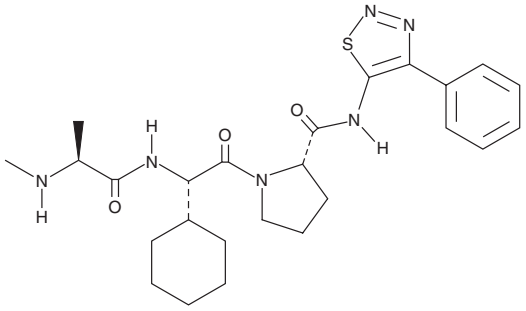
PRODUCT INFORMATION

GDC-0152

Item No. 17810

CAS Registry No.:	873652-48-3
Formal Name:	N-methyl-L-alanyl-(2S)-2-cyclohexylglycyl-N-(4-phenyl-1,2,3-thiadiazol-5-yl)-L-prolinamide
MF:	$C_{25}H_{34}N_6O_3S$
FW:	498.6
Purity:	≥95%
UV/Vis.:	λ_{max}: 230, 255, 293 nm
Supplied as:	A crystalline solid
Storage:	-20°C
Stability:	≥4 years



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

Laboratory Procedures

GDC-0152 is supplied as a crystalline solid. A stock solution may be made by dissolving the GDC-0152 in the solvent of choice. GDC-0152 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF), which should be purged with an inert gas. The solubility of GDC-0152 in ethanol and DMSO is approximately 10 mg/ml and approximately 25 mg/ml in DMF.

GDC-0152 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, GDC-0152 should first be dissolved in DMF and then diluted with the aqueous buffer of choice. GDC-0152 has a solubility of approximately 0.5 mg/ml in a 1:1 solution of DMF:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

Inhibitor of apoptosis proteins (IAPs), which block various signaling pathways leading to apoptotic cell death, are commonly over-expressed in cancer cells.[1] GDC-0152 is a potent inhibitor of specific IAPs that binds baculoviral IAP repeat (BIR) domains (K_is = 28, 14, 17, and 43 nM for XIAP BIR3, NL-IAP BIR, BIRC2 (c-IAP1) BIR3, and BIRC3 (c-IAP2) BIR3, respectively).[2] GDC-0152 induces activation of caspases, decreasing the viability of cancer cells without affecting normal cells.[2,3] It is orally bioavailable and suppresses tumor growth in breast cancer xenografts in mice.[2] GDC-0152 also induces NF-κB transcriptional activity, resulting in the expression of several cytokines, including TNF-α.[4] In dogs and rats, but not humans, this leads to a pronounced inflammatory response.[4]

References

1. Goyal, L. Cell death inhibition: Keeping caspases in check. *Cell* **104**, 805-808 (2001).
2. Flygare, J.A., Beresini, M., Budha, N., *et al.* Discovery of a potent small-molecule antagonist of inhibitor of apoptosis (IAP) proteins and clinical candidate for the treatment of cancer (GDC-0152). *J. Med. Chem.* **55(9)**, 4101-4113 (2012).
3. Hu, R., Li, J., Liu, Z., *et al.* GDC-0152 induces apoptosis through down-regulation of IAPs in human leukemia cells and inhibition of PI3K/Akt signaling pathway. *Tumour Biol.* **36(2)**, 577-584 (2015).
4. Erickson, R.I., Tarrant, J., Cain, G., *et al.* Toxicity profile of small-molecule IAP antagonist GDC-0152 is linked to TNF-α pharmacology. *Toxicol. Sci.* **131(1)**, 247-258 (2013).

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