Drug Monograph

Drug Name: **Scenesse® (afamelanotide) implant**
Drug Class: **Melanocortin Receptor Agonist Agents**
Prepared For: MO HealthNet
Prepared By: Conduent

☒ **New Criteria** ☐ **Revision of Existing Criteria**

Executive Summary

Purpose:	The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be made available on an open access basis to prescribers, require a clinical edit or require prior authorization for use.
Dosage Forms:	Scenesse is available as an implant containing 16 mg of afamelanotide.
Manufacturer:	Distributed by: Clinuvel, Inc., Burlingame, CA 94010.
Summary of Findings:	The efficacy and safety of Scenesse was established in two Phase 3 trials conducted in the European Union and in the United States (N=167). Patients were randomized 1:1 to receive a subcutaneous implant of Scenesse or placebo every 60 days for a six-month and a nine-month period, respectively. In the United States, the median duration of pain-free time was longer over a 6-month period in the afamelanotide group compared to placebo (64.1 hours vs. 40.5 hours; *P=0.04*). In the European Union study, the median duration of pain-free survival was longer over a 9-month period in the afamelanotide group compared to placebo (6.0 vs. 0.75; *P=0.005*). In both trials, quality of life improved with Scenesse therapy. Adverse events were mostly mild; serious adverse events were not thought to be related to the study drug.
Status Recommendation:	☒ Clinical Edit ☐ PA Required ☐ Open Access ☐ PDL
Type of PA Criteria:	☒ Appropriate Indications ☐ Non-Preferred ☐ No PA Required ☐ Preferred

Purpose

The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be considered a prior authorization drug, a clinical edit drug or an open access drug. While prescription expenditures are increasing at double-digit rates, payers are evaluating ways to control these costs by influencing prescriber behavior and guide appropriate medication usage. This review will assist in the achievement of qualitative and economic goals related to health care resource utilization. Restricting the use of certain medications can reduce costs by requiring documentation of appropriate indications for use, and where appropriate, encourage the use of less expensive agents within a drug class.

Introduction [1,2]

Erythropoietic protoporphyria (EPP) is a rare autosomal recessive disorder caused by mutations leading to impairment in ferrochelatase (FECH) activity, an enzyme involved in heme production. The decrease in FECH activity leads to an accumulation of protoporphyrin IX (PPIX) in the body, which can react with light reaching the skin, causing intense pain and skin changes, including redness and thickening. Few EPP patients develop hepatic complications which can include cholelithiasis or chronic liver disease progressing to rapid acute liver failure. Erythropoietic protoporphyria comprises about 90% phenotypic presentations, but prevalence is not well characterized in the U.S. Prevalence estimates range from 1 in 75,000 and 1 in 200,000 in the Netherlands and Wales respectively and prevalence in 17 European countries is estimated at 1 in 140,000. Gold standard test for the diagnosis of EPP is biochemical analysis (PEE/Porphyrins Evaluation, Whole Blood).

Dosage Form [3]

Scenesse is available as an implant containing 16 mg of afamelanotide.

Manufacturer [3]

Distributed by: Clinuvel, Inc., Burlingame, CA 94010.

Indication(s) [3]

Scenesse is indicated to increase pain free light exposure in adult patients with a history of phototoxic reactions from EPP.

Clinical Efficacy [3,4,5] (mechanism of action/pharmacology, comparative efficacy)

Scenesse is a synthetic tridecapeptide and a structural analog of α-melanocyte stimulating hormone (α-MSH). Scenesse is a melanocortin receptor agonist and binds predominantly to MC1-R.

Pharmacokinetics:

Absorption	Tmax: 36 hours
Metabolism	Possibly hydrolysis, but metabolic profile has not been fully characterized
Excretion	N/A
Half-life	15 hours

Clinical Trials Experience

<table>
<tr><td>STUDY DESIGN (N=167)</td><td>Two vehicle-controlled, parallel-group Phase 3 clinical trials
(EU: NCT00979745; US: NCT01605136)</td></tr>
<tr><td>INCLUSION CRITERIA</td><td>• Male or female subjects with characteristic symptoms of EPP phototoxicity and a biochemically confirmed diagnosis of EPP
• Aged ≥18 years
• Willing to take precautions to prevent pregnancy until completion of the study (Day 180)</td></tr>
<tr><td>EXCLUSION CRITERIA</td><td>• Any allergy to afamelanotide or the polymer contained in the implant or to lidocaine or other local anesthetic to be used during the administration of the study medication
• EPP patients with significant hepatic involvement
• Personal history of melanoma or dysplastic nevus syndrome
• Current Bowen's disease, basal cell carcinoma, squamous cell carcinoma, or other malignant or premalignant skin lesions
• Any other photodermatosis such as polymorphic light eruption, actinic prurigo, discoid lupus erythematosus, chronic actinic dermatitis or solar urticaria
• Any evidence of clinically significant organ dysfunction or any clinically significant deviation from normal in the clinical or laboratory determinations
• Acute history of drug or alcohol abuse (in the last 6 months)
• Prior and concomitant therapy with medications which may interfere with the objectives of the study, including drugs that cause photosensitivity or skin pigmentation
• Female who is pregnant (confirmed by positive serum β-HCG pregnancy test prior to baseline) or lactating
• Females of child-bearing potential (pre-menopausal, not surgically sterile) not using adequate contraceptive measures (i.e., oral contraceptives, diaphragm plus spermicide, intrauterine device)</td></tr>
<tr><td>TREATMENT REGIMEN</td><td>Patients were randomly assigned 1:1 to receive a subcutaneous implant of afamelanotide or placebo every 60 days for a six-month and a nine-month period, respectively (U.S.: 3 doses, EU: 5 doses).</td></tr>
<tr><td>RESULTS</td><td>The primary efficacy endpoint was duration of direct sunlight exposure between 10:00am and 3:00pm (EU) and 10:00am and 6:00pm (US) on days when no pain was experienced (pain score of 0). Secondary endpoints included: combined sun exposure and phototoxic pain, sun exposure, quality of life, photoprovocation, phototoxicity, and safety and tolerability endpoints.

