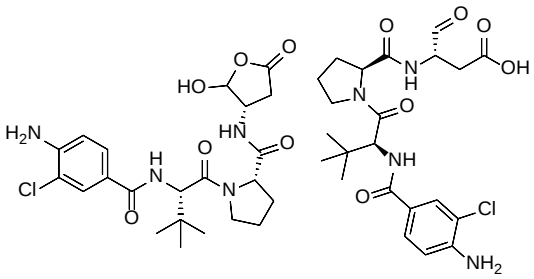
Product data sheet

MedKoo Cat#: 205941 Name: VRT-043198 CAS#: 244133-31-1 Chemical Formula: $C_{22}H_{29}ClN_4O_6$ Exact Mass: 480.1776 Molecular Weight: 480.94	
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:
VRT-043198, the active metabolite of VX-765 (Belnacasan), is a Caspase inhibitor. VRT-043198 exhibits 100- to 10,000-fold selectivity against other caspase-3 and -6 to -9. VRT-043198 inhibited the release of interleukin (IL)-1beta and IL-18, but it had little effect on the release of several other cytokines, including IL-1alpha, tumor necrosis factor-alpha, IL-6 and IL-8.

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	50.0	103.96

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.08 mL	10.40 mL	20.79 mL
5 mM	0.42 mL	2.08 mL	4.16 mL
10 mM	0.21 mL	1.04 mL	2.08 mL
50 mM	0.04 mL	0.21 mL	0.42 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. Wannamaker W, Davies R, Namchuk M, Pollard J, Ford P, Ku G, Decker C, Charifson P, Weber P, Germann UA, Kuida K, Randle JC. (S)-1-((S)-2-{[1-(4-amino-3-chloro-phenyl)-methanoyl]-amino}-3,3-dimethyl-butanoyl)-pyrrolidine-2-carboxylic acid ((2R,3S)-2-ethoxy-5-oxo-tetrahydro-furan-3-yl)-amide (VX-765), an orally available selective interleukin (IL)-converting enzyme/caspase-1 inhibitor, exhibits potent anti-inflammatory activities by inhibiting the release of IL-1beta and IL-18. J Pharmacol Exp Ther. 2007 May;321(2):509-16. doi: 10.1124/jpet.106.111344. Epub 2007 Feb 8. PMID: 17289835.

In vivo study

1. Wannamaker W, Davies R, Namchuk M, Pollard J, Ford P, Ku G, Decker C, Charifson P, Weber P, Germann UA, Kuida K, Randle JC. (S)-1-((S)-2-{[1-(4-amino-3-chloro-phenyl)-methanoyl]-amino}-3,3-dimethyl-butanoyl)-pyrrolidine-2-carboxylic acid ((2R,3S)-2-ethoxy-5-oxo-tetrahydro-furan-3-yl)-amide (VX-765), an orally available selective interleukin (IL)-converting enzyme/caspase-1 inhibitor, exhibits potent anti-inflammatory activities by inhibiting the release of IL-1beta and IL-18. J Pharmacol Exp Ther. 2007 May;321(2):509-16. doi: 10.1124/jpet.106.111344. Epub 2007 Feb 8. PMID: 17289835.

7. Bioactivity
Biological target: VRT-043198 is an inhibitor of IL-converting enzyme (ICE)/caspase-1 with Kis of 0.8 nM and less than 0.6 nM for caspase-1 and caspase-4, respectively.

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In vitro activity

In cultures of peripheral blood mononuclear cells and whole blood from healthy subjects stimulated with bacterial products, VRT-043198 inhibited the release of interleukin (IL)-1beta and IL-18, but it had little effect on the release of several other cytokines, including IL-1alpha, tumor necrosis factor-alpha, IL-6 and IL-8. In contrast, VRT-043198 had little or no demonstrable activity in cellular models of apoptosis, and it did not affect the proliferation of activated primary T cells or T-cell lines.

Reference: J Pharmacol Exp Ther. 2007 May;321(2):509-16. https://jpet.aspetjournals.org/content/321/2/509.long

In vivo activity

VX-765 was efficiently converted to VRT-043198 when administered orally to mice, and it inhibited lipopolysaccharide-induced cytokine secretion. In addition, VX-765 reduced disease severity and the expression of inflammatory mediators in models of rheumatoid arthritis and skin inflammation. These data suggest that VX-765 is a novel cytokine inhibitor useful for treatment of inflammatory diseases.

Reference: J Pharmacol Exp Ther. 2007 May;321(2):509-16. https://jpet.aspetjournals.org/content/321/2/509.long

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.