

afamelanotide (Scenesse®)

Medicare Advantage Medical Policy #MNG-039

Original Effective Date: 01/01/2025

Current Effective Date: 01/01/2025

Applies to all products administered or underwritten by the Health Plan, unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Health Plan may consider afamelanotide (Scenesse®)‡ for the treatment of erythropoietic protoporphyria to be **eligible for coverage**.**

Patient Selection Criteria

Coverage eligibility for afamelanotide (Scenesse) will be considered when the following patient selection criteria are met:

- Patient has a diagnosis of erythropoietic protoporphyria (including X-linked protoporphyria) confirmed by ONE of the following:
 - Free erythrocyte protoporphyrin level above the normal reference range for the reporting laboratory; OR
 - Molecular genetic testing consistent with the diagnosis; AND
- Patient is greater than or equal to 18 years of age; AND
- Patient has a history of at least one porphyric phototoxic reaction (e.g. skin burning, pain, stinging, redness, swelling); AND
- Patient does NOT have any of the following:
 - Current Bowen's disease, basal cell carcinoma, squamous cell carcinoma, or other malignant or premalignant skin lesions; OR
 - Personal history of melanoma or dysplastic nevus syndrome.

When Services Are Considered Not Medically Necessary

Based on review of available data, the Health Plan considers the use of afamelanotide (Scenesse) in patients with current Bowen's disease, basal cell carcinoma, squamous cell carcinoma, other malignant or premalignant skin lesions, or a history of melanoma or dysplastic nevus syndrome to be **not medically necessary**.**

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When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Health Plan considers the use of afamelanotide (Scenesse) when the patient selection criteria are not met (except those denoted to be **not medically necessary****) to be **investigational**.*

Background/Overview

Scenesse is a subcutaneous implant indicated to increase pain free light exposure in adult patients with a history of phototoxic reactions from erythropoietic protoporphyria. It is a first in class melanocortin 1 receptor (MC1-R) agonist that increases skin pigmentation by increasing melanin production and reducing free radical formation and cytokine production. The implant should be inserted subcutaneously above the anterior supra-iliac crest by a healthcare provider every 2 months. Although there is still limited clinical experience with this therapy, it appears that toxicities associated with Scenesse are minimal. The major adverse events noted are nausea and headache. Additionally, temporary skin darkening is expected with the treatment.

Erythropoietic Protoporphyrin (EPP) is a rare inherited condition that is caused by altered activity of an enzyme in the heme biosynthetic pathway (either ferrochelatase [FECH] or delta-aminolevulinic acid synthase [ALAS2]). The disease can be categorized into one of two subtypes: classic EPP or X-linked EPP (XLP). In classic EPP, there is a mutation in the *FECH* gene, and in XLP there is a gain-of-function mutation in the erythroid form of the ALAS2 enzyme. Both of these mutations result in the characteristic symptoms of painful, nonblistering photosensitivity that occurs acutely after sunlight exposure but leaves little residual skin damage. EPP is estimated to occur in 2 to 5 per million individuals, although the exact prevalence is unknown. It is diagnosed either biochemically with elevated metal free erythrocyte protoporphyrin or with molecular genetic testing noting a mutation in the *FECH* or *ALAS2* genes. Because the condition is so rare, some laboratories may not be equipped to measure true metal free erythrocyte protoporphyrin and instead measure total erythrocyte protoporphyrin, a nonspecific finding that can occur in many conditions. To prevent diagnostic uncertainty, a lab such as the Porphyrin Laboratory at the University of Texas Medical Branch at Galveston or Mayo Medical Laboratories should be used to obtain biochemical test results.

Prior to approval of Scenesse, there was no effective treatment available for EPP and patients were treated with the best supportive care including light avoidance, sun protection (e.g. complete light blocking creams), clothing, and vitamin D supplementation to correct for deficiency. Scenesse can improve sun tolerance in these patients, but it should be noted that it does not affect porphyrin production or alter the underlying disease process.

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FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Scenesse was approved in October 2019 to increase pain free light exposure in adult patients with a history of phototoxic reactions from erythropoietic protoporphyria.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The efficacy and safety of Scenesse was evaluated in two vehicle-controlled, parallel-group clinical trials in patients with EPP, CUV039 and CUV029.

Study CUV039 was conducted in the United States and enrolled 93 subjects, of whom 48 received Scenesse and 45 received vehicle. Subjects received three implants administered subcutaneously every 2 months 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 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 Scenesse and 40.5 hours for subjects receiving vehicle. Notable secondary endpoints were number of phototoxic reactions and quality of life. In this study, the median number of phototoxic reactions was similar between the two groups (46 reactions vs 43 reactions for Scenesse vs placebo, respectively). Quality of life improvement was noted using the EPP-quality of life (EPP-QOL) tool with higher scores indicating greater quality of life. The mean EPP-QOL was 51 points in the Scenesse group vs 37 points in the placebo group.

Study CUV029 was conducted in the European Union and enrolled 74 subjects, of whom 38 received Scenesse and 36 received vehicle. 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. 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 hours for subjects in the Scenesse group and 0.75 hours for subjects in the vehicle group. Notable secondary endpoints were number of phototoxic reactions and quality of life. In this study, the median number of phototoxic reactions was significantly lower in the Scenesse group than the placebo group (77 vs 146, respectively). Quality of life improvement was also noted using the

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EPP-QOL tool. The mean EPP-QOL was 85 points in the Scenesse group vs 73 points in the placebo group.

References

1. Scenesse [package insert]. Clinuvel Inc. Burlingame, CA. Updated April 2020.
2. Erythropoietic protoporphyria and X-linked protoporphyria. UpToDate. Updated January 2020.
3. Scenesse Drug Evaluation. Express Scripts. Updated January 2020.

Policy History

Original Effective Date: 01/01/2025

Current Effective Date: 01/01/2025

10/15/2024 UM Committee review

Next Scheduled Review Date: 10/2025

Coding

The five character codes included in the Health Plan Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2023 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

The responsibility for the content of the Health Plan Medical Policy Coverage Guidelines is with the Health Plan and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in the Health Plan Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of the Health Plan Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No codes
HCPCS	J7352

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ICD-10 Diagnosis	All related Diagnoses
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*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
 - 1. Consultation with technology evaluation center(s);
 - 2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
 - 3. Reference to federal regulations.

**Medically Necessary (or “Medical Necessity”) - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

- A. In accordance with nationally accepted standards of medical practice;
- B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
- C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient’s health insurance contract contains language that differs from the Health Plan Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Health Plan

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recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

Medicare Advantage Members

Established coverage criteria for Medicare Advantage members can be found in Medicare coverage guidelines in statutes, regulations, National Coverage Determinations (NCD)s, and Local Coverage Determinations (LCD)s. To determine if a National or Local Coverage Determination addresses coverage for a specific service, refer to the Medicare Coverage Database at the following link: <https://www.cms.gov/medicare-coverage-database/search.aspx>. You may wish to review the Guide to the MCD Search here: <https://www.cms.gov/medicare-coverage-database/help/mcd-bene-help.aspx>.

When coverage criteria are not fully established in applicable Medicare statutes, regulations, NCDs or LCDs, internal coverage criteria may be developed. This policy is to serve as the summary of evidence, a list of resources and an explanation of the rationale that supports the adoption of this internal coverage criteria.