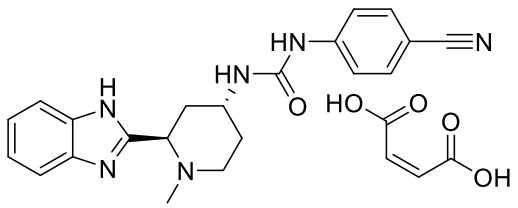
Product data sheet

MedKoo Cat#: 564805 Name: Glasdegib Maleate CAS#: 2030410-25-2 (maleate) Chemical Formula: $C_{25}H_{26}N_6O_5$ Molecular Weight: 490.52	
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:
Glasdegib Maleate is a potent and orally bioavailable inhibitor of smoothened.

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	49.05	100.0

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.04 mL	10.19 mL	20.39 mL
5 mM	0.41 mL	2.04 mL	4.08 mL
10 mM	0.20 mL	1.02 mL	2.04 mL
50 mM	0.04 mL	0.20 mL	0.41 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. Sadarangani A, Pineda G, Lennon KM, Chun HJ, Shih A, Schairer AE, Court AC, Goff DJ, Prashad SL, Geron I, Wall R, McPherson JD, Moore RA, Pu M, Bao L, Jackson-Fisher A, Munchhof M, VanArsdale T, Reya T, Morris SR, Minden MD, Messer K, Mikkola HK, Marra MA, Hudson TJ, Jamieson CH. GLI2 inhibition abrogates human leukemia stem cell dormancy. J Transl Med. 2015 Mar 21;13:98. doi: 10.1186/s12967-015-0453-9. PMID: 25889765; PMCID: PMC4414375.

In vivo study

1. Sadarangani A, Pineda G, Lennon KM, Chun HJ, Shih A, Schairer AE, Court AC, Goff DJ, Prashad SL, Geron I, Wall R, McPherson JD, Moore RA, Pu M, Bao L, Jackson-Fisher A, Munchhof M, VanArsdale T, Reya T, Morris SR, Minden MD, Messer K, Mikkola HK, Marra MA, Hudson TJ, Jamieson CH. GLI2 inhibition abrogates human leukemia stem cell dormancy. J Transl Med. 2015 Mar 21;13:98. doi: 10.1186/s12967-015-0453-9. PMID: 25889765; PMCID: PMC4414375.

7. Bioactivity
Biological target:

PF 04449913 maleate is a potent Smo antagonist (IC_{50} = 5 nM).

In vitro activity

Glasdegib (PF-04449913) inhibits sonic hedgehog (Shh) stimulated luciferase expression in mouse embryonic fibroblasts with an IC50 of 6.8 nM; and significantly reduces medulloblastoma growth in a Ptch1+/-p53+/- allograft model at doses that decreased murine Shh target gene expression. In stromal co-culture experiments, FACS analysis demonstrates a significant reduction in BC LSC by

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Glasdegib (PF-04449913) when compared with normal progenitors. Importantly, human BC LSC engrafted RAG2-/-γC-/- mice treated daily with Glasdegib (PF-04449913) compared with vehicle treated controls have a significant spleen weight reduction (p=0.006). This reduction in leukemic burden corresponded with decreased GLI2 protein expression, as determined by both nanoproteomic analysis of FACS purified human progenitors and GLI2 confocal fluorescence microscopic analysis of splenic sections.

Reference: J Transl Med. 2015 Mar 21;13:98. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/25889765/

In vivo activity

Human BC LSC engrafted RAG2-/-γC-/- mice treated daily with Glasdegib (PF-04449913) compared with vehicle treated controls had a significant spleen weight reduction (p=0.006). When CD34+ cord blood engrafted NSG mice are treated with Glasdegib (PF04449913), the frequency of human CD45+ cells, progenitors and both myeloid and lymphoid cell fate commitment remained comparable to vehicle treated controls indicating that unlike LSC, normal human HSC cell fate decisions are Hh pathway independent. These results highlight the important niche dependent effects of selective SMO inhibition that induce GLI2 downregulation in a cell type and context specific manner.

Reference: J Transl Med. 2015 Mar 21;13:98. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/25889765/