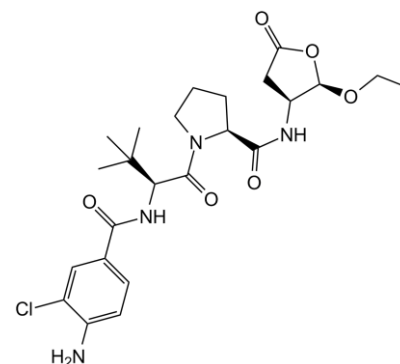


Product Data Sheet

Chemical Properties

Product Name:	VX-765
Cas No.:	273404-37-8
M.Wt:	508.99
Formula:	C ₂₄ H ₃₃ ClN ₄ O ₆



Chemical Name:	(2S)-1-[(2S)-2-[(4-amino-3-chlorobenzoyl)amino]-3,3-dimethylbutanoyl]-N-[(2R,3S)-2-ethoxy-5-oxoxolan-3-yl]pyrrolidine-2-carboxamide
Canonical SMILES:	<chem>CCOC1C(CC(=O)O1)NC(=O)C2CCCN2C(=O)C(C(C)(C)C)NC(=O)C3=CC(=C(C=C3)N)Cl</chem>
Solubility:	>25.5mg/mL in DMSO
Storage:	Desiccate at -20°C
General tips:	For obtaining a higher solubility , please warm the tube at 37° C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20° C for several months.
Shopping Condition:	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request

Biological Activity

Targets :	Caspase
Pathways:	Apoptosis >> Caspase
Description:	

VX-765, an orally- absorbed pro-drug of VRT-043198, is a potent and selective inhibitor of caspase-1 which belongs to the ICE/caspase-1 sub-family caspases. Caspase-1, known as interleukin (IL)-1-converting enzyme, is responsible for the processing of a

key inflammatory mediator IL-1 β from an inactive precursor to an active, secreted protein. In response to intracellular bacteria, caspase-1 is also reported to be involved in a rapid programme of cell death, termed pyroptosis in macrophages [1].

VX-765 is usually metabolized to an active molecular VRT-043198. In cultures of peripheral blood mononuclear cells stimulated with bacterial products, VRT-043198 inhibited the release of Interleukin (IL)-1 β and IL-18, but had no effect on the secretion of other cytokines such as IL- α , TNF α , IL-6 and IL-8 [2].

This product is also used in other models to illustrate the function of Caspase-1. Oral administration of VX-765 significantly reduced the severity of diseases and the inflammatory cytokines and chemokines secretion in the mouse model of rheumatoid arthritis and skin inflammation[1]. In addition, recent study demonstrated that VX-765 prevents CD4 T-cell pyroptotic death in a dose-dependent manner in HIV-infected lymphoid tissues [3].

Reference:

1. Denes A, Lopez-Castejon G, Brough D. Caspase-1: is IL-1 just the tip of the ICEberg. *Cell Death Dis* 2012,3:e338.

2. Wannamaker W, Davies R, Namchuk M, Pollard J, Ford P, Ku G, et al.

(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-1 β and IL-18. *J Pharmacol Exp Ther* 2007,321:509-516.

3. Doitsh G, Galloway NL, Geng X, Yang Z, Monroe KM, Zepeda O, et al. Cell death by pyroptosis drives CD4 T-cell depletion in HIV-1 infection. *Nature* 2014,505:509-514.

Product Citations

1. Zaccara, Gaetano, and Dieter Schmidt. "Do traditional anti-seizure drugs have a future A review of potential anti-seizure drugs in clinical development." *Pharmacological research* 104 (2016): 38-48. PMID:26689774

Caution

FOR RESEARCH PURPOSES ONLY.

NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

Specific storage and handling information for each product is indicated on the product datasheet. Most ApexBio products are stable under the recommended conditions. Products are sometimes shipped at a temperature that differs from the recommended storage temperature. Short-term storage of many products are stable in the short-term at temperatures that differ from that required for long-term storage. We ensure that the product is shipped under conditions that will maintain the quality of the reagents. Upon receipt of the product, follow the storage recommendations on the product data sheet.

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