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

Last Approval: 04/15/2026
Next Review Due By: April 2027

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 photodermatoses characterized by acute, non-blistering photosensitivity, typically presenting as severe burning, stinging, and erythema within minutes of sunlight or visible-light exposure, often with minimal objective skin findings, yet they cause major functional impairment and significantly reduce quality of life. EPP results from partial deficiency of the ferrochelatase (FECH) enzyme in the heme biosynthetic pathway, producing accumulation of metal-free protoporphyrin IX (PPIX), a light-sensitive molecule, in erythrocytes, plasma, and the liver. XLPP arises from gain-of-function variants in ALAS2, the erythroid-specific, rate-limiting enzyme of heme synthesis, leading to overproduction of PPIX. A third, rarer protoporphyria—CLPX-associated EPP (EPP2)—has also been described, further demonstrating that dysregulation of heme biosynthesis at multiple regulatory points can produce the same toxic accumulation of PPIX (Balwani 2017; Balwani 2019; Langendonk 2015; Mittal & Anderson 2025).

All forms of protoporphyria carry risk for hepatobiliary complications because PPIX is insoluble and excreted through bile. Approximately 20–30% of individuals develop biochemical liver abnormalities, and 1–5% progress to severe cholestatic hepatopathy or liver failure. Consensus guidelines emphasize annual monitoring, vaccination against hepatitis A and B, avoidance of hepatotoxins such as alcohol, and early recognition of rising erythrocyte PPIX as a marker of hepatic risk.

Diagnosis is clinical and biochemical. In all protoporphyrias, characteristic symptoms are an essential component of diagnosis and must be interpreted alongside laboratory findings. Biochemical confirmation requires elevated total erythrocyte protoporphyrin levels with fractionation to demonstrate a predominantly metal-free protoporphyrin fraction (typically >85% in EPP and 50–85% in XLPP). Hematofluorometric ZPP alone is inadequate for diagnosis. Genetic testing for FECH, ALAS2, or CLPX variants is supportive but not required to establish the diagnosis.

The condition typically manifests in infancy or early childhood; however, in some cases, onset may not occur until adolescence or adulthood. EPP and XLPP represent two of the most common pediatric onset prophyrias with an estimated prevalence ranging from 1 in 74,000 to 1 in 200,000, though under-recognition likely contributes to underestimation. 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. Before the availability of disease-modifying therapy, management relied almost entirely on strict light avoidance, including protective clothing, sunscreens, and window films. Such strategies reduce but do not eliminate phototoxic reactions, and long-term light avoidance is strongly associated with social isolation, emotional distress, and impairment in education/employment. Patients often also require vitamin D supplementation due to chronic avoidance of sunlight (Balwani 2017).

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Scenesse (afamelanotide) is a synthetic analog of α-melanocyte–stimulating hormone (α-MSH) that increases eumelanin production through activation of the melanocortin-1 receptor (MC1R), enhancing the skin's natural photoprotective capacity. It is FDA-approved to increase pain-free light exposure in adults with a history of phototoxic reactions from EPP. It is administered as a 16 mg subcutaneous implant every 2 months, placed above the anterior supra-iliac crest by a trained healthcare professional. Once inserted, the implant slowly dissolves and is fully bioresorbed over approximately 50–60 days, providing a sustained therapeutic effect throughout the dosing interval. XLPP treatment remains off-label in the United States, though biochemical and clinical responses are similar due to shared PPIX-mediated phototoxic mechanisms (FDA 2019).

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

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   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
CLINUVEL (2025) released preliminary results from its post-authorisation pharmacokinetic and safety study CUV052, evaluating SCENESSE® (afamelanotide) in both adult and adolescents aged 12–17 years with erythropoietic protoporphyria (EPP). The study enrolled 38 patients (14 adults, 14 adolescents) across European EPP expert centers and represents the first formal clinical evaluation of afamelanotide in an adolescent population. Premilimary findings indicate that SCENESSE® was well tolerated in adolescents, with a safety profile consistent

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with long-term adult use. All treatment-related adverse events were mild and resolved during the study, with no treatment-related serious adverse events reported. Biochemical and pharmacokinetic analyses demonstrated that the controlled-release profile of the implant in adolescents was comparable to adults, although adolescents showed slightly higher detectable plasma drug exposure, remaining within historically observed adult ranges. All eligible adolescent participants elected to continue treatment under special-access provisions.

Langendonk et al. (2015) evaluated the safety and efficacy of afamelanotide in treating photosensitivity in patients with EPP in two pivotal multicenter, randomized, double-blind, placebo-controlled Phase 3 trials. The inclusion criteria required participants to be ≥18 years of age with biochemically confirmed EPP, able to complete detailed daily diaries of sun exposure and symptoms, while exclusion criteria eliminated individuals with significant hepatic dysfunction, skin cancer or premalignant lesions, other photodermatoses, pregnancy, or recent substance misuse. The outcome criteria focused on the primary endpoint of pain-free direct sunlight exposure time, alongside secondary measures including phototoxic reaction frequency and severity, patient-reported pain scores, quality-of-life indices (EPP-QOL, DLQI), and photoprovocation testing in a U.S. subgroup. Across 168 randomized participants in the EU (nine-month, five-implant regimen) and U.S. (six-month, three-implant regimen) trials, the results consistently favored afamelanotide: treated patients achieved significantly longer pain-free sunlight exposure (e.g., U.S. median 69.4 vs. 40.8 hours, P = 0.04; EU median 6.0 vs. 0.8 hours, P = 0.005) and, in the EU study, experienced fewer phototoxic reactions (77 vs. 146, P = 0.04), along with meaningful improvements in quality-of-life measures. Adverse events were generally mild to moderate, and no treatment-related serious adverse events occurred. Limitations included partial unblinding from pigment changes, persistent sun-avoidant behavior that reduced sunlight-challenge opportunities, differences in trial duration and ambient light conditions between regions, and subjectivity inherent in diary-based exposure reporting. Overall, the trials concluded that afamelanotide has an acceptable safety profile and provides clinically meaningful improvements in light tolerance and quality of life, reinforcing its therapeutic value for adults with EPP.

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.

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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

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

04/15/2026 Policy reviewed. No changes to coverage criteria. Updated Overview, Summary of Medical Evidence, and References.
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

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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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