PRODUCT INFORMATION

Dolutegravir-d_5

Item No. 25755

Formal Name: (4R,12aS)-N-((2,4-difluorophenyl-3,5,6-d_3)methyl-d_2)-7-hydroxy-4-methyl-6,8-dioxo-3,4,6,8,12,12a-hexahydro-2H-pyrido[1',2':4,5]pyrazino[2,1-b][1,3]oxazine-9-carboxamide

MF: $C_{20}H_{14}D_5F_2N_3O_5$

FW: 424.4

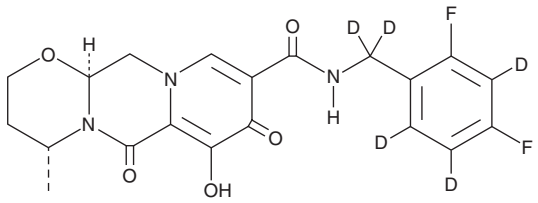
Chemical Purity: ≥95% (Dolutegravir)

Deuterium Incorporation: ≥99% deuterated forms (d_1-d_5); ≤1% d_0

Supplied as: A 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

Dolutegravir-d_5 is intended for use as an internal standard for the quantification of dolutegravir (Item No. 22191) by GC- or LC-MS. The accuracy of the sample weight in this vial is between 5% over and 2% under the amount shown on the vial. If better precision is required, the deuterated standard should be quantitated against a more precisely weighed unlabeled standard by constructing a standard curve of peak intensity ratios (deuterated *versus* unlabeled).

Dolutegravir-d_5 is supplied as a solid. A stock solution may be made by dissolving the dolutegravir-d_5 in the solvent of choice, which should be purged with an inert gas. Dolutegravir-d_5 is soluble in organic solvents such as DMSO and dimethyl formamide. The solubility of dolutegravir-d_5 in these solvents is approximately 2.5 and 5 mg/ml, respectively. Dolutegravir-d_5 is also slightly soluble in ethanol.

Description

Dolutegravir is a potent inhibitor of HIV integrase with an IC_{50} value of 2.7 nM for HIV-1 integrase-catalyzed strand transfer *in vitro*.[1] It inhibits HIV-1 viral replication (EC_{50} = 0.51 nM) in peripheral blood mononuclear cells (PBMCs). The cytotoxic concentration (CC_{50}) values for dolutegravir in unstimulated and stimulated PBMCs are 189 and 52 µM, respectively, resulting in a therapeutic index of at least 9,400. It prevents replication of several HIV-1 strains (EC_{50}s = 0.36-2.1 nM) that are resistant to nucleoside reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), and protease inhibitors and impairs their ability to infect CIP4 cells.[1,2] Formulations containing dolutegravir have been used to treat HIV-1 infection in humans.[3]

References

1. Kobyayshi, M., Yoshinaga, T., Seki, T., *et al.* *In vitro* antiretroviral properties of S/GSK1349572, a next-generation HIV integrase inhibitor. *Antimicrob. Agents and Chemother.* **55(2)**, 813-821 (2011).
2. Hare, S.A., Smith, S.J., Métifiot, M., *et al.* Structural and functional analyses of the second-generation integrase strand transfer inhibitor dolutegravir (S/GSK1349572). *Mol. Pharmacol.* **80(4)**, 565-572 (2011).
3. Venter, W.D.F., Clayden, P., and Serenata, C. The ADVANCE study: A groundbreaking trial to evaluate a candidate universal antiretroviral regimen. *Curr. Opin. HIV AIDS* **12(4)**, 351-354 (2017).

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