

**ANNEX I**

**SUMMARY OF PRODUCT CHARACTERISTICS**

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

## **1. NAME OF THE MEDICINAL PRODUCT**

SCENESSE 16 mg implant

## **2. QUALITATIVE AND QUANTITATIVE COMPOSITION**

The implant contains 16 mg of afamelanotide (as acetate).  
For the full list of excipients, see section 6.1.

## **3. PHARMACEUTICAL FORM**

Implant.  
Solid white to off-white rod approximately 1.7 cm in length and 1.5 mm in diameter.

## **4. CLINICAL PARTICULARS**

### **4.1 Therapeutic indications**

SCENESSE is indicated for prevention of phototoxicity in adult patients with erythropoietic protoporphyria (EPP).

### **4.2 Posology and method of administration**

SCENESSE should only be prescribed by specialist physicians in recognised porphyria centres and administration should be performed by a physician trained and accredited by the marketing authorisation holder to administer the implant.

#### Posology

One implant is administered every 2 months prior to expected and during increased sunlight exposure. The overall duration of treatment is at the specialist physician's discretion (see sections 4.4 and 5.1).

#### Special populations

For patients with renal or hepatic impairment see sections 4.3 and 5.2.

#### *Elderly population*

Due to limited data in treatment of elderly patients, the use of afamelanotide is not recommended (see section 4.4).

#### *Paediatric population*

The safety and efficacy of afamelanotide in children and adolescents aged to 17 years have not yet been established.  
No data are available.

#### Method of administration

For subcutaneous use.

#### Instruction for use

- Take the packed implant out of the refrigerator and allow the medicinal product to warm up to ambient temperature.
- Have the patient sit in a comfortable position or lie on his/her back with the upper part of the body slightly raised.
- Disinfect the skin above the supra-iliac crest.
- Anaesthetise the insertion area if deemed necessary and in consultation with the patient.
- Select a 14 gauge (1.6 mm inner diameter) catheter with needle.
- Mark 1.5 to 2 cm on the catheter shaft using surgical ink.
- Hold the catheter at its base using a sterile technique, pinch and hold the skinfold cranial to, or overlying the patient's supra-iliac crest with two fingers.
- With the bevel of the needle facing upwards, insert the catheter laterally 1.5 to 2 cm into the subcutaneous layer at a 30 to 45 degree angle to the skin surface in one continuous flowing movement.
- With the catheter in place, aseptically remove the implant from the vial.
- Remove the needle from within the catheter using a sterile technique.
- Transfer the implant to the outlet of the catheter.
- Using a suitable device (such as a stylet) gently push the implant down the full length of the catheter lumen.
- Apply some pressure to the insertion area with your finger while removing the stylet and the catheter.
- Confirm insertion of the implant by palpating the skin with subcutis cranial to/overlying the suprailiac crest until the implant is located. Always verify the presence of the implant, if in doubt of its presence, check whether the implant has remained in the catheter. If the implant has not been administered during the procedural steps described above, discard the implant and administer a new implant. Do not administer a new implant unless it has been unequivocally confirmed that the first one had not been inserted.
- Apply a small pressure dressing to the injection site.
- Observe the patient for 30 minutes to ensure that you will notice if the patient develops an allergic or hypersensitivity reaction (immediate type).

The implant can be surgically removed if needed.

#### **4.3 Contraindications**

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1
- Presence of severe hepatic disease
- Hepatic impairment (see section 5.2)
- Renal impairment (see section 5.2)

#### **4.4 Special warnings and precautions for use**

##### Hypersensitivity

Uncommon occurrences of hypersensitivity reactions, including anaphylaxis, have been reported following administration of SCENESSE. Appropriate medical support measures should be readily available when SCENESSE is administered. If a serious hypersensitivity reaction occurs, appropriate medical treatment should be initiated, the implant should be removed if needed and further treatment with SCENESSE should be discontinued (see section 4.8).

##### Concomitant disorders not studied

Clinically significant disorders of the gastrointestinal, cardiovascular, respiratory, endocrine (including diabetes, Cushing's disease, Addison's disease, Peutz-Jeghers syndrome), neurological (including seizures) and haematological (especially anaemia) systems have not been evaluated.

A careful decision must be made whether to treat patients with any of these conditions with this medicinal product. If such patients are treated they must be monitored after each implant administration, including vital signs, routine haematology, and biochemistry.

