

Appeal Letter Guide

Overcoming denials

This sample letter shows what information and supplemental documentation you may include when requesting approval for YORVIPATH® (palopegteriparatide) in the event of a denial.

Important Safety Information

INDICATION AND LIMITATIONS OF USE

YORVIPATH (palopegteriparatide) is indicated for the treatment of hypoparathyroidism in adults.

- YORVIPATH was not studied for acute post-surgical hypoparathyroidism.
- YORVIPATH's titration scheme was only evaluated in adults who first achieved an albumin-corrected serum calcium of at least 7.8 mg/dL using calcium and active vitamin D treatment.

CONTRAINDICATIONS

YORVIPATH is contraindicated in patients with severe hypersensitivity to palopegteriparatide or to any of its excipients. Hypersensitivity reactions, including anaphylaxis, angioedema, and urticaria, have been observed with parathyroid hormone (PTH) analogs.

WARNINGS AND PRECAUTIONS

Risk of Unintended Changes in Serum Calcium Levels Related to Number of Daily Injections

Use only one YORVIPATH injection to achieve the recommended once daily dosage. Using two YORVIPATH injections to achieve the recommended once daily dosage increases the variability of the total delivered dose, which can cause unintended changes in serum calcium levels, including hypercalcemia and hypocalcemia.

Serious Hypercalcemia

Serious events of hypercalcemia requiring hospitalization have been reported with YORVIPATH. The risk is highest when starting or increasing the dose of YORVIPATH but may occur at any time. Measure serum calcium 7 to 10 days after any dose change or if there are signs or symptoms of hypercalcemia, and at a minimum of every 4 to 6 weeks once the maintenance dose is achieved. Treat hypercalcemia if needed. If albumin-corrected serum calcium is greater than 12 mg/dL, withhold YORVIPATH for at least 2-3 days. For less serious hypercalcemia, adjust the dose of YORVIPATH, active vitamin D, and/or calcium supplements.

Please see Important Safety Information throughout and accompanying full Prescribing Information for YORVIPATH.

A

Formulary exception statement

Ensure you state your request for approval based on the reason for denial. You may also amend this statement to request approval for YORVIPATH®, if your patient:

- Was denied due to YORVIPATH not being on formulary
- Was approved for treatment with a different product
- Did not meet their plan’s medical criteria

B

Clinical findings

Ensure that you give a comprehensive profile for your patient with attached documentation. Submitting this letter without the attached clinical findings may result in additional delays or denials.

C

Etiology statement

Establish the cause of your patient’s hypoparathyroidism. An etiology statement for both postsurgical and nonsurgical cases has been provided in this sample.

[In the event of a denial, fill out this sample letter based on your patient’s individual criteria and treatment experience.]

DATE: [Date of Submission]

ATTN: [Appeals Reviewer]
[Payor Name]
[Payor Contact Name if in previous denial letter]
[Payor Address]

RE: [First, Second, External Appeal for Hypoparathyroidism Treatment With YORVIPATH®]

Patient Name and Date of Birth: [Patient Full Name] [DOB]

Member ID and Group Number: [Insurance ID #] [Insurance group #]

Therapy	Date of Denial	Reference Number	ICD-10	Diagnosis
YORVIPATH® (palopegteriparatide)	[Denial Date]	[Reference Number]	[E20.9, E89.2]	Hypoparathyroidism

To Whom It May Concern:

I am writing this on behalf of my patient, [Patient Full Name, DOB], to request approval for the treatment of hypoparathyroidism with YORVIPATH. I have received your letter dated [Denial Letter Date] denying coverage of YORVIPATH.

[Patient Full Name] is a [Patient Age]-year-old [Male/Female] who was diagnosed with hypoparathyroidism on [Diagnosis Date]. In my independent medical judgment, [Patient Full Name] meets medical necessity.

Per the denial letter, YORVIPATH is not on formulary for the treatment of hypoparathyroidism. As a medical expert in the field of endocrinology and hypoparathyroidism, I have determined that [Patient Full Name] has hypoparathyroidism, and treatment with YORVIPATH is medically necessary. I am requesting a **formulary exception** for YORVIPATH based on the rationale included in this letter.

Please see the diagnosis criteria and attached clinicals:

PTH Level: [Result; Date]
24-hour Urine Calcium: [Result; Date]
Serum Calcium Level: [Result; Date]
Serum 25(OH) Vitamin D: [Result; Date]
Daily Calcium Supplement Dose: [___ mg elemental calcium/day; Date]
Daily Active Vitamin D (Calcitriol) Dose: [___ mcg/day; Date]
Date of Surgery (if applicable): [Date]

[Hypoparathyroidism is an endocrine disease caused by insufficient levels of PTH.1 It most often occurs after thyroid surgery, but may also occur following parathyroidectomy or other neck surgeries.2]
[Hypoparathyroidism has a nonsurgical origin in approximately 25% of patients with the disease, often due to genetic mutations or autoimmune disease.3]

Treatment for hypoparathyroidism is medically necessary for [Patient Full Name]. On behalf of the patient, I am requesting approval for use and subsequent payment for the treatment of hypoparathyroidism with YORVIPATH.

