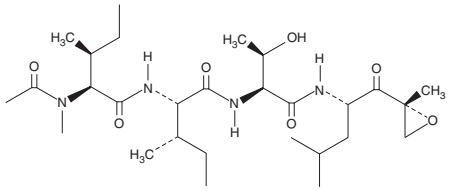
PRODUCT INFORMATION

Epoxomicin

Item No. 10007806

CAS Registry No.:	134381-21-8
Formal Name:	N-acetyl-N-methyl-L-isoleucyl-L-isoleucyl-N-[(1S)-3-methyl-1-[[(2R)-2-methyloxiranyl]carbonyl]butyl]-L-threoninamide
Synonym:	BU 4061T
MF:	$C_{28}H_{50}N_4O_7$
FW:	554.7
Purity:	≥98%
Supplied as:	A solution in DMSO
Storage:	-20°C
Stability:	≥2 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Description

Epoxomicin is a potent anti-tumor agent isolated from *Actinomycetes* that is used as a selective and irreversible inhibitor of the 20S proteasome. It inhibits proteasome activity in cell growth assays with an IC_{50} value of 4 nM and demonstrates potent cytotoxicity against B16-F10, HCT116, and Moser solid tumor cells, as well as P388 and K562 leukemia cells with IC_{50} values ranging from 2-44 nM.[1,2] By inhibiting osteoblast proteasome activity, epoxomicin stimulates bone formation at concentrations as low as 10 nM.[3] Intraperitoneal injection of 1.5 mg/kg epoxomicin given daily for two weeks induces Parkinson's-like symptoms in rats and addition of 100 nM epoxomicin to rat ventral midbrain cultures results in apoptosis specific to dopaminergic neurons.[4,5] Epoxomicin-induced parkinsonism can be a useful model to examine mechanisms and therapies for the disease.

References

1. Kim, K.B., Myung, J., Sin, N., *et al.* Proteasome inhibition by the natural products epoxomicin and dihydroeponemycin: Insights into specificity and potency. *Bioorg. Medicinal Chem. Letters* **9(23)**, 3335-3340 (1999).
2. Hanada, M., Sugawara, K., Kaneta, K., *et al.* Epoxomicin, a new antitumor agent of microbial origin. *J. Antibiotics* **45(11)**, 1746-1752 (1992).
3. Garrett, I.R., Chen, D., Gutierrez, G., *et al.* Selective inhibitors of the osteoblast proteasome stimulate bone formation *in vivo* and *in vitro*. *J. Clin. Invest.* **111(11)**, 1771-1782 (2003).
4. McNaught, K.St.M., Perl, D.P., Brownell, A.-L., *et al.* Systemic exposure to proteasome inhibitors causes a progressive model of Parkinson's disease. *Ann. Neurol.* **56(1)**, 149-162 (2004).
5. Rideout, H.J., Lang-Rollin, I.C.J., Savalle, M., *et al.* Dopaminergic neurons in rat ventral midbrain cultures undergo selective apoptosis and form inclusions, but do not up-regulate iHSP70, following proteasomal inhibition. *J. Neurochem.* **93(5)**, 1304-1313 (2005).

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