

Product Data Sheet

Product Name: Dapivirine (TMC120)

Cat. No.: GC14452

Chemical Properties

Cas. No. 244767-67-7

Chemical Name 4-[[4-(2,4,6-trimethylanilino)pyrimidin-2-yl]amino]benzonitrile

SMILES CC1=CC(=C(C(=C1)C)NC2=NC(=NC=C2)NC3=CC=C(C=C3)C#N)C

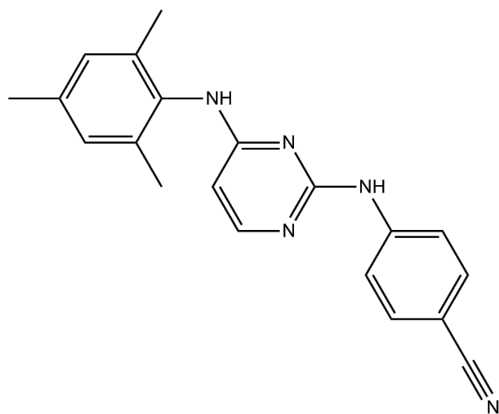
Formula $C_{20}H_{19}N_5$ M.Wt 329.4

Solubility $\geq 13.5\text{mg/mL}$ in DMSO Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice. All other available size: ship with RT, or blue ice upon request.

Structure



Background

Dapivirine (TMC 120, TMC 120 R147681) is a NNRTI for HIV reverse transcriptase with IC_{50} of 24 nM, inhibits a broad panel of HIV-1 isolates from different classes, including a wide range of NNRTI-resistant isolates. IC_{50} value: 24 nM [1]. Target: HIV reverse transcriptase; NNRTIs in vitro: TMC120-R147681 is a diarylpyrimidine with high activity against wild-type and mutant HIV. A 24-h treatment with 1,000 nM UC-781 or 100 nM TMC120-R147681 prevented cell-free HIV infection, whereas 10-fold-higher concentrations blocked cell-associated HIV, TMC120-R147681 apparently blocked

Caution: Product has not been fully validated for medical applications. For research use only.

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infection in the primary cultures at a 10 nM concentration, but secondary cultures revealed that a 100 nM concentration was needed to completely prevent proviral integration [1]. Dapivirine is well tolerated by epithelial cells, T cells, macrophages, and cervical tissue explants with CC50 (50% cytotoxic concentration) of 10 μ M to 20 μ M. Dapivirine potently inhibits infection by both X4- and R5-utilizing HIV-1 strains with IC50 of 1.46 nM in cell-based assays. Dapivirine potently inhibits HIV-1BaL infection of human ectocervical explant tissue in a dose-dependent manner, as evaluated by the reduction in both p24 release and provirus content in cultured explants. Dapivirine inhibits the transmission of virus to permissive T cells in a dose-dependent manner, with an IC50 of 0.1 nM. Dapivirine results in significant inhibition of HIV infection when explants are challenged with virus immediately with IC90 of 100 nM. Dapivirine is also able to inhibit viral dissemination by migratory cells [2]. *in vivo*: Dapivirine-containing gel at vaginal level inhibits cell-associated HIV infection in mice [3]. More placebo (7 of 12) than Dapivirine (3 of 24) gel users has positive vaginal swab results, with white blood cells being the most common finding. Dapivirine (0.05%) results in Cmax of 715 pg/mL, AUC of 15 ng $\times$ h/mL and T1/2 of 89.87 hours in plasma after 14 days post-dose. Mean Dapivirine (0.05%) concentrations in vaginal fluids collected at the introitus, mid vagina, and cervix are in the range of 62-265 μ g/g on day 1 [4].

References:

- [1]. Van Herrewege Y, et al. In vitro evaluation of nonnucleoside reverse transcriptase inhibitors UC-781 and TMC120-R147681 as human immunodeficiency virus microbicides. *Antimicrob Agents Chemother.* 2004 Jan;48(1):337-9.
- [2]. Fletcher P, et al. Inhibition of human immunodeficiency virus type 1 infection by the candidate microbicide dapivirine, a nonnucleoside reverse transcriptase inhibitor. *Antimicrob Agents Chemother.* 2009 Feb;53(2):487-95.
- [3]. Di Fabio S, et al. Inhibition of vaginal transmission of HIV-1 in hu-SCID mice by the non-nucleoside reverse transcriptase inhibitor TMC120 in a gel formulation. *AIDS.* 2003 Jul 25;17(11):1597-604.
- [4]. Nel AM, et al. Pharmacokinetics of 2 dapivirine vaginal microbicide gels and their safety vs. Hydroxyethyl cellulose-based universal placebo gel. *J Acquir Immune Defic Syndr.* 2010 Oct;55(2):161-9.

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