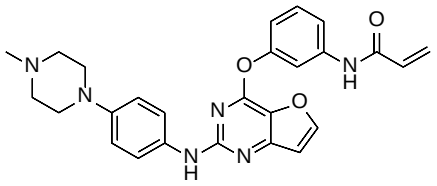
Product data sheet

MedKoo Cat#: 327020 Name: Poseltinib CAS#: 1353552-97-2 Chemical Formula: $C_{26}H_{26}N_6O_3$ Exact Mass: 470.2066 Molecular Weight: 470.53	
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:
Poseltinib, also known HM-71224 and LY3337641, is a tyrosine kinase inhibitor. Poseltinib is an experimental Bruton's tyrosine kinase inhibitor for the treatment of rheumatoid arthritis. HM71224 irreversibly bound to and inhibited Btk (IC50 = 1.95 nM). The compound also inhibited the phosphorylation of Btk and its downstream molecules such as PLCγ2, in activated Ramos B lymphoma cells and primary human B cells in a dose-dependent manner. Furthermore, HM71224 effectively inhibited the production of tumor necrosis factor (TNF)-α, interleukin (IL)-6, and IL-1β by human monocytes, and osteoclast formation by human monocytes. HM71224 inhibits Btk in B cells and monocytes and ameliorates experimental arthritis in a mouse model. HM71224 is a potential novel therapeutic agent for rheumatoid arthritis in humans.

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	100.0	212.53

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.13 mL	10.63 mL	21.25 mL
5 mM	0.43 mL	2.13 mL	4.25 mL
10 mM	0.21 mL	1.06 mL	2.13 mL
50 mM	0.04 mL	0.21 mL	0.43 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. Kim YY, Park KT, Jang SY, Lee KH, Byun JY, Suh KH, Lee YM, Kim YH, Hwang KW. HM71224, a selective Bruton's tyrosine kinase inhibitor, attenuates the development of murine lupus. Arthritis Res Ther. 2017 Sep 26;19(1):211. doi: 10.1186/s13075-017-1402-1. PMID: 28950886; PMCID: PMC5615432.

In vivo study

1. Kim YY, Park KT, Jang SY, Lee KH, Byun JY, Suh KH, Lee YM, Kim YH, Hwang KW. HM71224, a selective Bruton's tyrosine kinase inhibitor, attenuates the development of murine lupus. Arthritis Res Ther. 2017 Sep 26;19(1):211. doi: 10.1186/s13075-017-1402-1. PMID: 28950886; PMCID: PMC5615432.

7. Bioactivity
Biological target: Poseltinib is a Bruton's tyrosine kinase (BTK) inhibitor with IC50 =1.95 nM.

Product data sheet

In vitro activity

To characterize the inhibitory effect of HM71224 on the BCR signaling pathway, the activation of BTK and PLCγ2, the physiological substrate of BTK, following stimulation with anti-IgM was examined in human Ramos B lymphoma cells. HM71224 blocked both autophosphorylation of BTK and phosphorylation of PLCγ2 with IC50 values of less than 10 nM (Fig. 1a). To explore the inhibitory effect of HM71224 on the FcγR signaling cascade, the production of the inflammatory cytokines TNF-α and IL-6 was evaluated following stimulation with anti-IgG in human monocyte THP-1 cells. Production of both TNF-α and IL-6 effectively decreased in a dose-dependent manner (Fig. 1b and c).

Reference: Arthritis Res Ther. 2017 Sep 26;19(1):211. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5615432/

In vivo activity

HM71224 had therapeutic effects related to the amelioration of kidney damage caused by lupus-like renal inflammation. Intrarenal B cells can contribute to renal damage and inflammation by enhancing the immunological response as antigen-presenting cells, inducing cytokine-promoting T cell proliferation and lymphatic angiogenesis, and enhancing the local immune response to persisting autoantigens in the tubulointerstitium. In both MRL/lpr and NZB/W F1 mice, activation of TLR9 caused accelerated LN. On the other hand, LN develops via unique mechanisms in each strain like the highly heterogenous nature of SLE. NZB/W F1 mice promote the renal damages B cell dependent manner including secretion of autoantibody, whereas MRL/lpr mice develop the renal damages via antigen presentation and cytokine production by B cells, not secretion of autoantibodies. HM71224 markedly reduced splenic B cell numbers, including those of germinal center B cells, plasma B cells, and activated B cells. HM71224 also had inhibiroty effects on BCR and FcR signaling. These mechanisms of action of HM71224 might lead to significant amelioration of renal injury and lymphocyte infiltration in both animal models, although differences in strains in the pathogenesis of LN can lead to different degrees of therapeutic drug efficacy. It is possible that the therapeutic effects of HM71224 in glomerulonephritis, interstitial nephritis, and vessel inflammation in murine LN were mediated by B cell inhibition.

Reference: Arthritis Res Ther. 2017 Sep 26;19(1):211. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5615432/