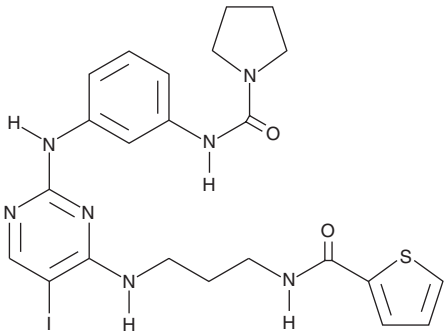
PRODUCT INFORMATION

BX-795

Item No. 14932

CAS Registry No.:	702675-74-9
Formal Name:	N-[3-[[5-iodo-4-[[3-[(2-thienylcarbonyl)amino]propyl]amino]-2-pyrimidinyl]amino]phenyl]-1-pyrrolidinecarboxamide
MF:	$C_{23}H_{26}IN_7O_2S$
FW:	591.5
Purity:	≥98%
UV/Vis.:	λ_{max}: 247 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

BX-795 is supplied as a crystalline solid. A stock solution may be made by dissolving the BX-795 in the solvent of choice, which should be purged with an inert gas. BX-795 is soluble in organic solvents such as DMSO and dimethyl formamide (DMF). The solubility of BX-795 in these solvents is approximately 11.1 and 12.5 mg/ml, respectively.

BX-795 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, BX-795 should first be dissolved in DMF and then diluted with the aqueous buffer of choice. BX-795 has a solubility of approximately 0.2 mg/ml in a 1:4 solution of DMF:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

BX-795 is a multi-kinase inhibitor that is an ATP-competitive inhibitor of 3-phosphoinositide-dependent protein kinase 1 (PDK1) and TANK-binding kinase 1 (TBK1; IC_{50}s = 6 and 11 nM, respectively).[1,2] It also inhibits the CAMK family kinases AMPK-related kinase 5 (NUAK1; IC_{50} = 5 nM) and microtubule affinity-regulating kinase 1 (MARK1), MARK2, MARK3, and MARK4 (IC_{50}s = 55, 53, 81, and 19 nM, respectively), as well as the MAP3K kinases mixed-lineages kinase 1 (MLK1), MLK2, and MLK3 (IC_{50}s = 50, 46, and 42 nM, respectively). BX-795 is selective for these kinases over five additional kinases (IC_{50}s = >1,100 nM) but does inhibit the receptor tyrosine kinase VEGFR, as well as IκB kinase ε (IKKε) and Aurora B kinase (IC_{50}s = 41 and 31 nM, respectively).[1] It inhibits phosphorylation of Akt at Thr^{308} and p70 ribosomal S6 kinase 1 (p70S6K1) at Thr^{389} in PC3 prostate cancer cells (IC_{50} = 300 nM).[1] BX-795 (1 µM) also inhibits the secretion of IFN-β induced by LPS or poly(I:C) in RAW 264.7 macrophages.[2] It inhibits the proliferation of PC3 prostate and MDA-MB-468 breast cancer cells (IC_{50}s = 250 and 720 nM, respectively). BX-795 (5 µM) inhibits the proliferation of $PDK1^{-/-}$ murine embryonic stem cells expressing either wild-type PDK1 or PDK1 with an alanine-to-glycine (L159G) mutation.[3]

References

1. Feldman, R.I., Wu, J.M., Polokoff, M.A., *et al.* Novel small molecule inhibitors of 3-phosphoinositide-dependent kinase-1. *J. Biol. Chem.* **280(20)**, 19867-19874 (2005).
2. Clark, K., Plater, L., Peggie, M., *et al.* Use of the pharmacological inhibitor BX795 to study the regulation and physiological roles of TBK1 and IκB kinase ε: A distinct upstream kinase mediates Ser-172 phosphorylation and activation. *J. Biol. Chem.* **284(21)**, 14136-14146 (2009).
3. Tamgüney, T., Zhang, C., Fiedler, D., *et al.* Analysis of 3-phosphoinositide-dependent kinase-1 signaling and function in ES cells. *Exp. Cell Res.* **314(11-12)**, 2299-2312 (2008).

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