Deforolimus (Ridaforolimus) Datasheet

**Technical Data**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular Weight (MW)</td>
<td>990.21</td>
</tr>
<tr>
<td>Formula</td>
<td>C₅₃H₆₄NO₁₄P</td>
</tr>
<tr>
<td>CAS No.</td>
<td>572924-54-0, 697252-87-2</td>
</tr>
<tr>
<td>Synonyms</td>
<td>AP23573, MK-8869</td>
</tr>
<tr>
<td><strong>Solubility (25°C)</strong></td>
<td></td>
</tr>
<tr>
<td>DMSO</td>
<td>198 mg/mL</td>
</tr>
<tr>
<td>Water</td>
<td>&lt;1 mg/mL</td>
</tr>
<tr>
<td>Ethanol</td>
<td>&lt;1 mg/mL</td>
</tr>
<tr>
<td><strong>Storage</strong></td>
<td></td>
</tr>
<tr>
<td>Powder</td>
<td>2 years, -20°C</td>
</tr>
<tr>
<td>in DMSO</td>
<td>2 weeks, 4°C in DMSO</td>
</tr>
<tr>
<td>Powder</td>
<td>6 months, -80°C in DMSO</td>
</tr>
</tbody>
</table>

**Biological Activity**

**In vitro**

Treatment of HT-1080 cells with Deforolimus induces a dose-dependent inhibition of phosphorylation of both S6 and 4E-BP1, with IC50 of 0.2 nM and 5.6 nM respectively, and leads to a decrease in cell size, an increase in the proportion of cells in the G1 phase of the cell cycle, and inhibition of glucose uptake. Deforolimus displays significant antiproliferative activity to a broad panel of cell lines with EC50 of 0.2-2.3 nM. Deforolimus potently and selectively inhibits VEGF production in a dose-dependent manner. [1] Deforolimus treatment significantly induces growth suppression in human NSCLC cell lines with IC50 values of 2.45-8.83 nM, with the exception of H157 with IC50 of >20 nM. Deforolimus treatment (2.8-5.9 nM) significantly dephosphorylates p70S6KThr389 in A499, H1703 and H157 cells, except H1666 that may express a resistant variant of mTORC1, and causes increased phosphorylation of pAKTThr473 and p4E-BP1Thr37/46 in A549 and H1703 cells. Deforolimus in combination with the MEK inhibitors, CI-1040 or PD0325901 exhibits dose-dependent synergism in lung cancer cell lines, which is associated with the suppression of proliferation rather than enhancement of cell death, involving the inhibition of ribosomal biogenesis by 40% within 24 hours and a decreased polyeclosomal ratio. [2]

**In vivo**

Administration of Deforolimus exerts significant antitumor effects in mice bearing PC-3 (prostate), HCT-116 (colon), MCF7 (breast), PANC-1 (pancreas) or A549 (lung) xenografts in a dose-dependent manner, and inhibits mTOR signaling in the SK-LMS-1 xenograft model associated with inhibition of tumor growth. [1]

**Clinical Trials**

**Features**

**Protocol (Only for Reference)**

**Kinase Assay:** [1]

**Cell based target inhibition**

HT-1080 cells are treated with increasing concentrations of Deforolimus (0-100 nM) for 2 hours, prior to harvest. Cellular lysates are extracted in denaturing lysis buffer, resolved on SDS-PAGE and transferred to PVDF membranes. After blocking, membranes are incubated with primary antibodies for 1 hour, followed by appropriate HRP-conjugated secondary antibodies for 1 hour at room temperature. Immunoreactive proteins are detected using enhanced chemiluminescence and autoradiography performed by exposure to X-ray film. IC50 is determined from the inhibition of levels of phosphorylated ribosomal protein S6 (p-S6) and 4E-BP1 (p-4E-BP1).

**Cell Assay:** [2]

**Cell Lines**

Colo205, H1755, H1395, H1666, A549, H157, and H1703 cells

**Concentrations**

Dissolved in ethanol, final concentrations ~ 1 μM

**Incubation Time**

72-120 hours

**Methods**

Cells are seeded at 2.3 × 10⁴/mL, and serial dilutions of Deforolimus are added after 2 hours, for at least three cell doublings (72-120 hours). Deforolimus effects are measured using the CellTiter 96 Aqueous nonradioactive cell proliferation assay and Sulforhodamine B assays. For Deforolimus, growth effects are described as IC30 because rapamycin and its derivatives do not significantly impede cell proliferation.

**Animal Study:** [1]

**Animal Models**

Male and female athymic NC-nu mice with xenografts established by subcutaneous implantation of PC-3, A549, HCT-116, MCF7, PANC-1 and SK-LMS-1 tumors

**Formulation**

Dissolved in ethanol, and diluted in a vehicle of 4% ethanol, 5% Tween 80, and 5% propylene glycol

**Doses**

~10 mg/kg

**Administration**

Intraperitoneally
References

Customer Reviews

Data independently produced by Dr Neal M. Davies of Washington State University,
Deforolimus (Ridaforolimus) purchased from Selleck
Concentration-time profile in rat serum following administration of deforolimus formulations (10mg/kg) intravenously to rats (mean ± SEM)

Data independently produced by Dr Zhang of Tianjin Medical University,
Deforolimus (Ridaforolimus) purchased from Selleck
Breast cancer cells were pretreated with 100ng/ml EGF for 15 min and then treated with the indicated concentrations of Deforolimus for 24 hours.

PLEASE KEEP THE PRODUCT UNDER -20°C FOR LONG-TERM STORAGE.

NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE

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