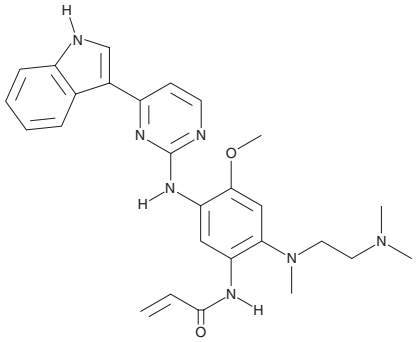
PRODUCT INFORMATION

AZ 5104

Item No. 17994

CAS Registry No.:	1421373-98-9
Formal Name:	N-[2-[[2-(dimethylamino)ethyl]methylamino]-5-[[4-(1H-indol-3-yl)-2-pyrimidinyl]amino]-4-methoxyphenyl]-2-propenamide
MF:	$C_{27}H_{31}N_7O_2$
FW:	485.6
Purity:	≥95%
UV/Vis.:	λ_{max}: 277, 313 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

AZ 5104 is supplied as a crystalline solid. A stock solution may be made by dissolving the AZ 5104 in the solvent of choice, which should be purged with an inert gas. AZ 5104 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide. The solubility of AZ 5104 in these solvents is approximately 30 mg/ml.

AZ 5104 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, AZ 5104 should first be dissolved in ethanol and then diluted with the aqueous buffer of choice. AZ 5104 has a solubility of approximately 0.5 mg/ml in a 1:1 solution of ethanol:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

AZ 5104 is an inhibitor of mutant EGFRs (IC_{50} = 2 nM for $EGFR^{L858R/T790M}$ and $EGFR^{T790M}$ for both) and an active metabolite of AZD 9291 (Item No. 16237).[1] It is selective for these mutant EGFRs over wild-type EGFR (IC_{50} = 33 nM). AZ 5104 is formed from AZD 9291 by the cytochrome P450 (CYP) isoform CYP3A.[2] It decreases proliferation of H1975 non-small cell lung cancer (NSCLC) cells containing the L858R activating and T790M resistance mutations (GI_{50} = 24 nM). AZ 5104 (2.5-10 mg/kg per day) reduces tumor growth in an H1975 mouse xenograft model.

References

1. Finlay, M.R., Anderton, M., Ashton, S., *et al*. Discovery of a potent and selective EGFR inhibitor (AZD9291) of both sensitizing and T790M resistance mutations that spares the wild type form of the receptor. *J. Med. Chem.* **57(20)**, 8249-8267 (2014).
2. Dickinson, P. A. , Vantarini, M. V., Collier, J., *et al*. Metabolic disposition of osimertinib in rats, dogs, and humans: Insights into a drug designed to bind covalently to a cysteine residue of epidermal growth factor receptor. *Drug Metab. Dispos.* **44(8)**, 1201-1212 (2016).

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