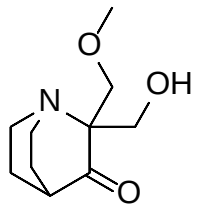
Product data sheet

MedKoo Cat#: 205945 Name: Eprenetapopt (APR-246) CAS#: 5291-32-7 Chemical Formula: $C_{10}H_{17}NO_3$ Exact Mass: 199.1208 Molecular Weight: 199.25	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
APR-246, also known as PRIMA-1MET and Eprenetapopt, is a quinuclidinone derivative that targets the Wrap53 gene with potential antineoplastic activity. p53 activator APR-246 binds to and activates transcription of the Wrap53 gene, which results in an increase in WRAP53 p53 antisense transcript levels and, potentially, an increase in native p53 activity; in turn, increased p53 activity may lead to an induction of cell cycle arrest and apoptosis in tumor cells. This agent may work synergistically with other antineoplastic agents.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	53.33	267.65
Water	45.0	225.85
Ethanol	32.50	163.11
DMF	30.0	150.56
PBS (pH 7.2)	5.0	25.09

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	5.02 mL	25.09 mL	50.19 mL
5 mM	1.00 mL	5.02 mL	10.04 mL
10 mM	0.50 mL	2.51 mL	5.02 mL
50 mM	0.10 mL	0.50 mL	1.00 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Liu DS, Duong CP, Haupt S, Montgomery KG, House CM, Azar WJ, Pearson HB, Fisher OM, Read M, Guerra GR, Haupt Y, Cullinane C, Wiman KG, Abrahmsen L, Phillips WA, Clemons NJ. Inhibiting the system xC-/glutathione axis selectively targets cancers with mutant-p53 accumulation. Nat Commun. 2017 Mar 28;8:14844. doi: 10.1038/ncomms14844. PMID: 28348409; PMCID: PMC5379068.

In vivo study

1. Liu DS, Duong CP, Haupt S, Montgomery KG, House CM, Azar WJ, Pearson HB, Fisher OM, Read M, Guerra GR, Haupt Y, Cullinane C, Wiman KG, Abrahmsen L, Phillips WA, Clemons NJ. Inhibiting the system xC-/glutathione axis selectively targets cancers with mutant-p53 accumulation. Nat Commun. 2017 Mar 28;8:14844. doi: 10.1038/ncomms14844. PMID: 28348409; PMCID: PMC5379068.

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7. Bioactivity

Biological target: APR-246 is a first-in-class, small molecule that restores wild-type p53 functions in TP53-mutant cells.

In vitro activity

Since APR-246 depletes GSH (glutathione) and system xC− blockade leads to cystine starvation, which in turn impairs GSH synthesis, it was examined whether their therapeutic combination would synergistically target mut-p53 cancer cells. APR-246 was applied to esophageal cell lines following SLC7A11 knockdown. Inhibiting SLC7A11 expression significantly enhanced the efficacy of APR-246, particularly against cancer cells with mut-p53 accumulation (Fig. 7a), resulting in synergistic induction of ROS and apoptosis (Fig. 7b,c; Supplementary Fig. 7a). Mechanistically, system xC− blockade in conjunction with APR-246 synergistically depleted intracellular GSH, resulting in mitochondrial ROS (reactive oxygen species) accumulation, lipid peroxidation and ultimately apoptotic cell death (Fig. 7h–k; Supplementary Fig. 7e–h).

Reference: Nat Commun. 2017 Mar 28;8:14844. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5379068/

In vivo activity

In FLO-1 xenografts, SLC7A11 knockdown significantly enhanced the anti-tumour activity of APR-246 (Fig. 8b,c; Supplementary Fig. 8k), leading to synergistic reduction of intratumoral GSH levels and improved animal survival (Fig. 8d,e). Consistent with this, the combination of SAS (sulfasalazine) with APR-246 at tolerated doses (Supplementary Fig. 8l,m) also conferred greater anti-tumour activity than single agents alone (Fig. 8f). Importantly, these findings were reproduced in a PDX model of mut-p53 high-expressing oesophageal cancer (Fig. 8g–i; Supplementary Fig. 8n–o). Analysis of these tumours revealed markedly reduced proliferation and increased apoptosis (Fig. 8j). These results demonstrate the therapeutic potential of combining system xC− inhibitors with APR-246 to synergistically target cancer cells with mut-p53 accumulation.

Reference: Nat Commun. 2017 Mar 28;8:14844. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5379068/