

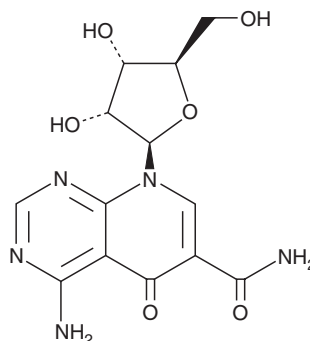
PRODUCT INFORMATION



API-1

Item No. 22081

CAS Registry No.: 36707-00-3
Formal Name: 4-amino-5,8-dihydro-5-oxo-8- β -D-ribofuranosyl-pyrido[2,3-d]pyrimidine-6-carboxamide
Synonym: NSC 177223
MF: C₁₃H₁₅N₅O₆
FW: 337.3
Purity: \geq 98%
UV/Vis.: λ_{max} : 275, 302 nm
Supplied as: A crystalline solid
Storage: -20°C
Stability: \geq 4 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

API-1 is supplied as a crystalline solid. A stock solution may be made by dissolving the API-1 in the solvent of choice. API-1 is soluble in DMSO, which should be purged with an inert gas. The solubility of API-1 in DMSO is approximately 2 mg/ml. API-1 is also slightly soluble in dimethyl formamide.

Description

API-1 is an inhibitor of Akt that reduces the level of phosphorylated Akt ($IC_{50} = \sim 0.8 \mu\text{M}$ in OVCAR3 cells) by binding to Akt and blocking its translocation to the cell membrane.¹ It reduces cell proliferation in various cancer cell lines, induces apoptosis, and, at a dose of 10 mg/kg per day, decreases tumor growth in a mouse xenograft model. API-1 inhibition of Akt leads to proteasomal degradation of the downstream mediator Mcl-1.² Likely independent of Akt binding, API-1 inhibits cell growth ($IC_{50}s = 2-5 \mu\text{M}$) and induces apoptosis in non-small cell lung and head and neck squamous cancer (NSCLC and HNSCC) cell lines with concomitant increases in caspase-3, -8, and -9 cleavage.³ It reduces the levels of cellular FLICE-inhibitory protein (c-FLIP), an important regulator of apoptosis, through ubiquitin- and proteasome-mediated degradation. It also has a synergistic effect on apoptosis in combination with TRAIL/APO-2L.

The information regarding the reduction in phosphorylated Akt levels, IC_{50} value, translocation, cell proliferation, and xenograft tumor growth was drawn from a paper that has been retracted; however, the information specified in the retraction statement has not been included.¹

References

1. Kim, D., Sun, M., He, L., *et al.* A small molecule inhibits Akt through direct binding to Akt and preventing Akt membrane translocation. *J. Biol. Chem.* **285**(11), 8383-8394 (2010).
2. Ren, H., Koo, J., Guan, B., *et al.* The E3 ubiquitin ligases β -TrCP and FBXW7 cooperatively mediates GSK3-dependent Mcl-1 degradation induced by the Akt inhibitor API-1, resulting in apoptosis. *Mol. Cancer* **12**(1), 146 (2013).
3. Li, B., Ren, H., Yue, P., *et al.* The novel Akt inhibitor API-1 induces c-FLIP degradation and synergizes with TRAIL to augment apoptosis independent of Akt inhibition. *Cancer Prev. Res. (Phila)*. **5**(4), 612-620 (2012).

WARNING

THIS PRODUCT IS FOR RESEARCH ONLY - NOT FOR HUMAN OR VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

SAFETY DATA

This material should be considered hazardous until further information becomes available. Do not ingest, inhale, get in eyes, on skin, or on clothing. Wash thoroughly after handling. Before use, the user must review the complete Safety Data Sheet, which has been sent via email to your institution.

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