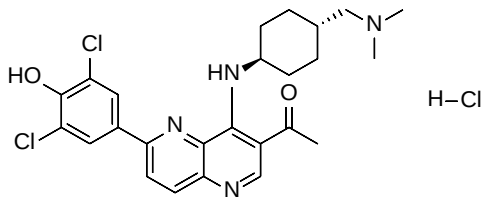
Product data sheet

MedKoo Cat#: 406520 Name: OTSSP167 HCl CAS#: 1431698-10-0 (HCl) Chemical Formula: $C_{25}H_{29}Cl_3N_4O_2$ Molecular Weight: 523.88	
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:
OTSSP167, also known as OTS167, is an orally available inhibitor of maternal embryonic leucine zipper kinase (MELK) with potential antineoplastic activity. Upon administration, OTS167 binds to MELK, which prevents both MELK phosphorylation and activation; thus inhibiting the phosphorylation of downstream MELK substrates. This may lead to an inhibition of both cell proliferation and survival in MELK-expressing tumor cells.

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	30.0	57.3

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.91 mL	9.54 mL	19.09 mL
5 mM	0.38 mL	1.91 mL	3.82 mL
10 mM	0.19 mL	0.95 mL	1.91 mL
50 mM	0.04 mL	0.19 mL	0.38 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. Muller J, Bolomsky A, Dubois S, Duray E, Stangelberger K, Plougonven E, Lejeune M, Léonard A, Marty C, Hempel U, Baron F, Beguin Y, Cohen-Solal M, Ludwig H, Heusschen R, Caers J. Maternal embryonic leucine zipper kinase inhibitor OTSSP167 has preclinical activity in multiple myeloma bone disease. Haematologica. 2018 Aug;103(8):1359-1368. doi: 10.3324/haematol.2017.185397. Epub 2018 May 10. PMID: 29748441; PMCID: PMC6068043.
2. Zhang Y, Zhou X, Li Y, Xu Y, Lu K, Li P, Wang X. Inhibition of maternal embryonic leucine zipper kinase with OTSSP167 displays potent anti-leukemic effects in chronic lymphocytic leukemia. Oncogene. 2018 Oct;37(41):5520-5533. doi: 10.1038/s41388-018-0333-x. Epub 2018 Jun 12. PMID: 29895969.

In vivo study

1. Muller J, Bolomsky A, Dubois S, Duray E, Stangelberger K, Plougonven E, Lejeune M, Léonard A, Marty C, Hempel U, Baron F, Beguin Y, Cohen-Solal M, Ludwig H, Heusschen R, Caers J. Maternal embryonic leucine zipper kinase inhibitor OTSSP167 has preclinical activity in multiple myeloma bone disease. Haematologica. 2018 Aug;103(8):1359-1368. doi: 10.3324/haematol.2017.185397. Epub 2018 May 10. PMID: 29748441; PMCID: PMC6068043.

7. Bioactivity
Biological target: OTSSP167 hydrochloride is a MELK inhibitor with an IC50 value of 0.41 nM.

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In vitro activity

The effects of the MELK inhibitor OTSSP167 on the proliferation of osteoclast progenitor cells and on the differentiation into osteoclasts were studied. Treatment of RAW264.7 cells with 25 nM OTSSP167 for 24 hours resulted in decreased MELK protein levels (Figure 1B). The effect of continuous OTSSP167 treatment on RAW264.7 and human PBMC (peripheral blood mononuclear cell) viability was assessed, and it was found that the viability of both osteoclast progenitor populations decreased (IC50: 12.8 nM and 43.2 nM, respectively) (Figure 1C). This coincided with an induction of G2/M cell cycle arrest (Online Supplementary Figure S1A). The decrease in progenitor viability corresponded with a decrease in both human (Figure 1D and and1F)1F) and murine (Figure 1E and 1H) osteoclast differentiation following continuous OTSSP167 treatment. Although the number of osteoclasts decreased, osteoclast size was markedly increased in human cultures treated with 10 nM OTSSP167, with a corresponding increase in the number of nuclei per osteoclasts (Figure 1G). This was not the case for RAW264.7 osteoclast cultures (Figure 1I).

Reference: Haematologica. 2018 Aug;103(8):1359-1368. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6068043/

In vivo activity

The potential of OTSSP167 as a therapy for MMBD (multiple myeloma bone disease) was assessed in vivo using the 5TGM.1 MM model. OTSSP167 treatment prevented the development of MMBD and this effect was similar at all dosing schedules tested (Figure 5A). OTSSP167 reduced the number of cortical perforations in MM-bearing mice (Figure 5B), without affecting cortical thickness (Ct.Th) (Online Supplementary Figure S1E). The loss of trabecular bone volume (Tb.BV/TV) that occurs in MM-bearing mice compared to healthy controls was completely prevented following treatment with OTSSP167 (Figure 5C). This was due to an increase in the number of trabeculae (Tb.N) (Figure 5D) and a decrease in trabecular separation (Tb.Sp) (Online Supplementary Figure S1F). As a result, trabecular connectivity density (Conn.Dn) was similar to healthy mice in OTSSP167-treated MM-bearing mice (Online Supplementary Figure S1G). Trabecular thickness was not affected in MM-bearing mice (Online Supplementary Figure S1H). Importantly, the observed prevention of MMBD in these mice does not appear to be solely due to a decreased tumor load following OTSSP167 treatment, as MMBD was prevented at a dose (7.5 mg/kg/2d) which had no effect on tumor load (Figure 5E).

Reference: Haematologica. 2018 Aug;103(8):1359-1368. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6068043/