Scenesse (afamelanotide)

NOTICE

This policy contains information which is clinical in nature. The policy is not medical advice. The information in this policy is used by Wellmark to make determinations whether medical treatment is covered under the terms of a Wellmark member's health benefit plan. Physicians and other health care providers are responsible for medical advice and treatment. If you have specific health care needs, you should consult an appropriate health care professional. If you would like to request an accessible version of this document, please contact customer service at 800-524-9242.

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Scenesse (afamelanotide) is a melanocortin 1 receptor (MC1-R) agonist indicated to increase pain free light exposure in adult patients with a history of phototoxic reactions from erythropoietic protoporphyria (EPP).

POLICY

Documentation Requirements

Submission of the following information is necessary to initiate the prior authorization review:

A. Initial therapy requests
    1. Documentation of increased level of protoporphyrin in peripheral red blood cells above with laboratory findings measuring metal-free protoporphyrin to be 85% or greater of total erythrocyte protoporphyrin
    2. Documentation confirming symptoms of erythropoietic protoporphyria phototoxicity
B. Continuation of therapy requests
    1. Documentation supporting the clinical benefit of Scenesse therapy

Criteria for Initial Approval

A. Scenesse (afamelanotide) may be considered **medically necessary** for the treatment of erythropoietic protoporphyria in adult members when all the following criteria are met:
   1. Member is 18 years of age or older
   2. Member has biochemically confirmed erythropoietic protoporphyria (e.g. elevated free protoporphyrin in peripheral erythrocytes)
   3. Member has protoporphyrin above the lab reference range in peripheral red blood cells
   4. Member has a history of phototoxic reactions despite sun and light protection measures
   5. Member will continue to maintain sun and light protection measures during treatment to prevent phototoxic reactions
   6. Member does not have any malignant or premalignant skin lesions
   7. Dose does not exceed one 16-mg implant every 2 months

Approval will be for **6 months**

Continuation of Therapy

A. Scenesse (afamelanotide) may be considered **medically necessary** for the continued treatment of erythropoietic protoporphyria in adult members when all the following criteria are met:
   1. Member continues to meet the relevant criteria identified in Criteria for Initial Approval
   2. Member has experienced a positive clinical response to therapy as evidenced by an improvement in or stabilization of disease symptoms and progression (i.e., increase in pain free time during light exposure, decrease in the number of phototoxic reactions, or continued maintenance of these measures)

Approval will be for **12 months**

Dosage and Administration

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

CLINICAL RATIONALE

Scenesse (afamelanotide) is a synthetic tridecapeptide and a structural analog of α-melanocyte stimulating hormone. Afamelanotide is a melanocortin receptor agonist and binds predominantly to the melanocortin 1 receptor (MC1-R), which leads to an increase in production of photoprotective eumelanin in the skin independently of exposure to sunlight or artificial ultraviolet light sources. Scenesse (afamelanotide) is the first melanocyte stimulating hormone agonist approved by the FDA and is the first agent indicated to increase pain free light exposure in adult patients with a history of phototoxic reactions from EPP. Scenesse (afamelanotide) provides an adjunctive treatment option to sun and light protection, which are the mainstays of treatment for EPP.

Scenesse (afamelanotide) should be administered by a healthcare professional proficient in the subcutaneous implantation procedure who has completed the training program provided by the manufacturer prior to administration of the Scenesse (afamelanotide) implant. A single Scenesse (afamelanotide) 16 mg implant is inserted subcutaneously above the anterior supra-iliac crest every 2 months. Sun and light protection measures should be maintained during treatment with Scenesse (afamelanotide) to prevent phototoxic reactions related to EPP.

Approaches to Treatment

EPP is a rare genetic disorder and inborn error of metabolism that usually manifests in infancy or early childhood as severe, painful photosensitivity. EPP results from a deficiency of ferrochelatase (FECH), the last enzyme in the heme biosynthetic pathway that inserts iron into protoporphyrin to form heme. Reduced FECH activity leads to an accumulation of mostly metal-free phototoxic protoporphyrin IX. Protoporphyrin

is released from the bone marrow into the circulation and taken up by the liver and vascular endothelium. Sun or visible light exposure, particularly in the visible blue-violet range, activates the protoporphyrin molecules, triggering singlet oxygen free-radical reactions that result in tissue and vessel damage. Symptoms develop in most patients within 30 minutes of sun exposure. Patients usually experience prodromal symptoms (e.g., itching and tingling) that can then progress to a severe burning pain, typically on the hands and face, often followed by erythema and edema. Possible complications of EPP include cholelithiasis and liver damage, which can result from accumulated hepatic protoporphyrin; severe liver disease, though rare, can occur in up to 5% of cases. Prevalence of EPP in the United States is not well characterized; worldwide prevalence estimates range from 1 in 75,000 individuals in the Netherlands to 1 in 200,000 individuals in the United Kingdom. EPP occurs across races and ethnic groups but is rare among blacks.

