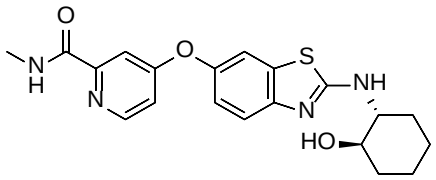
Product data sheet

MedKoo Cat#: 407110 Name: BLZ945 CAS#: 953769-46-5 Chemical Formula: $C_{20}H_{22}N_4O_3S$ Exact Mass: 398.1413 Molecular Weight: 398.48	
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:

BLZ945 is a potent and selective CSF-1R kinase inhibitor. BLZ945 showed effects of CSF1R inhibition on other tumor-infiltrating immune cells. BLZ945 attenuates the turnover rate of TAMs while increasing the number of CD8+ T cells that infiltrate cervical and breast carcinomas. BLZ945 decreases the growth of malignant cells in the mouse mammary tumor virus-driven polyomavirus middle T antigen (MMTV-PyMT) model of mammary carcinogenesis. BLZ945 prevents tumor progression in the keratin 14-expressing human papillomavirus type 16 (K14-HPV-16) transgenic model of cervical carcinogenesis.

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	59.44	149.17
Ethanol	3.0	7.53
Water	1.0	2.51
DMF	25.0	62.74
DMF:PBS (pH 7.2) (1:8)	0.11	0.28

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	2.51 mL	12.55 mL	25.10 mL
5 mM	0.50 mL	2.51 mL	5.02 mL
10 mM	0.25 mL	1.25 mL	2.51 mL
50 mM	0.05 mL	0.25 mL	0.50 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. Mao Y, Eissler N, Blanc KL, Johnsen JI, Kogner P, Kiessling R. Targeting Suppressive Myeloid Cells Potentiates Checkpoint Inhibitors to Control Spontaneous Neuroblastoma. Clin Cancer Res. 2016 Aug 1;22(15):3849-59. doi: 10.1158/1078-0432.CCR-15-1912. Epub 2016 Mar 8. PMID: 26957560.

In vivo study

1. Beckmann N, Giorgetti E, Neuhaus A, Zurbruegg S, Accart N, Smith P, Perdoux J, Perrot L, Nash M, Desrayaud S, Wipfli P, Frieauff W, Shimshek DR. Brain region-specific enhancement of remyelination and prevention of demyelination by the CSF1R kinase inhibitor BLZ945. Acta Neuropathol Commun. 2018 Feb 15;6(1):9. doi: 10.1186/s40478-018-0510-8. PMID: 29448957; PMCID: PMC5815182.

Product data sheet

7. Bioactivity

Biological target: BLZ945 is a CSF-1R (c-Fms) inhibitor with an IC50 of 1 nM.

In vitro activity

To uncover the essential factors contributing to the alterations in myelopoiesis, 28 soluble factors in tumor-conditioned media were ama;yzed and M-CSF was identified (Supplementary Fig. S3A and S3B) as the only factor that was absent in the culture medium but produced at high levels by all three tumor cell lines. Indeed, antagonizing CSF-1R during differentiation of CD34+ cells by a highly selective inhibitor (BLZ945) specifically limited the differentiation of macrophages and monocytes (Fig. 2D and Supplementary Fig. S3C) that had high expression of CSF-1R (Fig. 2E). However, it had no impact on DCs (Fig. 2D), because of their lower expression of CSF-1R (Supplementary Fig. S2E). Functionally, BLZ945 significantly recovered the potential of myeloid cells to stimulate T cells (Fig. 2F and 2G), with comparable effects on CD8+ and CD4+ subsets (Supplementary Fig. S3D and S3E). Notably, BLZ945 decreased monocytes and macrophages in cultures with only cytokines (Fig. 2D), but this did not lead to consistent changes of their T cell–activating capacities (Fig. 2F).

Reference: Clin Cancer Res. 2016 Aug 1;22(15):3849-59. https://clincancerres.aacrjournals.org/content/22/15/3849.long

In vivo activity

Multiple sclerosis (MS) is a chronic inflammatory disease affecting the central nervous system (CNS). While multiple effective immunomodulatory therapies for MS exist today, they lack the scope of promoting CNS repair, in particular remyelination. Microglia play a pivotal role in regulating myelination processes, and the colony-stimulating factor 1 (CSF-1) pathway is a key regulator for microglia differentiation and survival. Here, the effects of the CSF-1 receptor kinase inhibitor, BLZ945, on central myelination processes were investigated in the 5-week murine cuprizone model by non-invasive and longitudinal magnetic resonance imaging (MRI) and histology. Therapeutic 2-week BLZ945 treatment caused a brain region-specific enhancement of remyelination in the striatum/cortex, which was absent in the corpus callosum/external capsule. This beneficial effect correlated positively with microglia reduction, increased oligodendrocytes and astrogliosis.

Reference: Acta Neuropathol Commun. 2018 Feb 15;6(1):9. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5815182/