- YORVIPATH is indicated for the treatment of hypoparathyroidism in adults. YORVIPATH was not studied for acute post-surgical hypoparathyroidism. YORVIPATH’s titration scheme was only evaluated in adults who first achieved an albumin-corrected serum calcium of at least 7.8 mg/dL using calcium and active vitamin D treatment4

Important Safety Information

WARNINGS AND PRECAUTIONS (cont’d)

Serious Hypocalcemia

Serious events of hypocalcemia have been observed with PTH products, including YORVIPATH. The risk is highest when YORVIPATH is abruptly discontinued, but may occur at any time, even in patients who have been on stable doses of YORVIPATH. Measure serum calcium 7 to 10 days after any dose change or if there are signs or symptoms of hypocalcemia, and at a minimum of every 4 to 6 weeks once the maintenance dosage is achieved. Treat hypocalcemia if needed, and adjust the dose of YORVIPATH, active vitamin D, and/or calcium supplements if hypocalcemia occurs.

Potential Risk of Osteosarcoma

YORVIPATH is a PTH analog. An increased incidence of osteosarcoma (a malignant bone tumor) has been reported in male and female rats treated with PTH analogs, including teriparatide. Osteosarcoma occurrence in rats is dependent on teriparatide or PTH dose and treatment duration. Osteosarcoma has been reported in patients treated with teriparatide in the postmarketing setting; however, an increased risk of osteosarcoma has not been observed in observational studies in humans. There are limited data assessing the risk of osteosarcoma beyond 2 years of teriparatide use.

D

YORVIPATH data

You may include clinical trial results as part of your rationale for prescribing YORVIPATH.

• YORVIPATH® is a prodrug of PTH(1-34) designed to deliver continuous exposure to active PTH over 24 hours.⁴ In the phase 3 clinical trial, 68.9% (42 of 61) of YORVIPATH-treated patients met the efficacy assessment at week 26 compared with 4.8% (1 of 21) of patients in the placebo group (treatment difference: 64.2%; 95% CI: 49.5% to 78.8%)⁴

– The efficacy assessment of the phase 3 clinical trial was the proportion of patients who achieved all of the following at week 26: albumin-corrected serum calcium levels in the normal range (8.3 to 10.6 mg/dL); independence from conventional therapy (defined as requiring no active vitamin D and ≤ 600 mg/day of calcium supplementation, including no use of PRN doses) since week 22; no increase in study drug dose since week 22; no missing active vitamin D and calcium data since week 22; and study drug dose was ≤ 30 mcg/day during the entire 26-week treatment period⁴

• When allowing for dose up-titration to a maximum dose of 30 mcg/day in the open-label extension, 64% (39 out of 61) and 66% (40 out of 61) of YORVIPATH-treated patients were able to maintain normal albumin-corrected serum calcium and independence from active vitamin D and therapeutic doses of calcium at week 52 and week 78, respectively⁴

[Insert other clinical rationale in support of YORVIPATH treatment for your patient]

Based on the information provided above, I am requesting approval of YORVIPATH for [Patient Full Name]. Please do not hesitate to contact me if you require any additional information. I look forward to receiving your positive response to this letter at your earliest convenience. Thank you for your prompt attention to this matter.

Sincerely,

[Prescriber Full Name and credentials]

NPI: [NPI]

Address: [Prescriber Address]

City, State, Zip Code: [Prescriber City, State, Zip Code]

Phone: [Prescriber Phone Number]

Fax: [Prescriber Fax Number]

E

Patient-specific support for YORVIPATH

This is a space where you may provide additional support for why you think YORVIPATH is the right treatment for your patient. It is important to highlight your patient's clinical needs and how YORVIPATH may help.

CI = confidence interval; PRN = as needed; PTH = parathyroid hormone.

References: 1. Shoback DM, Bilezikian JP, Costa AG, et al. Presentation of hypoparathyroidism: etiologies and clinical features. *J Clin Endocrinol Metab.* 2016;101(6):2300-2312. doi:10.1210/je.2016-3909 2. Bollerslev J, Rejnmark L, Marcocci C, et al; European Society of Endocrinology. European Society of Endocrinology Clinical Guideline: treatment of chronic hypoparathyroidism in adults. *Eur J Endocrinol.* 2015;173(2):G1-G20. doi:10.1530/EJE-15-0629 3. Khan AA, Guyatt G, Ali DS, et al. Management of hypoparathyroidism. *J Bone Miner Res.* 2022;37(12):2663-2677. doi:10.1002/jbm.b.4716 4. Yorvipath. Prescribing information. Ascendis Pharma, Inc.; 2024.

