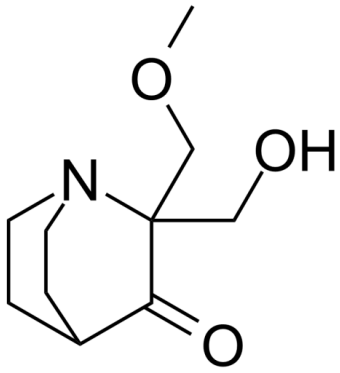
Data Sheet

Product Name:	PRIMA-1Met
Cat. No.:	CS-7614
CAS No.:	5291-32-7
Molecular Formula:	C10H17NO3
Molecular Weight:	199.25
Target:	Apoptosis; Autophagy; Ferroptosis; MDM-2/p53
Pathway:	Apoptosis; Autophagy
Solubility:	H2O : 50 mg/mL (250.94 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

PRIMA-1Met restores wild-type conformation and function to mutant **p53**, and triggers apoptosis in tumor cells. PRIMA-1Met also targets the selenoprotein thioredoxin reductase 1 (**TrxR1**), a key regulator of cellular redox balance. IC50 & Target: p53 activator[1] TrxR1 inhibitor[1] **In Vitro:** PRIMA-1Met inhibits both recombinant TrxR1 in vitro and TrxR1 in cells. Cellular TrxR1 activity is inhibited by PRIMA-1Met irrespective of p53 status. PRIMA-1Met can directly affect cellular redox status via targeting of TrxR1. Several small molecules have been shown to restore wild-type activity to mutant p53, including CP-31398, PRIMA-1 and PRIMA-1MET, MIRA, STIMA, PhiKan-083 and NSC319726. PRIMA-1 and its methylated analog PRIMA-1Met promote correct folding of mutant p53, induce cell death by apoptosis, and inhibit tumor growth in mice. PRIMA-1Met has also been shown to reactivate mutant forms of the p63 and p73 proteins that share high structural homology with p53[1]. PRIMA-1MET is a powerful apoptosis-inducing agent. PRIMA-1MET can enhance apoptosis in mutant p53 carrying cells, compared to the p53 null parental cells. Most p53 mutants are in complex with Hsp70 proteins. PRIMA-1MET treatment increases Hsp70 expression and nucleolar translocation, in parallel with the induction of nucleolar accumulation of mutant p53. Several lines of evidence suggest that PRIMA-1MET can also act independently of the p53 status of the cell. It can radiosensitize prostate carcinoma cell lines with mutant or wild type p53 and $p53^{-/-}$ cells as well. Introduction of mutant p53 (p53ser249 or p53gln248) into $p53^{-/-}$ hepatocarcinoma cells increases sensitivity to PRIMA-1MET without the induction of p53 target genes. PRIMA-1MET regularly induces apoptosis in mutant p53 expressing cells[2].

PROTOCOL (Extracted from published papers and Only for reference)

Kinase Assay: [1]Cells are plated in six-well plates at a density of 15 000 cells per cm^2. Next day, cells are treated with different concentrations of PRIMA-1Met (0, 25, 50, 75 and 100 μM) and harvested after 4, 12 and 24 h. The cells are lysed, and the clarified supernatants are used for either analysis of TrxR enzymatic activities or western blot. Total protein concentrations are determined with a Bradford reagent kit. Cellular TrxR activity is measured using an adapted Trx-dependent end point insulin reduction assay for microwell plates[1].

References:

[1]. Peng X, et al. APR-246/PRIMA-1MET inhibits thioredoxin reductase 1 and converts the enzyme to a dedicated NADPH oxidase. Cell Death Dis. 2013 Oct 24;4:e881.

[2]. Stuber G, et al. PRIMA-1MET induces nucleolar translocation of Epstein-Barr virus-encoded EBNA-5 protein. Mol Cancer. 2009 Mar 26;8:23.

CAIndexNames:

1-Azabicyclo[2.2.2]octan-3-one, 2-(hydroxymethyl)-2-(methoxymethyl)-

SMILES:

O=C1C(COC)(CO)N2CCC1CC2

Caution: Product has not been fully validated for medical applications. For research use only.

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