Small Molecules

MLN4924

Inhibits NEDD8-activating enzyme

Catalog # 74182 1 mg
74184 10 mg

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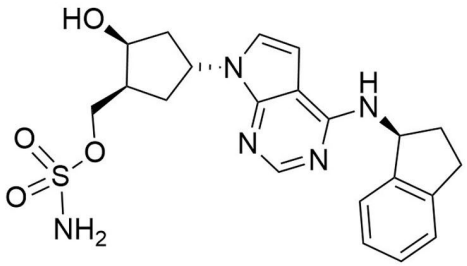
Product Description

MLN4924 inhibits cullin neddylation by directly targeting the NEDD8-activating enzyme that is essential for the activity of cullin-RING ligase (CRL) (Nawrocki et al.). The components of CRL are frequently up-regulated in human cancers (Zhao & Sun), and MLN4924 was reported to suppress the growth of human tumor xenografts in mice (Soucy et al.).

Molecular Name:	MLN4924
Alternative Names:	Pevonedistat
CAS Number:	905579-51-3
Chemical Formula:	$C_{21}H_{25}N_5O_4S$
Molecular Weight:	443.5 g/mol
Purity:	≥ 98%
Chemical Name:	sulfamic acid, [(1S,2S,4R)-4-[4-[[(1S)-2,3-dihydro-1H-inden-1-yl]amino]-7H-pyrrolo[2,3-d]pyrimidin-7-yl]-2-hydroxycyclopentyl]methyl ester
Structure:	

Properties

Physical Appearance:	A crystalline solid
Storage:	Product stable at -20°C as supplied. Protect product from prolonged exposure to light. For long-term storage, store with a desiccant. Stable as supplied for 12 months from date of receipt.
Solubility:	· DMSO ≤ 45 mM · Absolute ethanol ≤ 25 mM For example, to prepare a 10 mM stock solution in DMSO, resuspend 1 mg in 225 µL of DMSO. Prepare stock solution fresh before use. Information regarding stability of small molecules in solution has rarely been reported; however, as a general guide we recommend storage in DMSO at -20°C. Aliquot into working volumes to avoid repeated freeze-thaw cycles. The effect of storage of stock solution on compound performance should be tested for each application. Compound has low solubility in aqueous media. For use as a cell culture supplement, stock solution should be diluted into culture medium immediately before use. Avoid final DMSO concentration above 0.1% due to potential cell toxicity.

Published Applications

GENOME EDITING
· In combination with other small molecules ("CRISPY" mix), MLN4924 has been reported to increase precise CRISPR-Cas9 genome editing in human pluripotent stem cells (Riesenberg & Maricic).
CANCER RESEARCH
· By blocking NAE and proteasome, MLN4924 together with bortezomib inhibits AKT and mTOR and induces apoptosis in multiple myeloma cell lines (Gu et al.).

References

Gu Y et al. (2014) MLN4924, an NAE inhibitor, suppresses AKT and mTOR signaling via upregulation of REDD1 in human myeloma cells. Blood 123(21): 3269–76.
Nawrocki ST et al. (2012) MLN4924: a novel first-in-class inhibitor of NEDD8-activating enzyme for cancer therapy. Expert Opin Investig Drugs 21(10): 1563–73.
Riesenberg S & Maricic T. (2018) Targeting repair pathways with small molecules increases precise genome editing in pluripotent stem cells. Nat Commun 9(1): 2164.
Soucy TA et al. (2009) An inhibitor of NEDD8-activating enzyme as a new approach to treat cancer. Nature 458(7239): 732–6.
Zhao & Sun. (2013) Cullin-RING ligases as attractive anti-cancer targets. Curr Pharm Des 19(18): 3215–25.

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This product is hazardous. Please refer to the Safety Data Sheet (SDS).