### Sun protection

It is recommended that sun protection measures routinely adopted by each patient to manage their photosensitivity related to EPP and in accordance with their skin type (Fitzpatrick scale) are maintained during treatment with this medicinal product.

### Skin monitoring

Afamelanotide may induce darkening of pre-existing pigmentary lesions due to its pharmacological effect. A regular full body skin examination (every 6 months) is recommended to monitor all pigmentary lesions and other skin abnormalities.

If the skin changes noted are consistent with skin cancer or its precursors, or are ambiguous to the porphyria specialist, dermatology specialist consultation should be sought.

The two total full body skin examinations per year are intended to:

- detect early any skin cancers and their precursors induced by UV-exposure, as EPP patients can be expected to significantly increase their exposure to sunlight and UV light while on treatment with afamelanotide. EPP patients with fair skin may be more likely to request treatment and are more prone to developing UV light-associated skin changes, including cancer;
- detect and monitor changes in pigmentary lesions, thus allowing early detection of melanoma.

Special caution is warranted in patients with an

- individual or family history of melanoma (inclusive of *in-situ* melanoma, e.g. lentigo maligna) or suspected or confirmed susceptibility to cutaneous melanoma (CMM1, MIM #155600, synonyms: familial atypical mole-malignant melanoma syndrome, FAMMM; dysplastic naevus syndrome, DNS; B-K mole syndrome; CMM2 MIM #155601)

and/or an

- individual history of basal cell carcinoma, squamous cell carcinoma (inclusive of carcinoma *in situ*, e.g. Bowen's disease), Merkel cell carcinoma, or other malignant or premalignant skin lesions.

### Long-term use

Long-term safety data for afamelanotide are limited.

The safety of this medicinal product has not been evaluated in clinical studies of duration longer than 2 years (see section 4.2).

### Elderly

Since available data in treatment of the elderly are limited, afamelanotide should not be used in patients over 70 years of age. If such patients are treated they must be monitored after administration of every implant, including vital signs, routine haematology and biochemistry.

## **4.5 Interaction with other medicinal products and other forms of interaction**

No specific interaction studies have been performed with this medicinal product.

Pharmacokinetic data for afamelanotide or any of its metabolites are very limited. As an oligopeptide with a short half-life, afamelanotide is expected to be rapidly hydrolysed into shorter peptide fragments and into its individual amino acids. However, due to the lack of data caution is warranted.

Patients taking substances which reduce coagulation, such as vitamin K antagonists (e.g. warfarin), acetylsalicylic acid and non-steroidal anti-inflammatory drug (NSAIDs) may experience increased bruising or bleeding at the site of implantation.

#### **4.6 Fertility, pregnancy and lactation**

##### Women of childbearing potential/contraception in females

Women of childbearing potential have to use effective contraception during treatment with SCENESSE and for a period of three months thereafter.

##### Pregnancy

There are no or limited amounts of data from the use of afamelanotide in pregnant women. Animal studies are insufficient with respect to developmental toxicity (see section 5.3). A risk to newborns/infants cannot be excluded. SCENESSE should not be used during pregnancy and in women of childbearing potential not using effective contraception.

##### Breast-feeding

It is unknown whether afamelanotide or any of its metabolites are excreted in breast milk. No clinical data are available on the use of afamelanotide in breastfeeding women.

A risk to newborns/infants cannot be excluded. SCENESSE should not be used during breastfeeding.

##### Fertility

There are no clinical data on the effects of afamelanotide on fertility. Animal studies have not shown any harmful effect on fertility and reproduction.

#### **4.7 Effects on ability to drive and use machines**

Afamelanotide has moderate influence on the ability to drive and use machines, especially within 72 hours of administration. Following administration of this medicinal product, somnolence, fatigue, dizziness, and nausea have been reported. Patients should not drive or use machines in case they are affected by these symptoms.

#### **4.8 Undesirable effects**

##### Summary of the safety profile

The safety profile is based on pooled data from clinical studies in 425 patients. The most commonly reported adverse reactions are nausea, experienced by approximately 19% of subjects who received treatment with this medicinal product, headache (20%), and implant site reactions (21%; mainly discolouration, pain, haematoma, erythema). In most cases these adverse reactions are reported to be mild in severity.

Uncommon occurrences of hypersensitivity reactions, including anaphylaxis, have been reported in association with SCENESSE treatment (see section 4.4).

##### Tabulated list of adverse reactions

The adverse reactions reported during clinical studies conducted with afamelanotide are listed in the table below by MedDRA system organ class and frequency convention.

