Dabrafenib Mesylate

Cat. No.: HY-14660A
CAS No.: 1195768-06-9
Molecular Formula: C₂₄H₂₄F₃N₅O₅S₃
Molecular Weight: 615.67
Target: Raf
Pathway: MAPK/ERK Pathway
Storage: Powder
-20°C 3 years
4°C 2 years
In solvent
-80°C 6 months
-20°C 1 month

SOLVENT & SOLUBILITY

In Vitro: DMSO: ≥ 36 mg/mL (58.47 mM)

<table>
<thead>
<tr>
<th>Solvent Concentration</th>
<th>1 mg Mass</th>
<th>5 mg Mass</th>
<th>10 mg Mass</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mM</td>
<td>1.6242 mL</td>
<td>8.1212 mL</td>
<td>16.2425 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td>0.3248 mL</td>
<td>1.6242 mL</td>
<td>3.2485 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.1624 mL</td>
<td>0.8121 mL</td>
<td>1.6242 mL</td>
</tr>
</tbody>
</table>

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description: Dabrafenib Mesylate is a potent and selective Raf kinase inhibitor with IC₅₀s of 0.6 and 5.0 nM for RafV₆₀₀E and c-Raf, respectively.

IC₅₀ & Target

<table>
<thead>
<tr>
<th>IC₅₀ &amp; Target</th>
<th>BRafV₆₀₀E</th>
<th>CRAF</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.6 nM (IC₅₀)</td>
<td>5 nM (IC₅₀)</td>
<td></td>
</tr>
</tbody>
</table>

In Vitro: Dabrafenib (GSK2118436, 1 μM) with 0.01 μM GSK1120212 inhibits more than 90% of cell growth in the NRAS mutant clones. GSK2118436 is sufficient to reduce S6P phosphorylation in A375[1]. Dabrafenib suppresses the PolyP-mediated vascular barrier permeability, upregulation of inflammatory biomarkers, adhesion/migration of leukocytes, and activation and/or production of nuclear factor-κB, tumor necrosis factor-α, and interleukin-6[2]. Dabrafenib inhibits the release of HMGB1 and downregulates HMGB1-dependent inflammatory responses by enhancing the expressions of cell adhesion molecules (CAMs) in human endothelial cells[3].
**In Vivo**

Dabrafenib-treated females have mostly immature reproductive tracts with no evidence of ovulation, similar to age-matched controls; however, DAB-treated females have keratinized and histologically open vaginas[^5].

**PROTOCOL**

**Cell Assay[^1]**

For longer term proliferation assays, cells are plated and treated with compound or combination of compounds in RPMI-1640 containing 10% FBS for 12 days. Compound treatments are replaced at least once during the assay. After 12 days, cells are stained with 0.5% methylene blue in 50% ethanol. Images are captured using flatbed scanner.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

**Animal Administration[^5]**

The rat pups selected as the test system are derived from 26 10-week-old, time-mated, virus-antibody-free SD (Crl:CD[SD]) female rats. Mated females are observed for natural deliveries from Day 20 to 23 pc (day parturition completed is designated PND 0). Litter examinations are conducted when parturition is complete, on PNDs 3 and 6, and included gender identification, individual pup weights, and external morphologic examinations. Parturient dams and their litters are selected for study based on clinical signs and body weights, and selected dams and their litters are randomized into study groups based on clinical observations and PND 3 litter mean body weights. On PND 3 or 4, litters are culled to four males and five females, with minimal fostering only when necessary to obtain the desired sex ratio, such that natural litters are maintained as much as possible. Records are kept of fostered pups of original and foster dams. All pups are identified by paw tattoo. To the extent possible, nonlittermates are assigned to subsets. DAB is formulated as a suspension in vehicle, 0.5% hydroxypropylmethylcellulose K15M, and 0.1% (v/v) Tween80 in purified water, and is given to juvenile male and female rats orally by gavage at a dose volume of 5 ml/kg, based on daily body weight.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

**CUSTOMER VALIDATION**

- **Science.** 2017 Dec 1;358(6367). pii: eaan4368.
- **Mol Ther Oncolytics.** 2019 Feb 5;12:235-245.

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**REFERENCES**


