# Molina Clinical Policy
# Scenesse (afamelanotide) Implant: Policy No. 367b MEDICARE

**Last Approval: 04/09/2025**
**Next Review Due By: April 2026**

## DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. Policies are not a supplementation or recommendation for treatment; Providers are solely responsible for the diagnosis, treatment, and clinical recommendations for the Member. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (e.g., will be paid for by Molina) for a particular Member. The Member's benefit plan determines coverage – each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their Providers will need to consult the Member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a Member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of the Federal government or CMS for Medicare. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this MCP and provide the directive for all Medicare members. References included were accurate at the time of policy approval and publication.

## OVERVIEW

**Erythropoietic Protoporphyria (EPP)** and **X-linked protoporphyria (XLPP)** are inherited cutaneous porphyrias characterized clinically by acute non-blistering photosensitivity that leads to a significantly reduced quality of life. EPP is characterized by a deficiency of the ferrochelatase (FECH) enzyme in the heme biosynthetic pathway, resulting in the accumulation of protoporphyrin IX, a light-sensitive molecule, in erythrocytes and plasma. This causes severe, painful cutaneous photosensitivity and incapacitating burning and itching sensations in the skin during or after exposure to sunlight, even with some forms of artificial light and an overcast sky, that can last for days after exposure (Balwani 2017; Balwani 2019; Langendonk 2015). EPP may potentially cause complications with the liver and gallbladder. An estimated 20%-30% of EPP patients have some degree of liver dysfunction (i.e., mild with minor elevations in liver enzymes), and up to 5% may develop more advanced liver disease, which may be accompanied by motor neuropathy and can lead to liver failure.

Diagnosis is based on symptoms and increased levels of protoporphyrin in red blood cells and plasma. The diagnostic gold standard for EPP is biochemical analysis interpreted in the context of clinical characteristics. The condition typically manifests in infancy or early childhood; however, in some cases, onset may not occur until adolescence or adulthood. EPP and XLPP together rank as the third most frequent type of Porphyria, with an estimated occurrence of 2 to 5 cases per million individuals. Among children, they are the most prevalent form of Porphyria. Erythropoietic Protoporphyria affects both genders equally, occurring in approximately 1 out of every 74,300 people. In XLPP, the genetic defect is a gain-of-function mutation, usually a four-base deletion, in the gene that encodes the enzyme 5-aminolevulinic acid synthase-2, the first and rate-controlling enzyme of heme synthesis in developing red blood cells. XLPP impacts both males and females, but males often experience a more severe version of the condition. The exact prevalence of XLPP remains unclear, with only a limited number of cases documented in families from Europe, South Africa, and Japan (American Porphyria Foundation date unknown).

There are few effective treatment options for EPP, and they mainly consist of supportive care. Cutaneous symptom management has primarily focused on strict light avoidance (e.g., the use of sun protective clothing, sunscreen, window tinting or films for the vehicle or house) (Balwani 2017). The long-term effects of light avoidance on physical and psychological wellbeing are unknown, but it has been linked to anxiety, social isolation, and poor quality of life. Other EPP treatments are symptomatic and supportive. Oral beta-carotene, a high potency form of oral beta-carotene, has been used to improve affected sunlight tolerance, but there is no evidence to support this treatment. Vitamin D supplements are recommended because EPP patients are likely to have low vitamin D levels due to avoiding sunlight.

**Scenesse (afamelanotide)** is indicated to increase pain-free exposure to light in adult patients with a history of EPP phototoxic reactions and received Orphan Drug designation on October 8, 2019. Scenesse a synthetic analog of α-melanocyte stimulating hormone, mimics the naturally occurring hormone by increasing melanin production in melanocytes, resulting in improved sunlight tolerance in EPP/XLPP patients. Scenesse is a melanocortin-1 receptor agonist that causes melanocytes to produce eumelanin, which pigments the epidermis and thus protects against light-induced phototoxicity. Scenesse is administered as an implant that slowly dissolves within 60 days.