Frequencies are defined as: very common ( $\geq 1/10$ ), common ( $\geq 1/100$  to  $< 1/10$ ), uncommon ( $\geq 1/1,000$  to  $< 1/100$ ), and rare ( $\geq 1/10,000$  to  $< 1/1,000$ ).

<b>System Organ Class</b>	<b>Very common</b>	<b>Common</b>	<b>Uncommon</b>	<b>Rare</b>
Infections and infestations		Influenza Upper respiratory tract infection	Cystitis Folliculitis Gastrointestinal infection Gastroenteritis	Candida infection
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		Melanocyte naevus	Haemangioma	
Blood and lymphatic system disorders				Leukopenia
Immune system disorders			Hypersensitivity, Anaphylaxis	
Metabolism and nutrition disorders			Decreased appetite Increased appetite	Hypercholesterolaemia
Psychiatric disorders			Depressed mood including depression Insomnia	Confusional state
Nervous system disorders	Headache	Dizziness Migraine Somnolence	Balance disorder Hyperaesthesia Lethargy Paraesthesia Poor quality sleep Presyncope  Restless leg syndrome Syncope	Dysgeusia Post-traumatic headache
Eye disorders			Dry eye Eye pain Ocular hyperaemia Photophobia Presbyopia	Eyelid oedema
Ear and labyrinth disorders			Tinnitus	
Cardiac disorders			Palpitations	Tachycardia
Vascular disorders		Flushing Hot flush	Haemorrhage Haematoma Hypertension	Diastolic hypertension
Respiratory, thoracic and mediastinal disorders			Sinus congestion	
Gastrointestinal disorders	Nausea	Abdominal pain including abdominal discomfort Diarrhoea Toothache Vomiting	Abdominal distension Defaecation disorders Dyspepsia Flatulence Gastroesophageal reflux disease Gastritis Irritable bowel syndrome Gingival pain Hypoesthesia oral Lip swelling	Bowel movement irregularity Cheilitis Gingival discolouration Lip discolouration Lip oedema Tongue discolouration

System Organ Class	Very common	Common	Uncommon	Rare
Skin and subcutaneous tissue disorders		Ephelides Erythema Pigmentation disorder Pruritus Rash including rash vesicular, rash erythematous, rash papular and rash pruritic	Acne Dermatitis contact Dry skin Eczema Hair colour changes Hyperhidrosis Nail pigmentation Papule Photosensitivity reaction Pigmentation lip Post inflammatory pigmentation change Pruritus generalised Skin burning sensation Skin discolouration Skin exfoliation Skin hyperpigmentation Skin hypopigmentation Skin irritation Skin lesion Seborrhoea Urticaria	Lichen planus Vitiligo
Musculoskeletal and connective tissue disorders		Musculoskeletal pain including back pain, arthralgia, pain in extremity and groin pain	Joint stiffness Muscle spasm Musculoskeletal stiffness Muscular weakness	Limb discomfort
Reproductive system and breast disorders			Breast tenderness Dysmenorrhoea Menstruation irregular	Libido decreased Menorrhagia Vaginal discharge
General disorders and administration site conditions		Asthenia Fatigue  Implant site disorders including implant site bruising, implant site discolouration, implant site erythema, implant site haematoma, implant site haemorrhage, implant site hypersensitivity, implant site hypertrophy, implant site induration, implant site irritation, implant site mass, implant site oedema, implant site pain, implant site pruritus, implant site reaction, implant site swelling, implant site urticaria,	Chills Feeling hot Hangover Malaise Oedema peripheral Oedema mucosal	

System Organ Class	Very common	Common	Uncommon	Rare
		implant site vesicles, implant site warmth  Influenza-like illness including cough, nasal congestion, nasopharyngitis, oropharyngeal pain, rhinitis  Pain Pyrexia		
Investigations			Alanine aminotransferase increased Aspartate aminotransferase increased Blood creatine phosphokinase increased Blood glucose increased Blood iron decreased Blood urine present Hepatic enzyme increased Liver function test abnormal Transaminases increased	Blood pressure diastolic increased Transferrin saturation decreased Weight increased
Injury, poisoning and procedural complications			Fall Wound	Procedural nausea Wound complication
Product issues			Device expulsion	

#### Reporting of suspected adverse reactions

Reporting of suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in [Appendix V](#)

### **4.9 Overdose**

There are no data available on symptoms or treatment of overdose with afamelanotide.

