09-J4000-38

Original Effective Date: 12/15/22

Reviewed: 11/12/25

Revised: 12/15/25

Subject: Afamelanotide (Scenesse) implant

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Erythropoietic protoporphyria (EPP) is a rare inherited metabolic disorder that results from one of two gene mutations: (1) the ferrochelatase (*FECH*) gene (90% of phenotypic cases), which causes a deficiency in activity of the FECH enzyme, or (2) delta-aminolevulinic acid synthase-2 (*ALAS2*) gene (10% of phenotypic cases), which results from a gain-of-function of erythroid-specific ALAS2. EPP arising from an *ALAS2* mutation is termed X-linked protoporphyria (XLPP). Both defective enzymes are in the heme biosynthesis pathway and result in increased red blood cell and plasma protoporphyrin IX (PPIX) levels (the photosensitizing precursor of heme). The excess protoporphyrin deposits in the skin or is excreted by the liver into bile. PPIX can be activated by the blue spectrum (400-410 nm, the Soret Band) of visible light; therefore, the major symptom is hypersensitivity of the skin to sunlight and some types of artificial light (e.g., fluorescent lights). Symptom severity varies among patients and clinical symptoms may include pain, burning, erythema, and edema of the exposed skin. The hands, arms, and face are the most commonly affected areas. If present, symptoms typically subside in 12 to 24 hours and heal without significant scarring. Blistering and scarring are characteristic of other types of cutaneous porphyria but are unusual in EPP. Other complications of EPP/XLPP may include hepatotoxicity (e.g., cirrhosis, liver failure) and gallbladder dysfunction (e.g., gallstones) as a result of precipitated protoporphyrin.

The prevalence of EPP is approximately 1 in 75,000 patients and is similar between males and females. EPP/XLPP should be suspected in children and adults with painful cutaneous photosensitivity who experience no blisters or scarring. Gallstones in children should also prompt genetic testing. Diagnosis is confirmed through genetic testing for *FECH* or *ALAS2* gene mutations and increased red blood cell and plasma protoporphyrin levels. Red blood cell protoporphyrin should also be fractionated to determine the proportions of metal-free and zinc protoporphyrin. In EPP, the proportion of red blood cell protoporphyrin that is metal-free is almost always greater than 85%. The presence of greater than

15% zinc protoporphyrin suggests XLPP. If measured, plasma coproporphyrin and urinary porphyrin levels are normal. Stool protoporphyrin may be elevated, but coproporphyrin level is normal.

Management of EPP/XLPP involves avoidance of sun exposure through use of protective clothing and opaque sunscreens, and symptomatic treatment includes cold compresses, nonsteroidal anti-inflammatory drugs (NSAIDs), and topical and/or oral corticosteroids. Afamelanotide (Scenesse) is a synthetic tridecapeptide and a structural analog of α-melanocyte stimulating hormone (α-MSH), which is a melanocortin receptor agonist and binds predominantly to MC1-R. Afamelanotide (Scenesse) increases production of eumelanin in the skin independently of exposure to sunlight or artificial UV light sources to provide photoprotection.

