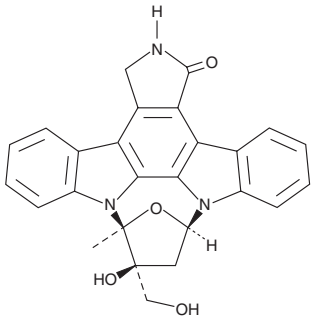
PRODUCT INFORMATION

Lestaurtinib

Item No. 12094

CAS Registry No.: 111358-88-4
Formal Name: 2,3,9S,10S,11,12R-hexahydro-10-hydroxy-10-(hydroxymethyl)-9-methyl-9,12-epoxy-1H-diindolo[1,2,3-fg:3',2',1'-kl]pyrrolo[3,4-i][1,6]benzodiazocin-1-one
Synonyms: A 154475.0, CEP-701, KT 5555, NSC 621867, SP 924
MF: $C_{26}H_{21}N_3O_4$
FW: 439.5
Purity: ≥98%
Supplied as: A crystalline solid
Storage: -20°C
Stability: ≥2 years



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

Laboratory Procedures

Lestaurtinib is supplied as a crystalline solid. A stock solution may be made by dissolving the lestaurtinib in the solvent of choice. Lestaurtinib is soluble in organic solvents such as DMSO and dimethyl formamide (DMF), which should be purged with an inert gas. The solubility of lestaurtinib in these solvents is approximately 3 and 5 mg/ml, respectively.

Lestaurtinib is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, lestaurtinib should first be dissolved in DMF and then diluted with the aqueous buffer of choice. Lestaurtinib has a solubility of approximately 0.05 mg/ml in a 1:20 solution of DMF:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

Janus-associated kinases (JAKs) are cytoplasmic tyrosine kinases that are required for activating the signaling of certain cytokines and growth factor receptors.[1,2] A JAK2 gene fusion mutation, $JAK2^{V617F}$, that causes unchecked activation of various growth factors and cytokines, has been linked to myeloproliferative disorders.[3] Lestaurtinib is a staurosporine analog that potently inhibits JAK2 kinase (IC_{50} = 1 nM) and downstream targets STAT5 (IC_{50} = 10-30 nM) and STAT3 in a human erythroleukemic cell line expressing the $JAK2^{V617F}$ mutation.[3,4] It has been used to reduce tumor growth in a xenograft model of pancreatic ductal adenocarcinoma, to inhibit cell growth in a trk-B overexpressing neuroblastoma xenograft model, and to block proliferation and induce apoptosis in Hodgkin lymphoma cell lines.[5-7] Lestaurtinib has since been reported to potently inhibit the epigenetic kinase PRK1 *in vitro* (IC_{50} = 8.6 nM), inducing hypophosphorylation of histone H3 threonine 11 and blocking androgen-dependent gene expression in prostate cancer cells at a concentration of 5 µM.[8]

References

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4. Hexner, E.O., Serdikoff, C., Jan, M., *et al. Blood* **111(12)**, 5663-5671 (2008).
5. Miknyoczki, S.J., Chang, H., Klein-Szanto, A., *et al. Clin. Cancer Res.* **5**, 2205-2212 (1999).
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CAYMAN CHEMICAL
1180 EAST ELLSWORTH RD
ANN ARBOR, MI 48108 · USA
PHONE: [800] 364-9897
[734] 971-3335
FAX: [734] 971-3640
CUSTSERV@CAYMANCHEM.COM
WWW.**CAYMANCHEM**.COM