Product Name: Pexmetinib (ARRY-614)

Revision Date: 6/30/2018

Product Data Sheet

Chemical Properties

Product Name: Pexmetinib (ARRY-614)
Cas No.: 945614-12-0
M.Wt: 556.64
Formula: C31H33FN6O3

Chemical Name: 1-(3-(tert-butyl)-1-(p-tolyl)-1H-pyrazol-5-yl)-3-(5-fluoro-2-((1-(2-hydroxyethyl)-1H-indazol-5-yl)oxy)benzyl)urea

Canonical SMILES: CC1=CC=C(N2C(NC(NCC3=CC(F)=CC=C3OC4=CC=C5C(C=NN5CCO)=C4)=C)CC(C(C)(C)C)=N2)C=C1

Solubility: ≥107.6 mg/mL in DMSO, <2.67 mg/mL in H2O, ≥113 mg/mL in EtOH

Storage: Store at -20°C

General tips: For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shopping Condition: Evaluation sample solution: ship with blue ice
All other available size: ship with RT, or blue ice upon request

Biological Activity

Targets: MAPK Signaling
Pathways: p38

Description:
Pexmetinib (ARRY-614) is a potent inhibitor of cytokine synthesis, via the dual inhibition of p38 mitogen-activated protein kinase (MAPK), and Tie2/Tek receptor tyrosine kinase. The in vitro IC50 values of ARR Y-614 for both Tie2 and p38 mitogen-activated protein kinase are 1000 ng/mL and
100 ng/mL, respectively [1, 2].

p38 is a group of mitogen-activated protein kinases. MAPKs are activated by the dual phosphorylation of Tyr and Thr residues in the Thr-Xaa-Tyr motif in subdomain VIII. Data indicated that p38 MAPK may mediate signaling to the nucleus [3].

ARRY-614 is active against MAPK and Tie2/Tek receptor tyrosine kinase in cells. In primary human bone marrow stromal cells, ARRY-614 inhibited basal cytokines with an IC50 value ranging from 50-100 nM [4].

In dose escalation or expansion cohorts, treatment with ARRY-614 either once daily or twice daily was applied to forty-five patients. ARRY-614 reduced the levels of circulating biomarkers and the p38 MAPK activation of bone marrow [1]. In ex vivo stimulated human whole blood, LPS-induced cytokines was inhibited by ARRY-614 with an IC50 value ranging from 50-120 nM. ARRY-614 inhibited the release of IL-6 from SEA- or LPS-challenged mice with an ED50 value less than 10 mg/kg. Combining ARRY-614 with lenalidomide inhibited both pro-inflammatory cytokines and tumor growth in vivo with higher potency, compared with either agent alone [4].

Reference:

Caution

FOR RESEARCH PURPOSES ONLY.

NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

Specific storage and handling information for each product is indicated on the product datasheet. Most ApexBio products are stable under the recommended conditions. Products are sometimes shipped at a temperature that differs from the recommended storage temperature. Shortterm storage of many products are stable in the short-term at temperatures that differ from that required for long-term storage. We ensure that the product is shipped under conditions that will maintain the quality of the reagents. Upon receipt of the product, follow the storage recommendations on the product data sheet.