## **5. PHARMACOLOGICAL PROPERTIES**

### **5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: Emollients and protectives, protectives against UV-radiation for systemic use, ATC code: D02BB02

#### Mechanism of action



Afamelanotide is a synthetic tridecapeptide and a structural analogue of  $\alpha$ -melanocyte stimulating hormone ( $\alpha$ -MSH). Afamelanotide is a melanocortin receptor agonist and binds predominantly to the melanocortin-1 receptor (MC1R). Its binding lasts longer than that of  $\alpha$ -MSH. This results in part from afamelanotide's resistance to immediate degradation by serum or proteolytic enzymes (see section 5.2). It presumably undergoes hydrolysis within a short time; its metabolites' pharmacokinetics and pharmacodynamics are not understood yet.

Afamelanotide is thought to mimic the endogenous compound's pharmacological activity by activating the synthesis of eumelanin mediated by the MC1R receptor.

Eumelanin contributes to photoprotection through different mechanisms including:

- strong broadband absorption of UV and visible light, where eumelanin acts as a filter
- antioxidant activity through scavenging of free radicals; and
- inactivation of the superoxide anion and increased availability of superoxide dismutase to reduce oxidative stress.

### Pharmacodynamic effects

Administration of afamelanotide may, therefore, result in increased production of eumelanin in the skin of the EPP patient independently of exposure to sunlight or artificial UV light. This can be accompanied by a darkening of the skin pigmentation in areas with melanocytes which gradually fades unless a further implant is administered.

### Clinical efficacy and safety

From the clinical development programme, there are limited data on dosing 4-6 implants/year.

In the pivotal clinical trial CUV039 a total of three 16 mg SCENESSE implants were administered at a two-month interval. It has been demonstrated that EPP patients receiving afamelanotide had more exposure to direct sunlight (10:00 to 18:00 hours) during a 180 day trial period compared to placebo recipients ( $p=0.044$ ; afamelanotide arithmetic mean: 115.6 h, median 69.4h; placebo mean 60.6h, median 40.8h).

In the supportive study CUV029 and a Post-Authorization Safety Study (PASS), five or up to six 16 mg SCENESSE implants were administered per year (at a two-month interval). The observed safety profile appears similar to that of the pivotal study CUV039.

### Paediatric population

The European Medicines Agency has deferred the obligation to submit the results of studies with SCENESSE in one or more subsets of the paediatric population in erythropoietic protoporphyria (see section 4.2 for information on paediatric use).

This medicinal product has been authorised under 'exceptional circumstances'. This means that due to the rarity of the disease it has not been possible to obtain complete information on this medicinal product.

The European Medicines Agency will review any new information which may become available every year and this SmPC will be updated as necessary.

## **5.2 Pharmacokinetic properties**

Dose-finding studies have not been conducted.

The pharmacokinetics of afamelanotide have not been fully characterised yet, i.e. distribution, metabolism or excretion are not clear. No pharmacokinetic information is available on any of its metabolites (active or inactive).

Half-life is approximately 30 minutes.

Following subcutaneous administration of the implant, most of the active substance is released within the first 48 hours with over 90% released by day 5. Plasma levels of afamelanotide are maintained

over a number of days. In most clinical studies afamelanotide plasma levels were below the limit of quantitation by day 10. The implant is absorbed by the body within 50 to 60 days after administration.

Data on possible interactions or effects in special populations, e.g. in patients with hepatic or renal impairment are not available.

#### Paediatric population

No data are available.

### **5.3 Preclinical safety data**

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, toxicity to reproduction and development.

In repeated dose toxicity studies, the only finding of relevance was an increase in melanin pigmentation in the dog, which is consistent with the active substance's pharmacological activity. This effect was observed only at exposure levels approximately 8 times higher than human exposure. Inflammation was observed in the Harderian gland in the rat. This finding is not considered relevant to human safety since the Harderian gland is not present in man.

In a fertility study no effects on the reproductive function of male or female Sprague-Dawley rats were observed after subcutaneous application of afamelanotide. A study in Sprague-Dawley rats showed no adverse effects on embryo-fetal development at exposures approximately 135-fold the human exposure (based on  $C_{max}$ ). A second study on embryo-fetal development in Lister-Hooded rats did not achieve sufficient exposure. Pre- and post-natal development of Sprague-Dawley rats was not affected at exposures of about 135-times the human exposure (based on  $C_{max}$ ).

## **6. PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

Poly (DL-lactide-co-glycolide)

### **6.2 Incompatibilities**

Not applicable.