## COVERAGE POLICY

**Scenesse (afamelanotide)** for the treatment of Erythropoietic Protoporphyria (EPP) or X-linked protoporphyria (XLPP) may be **considered medically necessary** when ALL the following documented clinical criteria are met:

1. Member is ≥ 18 years old

2. Definitive diagnosis of EPP or XLPP confirmed by genetic testing AND Gene sequencing shows a FECH, CLPX, or ALAS2 mutation

3. Biochemical finding of a marked increase of EPP (e.g., elevated free protoporphyrin in peripheral erythrocytes) confirmed by ONE of the following tests:
    a. Elevated total erythrocyte protoporphyrin (e.g., 300 to 8,000 mcg/dL) **Normal ranges up to 80 mcg/dL*
    b. Elevated Erythrocyte fractionation shows ≥ 50% metal-free vs. zinc protoporphyrin
    **Generally, metal-free protoporphyrin represents > 85% of total porphyrin in EPP and 50-85% of total porphyrins in XLPP*

4. Evidence of EPP/XLPP-associated acute non-blistering cutaneous reactions (e.g., pain, stinging, redness, swelling, blanching) following exposure to sun

5. Absence of ALL the following contraindications:
    a. Any malignant or premalignant skin lesions (e.g., melanoma, dysplastic nevus syndrome, Bowen's disease, basal cell, or squamous cell carcinomas, etc.) as evidenced by a baseline full body skin examination for pre-existing skin lesions
    b. Significant hepatic involvement, dysfunction, or failure
    c. Any other photodermatosis such as polymorphic light eruption, actinic prurigo, discoid lupus erythematosus, chronic actinic dermatitis or solar urticaria

6. Documentation in Member's medical chart of ALL the following:
    a. Sun avoidance and use of sunscreen, protective clothing, and pain medication have proven inadequate in controlling EPP-associated painful skin reactions
    b. Member will continue to maintain sun and light protection measures during treatment to prevent phototoxic reactions

5. Prescriber agrees to submit documentation of full-body skin examination twice annually to monitor pre-existing and new skin pigmentary lesions

**Continuation of Therapy**

Continued administration of Scenesse (afamelanotide) for the treatment of Erythropoietic Protoporphyria (EPP) or X-linked protoporphyria (XLPP) may be **considered medically necessary** when ALL the following clinical criteria are met:

1. Member has met initial criteria for Scenesse therapy

2. Scenesse therapy may be re-authorized when stabilization of disease, or absence of disease progression, is documented by at least ONE of the following:
    a. Decreased severity and number of phototoxic reactions
    b. An increase in pain-free time during light exposure
    c. Improvement in acute non-blistering cutaneous reactions (e.g., pain, stinging, redness, swelling, blanching) following exposure to sun
    d. Improvement on a pain-intensity Likert scale or quality of life questionnaire

3. Continuous adherence to therapy as verified by member's claim history (review member's prescription claims history for compliance)

4. Documentation received of a full skin examination by the Prescriber/Dermatologist within the last six months to monitor pre-existing and new skin pigmentary lesions

5. Member has not experienced unacceptable toxicity, significant non-anaphylactic reaction(s), or anaphylaxis from Scenesse (afamelanotide) Implant therapy

**DOCUMENTATION REQUIREMENTS.** Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

## DRUG INFORMATION

**ROUTE OF ADMINISTRATION:** Subcutaneous Implantation

**DRUG CLASS:** Alpha-Melanocyte Stimulating Hormone Analog, Synthetic

**FDA-APPROVED USES:** Erythropoietic Protoporphyria (EPP)
*To increase pain free light exposure in adult patients with a history of phototoxic reactions from EPP*

**COMPENDIAL APPROVED OFF-LABELED USES:** None

**DOSING CONSIDERATIONS:** The recommended dose is a single implant (16 mg) inserted every 2 months

**MONITORING PARAMETERS:** Full body skin examination (twice yearly) per approved labeling

**DURATION OF APPROVAL:**
1. Initial authorization: **6 months**
2. Continuation of treatment: Re-authorization is required every **6 months** to determine continued need based on member meeting 'Continuation of Therapy' criteria

**QUANTITY LIMITATIONS:**
1. ONE implant every 2 months
2. THREE implants per year for seasonal coverage (most likely during spring and summer) is recommended. The recommended maximum number of implants is FOUR per year
    a. For requests beyond THREE implants a year medical justification is required. Prescriber must submit all relevant supporting documentation for clinical staff review

## SUMMARY OF MEDICAL EVIDENCE

***Clinical Trials***
In February 2025, CLINUVEL shared initial findings from its post-authorisation study, CUV052, focusing on SCENESSE® (afamelanotide) for both adult and adolescent (ages 12–17) patients with erythropoietic protoporphyria (EPP). Once the final analyses are complete, the data will be incorporated into a regulatory submission aimed at broadening the approved use of SCENESSE® to include adolescent patients.