<table>
<tr><th>Endpoint</th><th>Afamelanotide</th><th>Placebo</th><th>P-Value</th></tr>
<tr><td colspan="4">EU Trial</td></tr>
<tr><td>No. of patients</td><td>38</td><td>36</td><td></td></tr>
<tr><td>No. of hours in direct sunlight between 10am-3pm without pain (median)</td><td>6.0</td><td>0.75</td><td>Not reported in prescribing information</td></tr>
<tr><td colspan="4">US Trial</td></tr>
<tr><td>No. of patients</td><td>48</td><td>45</td><td></td></tr>
<tr><td>No. of hours in direct sunlight between 10am-3pm without pain (median)</td><td>64.1</td><td>40.5</td><td>Not reported in prescribing information</td></tr>
</table>
</td></tr>
<tr><td>SAFETY</td><td>Discussed in the Adverse Effects section below.</td></tr>
</table>

Contraindications [3,4]

- None

Warnings and Precautions [3,4]

- Skin Monitoring: 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.

Adverse Effects [3,4]

Most common, ≥2%	Scenesse N=125 n (%)	Vehicle N=119 n (%)
Implant site reaction[1]	26 (21)	12 (10)
Nausea	24 (19)	17 (14)
Oropharyngeal pain	9 (7)	6 (5)
Cough	8 (6)	4 (3)
Fatigue	7 (6)	3 (3)
Skin hyperpigmentation[2]	5 (4)	0 (0)
Dizziness	5 (4)	4 (3)
Melanocytic nevus	5 (4)	2 (2)
Respiratory tract infection	5 (4)	3 (3)
Somnolence	3 (2)	1 (1)
Non-acute porphyria	2 (2)	0 (0)
Skin irritation	2 (2)	0 (0)

[1] Implant site reaction includes: implant site bruising, discoloration, erythema, hemorrhage, hypertrophy, irritation, nodule, pain, pruritus, swelling; injection site bruising and expelled implant
[2] Skin hyperpigmentation includes skin hyperpigmentation, pigmentation lip (subject also had skin hyperpigmentation), and pigmentation disorder.

Drug Interactions [3,4]

- None

Dosage and Administration [3,4]

- Scenesse should be administered by a healthcare professional who is proficient in the subcutaneous implantation procedure and has completed training prior to administration.
- Insert a single implant, containing 16 mg of afamelanotide, using an SFM Implantation Cannula or other implantation devices that have been determined by the manufacturer to be suitable for implantation of Scenesse.
- Administer Scenesse subcutaneously every 2 months.

Cost

Generic Name	Brand Name	Manufacturer	Dose	Cost**
Afamelanotide	Scenesse	Clinuvel, Inc.	16 mg implant placed subcutaneously every 2 months	N/A

** Wholesale Acquisition Cost

Conclusion

Scenesse is a synthetic tridecapeptide and a structural analog of α-melanocyte stimulating hormone (α-MSH). It is a melanocortin receptor agonist and binds predominantly to MC1-R. Scenesse is indicated to increase pain free light exposure in adult patients with a history of phototoxic reactions from erythropoietic protophorphyria (EPP). The efficacy and safety of Scenesse was established in two Phase 3 trials. Patients were randomized 1:1 to receive a subcutaneous implant of Scenesse or placebo every 60 days for a six-month and a nine-month period, respectively. In the US and EU, the median duration of pain-free time was longer in the afamelanotide group compared to placebo. In both trials, quality of life improved with Scenesse therapy. The most common adverse reactions are implant site reaction, nausea, oropharyngeal pain, cough, fatigue, dizziness, skin hyperpigmentation, somnolence, melanocytic nevus, respiratory tract infection, non-acute porphyria, and skin irritation. Due to its highly specific indication and place in therapy, utilization management, such as clinical protocols and/or prior authorizations, should be considered to ensure appropriate utilization.

Recommendation

The MO Healthnet Division recommends a clinical edit for this drug.

References

1) National Organization for Rare Disorders. Erythropoietic Protoporphyria and X-Linked Protoporphyria. https://rarediseases.org/rare-diseases/erythropoietic-protoporphyria/. Accessed February 13, 2022.
2) IPDanalytics. Scenesse New Drug Approval. Accessed February 12, 2022.
3) Scenesse [package insert]. Burlingame, CA: Clinuvel, Inc.; 2020.
4) U.S. National Library of Medicine. Phase III Confirmatory Study in Erythropoietic Protoporphyria (EPP). https://clinicaltrials.gov/ct2/show/results/NCT00979745?term=NCT00979745&draw=2&rank=1&view=results. Accessed February 13, 2022.
5) Langendonk JG, Balwani M, Anderson KE, et al. Afamelanotide for Erythropoietic Protoporphyria. N Engl J Med. 2015 Jul 2;373(1):48-59. doi: 10.1056/NEJMoa1411481. PMID: 26132941; PMCID: PMC4780255.

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