### **6.3 Shelf life**

4 years.

### **6.4 Special precautions for storage**

Store in a refrigerator (2°C - 8°C)

### **6.5 Nature and contents of container**

Type I amber glass vial sealed with a PTFE coated rubber stopper.  
Pack of one vial containing one implant.

### **6.6 Special precautions for disposal and other handling**

For instructions on correct administration and preparation see section 4.2.  
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

**7. MARKETING AUTHORISATION HOLDER**

CLINUVEL EUROPE LIMITED  
10 Earlsfort Terrace  
Dublin 2  
D02 T380  
Ireland

**8. MARKETING AUTHORISATION NUMBER(S)**

EU/1/14/969/001

**9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date of first authorisation: 22 December 2014  
Date of latest renewal: 19 November 2019

**10. DATE OF REVISION OF THE TEXT**

Detailed information on this medicinal product is available on the website of the European Medicines Agency <http://www.ema.europa.eu>.

## **ANNEX II**

- A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE**
- B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE**
- C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION**
- D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT**
- E. SPECIFIC OBLIGATIONS TO COMPLETE POST-AUTHORISATION MEASURES FOR THE MARKETING AUTHORISATION UNDER EXCEPTIONAL CIRCUMSTANCES**

## **A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE**

Name and address of the manufacturer(s) responsible for batch release

CLINUVEL EUROPE LIMITED  
Alexandra House  
The Sweepstakes  
Ballsbridge  
Dublin 4  
D04 C7H2  
Ireland

## **B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE**

Medicinal product subject to restricted medical prescription (see Annex I: Summary of Product Characteristics, section 4.2).

## **C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION**

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

## **D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT**

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.
- Within 60 days of an important (pharmacovigilance or risk minimisation) milestone being reached

- **Additional risk minimisation measures**

Education and training programme for physicians

Prior to launch of SCENESSE in each Member State, the Marketing Authorisation Holder (MAH) must agree the content and format of the educational package, including communication media, distribution modalities, and any other aspects, with the National Competent Authority. The MAH shall also agree the details of the controlled access programme to ensure distribution of SCENESSE only to centres where the physicians received the educational materials and have been trained.

The MAH shall ensure that in each Member State where SCENESSE is marketed, all healthcare professionals who are expected to use the product are provided with the following educational package and trained:

- Summary of product characteristics,
- Face to face training material,
- Educational video,
- Registry information sheet.

The face to face training material, including the educational video, shall contain the following key messages:

- Demonstration of the correct application technique, highlighting the measures needed to ensure the implant is not damaged during use.
- The importance of maintaining aseptic conditions.
- Methods to prevent or minimise application errors and application site reactions

Registry information sheet shall contain the following key messages:

- The importance of recruiting and entering patients in the EU Registry,
- How to access and use the EU Registry.

#### **E. SPECIFIC OBLIGATIONS TO COMPLETE POST-AUTHORISATION MEASURES FOR THE MARKETING AUTHORISATION UNDER EXCEPTIONAL CIRCUMSTANCES**

This being an approval under exceptional circumstances and pursuant to Article 14(8) of Regulation (EC) No 726/2004, the MAH shall conduct, within the stated timeframe, the following measures:

<b>Description</b>	<b>Due date</b>
<b>Disease registry</b> Prior to launch in Member States, the MAH shall establish a disease registry to gather long term safety data and outcome endpoints in patients with EPP. The registry should collect data from both patients and physicians.	Draft protocol to be submitted 2 months after notification of the European Commission decision Intermediate reports: annual submission.

**ANNEX III**  
**LABELLING AND PACKAGE LEAFLET**

## **A. LABELLING**



**PARTICULARS TO APPEAR ON THE OUTER PACKAGING****OUTER CARTON****1. NAME OF THE MEDICINAL PRODUCT**

SCENESSE 16 mg implant  
afamelanotide

**2. STATEMENT OF ACTIVE SUBSTANCE(S)**

Each implant contains 16 mg afamelanotide (as acetate).

**3. LIST OF EXCIPIENTS**

Poly (DL-lactide-co-glycolide).

**4. PHARMACEUTICAL FORM AND CONTENTS**

1 implant

**5. METHOD AND ROUTE(S) OF ADMINISTRATION**

Read the package leaflet before use  
Subcutaneous use

**6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN**

Keep out of the sight and reach of children.