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Important Safety Information

WARNINGS AND PRECAUTIONS (cont'd)

YORVIPATH is not recommended in patients who are at increased risk of osteosarcoma, such as patients with:

- Open epiphyses. YORVIPATH is not approved in pediatric patients.
- Metabolic bone diseases other than hypoparathyroidism, including Paget's disease of bone.
- Unexplained elevations of alkaline phosphatase.
- Bone metastases or a history of skeletal malignancies.
- History of external beam or implant radiation therapy involving the skeleton.
- Hereditary disorders predisposing to osteosarcoma.

Instruct patients to promptly report clinical symptoms (e.g., persistent localized pain) and signs (e.g., soft tissue mass tender to palpation) that could be consistent with osteosarcoma.

Orthostatic Hypotension

Orthostatic hypotension has been reported with YORVIPATH. Associated signs and symptoms may include decreased blood pressure, dizziness (including postural dizziness), palpitations, tachycardia, presyncope, or syncope. Such symptoms can be managed by dosing at bedtime, while reclining. YORVIPATH should be administered initially when the patient can sit or lie down due to the potential of orthostatic hypotension.

Please see Important Safety Information throughout and accompanying full Prescribing Information for YORVIPATH.

Important Safety Information

WARNINGS AND PRECAUTIONS (cont'd)

Risk of Digoxin Toxicity with Concomitant Use of Digitalis Compounds

YORVIPATH increases serum calcium, and therefore, concomitant use with digoxin (which has a narrow therapeutic index) may predispose patients to digitalis toxicity if hypercalcemia develops. Digoxin efficacy may be reduced if hypocalcemia is present. When YORVIPATH is used concomitantly with digoxin, measure serum calcium and digoxin levels routinely, and monitor for signs and symptoms of digoxin toxicity. Refer to the digoxin prescribing information for dose adjustments, if needed.

ADVERSE REACTIONS

The most common adverse reactions ($\geq 5\%$) in patients treated with YORVIPATH were injection site reactions (39%), vasodilatory signs and symptoms (28%), headache (21%), diarrhea (10%), back pain (8%), hypercalcemia (8%) and oropharyngeal pain (7%).

DRUG INTERACTIONS

Drugs Affected by Serum Calcium

Digoxin: YORVIPATH increases serum calcium, therefore, concomitant use with digoxin (which has a narrow therapeutic index) may predispose patients to digitalis toxicity if hypercalcemia develops. Digoxin efficacy may be reduced if hypocalcemia is present. When YORVIPATH is used concomitantly with digoxin, measure serum calcium and digoxin levels, and monitor for signs and symptoms of digoxin toxicity. Adjustment of the digoxin and/or YORVIPATH dose may be needed.

Drugs Known to Affect Serum Calcium

Drugs that affect serum calcium may alter the therapeutic response to YORVIPATH. Measure serum calcium more frequently when YORVIPATH is used concomitantly with these drugs, particularly after these drugs are initiated, discontinued, or dose adjusted.

USE IN SPECIFIC POPULATIONS

Pregnancy

Available data from reports of pregnancies in the clinical trials from drug development are insufficient to identify a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. If YORVIPATH is administered during pregnancy, or if a patient becomes pregnant while receiving YORVIPATH, healthcare providers should report YORVIPATH exposure by calling 1-844-442-7236.

Lactation

Monitor infants breastfed by females treated with YORVIPATH for symptoms of hypercalcemia or hypocalcemia. Consider monitoring serum calcium in the breastfed infant.

You are encouraged to report side effects to FDA at (800) FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Ascendis Pharma at 1-844-442-7236.

Please see Important Safety Information throughout and accompanying full Prescribing Information for YORVIPATH.

References: 1. Shoback DM, Bilezikian JP, Costa AG, et al. Presentation of hypoparathyroidism: etiologies and clinical features. *J Clin Endocrinol Metab.* 2016;101(6):2300-2312. doi:10.1210/jc.2015-3909 2. Bollerslev J, Rejnmark L, Marcocci C, et al; European Society of Endocrinology. European Society of Endocrinology Clinical Guideline: treatment of chronic hypoparathyroidism in adults. *Eur J Endocrinol.* 2015;173(2):G1-G20. doi:10.1530/EJE-15-0628 3. Khan AA, Guyatt G, Ali DS, et al. Management of hypoparathyroidism. *J Bone Miner Res.* 2022;37(12):2663-2677. doi:10.1002/jbmr.4716 4. Yorvipath. Prescribing information. Ascendis Pharma, Inc.; 2024.