

#9900 Store at -20°C

PD98059 (MEK1 Inhibitor)

- Small 1.5 mg lyophilized powder
- Large 5 mg lyophilized powder

Orders ■ 877-616-CELL (2355)
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This product is for *in vitro* research use only and is not intended for use in humans or animals. This product is not intended for use as a therapeutic or in diagnostic procedures.

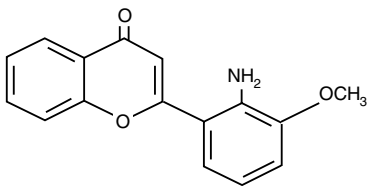
Description: PD98059 (MEK1 Inhibitor) is soluble in DMSO at 10–100 mM. For use with *in vitro* or cell-based assays, it may be diluted into aqueous buffers to yield desired concentrations (<100 μM) with final DMSO concentrations of ~0.1%. IC₅₀ values for inhibitory activity against MEK1 are around 5–10 μM. For experiments with cultured cells, CST recommends pretreating with this inhibitor for one hour prior to stimulation.

Background: MEK1 and MEK2, also called MAPK or Erk kinases, are dual-specificity protein kinases that function in a mitogen activated protein kinase cascade controlling cell growth and differentiation (1–3). Activation of MEK1 and MEK2 occurs through phosphorylation of two serine residues at positions 217 and 221 (in the activation loop of subdomain VIII) by Raf-like molecules. MEK1/2 is activated by a wide variety of growth factors and cytokines and also by membrane depolarization and calcium influx (1–4). Constitutively active forms of MEK1/2 are sufficient for the transformation of NIH/3T3 cells or the differentiation of PC12 cells (4). MEK activates p44 and p42 MAP kinase by phosphorylating both threonine and tyrosine residues at sites located within the activation loop of kinase subdomain VIII.

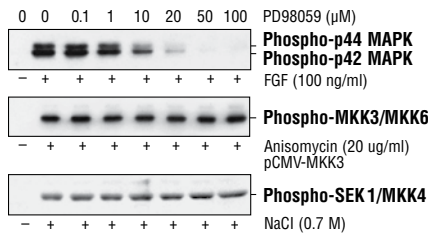
PD98059 (MEK1 Inhibitor) has been shown to act *in vivo* as a highly selective inhibitor of MEK1 activation and the MAP kinase cascade (1–4). PD98059 binds to the inactive forms of MEK1 and prevents activation by upstream activators such as c-Raf (3)

Specificity/Sensitivity: PD98059 (MEK1 Inhibitor) inhibits activation of MEK1 and MEK2 with IC₅₀ values of 4 μM and 50 μM, respectively (1–3). Testing at CST and by others (3) has shown that PD98059 does not inhibit activation of other highly related dual-specificity protein kinases or the activity of over 18 other Ser/Thr protein kinases. As shown in the Western blot, at concentrations up to 100 μM, PD98059 does not inhibit activation of MKK3 or SEK (MKK4) as determined by measuring phosphorylation at its activation site. We have also found no inhibition of MKK6 or related family members.

Molecular Formula: C₁₆H₁₃NO₃



Molecular Weight: 267.28



SK-N-MC cells were pretreated with varying amounts of MEK1 Inhibitor for 1 hour, then treated with FGF for 30 minutes. Cell extracts were blotted with Phospho-p44/p42 MAP Kinase (Thr202/Tyr204) Antibody #9101 (top). COS cells were transfected with pCMV-MKK3 for 22 hours, pretreated with varying amounts of MEK1 Inhibitor for 1 hour, then treated with anisomycin for 30 minutes. Cell extracts were blotted with Phospho-MKK3/MKK6 (Ser189/207) Antibody #9231 (middle). 293 cells were pretreated with varying amounts of MEK1 Inhibitor for 1 hour, then treated with sodium chloride for 30 minutes. Cell extracts were blotted with Phospho-SEK1/MKK4 (Thr261) Antibody #9151 (bottom).

Directions for Use: Supplied as a lyophilized yellow powder. For 20 mM stock, reconstitute 1.5 mg in 280 μl DMSO (5 mg in 933.3 μl). For 50 mM stock, reconstitute 1.5 mg in 112 μl DMSO (5 mg in 373.3 μl). Store in aliquots at -20°C. See enclosed MSDS for further information. This product is for *in vitro* research use only and is not intended for use in humans or animals.

Selected Application References:

Badache, A. et al. (2001) Interleukin 6 inhibits proliferation and, in cooperation with an epidermal growth factor receptor autocrine loop, increases migration of T47D breast cancer cells. *Cancer Res.* 61, 383–391.

Wei, S. et al. (2000) Direct tumor lysis by NK cells uses a C348Ras-independent mitogen-activated protein kinase signal pathway. *J. Immunol.* 165, 3811–3819.

Lee, S.H. et al. (2000) Maintenance of vascular integrity in the embryo requires signaling through the fibroblast growth factor receptor. *J. Biol. Chem.* 275, 33679–33687.

Bommhardt, U. et al. (2000) MEK activity regulates negative selection of immature CD4⁺CD8⁺ thymocytes. *J. Immunol.* 164, 2326–2337.

Hardingham, G.E. et al. (2001) Nuclear calcium signaling controls CREB-mediated gene expression triggered by synaptic activity. *Nat. Neuro.* 4, 261–267.

Degryse, B. et al. (2001) The high mobility group (HMG) boxes of the nuclear protein HMG1 induce chemotaxis and cytoskeleton reorganization in rat smooth muscle cells. *J. Cell Biol.* 152, 1197–1206.

Entrez-Gene ID # 5604
Swiss-Prot Acc. # Q02750

Storage: Lyophilized: -20°C, stable at least one year. Reconstituted: -20°C, stable at least one year.

For application specific protocols please see the web page for this product at www.cellsignal.com.

Companion Products:

- Phospho-p44/42 MAP Kinase (Thr202/Tyr204) Antibody #9101
- Phospho-p44/42 MAPK (Thr202/Tyr204) (E10) Mouse mAb #9106
- p44/42 MAP Kinase Assay Kit (nonradioactive) #9800
- U0126 (MEK1/2 Inhibitor) #9903

Please visit www.cellsignal.com for a complete listing of recommended companion products.

Background References:

(1) Crews, C.M. et al. (1992) *Science* 258, 478–480.

(2) Alessi, D.R. et al. (1994) *EMBO J.* 13, 1610–1619.

(3) Rosen, L.B. et al. (1994) *Neuron* 12, 1207–1221.

(4) Cowley, S. et al. (1994) *Cell* 77, 841–852.