**7. OTHER SPECIAL WARNING(S), IF NECESSARY****8. EXPIRY DATE**

EXP

**9. SPECIAL STORAGE CONDITIONS**

Store in a refrigerator.

<b>10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE</b>
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Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

<b>11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER</b>
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CLINUVEL EUROPE LIMITED  
10 Earlsfort Terrace  
Dublin 2  
D02 T380  
Ireland

<b>12. MARKETING AUTHORISATION NUMBER(S)</b>
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EU/1/14/969/001

<b>13. BATCH NUMBER</b>
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BN

<b>14. GENERAL CLASSIFICATION FOR SUPPLY</b>
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<b>15. INSTRUCTIONS ON USE</b>
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<b>16. INFORMATION IN BRAILLE</b>
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Justification for not including Braille accepted.

<b>17. UNIQUE IDENTIFIER – 2D BARCODE</b>
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2D barcode carrying the unique identifier included.

<b>18. UNIQUE IDENTIFIER - HUMAN READABLE DATA</b>
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PC  
SN  
NN

<b>MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS</b> <b>VIAL</b>
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<b>1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION</b>
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SCENESSE 16 mg implant  
afamelanotide  
Subcutaneous use

<b>2. METHOD OF ADMINISTRATION</b>
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Read the package leaflet before use.

<b>3. EXPIRY DATE</b>
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EXP

<b>4. BATCH NUMBER</b>
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BN

<b>5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT</b>
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1 implant

<b>6. OTHER</b>
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## **B. PACKAGE LEAFLET**

## **Package leaflet: Information for the patient**

### **SCENESSE 16 mg implant** afamelanotide

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

**Read all of this leaflet carefully before you start using this medicine because it contains important information for you.**

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor.
- If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. See section 4.

#### **What is in this leaflet**

1. What SCENESSE is and what it is used for
2. What you need to know before you receive SCENESSE
3. How SCENESSE is given
4. Possible side effects
5. How SCENESSE is stored
6. Contents of the pack and other information

#### **1. What SCENESSE is and what it is used for**

SCENESSE contains the active substance afamelanotide (as acetate). Afamelanotide is a synthetic form of a body hormone called alpha-melanocyte stimulating hormone ( $\alpha$ -MSH). Afamelanotide works in a way similar to the natural hormone, by making skin cells produce eumelanin which is a brown-black type of melanin pigment in the body.

Afamelanotide is used to increase the tolerance to sunlight in adults with a confirmed diagnosis of erythropoietic protoporphyria (EPP). EPP is a condition in which patients have an increased sensitivity to sunlight, which can cause toxic effects such as pain and burning. By increasing the amount of eumelanin, SCENESSE can help to delay the onset of pain due to skin photosensitivity (sensitive to sunlight).

#### **2. What you need to know before you receive SCENESSE**

##### **Do not use SCENESSE**

- if you are allergic to afamelanotide or any of the other ingredients of this medicine (listed in section 6).
- if you have any severe condition of the liver.
- if you have liver problems.
- if you have kidney problems.

##### **Warnings and precautions**

Talk to your doctor before receiving SCENESSE if you have or have ever had:

- heart problems or severe breathing problems;
- gastrointestinal problems;
- diabetes;

- Cushing's disease (a hormone disorder where the body produces too much of the hormone cortisol);
- Addison's disease (a disorder of the adrenal glands causing a lack of some hormones);
- Peutz-Jeghers syndrome (a disorder that causes blockage of the bowel and where your hands, soles of your feet and surface of your lips may have brown freckles);
- epilepsy (or have been told that you are at risk of having fits);
- anaemia (low counts of red blood cells in your blood);
- melanoma (an aggressive type of skin cancer), including in-situ melanoma, e.g. lentigo maligna; or if you have certain inherited conditions that increase the risk of developing a melanoma;
- skin cancer of the types, basal cell carcinoma or squamous cell carcinoma (inclusive of carcinoma *in situ*, e.g. Bowen's disease), Merkel cell carcinoma or other malignant or premalignant skin problems.

Talk to your doctor before receiving SCENESSE if you are over 70 years of age.

If you have ever had any of these conditions your doctor may have to monitor you more closely during your treatment.

### Sun protection

Do not change the sun protection measures you normally follow to manage your EPP and according to your skin phototype (UV sensitivity). Keep in mind that increased exposure to UV light will contribute to skin cancer development.

### Skin monitoring

Because this medicine increases eumelanin, in most treated patients the skin will darken. This is an expected response to this medicine, and the darkening will slowly fade unless another implant is used.

