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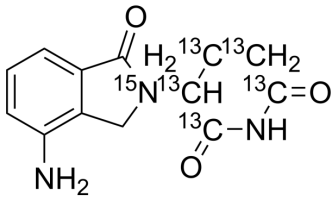
Lenalidomide-$^{13}C_5$,^{15}N

Cat. No.:	HY-A0003S2
Molecular Formula:	$C_8{}^{13}C_5H_{13}N_2{}^{15}NO_3$
Molecular Weight:	265.22
Target:	Ligands for E3 Ligase; Apoptosis; Molecular Glues; Isotope-Labeled Compounds
Pathway:	PROTAC; Apoptosis; Others
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	Lenalidomide-$^{13}C_5$,^{15}N is ^{15}N and ^{13}C labeled Lenalidomide (HY-A0003). Lenalidomide (CC-5013), a derivative of Thalidomide, acts as molecular glue. Lenalidomide is an orally active immunomodulator. Lenalidomide (CC-5013) is a ligand of ubiquitin E3 ligase cereblon (CRBN), and it causes selective ubiquitination and degradation of two lymphoid transcription factors, IKZF1 and IKZF3, by the CRBN-CRL4 ubiquitin ligase. Lenalidomide (CC-5013) specifically inhibits growth of mature B-cell lymphomas, including multiple myeloma, and induces IL-2 release from T cells[1][2].
In Vitro	Stable heavy isotopes of hydrogen, carbon, and other elements have been incorporated into drug molecules, largely as tracers for quantitation during the drug development process. Deuteration has gained attention because of its potential to affect the pharmacokinetic and metabolic profiles of drugs[1]. Lenalidomide is potent in stimulating T cell proliferation and IFN-γ and IL-2 production. Lenalidomide has been shown to inhibit production of pro inflammatory cytokines TNF-α, IL-1, IL-6, IL-12 and elevate the production of anti-inflammatory cytokine IL-10 from human PBMCs. Lenalidomide downregulates the production of IL-6 directly and also by inhibiting multiple myeloma (MM) cells and bone marrow stromal cells (BMSC) interaction, which augments the apoptosis of myeloma cells[3]. Dose-dependent interaction with the CRBN-DDB1 complex is observed with Thalidomide, Lenalidomide and Pomalidomide, with IC_{50} values of ~30 μM, ~3 μM and ~3 μM, respectively, These reduced CRBN expression cells (U266-$CRBN_{60}$ and U266-$CRBN_{75}$) are less responsive than the parental cells to antiproliferative effects Lenalidomide across a dose-response range of 0.01 to 10 μM[4]. Lenalidomide, a thalidomide analog, functions as a molecular glue between the human E3 ubiquitin ligase cereblon and CKIα is shown to induce the ubiquitination and degradation of this kinase, thus presumably killing leukemic cells by p53 activation[6]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	The toxicity of Lenalidomide doses up to 15, 22.5, and 45 mg/kg via IV, IP, and PO routes of administration. Limited by solubility in our PBS dosing vehicle, these maximum achievable Lenalidomide doses are well tolerated with the exception of one mouse death (of four total dosed) at the 15 mg/kg IV dose. Notably, no other toxicities are observed in the study at IV doses of 15 mg/kg (n=3) or 10 mg/kg (n=45) or at any other dose level through IV, IP, and PO routes[5]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

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