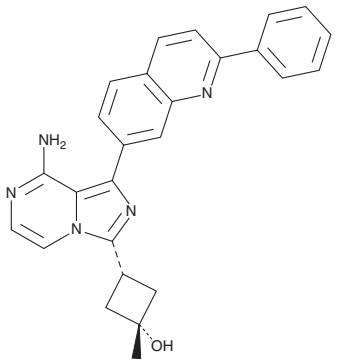
PRODUCT INFORMATION

Linsitinib

Item No. 17708

CAS Registry No.:	867160-71-2
Formal Name:	*cis*-3-[8-amino-1-(2-phenyl-7-quinolinyl)imidazo[1,5-a]pyrazin-3-yl]-1-methyl-cyclobutanol
Synonym:	OSI-906
MF:	$C_{26}H_{23}N_5O$
FW:	421.5
Purity:	≥98%
UV/Vis.:	λ_{max}: 210, 259, 352 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

Linsitinib is supplied as a crystalline solid. A stock solution may be made by dissolving the linsitinib in the solvent of choice, which should be purged with an inert gas. Linsitinib is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF). The solubility of linsitinib in these solvents is approximately 1, 20, and 25 mg/ml, respectively.

Linsitinib is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, linsitinib should first be dissolved in DMF and then diluted with the aqueous buffer of choice. Linsitinib has a solubility of approximately 0.03 mg/ml in a 1:30 solution of DMF:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

The binding of insulin-like growth factor 1 (IGF-1) to the IGF-1 receptor (IGF-1R) promotes cell growth while inhibiting apoptotic pathways. Overexpression of IGF-1R is found in certain solid tumors and hematologic neoplasias.[1,2] However, insulin receptor (InsR) signaling can compensate for IGF-1R inhibition.[3] Linsitinib is a dual inhibitor of IGF-1R and InsR kinases (IC_{50}s = 35 and 75 nM, respectively).[4] It also inhibits InsR-related receptor (IC_{50} = 75 nM) but is without effect (IC_{50} > 10 µM) against a large panel of other kinases.[4] Linsitinib inhibits proliferation of a variety of tumor cell lines *in vitro* and has antitumor efficacy in an IGF-1R-driven xenograft mouse model when administered orally.[4] A rapid, non-invasive method to predict the pharmacodynamic response to linsitinib has been reported.[3]

References

1. Scagliotti, G.V. and Novello, S. The role of the insulin-like growth factor signaling pathway in non-small cell lung cancer and other solid tumors. *Cancer Treat. Rev.* **38(4)**, 292-302 (2012).
2. McKinley, E.T., Bugaj, J.E., Zhao, P., *et al.* ^{18}FDG-PET predicts pharmacodynamic response to OSI-906, a dual IGF-1R/IR inhibitor, in preclinical mouse models of lung cancer. *Clin. Cancer Res.* **17(10)**, 3332-3340 (2011).
3. Buck, E., Gokhale, P.C., Koujak, S., *et al.* Compensatory insulin receptor (IR) activation on inhibition of insulin-like growth factor-1 receptor (IGF-1R): rationale for cotargeting IGF-1R and IR in cancer. *Mol. Cancer Ther.* **9(10)**, 2652-2664 (2010).
4. Mulvihill, M.J., Cooke, A., Rosenfeld-Franklin, M., *et al.* Discovery of OSI-906: A selective and orally efficacious dual inhibitor of the IGF-1 receptor and insulin receptor. *Future Med. Chem.* **1(6)**, 1153-1171

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