

Product Data Sheet

Product Name: Palovarotene

Cat. No.: GC14304

Chemical Properties

Cas. No. 410528-02-8

Chemical Name 4-[(E)-2-[5,5,8,8-tetramethyl-3-(pyrazol-1-ylmethyl)-6,7-dihydronaphthalen-2-yl]ethenyl]benzoic acid

SMILES CC1(CCC(C2=C1C=C(C(=C2)C=CC3=CC=C(C(=C3)C(=O)O)CN4C=CC=N4)(C)C)C

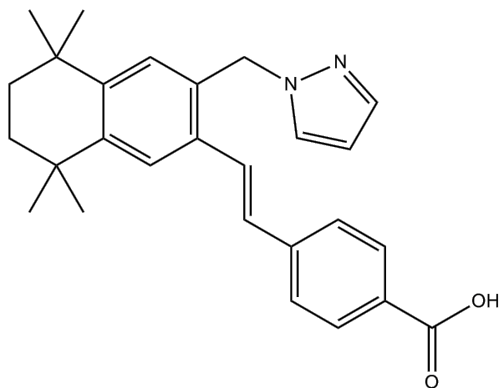
Formula C₂₇H₃₀N₂O₂ M.Wt 414.54

Solubility ≥ 41.5mg/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



Protocol

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

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**Animal
experiment:**

Rats[1] A total of 110 young adult pathogen-free male Sprague Dawley rats (*Rattus norvegicus*; 400-600 g) are used. Rats receive via oral gavage (100 μ L) either Palovarotene (1.0 mg/kg) or vehicle as control (5% DMSO in corn oil) prepared every other day for 14 days, starting at postoperative day 1 (POD-1) or POD-5. Rats are euthanized at indicated time points post-injury for ex vivo end point analysis by micro-computed CT (μ CT), histology and RT-PCR gene transcript expression. Mice[2] One-month-old *Acvr1cR206H/+* mice are provided doxycycline chow for 3 days to induce mutant gene expression globally. Mouse quadriceps muscles are injured by injection with 50 μ L of 10mM cardiotoxin. Beginning on the day of injury, Palovarotene or vehicle (1:4 DMSO in corn oil) is administered daily for 14 days by oral gavage (100 mg/mouse from days 1 to 3 and 15mg/mouse from days 4 to 14) using a 20-gauge gavage needle. Palovarotene solution in DMSO is stored at -20°C under argon and diluted (1:4) with corn oil for administration.

References:

- [1]. Pavey GJ, et al. Targeted stimulation of retinoic acid receptor- γ mitigates the formation of heterotopic ossification in an established blast-related traumatic injury model. *Bone*. 2016 Sep;90:159-67.
- [2]. Chakkalakal SA, et al. Palovarotene Inhibits Heterotopic Ossification and Maintains Limb Mobility and Growth in Mice With the Human ACVR1(R206H) Fibrodysplasia Ossificans Progressiva (FOP) Mutation. *J Bone Miner Res*. 2016 Sep;31(9):1666-75.
- [3]. Lees-Shepard JB, et al. Palovarotene reduces heterotopic ossification in juvenile FOP mice but exhibits pronounced skeletal toxicity. *Elife*. 2018 Sep 18;7. pii: e40814.

Background

Palovarotene is a nuclear retinoic acid receptor γ (RAR- γ) agonist. Palovarotene suppresses post-traumatic chondrogenesis and osteogenesis and mitigated trauma-induced ectopic bone formation. Palovarotene inhibits subcutaneous and intramuscular heterotopic ossification (HO) in mice. Palovarotene is given orally for 14 days at 1 mg/kg/day starting on post-operative day (POD) 1 or POD-5, and HO amount, wound dehiscence and related processes are

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monitored for up to 84 days post injury. Compared to vehicle-control animals, Palovarotene significantly decreases HO by 50 to 60% regardless of when the treatment started and if infection is present[1]. Starting from day 1 of injury, half of the Acvr1cR206H/+ mice are treated with Palovarotene by daily gavage for 14 days and the other half received vehicle as control. Analysis by mCT and 3D image reconstruction at day 14 shows that large HO tissue masses have formed in the targeted leg of Acvr1cR206H/+ mutant mice receiving vehicle, but HO formation is greatly diminished in Palovarotene-treated companions by more than 80% based on bone volume/total volume quantification[2].

Reference:

- [1]. Pavey GJ, et al. Targeted stimulation of retinoic acid receptor- γ mitigates the formation of heterotopic ossification in an established blast-related traumatic injury model. *Bone*. 2016 Sep;90:159-67.
- [2]. Chakkalakal SA, et al. Palovarotene Inhibits Heterotopic Ossification and Maintains Limb Mobility and Growth in Mice With the Human ACVR1(R206H) Fibrodysplasia Ossificans Progressiva (FOP) Mutation. *J Bone Miner Res*. 2016 Sep;31(9):1666-75.
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