Your doctor will need to regularly check your skin (full body) to monitor changes in moles (e.g. darkening) or other skin abnormalities. This is recommended to be performed every 6 months.

Please inform your doctor about new or changing skin abnormalities. Arrange for an early appointment with your porphyria specialist if pigmented lesions like moles grow or if other growing, non-healing, weeping, plaque-like, wart-like, or ulcerated lesions appear. A referral to a dermatology specialist might be necessary.

### **Children and adolescents**

This medicine should not be given to children and adolescents under 18 years of age because it has not been tested in this age group.

### **Other medicines and SCENESSE**

Tell your doctor if you are taking, have recently taken or might take any other medicines.

Tell your doctor if you are taking anticoagulant medicines used to prevent blood clots. These may include-warfarin, acetylsalicylic acid (a substance present in many medicines used to relieve pain and lower fever or to prevent blood clotting) and a group of medicines called non-steroidal anti-inflammatory drug (NSAIDs), used to treat common ailments, such as arthritis, headaches, mild fever, rheumatism and sore throats. This is because patients taking such medicines may experience increased bruising or bleeding at the site of the implant.

## **Pregnancy and breastfeeding**

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, you should not receive SCENESSE, since it is not known how it will affect your unborn baby or the breastfed infant.

Women who could become pregnant should use adequate contraception such as oral contraceptives, diaphragm plus spermicide, intrauterine device (also known as a coil) during treatment and for three months after the last SCENESSE implantation.

## **Driving and using machines**

There is a risk of feeling drowsy and tired when using this medicine, especially within 72 hours of administration. If you are affected, do not drive or use any tools or machines. If you suffer from continued drowsiness, then you should speak to your doctor.

## **3. How to use SCENESSE**

The implant will be inserted by a doctor who has been trained in the administration procedure. The doctor will decide with you the most suitable time and the site for inserting the implant.

One implant is injected every 2 months prior to expected and during increased sunlight exposure. The number of implants per year and the overall duration of treatment is decided by your specialist physician.

The implant is given as injection under your skin using a catheter tube and needle (subcutaneous use). Before inserting this medicine, your doctor may decide to give you a local anaesthetic to numb the area where the implant is to be inserted. The implant is inserted directly under the skin folds on your waist or abdomen in an area known as the supra-iliac crest.

At the end of the insertion procedure, you may be able to feel the implant under your skin. Over time the implant will be absorbed by the body, this will happen within 50 to 60 days after implantation.

If you experience discomfort and are concerned, speak to your doctor. The implant may be removed by a simple surgical procedure if needed.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

## **4. Possible side effects**

Like all medicines, this medicine can cause side effects, although not everybody gets them.

The following side effects are considered to be:

**Very common** (may affect more than 1 in 10 people):

- nausea (feeling sick),
- headache.

**Common** (may affect up to 1 in 10 people):

- flu, upper respiratory tract infection (colds),
- general changes to the skin including darkening of freckles and moles,
- rash with small blisters, itch, rash, red rash, itchy rash,
- dizziness, drowsiness and migraine (severe headache),
- hot flushes, flushing, feeling hot and redness of the skin,
- abdominal (tummy) pain, toothache, diarrhoea and vomiting,
- pain in arms and legs, pain or weakness in muscles and bones, back pain,

- fatigue, pain, fever, reactions at the implant site including pain, bruising, swelling, bleeding, itching and changes to the colour of overlying skin, flu-like illness, cough, blocked nose, inflamed nose and throat.

**Uncommon** (may affect up to 1 in 100 people):

- urinary tract infection, infected hair follicle, infection in stomach and intestines,
- hypersensitivity and severe allergic reaction including anaphylaxis (signs may include: a rash, swallowing or breathing problems, swelling of your lips, face, throat or tongue)
- decreased or increased appetite,
- depressed mood including depression, inability to sleep, poor quality sleep,
- fainting, fainting sensation, weakness, inability to get legs comfortable, disturbance of balance,
- dry eye, eye pain, red eyes, difficulty focusing on objects, sensitivity in eyes to light, ringing in ears,
- palpitations, bruising, bleeding, high blood pressure,
- blocked sinuses,
- inflamed stomach and intestines, heartburn, irritable bowel syndrome, wind, lip swelling, reduce sense of touch in the mouth, gum pain,
- acne, eczema, red swelling on skin, dry skin, hair colour changes, excessive sweating, pigmentation in nails, colouration on lip, skin peeling, skin burning sensation, changes to the colour of the skin including loss of colour, oily skin, hives,
- joint stiffness, stiffness of muscle and bones, sudden muscle contraction, sore muscle,
- breast tenderness, irregular period, painful period,
- chills, feeling hot, hangover, malaise, swelling in legs or hands,
- abnormal liver function tests, decreased iron binding, increased sugar level, decreased blood iron level, blood in urine,
- fall and wound,
- device expulsion.

