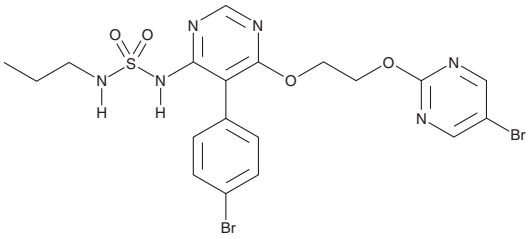
PRODUCT INFORMATION

Macitentan

Item No. 23304

CAS Registry No.: 441798-33-0
Formal Name: N-[5-(4-bromophenyl)-6-[2-[(5-bromo-2-pyrimidinyl)oxy]ethoxy]-4-pyrimidinyl]-N'-propyl-sulfamide
Synonyms: ACT-064992, Actelion-1
MF: $C_{19}H_{20}Br_2N_6O_4S$
FW: 588.3
Purity: ≥98%
UV/Vis.: λ_{max}: 215 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

Macitentan is supplied as a crystalline solid. A stock solution may be made by dissolving the macitentan in the solvent of choice, which should be purged with an inert gas. Macitentan is soluble in organic solvents such as DMSO and dimethyl formamide (DMF). The solubility of macitentan in these solvents is approximately 33 mg/ml.

Macitentan is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, macitentan should first be dissolved in DMF and then diluted with the aqueous buffer of choice. Macitentan has a solubility of approximately 0.12 mg/ml in a 1:7 solution of DMF:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

Macitentan is a dual antagonist of the endothelin (ET) receptors type A and B (IC_{50}s = 0.5 and 391 nM in a radioligand binding assay using recombinant ET_A and ET_B, respectively).[1] Macitentan inhibits intracellular calcium increases induced by the endothelin isoform ET-1 in human pulmonary arterial smooth muscle cells (HPASMCs; IC_{50} = 0.9 nM), contractions of isolated rat aortic rings (pA_2 = 7.6 for ET_A), and sarafotoxin S6c-induced contractions of isolated rat tracheal rings (pA_2 = 5.9 for ET_B). Macitentan increases plasma ET-1 concentrations in normotensive rats and decreases mean arterial blood pressure in DOCA-salt hypertensive rats (ED_{50} = 1 mg/kg). Oral administration (30 mg/kg per day) prevents development of pulmonary hypertension and right ventricle hypertrophy in a rat model of hypertension induced by monocrotaline (Item No. 16666). It also decreases the number of vascular and tubule-interstitial lesions and amount of glomerular damage in a rat model of diabetes induced by streptozotocin (Item No. 13104). Formulations containing macitentan have been used for the treatment of pulmonary arterial hypertension.

Reference

1. Iglarz, M., Binkert, C., Morrison, K., *et al*. Pharmacology of macitentan, an orally active tissue-targeting dual endothelin receptor antagonist. *J. Pharmacol. Exp. Ther.* **327(3)**, 736-745 (2008).

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