Afamelanotide (Scenesse)'s efficacy was evaluated in two published phase III, multicenter, randomized, double-blind, placebo-controlled trials. One was conducted in the European Union (74 patients: 38 treatment arm and 36 placebo arm), and the other in the United States (94 patients: 48 treatment arm and 45 placebo arm). Eligibility criteria included the following: 18 years of age or older, biochemically confirmed erythropoietic protoporphyria, and no clinically significant hepatic or other organ dysfunction, skin cancer, or premalignant lesions or other photodermatoses. Patients were randomized in a 1:1 ratio to receive a subcutaneous implant containing either afamelanotide 16 mg or placebo every 60 days. Patients enrolled in the European Union (EU) study received five total implants over the course of the trial, and those in the United States (US) study received a total of three implants during the trial period. The primary end point was the duration of direct exposure to sunlight without pain between 10 am and 3 pm in the EU trial and 10 am and 6 pm in the US trial. The intensity and duration of pain and exposure to sunlight and shade were recorded daily by the patients in a diary over the 270-day and 180-day trial period, respectively. Pain was scored on an 11-point Likert pain-intensity scale (scores range from 0 to 10; higher scores indicating greater severity). Phototoxic reactions and their durations were defined as pain with a Likert score of 4 or higher occurring in light-exposed skin for one or more consecutive days. Quality of life was assessed with the use of the Erythropoietic Protoporphyria Quality-of-Life (EPP-QOL) questionnaire (scores range from 0 to 100; higher scores indicate higher QOL) and the Dermatology Life Quality Index (scores range from 0 to 30; lower scores indicate improved QOL). The median pain-free time in direct sunlight was 6 hours for afamelanotide and 0.8 hours for placebo (p=0.005) in the EU study and 69.4 hours for afamelanotide and 40.8 hours for placebo (p=0.04) in the US study. The total number of phototoxic reactions was reduced in the EU trial (77 versus 146; p=0.04) but no significant changes were seen in the US trial (46 versus 43 reactions). The EPP-QOL improved in the afamelanotide group in both the EU and US studies; however, the Dermatology Life Quality Index did not change in either study.

The most common adverse reactions (incidence > 2%) associated with afamelanotide (Scenesse) are implant site reactions, nausea, oropharyngeal pain, cough, fatigue, dizziness, skin hyperpigmentation, somnolence, melanocytic nevus, respiratory tract infection, non-acute porphyria, and skin irritation.

POSITION STATEMENT:

The administration of afamelanotide (Scenesse) **meets the definition of medical necessity** when **ALL** of the following are met:

1. Member is 18 years of age or older with a diagnosis of erythropoietic protoporphyria (EPP) or X-linked protoporphyria (XLPP)

2. Member has increased total erythrocyte protoporphyrin levels (i.e., equal to or greater than 300 mcg/dL) and one of the following ("a" or "b"): – Laboratory documentation must be submitted
    a. Genetic test demonstrating a ferrochelatase (FECH) gene mutation or a delta-aminolevulinate synthase-2 (ALAS2) gain-of-function gene mutation
    b. An increased percentage of erythrocyte metal-free protoporphyrin (e.g., generally greater than 85% of the total protoporphyrin) rather than zinc protoporphyrin
3. Member has a history of pain associated with phototoxic reactions (e.g., burning, erythema, edema of the exposed skin) due to EPP/XLPP
4. Member does not have any malignant or premalignant skin lesions (e.g., melanoma, dysplastic nevus syndrome, Bowen's disease, basal cell or squamous cell carcinomas) as evidenced by a baseline full body skin examination
5. The medication is prescribed by, or in consultation with, a hematologist, dermatologist or specialist with expertise in the diagnosis and management of EPP/XLPP
6. The dose does not exceed one 16-mg implant every 2 months
7. The administration is conducted by a healthcare professional who has completed requisite procedural training provided by the product manufacturer

Approval duration: 6 months

Afamelanotide (Scenesse) is considered **experimental or investigational** for any other indications due to insufficient evidence in the peer-reviewed medical literature to support safety, efficacy, and net health outcome.

Continuation of afamelanotide (Scenesse) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. An authorization or reauthorization has been previously approved for afamelanotide (Scenesse) for the prevention of pain associated with phototoxic reactions (e.g., pain, burning, erythema, and edema of the exposed skin) from EPP/XLPP by Florida Blue or another health plan in the past 2 years, **OR** the member has previously met all indication-specific criteria for coverage – Documentation that the member has been treated with afamelanotide (starting on samples is not approvable) within the past 90 days
2. Member has experienced a positive clinical response (i.e., reduction in phototoxic reactions such as pain, burning, erythema, and edema of the exposed skin)
3. Member does not have any malignant or premalignant skin lesions (e.g., melanoma, dysplastic nevus syndrome, Bowen's disease, basal cell or squamous cell carcinomas) as evidenced by a baseline full body skin examination
4. The medication is prescribed by, or in consultation with, a hematologist, dermatologist or specialist with expertise in the diagnosis and management of EPP/XLPP
5. The dose does not exceed one 16-mg implant every 2 months
6. The administration is conducted by a healthcare professional who has completed requisite procedural training provided by the product manufacturer