**Rare** (may affect up to 1 in 1000 people):

- fungal infection,
- decrease white blood cells,
- increased cholesterol,
- confusion, headache following injury, abnormal taste sensation,
- swollen eye lids,
- fast heart rate,
- irregular bowel movements, inflamed lips, discoloured gums, lips and tongue,
- red or brownish nodules on the skin (called “Lichen planus”), vitiligo,
- heavy prolonged period, discharge from vagina, decreased sex drive,
- increase in body weight,
- wound complication, nausea following implant insertion.

**Reporting of side effects**

If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in [Appendix V](#). By reporting side effects you can help provide more information on the safety of this medicine.

**5. How SCENESSE is stored**

Keep this medicine out of the sight and reach of children.

This medicine must not be used after the expiry date which is stated on the vial and the outer carton. Your doctor will check the expiry date before an implant is used.

Store in a refrigerator (2°C - 8°C).



Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

## **6. Contents of the pack and other information**

### **What SCENESSE contains**

- The active substance is afamelanotide. One implant contains 16 mg of afamelanotide (as acetate).
- The other ingredient is poly (D,L-lactide-co-glycolide).

### **What SCENESSE looks like and contents of the pack**

The implant is a solid white to off-white rod approximately 1.7 cm in length and 1.5 mm in diameter in an amber glass vial sealed with a PTFE coated rubber stopper.

Pack size of one vial containing one implant.

### **Marketing Authorisation Holder**

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### **Manufacturer**

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### **This leaflet was last revised in**

This medicine has been authorised under 'exceptional circumstances'. This means that because of the rarity of this disease, for scientific reasons, and for ethical reasons it has been impossible to get complete information on this medicine.

The European Medicines Agency will review any new information on this medicine every year and this leaflet will be updated as necessary.

### **Other sources of information**

Detailed information on this medicine is available on the European Medicines Agency web site: <http://www.ema.europa.eu>. There are also links to other websites about rare diseases and treatments.

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The following information is intended for healthcare professionals only:

### Method of administration

SCENESSE is administered subcutaneously under aseptic conditions as described below. Administration should be performed by a physician trained and accredited by the marketing authorisation holder to administer the implant.

#### Instruction for use

- Take the packed implant out of the refrigerator and allow the medicinal product to warm up to ambient temperature.
- Have the patient sit in a comfortable position or lie on his/her back with the upper part of the body slightly raised.
- Disinfect the skin above the supra-iliac crest.
- Anaesthetize the insertion area if deemed necessary and in consultation with the patient.
- Select a 14 gauge (1.6 mm inner diameter) catheter with needle.
- Mark 1.5 to 2 cm on the catheter shaft using surgical ink.
- Hold the catheter at its base using a sterile technique, pinch and hold the skinfold cranial to, or overlying the patient's supra-iliac crest with two fingers.
- With the bevel of the needle facing upwards, insert the catheter laterally 1.5 to 2 cm into the subcutaneous layer at a 30 to 45 degree angle to the skin surface in one continuous flowing movement.
- With the catheter in place, aseptically remove the implant from the vial.
- Remove the needle from within the catheter using a sterile technique.
- Transfer the implant to the outlet of the catheter.
- Using a suitable device (such as a stylet) gently push the implant down the full length of the catheter lumen.
- Apply some pressure to the insertion area with your finger while removing the stylet and the catheter.
- Confirm insertion of the implant by palpating the skin with subcutis cranial to/overlying the suprailiac crest until the implant is located. Always verify the presence of the implant, if in doubt of its presence, check whether the implant has remained in the catheter. If the implant has not been administered during the procedural steps described above, discard the implant and administer a new implant. Do not administer a new implant unless it has been unequivocally confirmed that the first one had not been inserted.
- Apply a small pressure dressing to the injection site.
- Observe the patient for 30 minutes to ensure that you will notice if the patient develops an allergic or hypersensitivity reaction (immediate type).

The implant can be surgically removed if needed.