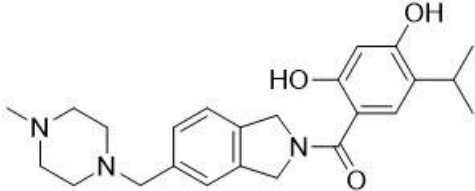


Product data sheet



MedKoo Cat#: 200317 Name: Onalespib free base CAS#: 912999-49-6 (free base) Chemical Formula: C ₂₄ H ₃₁ N ₃ O ₃ Exact Mass: 409.23654 Molecular Weight: 409.52		
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:

Onalespib, also known as AT13387, is a synthetic, orally bioavailable, small-molecule inhibitor of heat shock protein 90 (Hsp90) with potential antineoplastic activity. Hsp90 inhibitor AT13387 selectively binds to Hsp90, thereby inhibiting its chaperone function and promoting the degradation of oncogenic signaling proteins involved in tumor cell proliferation and survival. Hsp90, a chaperone protein upregulated in a variety of tumor cells, regulates the folding, stability and degradation of many oncogenic signaling proteins.

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	20.0	48.8

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.44	12.21	24.42
5 mM	0.49	2.44	4.88
10 mM	0.24	1.22	2.44
50 mM	0.05	0.24	0.49

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

- Lundsten S, Spiegelberg D, Stenerlöw B, Nestor M. The HSP90 inhibitor onalespib potentiates 177Lu-DOTATATE therapy in neuroendocrine tumor cells. *Int J Oncol.* 2019 Dec;55(6):1287-1295. doi: 10.3892/ijo.2019.4888. Epub 2019 Sep 30. PMID: 31638190; PMCID: PMC6831206.
- Mehta RK, Pal S, Kondapi K, Sitto M, Dewar C, Devasia T, Schipper MJ, Thomas DG, Basrur V, Pai MP, Morishima Y, Osawa Y, Pratt WB, Lawrence TS, Nyati MK. Low-Dose Hsp90 Inhibitor Selectively Radiosensitizes HNSCC and Pancreatic Xenografts. *Clin Cancer Res.* 2020 Oct 1;26(19):5246-5257. doi: 10.1158/1078-0432.CCR-19-3102. Epub 2020 Jul 27. PMID: 32718999; PMCID: PMC7541797.

In vivo study

- Lundsten S, Spiegelberg D, Raval NR, Nestor M. The radiosensitizer Onalespib increases complete remission in 177Lu-DOTATATE-treated mice bearing neuroendocrine tumor xenografts. *Eur J Nucl Med Mol Imaging.* 2020 Apr;47(4):980-990. doi: 10.1007/s00259-019-04673-1. Epub 2020 Jan 7. PMID: 31912256; PMCID: PMC7075859.
- Mehta RK, Pal S, Kondapi K, Sitto M, Dewar C, Devasia T, Schipper MJ, Thomas DG, Basrur V, Pai MP, Morishima Y, Osawa Y, Pratt WB, Lawrence TS, Nyati MK. Low-Dose Hsp90 Inhibitor Selectively Radiosensitizes HNSCC and Pancreatic Xenografts. *Clin Cancer Res.* 2020 Oct 1;26(19):5246-5257. doi: 10.1158/1078-0432.CCR-19-3102. Epub 2020 Jul 27. PMID: 32718999; PMCID: PMC7541797.

Product data sheet



7. Bioactivity

Biological target:

Onalespib (AT13387) is a long-acting second-generation Hsp90 inhibitor with a Kd of 0.71 nM

In vitro activity

The effect of AT13387 on in vitro radio-sensitization was assessed using a clonogenic assay. The amplitude of the effects of 100 nM AT13387 on the global proteome was significantly lower than that of 3 μ M AT13387. Interestingly, except for Hsp70, the abundance of any other protein did not reach beyond the 1.5-fold abundance (log scale) level. The magnitude observed on protein levels (total 2145 significantly affected protein out of 5086) suggests that the 3 μ M AT13387 concentration would not be selective. Therefore, when given at a dose producing such drug levels in patients, it seems unlikely that the cumulative effect of the drug would be selective for cancer treatment. Altogether, the data suggest that a sub-toxic concentration of AT13387 can cause radio-sensitization regardless of the specific oncogenic driver(s) present in the cell lines.

Clin Cancer Res. 2020 Oct 1; 26(19): 5246–5257. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7541797/>

In vivo activity

Following the determination of the pharmacokinetic profile of AT13387, it was sought to determine the duration for which AT13387 can exert its effects in vivo. To investigate these effects, a single 40 mg/kg dose of AT13387 was administered at 0 hours, and a second 40 mg/kg dose at 96 hours, to mice bearing UMSCC74B xenografts. The expression of Hsp70 was analyzed in the tumor at the various time points as previously described. Following administration, pharmacodynamics studies showed that the expression of chaperone protein Hsp70, our biomarker for Hsp90 activity, was upregulated after AT13387 treatment (Figure 5B). This result was confirmed by densitometry analysis, which showed an 8-fold upregulation of Hsp70 expression at 24 and 120 hours (Figure 5B). Nearly 2 to 5-fold increased Hsp70 expression was demonstrated using immunohistochemistry (Figure 5C). This upregulation suggests that AT13387 treatment showed the desired inhibitory effect of Hsp90 inhibition in vivo. This indicates a potential role of the immune component in radiosensitization by AT13387.

Clin Cancer Res. 2020 Oct 1; 26(19): 5246–5257. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7541797/>

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.