Product Name: VX-702

Revision Date: 11/5/2019

Product Data Sheet

Chemical Properties

Product Name: VX-702
Cas No.: 479543-46-9; 745833-23-2
M.Wt: 404.33
Formula: C19H12F4N4O2

Chemical Name: 6-(N-carbamoyl-2,6-difluoroanilino)-2-(2,4-difluorophenyl)pyridine-3-carboxamide

Canonical SMILES: C1=CC(=C(C=C1)F)N(C2=NC(=C(C=C2)C(=O)N)C3=C(C=C(C3)F)F)C(=O)N)F

Solubility: ≥20.2mg/mL in DMSO

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:

VX-702 is a selective inhibitor of p38α MAPK with IC50 value ranges from 4 nM to 20 nM [1]. P38 mitogen-activated protein kinases (p38 MAPK), also named as MAPK14, are a class of mitogen-activated protein kinases and play an important role in a signaling cascade controlling cellular responses to cytokines and stress [1-3]. VX-702 is a potent p38α MAPK inhibitor and is designed as for greater affinity and greater
selectivity compared with the first reported p38α MAPK inhibitors. When tested with PLTs (platelets), VX-702 caused better maintenance of PLT mitochondrial, functional, structural and metabolic parameters during 7 days storage and restored PLTs properties following an extended interruption of agitation to levels of continuously agitated PLTs [2, 4]. In the isolated perfused rat kidney (IPRK) model, administration of VX-702 at a range of doses between 100 and 600 ng/mL showed linear excretion and the clearance data were consistent with net reabsorption by the kidney. Further, VX-702 was showed not a substrate for renal organic anion and organic cation transport systems [3].

Reference:

Protocol

Cell experiment:

<table>
<thead>
<tr>
<th>Cell lines</th>
<th>blood platelets</th>
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</thead>
<tbody>
<tr>
<td>Preparation method</td>
<td>The solubility of this compound in DMSO is &gt; 20.2 mg/mL. General tips for obtaining a higher concentration: Please warm the tube at 37 ℃ for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20℃ for several months.</td>
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<tr>
<td>Reacting conditions</td>
<td>In an ex vivo blood assay primed with LPS, VX-702 dose-dependently inhibited the production of IL-6, IL-1β and TNFα with the IC50 of 59, 122 and 99 ng/ml, respectively. In gel-filtered platelets were prepared from healthy individuals, the activation was completely or partially inhibited by pre-incubation with 1 μM of VX-702 (IC50 = 4 to 20 nM). VX-702 had no effect on platelet aggregation induced by any of the p38 MAPK agonists, such as thrombin, SFLLRN, AYPGKF and collagen, in the presence or absence of platelet inhibitors, such as aspirin, heparin or apyrase. VX-702 did not directly cause platelet aggregation or induce Ca2+ mobilization, or affect basal aggregation induced by shear stress. VX-702 did not significantly affect platelet function and would not be expected to contribute to an elevated risk of hematological side effects in treated patients.</td>
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Applications
Animal experiment [3]:

Animal models: Mouse collagen-induced arthritis

Dosage form: Oral administration, 0.1 mg/kg, 5 mg/kg, twice daily

Applications: VX-702 (0.1 mg/kg twice daily) was equivalent to methotrexate (a commonly used disease modifying antirheumatic drug [DMARD]; also at 0.1 mg/kg) in mouse collagen-induced arthritis. VX-702 (5 mg/kg, twice daily) was found to be equivalent to prednisolone (10 mg/kg, once daily) in the same model, as measured by the percentage inhibition of wrist joint erosion and an inflammation score. Male Sprague Dawley rats with myocardial damage after ischemia-reperfusion injury were randomized to receive either vehicle or VX-702 (5 or 50 mg/kg). The results suggested that phosphor MK2 was markedly increased in the ischemic zone tissue compared with the non-ischemic zone tissue in the vehicle group. This effect was dose-dependently reduced in the VX-702 groups. VX-702 selectively inhibited activation of p38 MAPK after ischemia, with no effects on ERKs and JNKs. The MI/AAR ratio was significantly reduced in the 50-mg/kg group compared with the other two groups. Oral administration of VX-702 reduced myocardial damage after ischemia-reperfusion injury.

Other notes: Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

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. Short term 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.