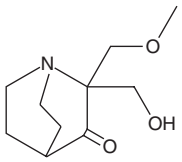
PRODUCT INFORMATION

PRIMA-1^{MET}

Item No. 9000487

CAS Registry No.: 5291-32-7
Formal Name: 2-(hydroxymethyl)-2-(methoxymethyl)-1-azabicyclo[2.2.2]octan-3-one
Synonym: APR 246
MF: $C_{10}H_{17}NO_3$
FW: 199.3
Purity: ≥95%
Supplied as: A crystalline solid
Storage: -20°C
Stability: ≥4 years



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

Laboratory Procedures

PRIMA-1^{MET} is supplied as a crystalline solid. A stock solution may be made by dissolving the PRIMA-1^{MET} in the solvent of choice, which should be purged with an inert gas. PRIMA-1^{MET} is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide. The solubility of PRIMA-1^{MET} in these solvents is approximately 25, 20, and 30 mg/ml, respectively.

Further dilutions of the stock solution into aqueous buffers or isotonic saline should be made prior to performing biological experiments. Ensure that the residual amount of organic solvent is insignificant, since organic solvents may have physiological effects at low concentrations. Organic solvent-free aqueous solutions of PRIMA-1^{MET} can be prepared by directly dissolving the crystalline solid in aqueous buffers. The solubility of PRIMA-1^{MET} in PBS (pH 7.2) is approximately 5 mg/ml. We do not recommend storing the aqueous solution for more than one day.

Description

Mutations in the p53 tumor suppressor are found in many different neoplastic cells. PRIMA-1 (Item No. 63520) is a unique anti-oncogenic substance that re-activates the apoptotic function of mutant p53 *via* conformational modulation of function-specific epitopes.[1,2] PRIMA-1^{MET} is a methylated derivative of PRIMA-1 that restores tumor-suppressor function to mutant p53 and induces cell death in various cancer cell lines.[3] PRIMA-1^{MET} can synergize with chemotherapeutic drugs to induce tumor cell apoptosis.[4] At 25-50 µM, it can also dose-dependently inhibit thioredoxin reductase, a key regulator of cellular redox balance.[5]

References

1. Bykov, V.J.N., Issaeva, N., Shilov, A., *et al.* Restoration of the tumor suppressor function to mutant p53 by a low-molecular-weight compound. *Nat. Med.* **8(3)**, 282-288 (2002).
2. Lane, D.P. and Hupp, T.R. Drug discovery and p53. *Drug Discov. Today* **8(8)**, 347-355 (2003).
3. Aryee, D.N., Niedan, S., Ban, J., *et al.* Variability in functional p53 reactivation by PRIMA-1^{Met}/APR-246 in Ewing sarcoma. *Br. J. Cancer* **109(10)**, 2696-2704 (2013).
4. Bykov, V.J., Zache, N., Stridh, H., *et al.* PRIMA-1^{MET} synergizes with cisplatin to induce tumor cell apoptosis. *Oncogene* **24(21)**, 3484-3491 (2005).
5. Peng, X., Zhang, M.Q., Conserva, F., *et al.* APR-246/PRIMA-1^{MET} inhibits thioredoxin reductase 1 and converts the enzyme to a dedicated NADPH oxidase. *Cell Death Dis.* **4(10)**, e881 (2013).

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