Approval duration: 1 year

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- Afamelanotide (Scenesse) 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).
- A single 16-mg afamelanotide (Scenesse) implant is inserted subcutaneously by a trained, proficient healthcare professional using an SFM Implantation Cannula or other implantation devices that have been determined by the manufacturer to be suitable for implantation.
- Afamelanotide (Scenesse) may be inserted every 2 months above the anterior supra-iliac crest.
- Patients should contact their healthcare provider if the implant is expelled.
- Patients should monitor the insertion site report any reaction observed to their healthcare provider.
- Patients should maintain sun and light protection measures during treatment to prevent phototoxic reactions related to EPP/XLPP.

Dose Adjustments

- The effect of renal or hepatic impairment on the pharmacokinetics of afamelanotide (Scenesse) is unknown.

Drug Availability

- Afamelanotide (Scenesse) implant, 16 mg, for subcutaneous administration (NDC 73372-0116-1) is supplied in a Type I amber glass vial sealed with a PTFE coated rubber stopper.
- Each vial contains one afamelanotide implant and is packaged individually in a cardboard box.
- Afamelanotide (Scenesse) should be stored in a refrigerator at 2°C – 8°C (36°F-46°F) and protected from light.

PRECAUTIONS:

Boxed Warning

- None

Contraindications

- Known hypersensitivity to afamelanotide (Scenesse) or to any of the excipients

Precautions/Warnings

- **Skin monitoring:** May induce darkening of pre-existing nevi and ephelides due to its pharmacological effect. A regular full body skin examination (twice yearly) is recommended to monitor all nevi and other skin abnormalities.
- Hypersensitivity: Serious hypersensitivity reactions, including anaphylaxis, have been reported. If a serious hypersensitivity reaction occurs, initiate appropriate therapy and remove the afamelanotide (Scenesse) implant if needed. The patient should not receive any further treatment with afamelanotide (Scenesse).

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

J7352	Afamelanotide implant, 1 mg

ICD-10 Diagnosis Codes That Support Medical Necessity

E80.0	Hereditary erythropoietic porphyria

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request

DEFINITIONS:

Bowen's disease - an early form of squamous cell skin cancer that appears as a red, scaly patch; it is sometimes referred to as squamous cell carcinoma in situ.

Dysplastic nevus syndrome - a risk factor for developing cutaneous melanoma; it is also known as atypical mole syndrome.

Erythropoietic protoporphyria - a rare inherited metabolic disorder of the heme biosynthesis pathway that results in increased red blood cell and plasma protoporphyrin levels; it also includes X-linked protoporphyria.

RELATED GUIDELINES:

None

OTHER:

None

REFERENCES:

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3. Langendonk JG, Balwani M, Anderson KE, et al. Afamelanotide for Erythropoietic Protoporphyria. *N Engl J Med*. 2015;373(1):48-59. doi:10.1056/NEJMoa1411481.
4. Micromedex Healthcare Series [Internet Database]. Greenwood Village, CO: Thomson Healthcare. Updated periodically. Accessed 10/27/25.
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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 11/12/25.

GUIDELINE UPDATE INFORMATION:

12/15/22	New Medical Coverage Guideline – Afamelanotide (Scenesse) for the prevention of pain associated with phototoxic reactions from genetically confirmed erythropoietic protoporphyria/ X-linked protoporphyria
1/15/24	Review and revision of the guideline, consisting of revising the position statement to include percentage of metal-free versus zinc protoporphyrin as an alternative to genetic testing and updating the references.
12/15/24	Review and revision of the guideline, consisting of revising the position statement to require only laboratory documentation for genetic testing, adding hypersensitivity

	reactions to the warnings/precautions and contraindication sections, and updating the references.
12/15/25	Review and revision of the guideline, consisting of updating the references.