Mitsubishi Tanabe Pharma America, Inc. (MTPA), is conducting a phase 3 trial (randomized, double-blind, placebo-controlled study) aimed at evaluating the safety, effectiveness, and tolerability of dersimelagon (MT-7117) in treating EPP and X-linked protoporphyria (XLPP). This investigational oral medication is being studied for its potential to extend the duration patients can remain in sunlight without experiencing early symptoms like burning, itching, or stinging, or developing a full phototoxic reaction. Dersimelagon is a novel synthetic compound targeting the melanocortin 1 receptor (MC1R). While it shows promise as a treatment for phototoxicity caused by EPP or XLPP, it is still investigational and not approved by regulatory authorities, including the FDA. It has received both Fast Track and Orphan Drug Designations from the U.S. FDA.

Langendonk et al. (2015) evaluated the safety and efficacy of afamelanotide in treating photosensitivity in patients with EPP in two Phase 3 multicenter, randomized, double-blind, placebo-controlled trials. The two parallel group clinical trials were conducted in the European Union (EU) (n=74) and the United States (US) (n=94) and served as the basis for FDA approval. Adults with EPP were randomly assigned to receive either Scenesse 16 mg or a placebo form of the implant subcutaneously every 60 days. Participants in the US trial received three implants over the course of six months, while those in the EU trial received five implants over the course of nine months. Both trials measured the number of hours a patient could be exposed to direct sunlight without experiencing pain. The primary efficacy endpoint was the duration of pain-free direct exposure to sunlight (10 am to 3 pm in the EU trial vs. 10 am to 6 pm in the US trial). In the U.S. trial, sunlight tolerance was assessed for a greater number of hours per day, and most of the study period occurred during the summer months. The primary outcome in the US trial was in direct sunlight, whereas the primary outcome in the EU trial was in direct sunlight and shade During the study period, the type and duration of sun exposure, the number and severity of phototoxic reactions, and adverse events (AEs) were all recorded. The number of study drug doses administered (3 doses vs. 5 doses), trial duration (6 months vs. 9 months), and time windows within a day in which time spent outdoors was recorded (10 am to 3 pm in the EU trial and 10 am to 6 pm in the US trial) differed between trials.

| Source | Trial | Location, Duration, # Enrolled | Primary Outcome(s) |
|---|---|---|---|
| Langendonk 2015 (NCT00979745) | CUV029 | European Trial<br>9 months (5 doses)<br>5 implants then followed for 270 days<br>N=74 [Scenesse 16mg (n=38); placebo (n=36)] | Time (hours) in light with no pain between 10:00 to 15:00/person/study period |
| Langendonk 2015 (NCT01605136) | CUV039 | United States Trial<br>6 months (3 doses)<br>3 implants then followed for 180 days<br>N=94 [Scenesse 16mg (n=48); placebo (n=45)] | Time (hours) in light with no pain between 10:00 and 18:00/person/study period |

*Participants were mostly Caucasian (98%), the mean age was 40 years (range 18 to 74 years), and 53% of subjects were male and 47% were female. Pain was rated on an 11-point Likert pain-intensity scale (with scores ranging from 0 to 10; higher scores indicating greater severity of symptoms).*

- EU trial: Five implants were administered to 74 patients (N = 74) over 9 months; 38 (n = 38) received afamelanotide, and 36 participants (n = 36) received a placebo. After 9 months, the median duration of pain-free time was 6 hours with afamelanotide and 0.8 hours with placebo. The total number of phototoxic reactions after 9 months was significantly lower with afamelanotide in study 2 (77 vs. 146 reactions). This analysis did not include sun exposure on days when subjects reported spending time in both direct sunlight and shade.

- U.S. trial: Three implants were administered to 93 subjects (N = 93) over 6 months; 48 (n = 48) received afamelanotide and 45 (n = 45) received a placebo subcutaneously every 2 months. The median total number of hours spent in direct sunlight between 10 a.m. and 6 p.m. on pain-free days was 69.4 hours for the Scenesse group versus 41 hours for the placebo group over 180 days. After 6 months, patients who received afamelanotide had 70% more pain-free time in direct sunlight than those who received placebo (median: 69.4 hours vs 40.8 hours).

