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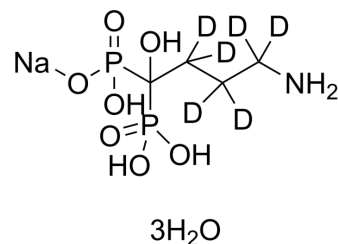
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Alendronate-d₆ sodium hydrate

Cat. No.:	HY-11101S
Molecular Formula:	C ₄ H ₁₂ D ₆ NNaO ₁₀ P ₂
Molecular Weight:	331.16
Target:	Isotope-Labeled Compounds
Pathway:	Others
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	Alendronate-d ₆ sodium hydrate is deuterated labeled Alendronate sodium hydrate (HY-11101). Alendronate sodium hydrate is a farnesyl diphosphate synthase inhibitor with IC ₅₀ of 460 nM.
In Vitro	<p>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].</p> <p>Alendronate, acting directly on osteoclasts, inhibits a rate-limiting step in the cholesterol biosynthesis pathway, essential for osteoclast function^[2]. Alendronate inhibits the isoprenoid biosynthesis pathway and interferes with protein prenylation, as a result of reduced geranylgeranyl diphosphate levels. Alendronate inhibits the incorporation of [³H]mevalonolactone into proteins of 18-25 kDa and into nonsaponifiable lipids, including sterols in osteoclasts^[3]. Alendronate causes a dose-dependent inhibition of [³H]MVA incorporation into sterols and a concomitant increase in incorporation of radiolabel into IPP and DMAPP^[4].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>
In Vivo	<p>Alendronate causes erosions in the rabbit stomach, but not antral ulceration in rats. Alendronate increases the incidence and size of indomethacin-induced antral ulcers. Alendronate also enhances indomethacin-induced gastric damage in the rat, and delays gastric ulcer healing^[5]. Alendronate (0.04-0.1 mg/kg twice weekly or 0.1 mg/kg weekly) partially blocks the establishment of bone metastases by human PC-3 ML cells and results in tumor formation in the peritoneum and other soft tissues. Alendronate pretreatment of mice (0.1 mg/kg twice weekly or weekly) and dosing along with taxol (10-50 mg/kg/day, twice weekly, or weekly) blocks the growth of PC-3 ML tumors in the bone marrow and soft tissues in a statistically significant manner and improves survival rates significantly by 4-5 weeks^[6].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>

REFERENCES

- [1]. Fisher JE, et al. Alendronate mechanism of action: geranylgeraniol, an intermediate in the mevalonate pathway, prevents inhibition of osteoclast formation, bone resorption, and kinase activation in vitro. *Proc Natl Acad Sci U S A.* 1999 Jan 5;96(1):133-8
- [2]. Keller RK, et al. Mechanism of aminobisphosphonate action: characterization of alendronate inhibition of the isoprenoid pathway. *Biochem Biophys Res Commun.* 1999 Dec 20;266(2):560-3.
- [3]. Bergstrom JD, et al. Alendronate is a specific, nanomolar inhibitor of farnesyl diphosphate synthase. *Arch Biochem Biophys.* 2000 Jan 1;373(1):231-41.

[4]. Elliott SN, et al. Alendronate induces gastric injury and delays ulcer healing in rodents. *Life Sci.* 1998;62(1):77-91.

[5]. Stearns ME, et al. Effects of alendronate and taxol on PC-3 ML cell bone metastases in SCID mice. *Invasion Metastasis.* 1996;16(3):116-31.

[6]. Russak EM, et al. Impact of Deuterium Substitution on the Pharmacokinetics of Pharmaceuticals. *Ann Pharmacother.* 2019 Feb;53(2):211-216.

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

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