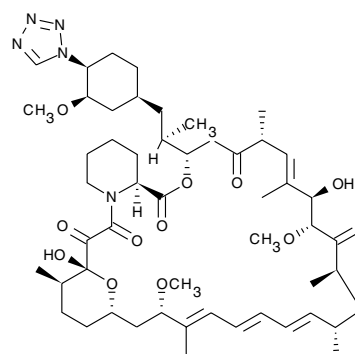
neuronal survival via extracellular signal-regulated kinase (ERK) and Akt." *Mol. Endocrinol.* **13**: 191-201 (1999). Morita, Y., *et al.* "Requirement for phosphatidylinositol-3'-kinase in cytokine-mediated germ cell survival during fetal oogenesis in the mouse." *Endocrinology* **140**: 941-949 (1999). Manna, S.K., and Aggarwal, B.B. "Interleukin-4 down-regulates both forms of tumor necrosis factor receptor and receptor-mediated apoptosis, NFkappaB, AP-1, and c-Jun N-terminal kinase." *J. Biol. Chem.* **273**: 33333-33341 (1998). Crowder, R.J., and Freeman, R.S. "Phosphatidylinositol 3-kinase and Akt protein kinase are necessary and sufficient for the survival of nerve growth factor-dependent sympathetic neurons." *J. Neurosci.* **18**: 2933-2943 (1998).

- Wortmannin inhibition of PI3-K also blocks many of the short-term metabolic effects induced by insulin receptor activation in isolated rat adipocytes without affecting the insulin receptor tyrosine kinase activity. Okada, T., *et al.* "Essential role of phosphatidylinositol 3-kinase in insulin-induced glucose transport and antilipolysis in rat adipocytes. Studies with a selective inhibitor wortmannin." *J. Biol. Chem.* **269**: 3568-3573 (1994). Moule, S.K., and Denton, R.M. "Multiple signaling pathways involved in the metabolic effects of insulin." *Am. J. Cardiol.* **80**: 41A-49A (1997).
- Inhibits platelet activating factor-induced MAP kinase activation in guinea pig neutrophils (200 - 300 nM). Ferby, I.M., *et al.* "Wortmannin inhibits mitogen-activated protein kinase activation induced by platelet-activating factor in guinea pig neutrophils." *J. Biol. Chem.* **269**: 30485-30488 (1994).
- Inhibits phospholipase D activation. Bonser, R.W., *et al.* "Demethoxyviridin and wortmannin block phospholipase C and D activation in the human neutrophil." *Br. J. Pharmacol.* **103**: 1237-1241 (1991).
- Sold for research use only; not for human drug, veterinary drug, food additive, clinical or household use.



endothelial cell (IC₅₀ = 2.6 nM) proliferation. After 28 days, zotarolimus stents from domestic juvenile swine exhibited less area stenosis (22.4% vs. 35.7%), less neointimal area (1.69 vs. 2.78 mm²), less neointimal thickness (0.25 vs. 0.38 mm), and greater lumen area (6.07 vs. 5.02 mm²) when compared to phosphorylcholine-coated stents. Garcia-Touchard, A., *et al.* "Zotarolimus-eluting stents reduce experimental coronary artery neointimal hyperplasia after 4 weeks." *Eur. Heart J.* **27**: 988-993 (2006).

- Zotarolimus was also designed for use in stents that have phosphorylcholine as a carrier.
- Zotarolimus is the active drug in the drug-eluting stents sold under the trade names Endeavor and ZoMaxx.
- **Sold for laboratory or manufacturing purposes only; not for human, veterinary, food, or household use.**
- This product is offered for R&D use in accordance with (i) 35 USC 271(e)+A13(1) in the U.S.; (ii) Section 69.1 of Japanese Patent Law in Japan; (iii) Section 11, No. 2 of the German Patent Act of 1981 in Germany; (iv) Section 60, Paragraph 5b of the U.K. Patents Act of 1977 in the U.K.; (v) Section 68B of the Patents Act of 1953 in New Zealand; (vi) such related legislation and/or case law as may be or become applicable in the aforementioned countries; and (vii) such similar laws and rules as may apply in various other countries.
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ZD-1839 – see Gefitinib (Cat. No. G-4408 on page 14).

Z-9040 Zotarolimus, >98%

[ABT-578] [40-Epi-(N1-tetrazolyl)-rapamycin]

(PLEASE INQUIRE ABOUT AVAILABILITY)

Size	US\$	€	£	¥
5 mg	148	123	81	17,800
25 mg	335	278	184	40,200
100 mg	685	569	377	82,200

M.W. 966.23 C₅₂H₇₉N₅O₁₂ [221877-54-9]

Storage: Store at or below -20 °C. **Solubility:** Soluble in DMSO. **Disposal:** A

- Zotarolimus (also known as ABT-578) is an analogue of rapamycin (sirolimus) that was designed to have a shorter *in vivo* half-life than rapamycin. Zotarolimus was found to be comparable in potency for inhibiting *in vitro* proliferation of both rat and human T cells and mechanistically similar to sirolimus in having high-affinity binding to the immunophilin FKBP12. Chen, Y.W., *et al.* "Zotarolimus, a novel sirolimus analogue with potent anti-proliferative activity on coronary smooth muscle cells and reduced potential for systemic immunosuppression." *J. Cardiovasc. Pharmacol.* **49**: 228-235 (2007).
- *In vitro*, zotarolimus inhibited FKBP-12 binding (IC₅₀ = 2.8 nM) and potently blocked smooth muscle cell (IC₅₀ = 2.9 nM) and



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