Both trials showed significant improvement in the primary endpoint with no significant AEs. Scenesse was superior to a placebo in increasing the amount of time patients spent directly exposed to sunlight without experiencing pain. Photosensitivity and improvements in sunlight tolerance were observed in the treatment groups when compared to the placebo group. The duration of pain-free time was longer in the afamelanotide group in both trials: a median duration of 69.4 hours vs. 40.8 hours in the placebo group in the US trial over a 6-month period, and a median duration of 6.0 hours vs. 0.75 hours in the EU trial over a 9-month period. The number of phototoxic reactions was also lower in the afamelanotide group (77 vs. 146) in the EU study. Limitations included the subjectivity of patients' pain assessments, the partial unblinding of patients due to increased skin pigmentation in patients who received Scenesse, and sun avoidance due to fear of painful reactions in patients in both groups who did not develop increased pigmentation. Overall, afamelanotide was associated with increased duration of sun exposure without pain, less severe phototoxic reactions, faster phototoxic reaction recovery time, and enhanced quality of life (QoL).

Afamelanotide was generally well tolerated in clinical trials. The majority of AEs were mild to moderate in severity, with headache, nausea, nasopharyngitis, and back pain being the most common.

Post-marketing requirements by the FDA indicate a thorough QT clinical study to adequately characterize the effect of afamelanotide on cardiac repolarization. A prospective, longitudinal, registry based observational cohort study assessing long-term safety related to primary AEs, skin cancer and implant-site reactions. Secondary AEs of interest include changes in pigmentary expressions, pregnancy outcomes, effects on lactation and breastfeeding infants, and implantation device malfunction or failure (Beitz JG; NDA approval letter).

***Non-Randomized Studies, Retrospective Reviews, and Other Evidence***
Leaf et al. (2024) assessed total of 36 patients with EPP or XLPP, of whom 29 (28 with EPP and 1 with XLPP) who received at least one dose of afamelanotide over a 20-month period. Among these, 26 patients (72.2%) received two or more implants. The study focused on impact on phototoxic symptoms, QoL, and certain laboratory parameters, including levels of metal-free erythrocyte protoporphyrin and plasma protoporphyrin. Outcome data were only available for those who returned for at least one additional implant (i.e., received two or more implants). Of the 26 patients (72.2%) that received two or more implants, the median time to onset of phototoxic symptoms following sunlight exposure increased significantly—from 12.5 minutes (IQR: 5–20) before treatment to 120 minutes (IQR: 60–240) after treatment ($p < 0.001$). QoL showed notable improvement during treatment, as indicated by two separate assessment tools, which demonstrated consistent results. However, no significant changes were observed in median levels of metal-free erythrocyte protoporphyrin, plasma protoporphyrin, or liver function markers before versus during treatment. These findings underscore afamelanotide's substantial benefits in improving light tolerance and quality of life for patients with protoporphyria, despite the lack of improvement in protoporphyrin levels or liver function indicators.

Minder et al. (2023) conducted a retrospective observational study to evaluate whether afamelanotide implants provide dose-dependent protection against liver damage in patients with EPP. Previous findings had shown improved liver function tests (LFTs) during treatment compared to pre-treatment levels. This study aimed to determine if this improvement was influenced by the dose frequency of afamelanotide. The analysis included 70 EPP patients and encompassed 2933 liver function tests, 1186 protoporphyrin (PPIX) measurements, and 1659 afamelanotide implant applications. Key factors assessed included the time elapsed since the prior afamelanotide dose, the number of doses received within the preceding year, and the impact of global radiation, with the majority of implants administered between March and September. Patient-specific differences had the most pronounced impact on PPIX levels and LFTs. PPIX levels significantly increased as the time since the last implant lengthened ($p < 0.0001$), while levels of ALAT and bilirubin decreased with more frequent doses over the previous year ($p = 0.012$ and $p = 0.0299$, respectively). Global radiation was found to influence PPIX levels ($p = 0.0113$) but had no effect on LFTs. These findings indicate that afamelanotide positively impacts both PPIX levels and liver enzyme profiles in a dose-dependent manner. The results suggest that administering 5–6 afamelanotide implants annually may help prevent EPP-related liver damage, particularly for patients with elevated erythrocyte PPIX concentrations above 20–30 µmol/L. For individuals with additional risk factors, such as liver steatosis or early signs of liver damage, a two-monthly implant schedule throughout the year is recommended to optimize outcomes.

