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Policy Number: 045.001

Title: Coverage Determination Policy for Scenesse (Afamelanotide)

Regions:	☒ **Texas**	☐ **Florida**	☐ **Indiana**	☐ **New Jersey**	☒ **New Mexico**

Impacted Areas:

☒ Network Management/Provider Services	☒ Utilization Management
☐ Member services	☐ Case management
☐ Quality Management	☐ Disease management
☐ Credentialing	☒ Claims
☐ IT	☐ Human resources
☐ Administration	☐ Finance
☐ Compliance/delegation	☒ Pharmacy
	☐ ALL

Available LCD/NCD/LCA: None

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Coverage Policy Number: 045.001

Line of Business: Medicare Part B

Policy Type: Prior Authorization

Coverage Determination:

Initial/New Requests

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).

WellMed will cover **Scenesse** for the treatment of **Erythropoietic Protoporphyria** in adult patients when **ALL** the following criteria are met:

1. Submission of medical records (e.g., chart notes, laboratory values, etc.) to support the diagnosis of Erythropoietic Protoporphyria (EPP) confirming **ONE** of the following:
   A. BOTH of the following:
      - Increased total erythrocyte protoporphyrin (usually 300 to 8000 mcg/dL; normal <80mcg/dL)
      - Increased percentage of erythrocyte metal-free protoporphyrin rather than zinc protoporphyrin (generally greater than 85% of total porphyrins)

   Or

   B. Molecular/genetic testing confirming one of the following genetic abnormalities
      - Ferrochelatase (FECH) gene mutation
      - Delta-aminolevulinate synthase-2 (ALAS2) gain-of-function gene mutation

   And

2. Patient is 18 years of age or older;
3. Patient has a history of phototoxic reactions due to EPP;
4. Scenesse dosing is in accordance with the United States Food and Drug Administration approved labeling;
5. Initial authorization will be for no more than 6 months

Renewal/Continuation of Therapy Requests

Scenesse is considered medically necessary for continued use when **ALL** of the following are met:

1. Patient has previously received Scenesse for the treatment of EPP
2. Patient has experienced a positive clinical response while on Scenesse by demonstrating **BOTH** of the following from pre-treatment baseline:
    - Reduction in phototoxic reactions
    - Increased duration of pain-free time in direct sunlight
3. Scenesse dosing is in accordance with the United States Food and Drug Administration approved labeling;
4. Reauthorization will be for no more than 12 months

FDA Approved Dose and Indication

FDA approved indications	Approved Dosing
Scenesse is indicated to increase pain free light exposure in adult patients with a history of phototoxic reactions from erythropoietic protoporphyria	A single implant (16 mg of Scenesse) subQ above the anterior supra-iliac crest every 2 months

General Background

Erythropoietic protoporphyria (EPP) is an inherited cutaneous porphyria characterized by painful, non-blistering photosensitivity occurring acutely after sunlight exposure but leaving little residual skin damage. It is caused by a deficiency of the enzyme ferrochelatase (FECH), which results from changes (mutations) in the FECH gene. Due to abnormally low levels of the FECH enzyme, excessive amounts of protoporphyrin accumulate in the bone marrow, blood plasma, and red blood cells. There are two main clinical manifestations of this disorder; cutaneous phototoxicity and hepatobiliary disease. Phototoxicity is the more common of these and it usually presents in early childhood as intolerance to sun-exposure with patients experiencing severe pain, described as burning, stinging, tingling, or a pricking sensation that may be accompanied or followed by redness, swelling, or blanching, lasting from minutes to days. Papulovesicles may form with prolonged exposure. In addition to sunlight, including sunlight passing through window glass or a car windshield, symptoms can also be elicited by non-sun exposures such as fluorescent lights and operating room lights. EPP is recognized as the most common porphyria in children and the third most common in adults, after porphyria cutanea tarda and acute intermittent porphyria.