Biochemical diagnosis of EPP is established in patients with significantly increased total erythrocyte protoporphyrin with a predominance (i.e., 85% to 100%) of metal-free protoporphyrin. In X-linked protoporphyria (XLP), a less common condition with a similar phenotype, total erythrocyte protoporphyrin is also elevated but with a lower fraction of metal-free protoporphyrin (i.e., 50% to 85% of the total). XLP also results from mutations in a different gene, the erythroid-specific aminolevulinic acid synthase (ALAS2) gene. Diagnosis of EPP can be confirmed by identification of biallelic mutations in the FECH gene.

The mainstays of therapy for EPP are sun/light avoidance (e.g., staying inside, seeking shade or only going out in early mornings and evenings) and photoprotection (e.g., protective clothing, sunglasses, physical sunscreens that protect against visible and violet light, tinting in car/home windows to absorb violet light). Phototoxic reactions can be severe, and the neuropathic pain triggered by activation of phototoxic protoporphyrin can be excruciating and does not respond to analgesics. Skin should be protected from sunlight with sunscreens containing zinc oxide or titanium dioxide, as conventional sunscreens are less effective due to a lack of protection against visible light. Sunlight avoidance affects patients' quality of life and often necessitates vitamin D supplementation. Other treatments for EPP (e.g., beta carotene, N-acetyl cysteine, vitamin C) have been described in the literature but lack clear supportive clinical data. Scenesse (afamelanotide) is the first FDA-approved treatment for adults with EPP and was found to increase the amount of pain-free time patients spent in direct sunlight compared with placebo. Because treatment with Scenesse (afamelanotide) does not influence the high levels of protoporphyrin that can lead to liver damage, treatment with Scenesse (afamelanotide) is unlikely to have any effect on liver disease complications. Liver transplant may be required in patients with end-stage liver disease secondary to protoporphyrin-related liver damage. Bone marrow transplant has been reported as a potential curative option for patients with EPP, but data are limited.

Efficacy

The efficacy of Scenesse was demonstrated in two placebo-controlled Phase 3 clinical trials designed to assess exposure to direct sunlight on days with no phototoxic pain in patients with EPP. The first study enrolled 93 patients, and the second study enrolled 74 patients. For the first study, the median total number of hours over 180 days spent in direct sunlight between 10 am and 6 pm on days with no pain was 64.1 hours for patients receiving Scenesse and 40.5 hours for patients receiving vehicle. For the second study, the median total number of hours over 270 days spent outdoors between 10 am and 3 pm on days with no pain for which "most of the day" was spent in direct sunlight was 6.0 hours for patients in the Scenesse group and 0.75 hours for patients in the vehicle group. Limitations included the partial unblinding of patients due to increased skin pigmentation in patients who received Scenesse and the finding of continued sun exposure avoidance (as evidenced by mean total hours in direct sunlight) due to fear of painful reactions in patients in both groups who did not develop increased pigmentation. Differences between trials with respect to pain-free sunlight exposure at baseline and during the trial were thought to be due in part to higher latitudes of European centers vs. centers in the United States. Differences between the two trials with respect to end points, the number of study drug doses administered, trial duration, recruitment periods, and data collected from the diaries may have also contributed to the differences in magnitude seen in the results

between the two trials. Photoprovocation testing on the dorsum of the hand and lower back was performed in 21 patients in the U.S. trial, with patients in the Scenesse group having a significantly higher tolerance to light at day 90 and day 120 based on the change from baseline in minimum symptom dose calculated using the irradiation output and time to first symptoms such as tingling or burning in the exposed areas ($p \leq 0.01$ and $p \leq 0.045$, respectively).

In conclusion, Scenesse was superior to placebo in increasing the duration of time patients spent directly exposed to sunlight without pain, with no major safety concerns. The subjective nature of the assessments and partial unblinding of patients due to visible skin pigmentation changes are limitations.

Safety

In clinical trials, most adverse events were mild to moderate in severity with the most common (occurring in ≥ 3% of patients) being implant site reaction, nausea, oropharyngeal pain, cough, fatigue, skin hyperpigmentation, dizziness, melanocytic nevus, and respiratory tract infection. Scenesse (afamelanotide) may lead to generalized increased skin pigmentation and darkening of pre-existing nevi and ephelides because of its pharmacologic effect. A full body skin examination twice yearly is recommended to monitor pre-existing and new skin pigmentary lesions.

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.

- J7352 - Afamelanotide implant, 1 mg

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POLICY HISTORY

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