**National and Specialty Organizations**

The medical guideline *Evidence Based Consensus Guidelines for Diagnosis and Management of Protoporphyria-Related Liver Dysfunction in Erythropoietic Protoporphyria and X-Linked Protoporphyria* (Levey et al. 2024) discusses management of EPP/XLPP in four critical areas: patients with normal liver function, those with mild-to-moderate liver dysfunction due to protoporphyria, individuals experiencing mild-to-moderate protoporphyria-related liver complications, and those with advanced or acute protoporphyric hepatopathy. These categories provide a structured approach to diagnosis, monitoring, and treatment tailored to the varying degrees of liver involvement in protoporphyrias. As for future directions, addressing protoporphyric hepatopathy—a serious potential complication—relies heavily on consensus-based guidance derived mainly from case reports and small studies. Given the rarity of this condition, randomized clinical trials are impractical. Advancing treatment approaches will depend on multicenter collaborative observational studies that rigorously monitor treatment impacts through frequent assessments of erythrocyte PPIX and plasma porphyrin levels. Additionally, investigating the natural progression of protoporphyrias could help identify risk factors and genetic contributors, enabling earlier detection and more effective intervention in the initial stages of liver dysfunction.

The Porphyrias Consortium of the Rare Diseases Clinical Research Network published *Evidence-based consensus*

*guidelines for the diagnosis and management of erythropoietic protoporphyria and X-linked protoporphyria* (Dickey et al. 2023) for the diagnosis and management of the phototoxic disorders erythropoietic protoporphyria and X-linked protoporphyria. This guideline defines the essential biochemical and genetic tests required for accurate diagnosis, offering insights into interpreting their outcomes. It covers strategies for symptom prevention, approaches to managing acute phototoxicity, and both pharmacologic and nonpharmacologic treatment options. It also emphasizes the necessity of routine monitoring for complications such as liver disease, iron, and vitamin D deficiencies, and provides recommendations for their management. It also delves into considerations for pregnancy, surgical procedures, and the safety of various treatments.

## CODING & BILLING INFORMATION

### CPT (Current Procedural Terminology)

| Code | Description |
|---|---|
| **11981** | Insertion, drug-delivery implant (i.e., bioresorbable, biodegradable, non-biodegradable) |

### HCPCS (Healthcare Common Procedure Coding System)

| Code | Description |
|---|---|
| **J7352** | Afamelanotide implant, 1 mg |

**AVAILABLE DOSAGE FORMS:** Subcutaneous implant containing 16 mg of afamelanotide.
*Implant is a bioresorbable sterile rod measuring approximately 1.7 cm in length and 1.45 mm in diameter. Supplied in a sealed glass vial packaged individually in a cardboard box; not supplied with an implantation device.*

**CODING DISCLAIMER.** Codes listed in this policy are for reference purposes only and may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry standard coding practices for all submissions. When improper billing and coding is not followed, Molina has the right to reject/deny the claim and recover claim payment(s). Due to changing industry practices, Molina reserves the right to revise this policy as needed.

## APPROVAL HISTORY

**04/09/2025** Policy reviewed. No changes to coverage criteria. Updated Overview, Summary of Medical Evidence and References. IRO Peer Review on March 20, 2025, by a practicing physician board-certified in Pathology - Hematology, Internal Medicine, Medical Oncology.
**04/10/2024** Policy reviewed, No changes to coverage criteria. Updated Summary of Medical Evidence and References.
**04/13/2023** Policy reviewed and updated. No changes in coverage criteria. Updated references section.
**04/13/2022** Policy reviewed and updated. No changes in coverage criteria. Updated references section.
**04/05/2021** Policy reviewed and updated. No changes in coverage criteria. Updated references. Clarifications in verbiage include:

- Updated prescriber specialty criterion from: Prescribed and administered by a dermatologist or a specialist *in the treatment of porphyria who has completed training for Scenesse administration*, TO: Prescribed and administered by a dermatologist or a specialist *with expertise in the diagnosis and management of EPP*.
- Removal of '*Prescriber must agree that the member will be monitored by a health care provider for at least 30 minutes after the implant administration*' since this is addressed by the criterion in the administration section ('Administration by a health care professional who is proficient in the subcutaneous implantation procedure and has completed the training program provided by the manufacturer)

**Q2 2020 P&T** New policy. IRO Specialist Peer Review: 4/12/2020. Practicing Physician. Board certified in Dermatology.

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21. United States Food and Drug Administration (FDA). News release: FDA approves first treatment to increase pain-free light exposure in patients with a rare disorder Published October 8, 2019. Accessed March 12, 2025. https://www.fda.gov/news-events/press-announcements/fda-approves-first-treatment-increase-pain-free-light-exposure-patients-rare-disorder