Available treatment modalities for patients with EPP are limited. Avoidance of strong sunlight, either from direct exposure or through windows glass and the use of protective clothing is essential to prevent phototoxic reactions. Systemic β-carotene has been shown to be of benefit in the treatment of EPP although good efficacy data are lacking. Narrow-band UVB phototherapy that provides exposure to UVB in the range of 311 to 313 nm, which stimulates melanin formation but does not activate porphyrins, has been described as beneficial. A number of other methods of photoprotection have been employed, with variable success. The clinical benefits of other treatments (oral cysteine, cholestyramine, cimetidine, etc) remain to be proven.

Scenesse is the 1st FDA-approved treatment to help patients with EPP increase their light exposure and it should be administered by a healthcare professional proficient in the subcutaneous implantation procedure and has completed the training program provided by the product manufacturer.

Mechanism of Action:

Afamelanotide is a synthetic tridecapeptide and a structural analog of alpha-melanocyte stimulating hormone. Afamelanotide is a melanocortin receptor agonist and binds predominantly to MC1-R.

Afamelanotide increases production of eumelanin in the skin independently of exposure to sunlight or artificial UV light sources.

Warnings:

Scenesse 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.

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

Implant site reaction includes: implant site bruising, discoloration, erythema, hemorrhage, hypertrophy, irritation, nodule, pain, pruritus, swelling; injection site bruising and erythema; and expelled implant.

Clinical Evidence

The efficacy of Scenesse was established in two parallel group clinical trials with patients with erythropoietic protoporphyria who received Scenesse or placebo form of the implant subcutaneously every two months. Patients in the European Union (74 patients) and the United States (93 patients) were randomly assigned, in a 1:1 ratio, to receive either afamelanotide or placebo (a total of five implants in the European Union study and three in the U.S study). The two trials differed in the number of days of follow-up, the time windows within a day in which time spent outdoors was recorded, and how the amount of time spent in direct sunlight on each day was characterized. The type and duration of sun exposure, number and severity of phototoxic reactions, and adverse events were recorded over the respective 180-day and 270-day study periods. The primary efficacy end point was the number of hours of direct exposure to sunlight without pain.

In the European Union study, 38 subjects received 16 mg of afamelanotide administered subcutaneously every 2 months. Subjects received five implants and were followed for 270 days. On each study day, subjects recorded the number of hours spent outdoors between 10 am and 3 pm, whether "most of the day" was spent in direct sunlight, shade, or a combination of both, and whether they experienced any phototoxic pain that day. The primary endpoint was the 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. This analysis does not include sun exposure on days for which subjects reported spending time in a combination of both direct sunlight and shade. 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 subjects in the afamelanotide group and 0.75 hours for subjects in the vehicle group.

In the U.S. study, 48 subjects received 16 mg of afamelanotide administered subcutaneously every 2 months. Subjects received three implants and were followed for 180 days. On each study day, subjects recorded the number of hours spent in direct sunlight between 10 am and 6 pm, the number of hours spent in shade between 10 am and 6 pm, and whether they experienced any phototoxic pain that day. The primary endpoint was the total number of hours over 180 days spent in direct sunlight between 10 am and 6 pm on days with no pain. 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 subjects receiving afamelanotide and 40.5 hours for subjects receiving vehicle.

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.

HCPCS Code

HCPCS Code	Description
J7352	Afamelanotide implant, 1 mg

Diagnosis Code	Description
E80.0	Hereditary Erythropoietic Porphyria

Dosage Form and Route of Administration	
16mg	Subcutaneous Implant

Acronyms

EPP = Erythropoietic protoporphyria

MC1-R = Melanocortin 1 receptor

FECH = Ferrochelatase

ALAS2 = Delta-aminolevulinate synthase-2

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.
4. Mittal S, Anderson KE. Erythropoietic protoporphyria and X-linked protoporphyria. In: UpToDate, Levy ML, Means RT, Tirnauer JS (Ed), UpToDate, Waltham, MA, 2020.
5. FDA News Release October 2019; FDA approves first treatment to increase pain-free light exposure in patients with a rare disorder; https://www.fda.gov/news-events/press-announcements/fda-approves-first-treatment-increase-pain-free-light-exposure-patients-rare-disorder.