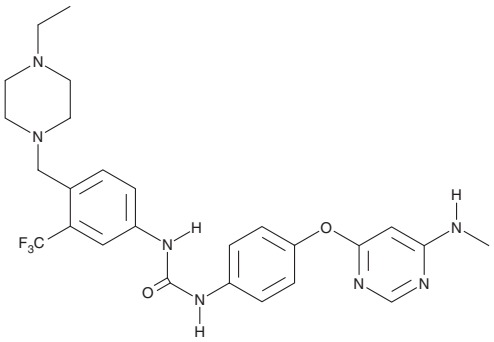
PRODUCT INFORMATION

AST-487

Item No. 19477

CAS Registry No.:	630124-46-8
Formal Name:	N-[4-[(4-ethyl-1-piperazinyl)methyl]-3-(trifluoromethyl)phenyl]-N'-[4-[[6-(methylamino)-4-pyrimidinyl]oxy]phenyl]-urea
Synonym:	NVP-AST-487
MF:	$C_{26}H_{30}F_3N_7O_2$
FW:	529.6
Purity:	≥98%
UV/Vis.:	λ_{max}: 262, 344 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

AST-487 is supplied as a crystalline solid. A stock solution may be made by dissolving the AST-487 in the solvent of choice, which should be purged with an inert gas. AST-487 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF). The solubility of AST-487 in ethanol and DMF is approximately 20 mg/ml and approximately 30 mg/ml in DMSO.

AST-487 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, AST-487 should first be dissolved in DMSO and then diluted with the aqueous buffer of choice. AST-487 has a solubility of approximately 0.3 mg/ml in a 1:2 solution of DMSO:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

AST-487 is an inhibitor of RET (IC_{50} = 0.88 µM), FLT3 (K_i = 0.52 µM), KDR (IC_{50} = 0.17 µM), c-Abl (IC_{50} = 0.02 µM), and c-Kit (IC_{50} = 0.5 µM).[1,2] It has been shown to inhibit RET autophosphorylation and activation of downstream effectors and to prevent the growth of human thyroid cancer cell lines with activating mutations of RET but not of lines without RET mutations.[1] In xenografts of NIH3T3 cells expressing oncogenic RET and of the MTC cell line TT in nude mice, AST-487 dose dependently inhibited tumor growth.[1] It also demonstrates antiproliferative effects on primary cells from acute myelocytic leukemia patients and on cell lines expressing FLT3-ITD or FLT3 kinase domain point mutants.[1]

References

1. Akeno-Stuart, N., Croyle, M., Knauf, J.A., *et al.* The RET kinase inhibitor NVP-AST487 blocks growth and calcitonin gene expression through distinct mechanisms in medullary thyroid cancer cells. *Cancer Res.* **67(14)**, 6956-6964 (2007).
2. Weisberg, E., Roesel, J., Bold, G., *et al.* Antileukemic effects of the novel, mutant FLT3 inhibitor NVP-AST487: effects on PKC412-sensitive and -resistant FLT3-expressing cells. *Blood* **112(13)**, 5161-5170 (2008).

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