**Product Data Sheet**

### Chemical Properties

**Product Name:** Cobimetinib

**Cas No.:** 934660-93-2

**M.Wt:** 531.31

**Formula:** C21H21F3IN3O2

**Synonyms:** GDC-0973; XL-518; GDC0973; XL518

**Chemical Name:** [3,4-difluoro-2-(2-fluoro-4-idoanilino)phenyl]-[3-hydroxy-3-[(2S)-3-(2-fluoro-4-iodoanilino)phenyl]azetidin-1-yl]methanone

**Canonical SMILES:** C1CCNC(C1)C2(CN(C2)C(=O)C3=C(C=C(C=C3)F)F)O

**Solubility:** $\geq 26.55 \text{ mg/mL in DMSO}$

**Storage:** Store at $-20^\circ C$

**General tips:** For obtaining a higher solubility, please warm the tube at $37^\circ C$ and shake it in the ultrasonic bath for a while. Stock solution can be stored below $-20^\circ C$ 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:** MEK1/2

**Description:**

Cobimetinib is a selective inhibitor of mitogen-activated protein kinase kinase (MEK) with IC50 value of 0.9 nM [1].

MEK is a kinase enzyme which selectively phosphorylates Ser/Thr and Tyr residues and involved in the mitogen-activated protein kinase (MAPK) signaling pathways that play an important role in
regulation of cell proliferation, survival, differentiation, motility and angiogenesis [2].

In a KRAS G13D and B-RAF G464V mutant MDA-MB-231T breast adenocarcinoma cells, Cobimetinib inhibited MEK with IC50 value of 0.2 nM [1]. In pharmacokinetic-pharmacodynamic (PK-PD) model, Cobimetinib showed a sustained tumor pharmacodynamic response due to longer residence in tumor than in plasma [3].

In WM-266-4 xenograft mice, Cobimetinib decreased %pERK in tumor with IC50 values of 0.78 (WM-266-4) and 0.52 mM. Also, Cobimetinib (3.89 mM) increased IC50 value in WM-266-4 mice. In A375 xenograft mice, Cobimetinib (0.3-30 mg/kg) showed antitumor efficacy in a dose-dependent way. Cobimetinib is currently in phase I clinical trials as a potential antitumor agent [3].

Reference:

Protocol

Cell experiment:

Cell lines  
KRAS G13D and B-RAF G464V mutant MDA-MB-231T breast adenocarcinoma cell lines

Preparation method  
The solubility of this compound in DMSO is >26.6 mg/mL. General tips for obtaining a higher concentration: Please warm the tube at 37°C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Reacting conditions

Applications  
In the biochemical activity c-Raf/MEK1/ERK study, cobimetinib inhibited MEK1 activity with a IC50 value of 0.9 nM. Additionally, in MDA-MB-231T breast adenocarcinoma cells with KRAS G13D and B-RAF G464V mutant, cobimetinib was found to be able to inhibit MEK with the IC50 value of 0.2 nM.

Animal experiment [3]:

Animal models  
MDA-MB-231T mouse xenograft model
<table>
<thead>
<tr>
<th>Dosage form</th>
<th>0.3-30 mg/kg, oral, qd</th>
</tr>
</thead>
<tbody>
<tr>
<td>Applications</td>
<td>In an MDA-MB-231T efficacy study, cobimetinib demonstrated tumor growth inhibition values of 60 and 93% at 1 and 3 mg/kg, respectively, and statistically significant tumor regression was observed at higher doses. Overall, predicted ED50 and ED90 values were 0.6 and around 3 mg/kg/day, respectively, in the latter case corresponding to peak circulating plasma levels in the range of 130 nM.</td>
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<tr>
<td>Other notes</td>
<td>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.</td>
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</table>

**Reference:**

**Product Citations**


**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.
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