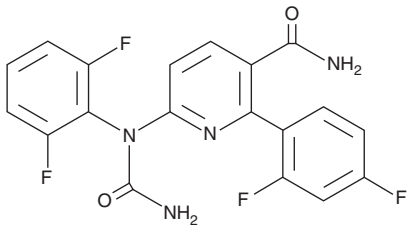
PRODUCT INFORMATION

VX-702

Item No. 13108

CAS Registry No.:	745833-23-2
Formal Name:	6-[(aminocarbonyl)(2,6-difluorophenyl) amino]-2-(2,4-difluorophenyl)-3-pyridinecarboxamide
MF:	$C_{19}H_{12}F_4N_4O_2$
FW:	404.3
Purity:	≥95%
UV/Vis.:	λ_{max}: 203, 240, 291 nm
Supplied as:	A crystalline solid
Storage:	-20°C
Stability:	≥4 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

VX-702 is supplied as a crystalline solid. A stock solution may be made by dissolving the VX-702 in the solvent of choice. VX-702 is soluble in organic solvents such as DMSO and dimethyl formamide, which should be purged with an inert gas. The solubility of VX-702 in these solvents is approximately 14 and 3 mg/ml, respectively.

VX-702 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, VX-702 should first be dissolved in DMSO and then diluted with the aqueous buffer of choice. VX-702 has a solubility of approximately 0.5 mg/ml in a 1:3 solution of DMSO:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

VX-702 is a third generation inhibitor of p38 mitogen-activated protein (MAP) kinases, binding to both p38α and p38β (K_d = 3.7 and 17 nM, respectively) in an ATP-competitive fashion.[1] It inhibits IL-6, IL-1β, and TNF-α production in LPS-primed blood with IC_{50} values of 59, 122, and 99 ng/ml, respectively.[1] VX-702, at 1 µM, inhibits activation of p38 in platelets by thrombin, U-46619 (Item No. 16450), or collagen but does not block platelet aggregation in response to collagen.[2] Although orally active, VX-702 provides only transient suppression of biomarkers of inflammation in ongoing rheumatoid arthritis.[3]

References

1. Goldstein, D.M., Kuglstatter, A., Lou, Y., *et al.* Selective p38α inhibitors clinically evaluated for the treatment of chronic inflammatory disorders. *J. Med. Chem.* **53(6)**, 2345-2353 (2010).
2. Kuliopulos, A., Mohanlal, R., and Covic, L. Effect of selective inhibition of the p38 MAP kinase pathway on platelet aggregation. *Thromb. Haemost.* **92(6)**, 1387-1393 (2004).
3. Damjanov, N., Kauffman, R.S., and Spencer-Green, G.T. Efficacy, pharmacodynamics, and safety of VX-702, a novel p38 MAPK inhibitor, in rheumatoid arthritis: Results of two randomized, double-blind, placebo-controlled clinical studies. *Arthritis Rheum.* **60(5)**, 1232-1241 (2009).

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