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.

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, e.g. from spring to early autumn. Three implants per year are recommended, depending on the length of protection required. The recommended maximum number of implants is four per year. The overall duration of treatment is at the specialist physician's discretion (see section 4.4).

Special populations

For elderly patients and patients with renal or hepatic impairment see sections 4.3 and 4.4:

Paediatric population

The safety and efficacy of afamelanotide in children and adolescents aged 0 to 17 years have not yet been established.
No data are available (see section 4.4).

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

Long-term use

Long-term safety data for afamelanotide are limited.
The safety of this medicinal product has not been evaluated in clinical trials of duration longer than 2 years (see section 4.2).

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:

a) 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 SCENESSE. 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;

b) 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.

Elderly

Since available data in treatment of the elderly are limited, SCENESSE 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.

Paediatric population

Use of SCENESSE is not recommended in the paediatric population due to the lack of data and the size of the implant which is not suitable for children.

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 should, 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. SCENESSE should not be used during pregnancy.

Breastfeeding

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. Animal studies are insufficient with respect to developmental toxicity (see section 5.3). A risk to newborns/infants cannot be excluded. SCENESSE should be avoided 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.

Tabulated list of adverse reactions

The adverse reactions reported during clinical trials conducted with SCENESSE are listed in the table below by MedDRA system organ class and frequency convention.
Frequencies are defined as: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000) and not known (cannot be estimated from the available data)

System Organ Class	Very common	Common	Uncommon
Infections and infestations		Upper respiratory tract infection	Influenza Gastrointestinal infection Gastroenteritis Folliculitis Candidiasis Nasopharyngitis

System Organ Class	Very common	Common	Uncommon
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			Haemangioma
Blood and lymphatic system disorders			Leukopenia
Metabolism and nutrition disorders		Decreased appetite	Hypercholesterolaemia Increased appetite
Psychiatric disorders			Depression Depressed mood Insomnia
Nervous system disorders	Headache	Migraine Dizziness Lethargy Somnolence	Syncope Restless leg syndrome Hyperaesthesia Presyncope Post-traumatic headache Burning sensation Poor quality sleep Dysgeusia
Eye disorders			Eyelid oedema Ocular hyperaemia Dry eye Presbyopia
Ear and labyrinth disorders			Tinnitus
Cardiac disorders			Palpitations Tachycardia
Vascular disorders		Flushing Hot flush	Haematoma Diastolic hypertension Hypertension
Respiratory, thoracic and mediastinal disorders			Dysphonia Sinus congestion Rhinitis Nasal congestion
Gastrointestinal disorders	Nausea	Abdominal pain Abdominal pain upper Diarrhoea Vomiting	Lip oedema Lip swelling Gastroesophageal reflux disease Gastritis Dyspepsia Cheilitis Abdominal distension Gingival pain Abdominal discomfort Toothache Abdominal symptom Bowel movement irregularity Flatulence Gingival discolouration Hypoaesthesia oral Lip discolouration Tongue discoloration
Skin and subcutaneous tissue disorders		Erythema Melanocytic naevus Pigmentation disorder	Lichen planus Rash vesicular Pruritus generalised

System Organ Class	Very common	Common	Uncommon
		Skin discolouration Skin hyperpigmentation Ephelides Pruritus	Rash Rash erythematous Rash papular Rash pruritic Skin irritation Vitiligo Acne Eczema Pigmentation lip Post inflammatory pigmentation change Seborrhoea Skin exfoliation Skin hypopigmentation Hair colour changes Hyperhidrosis
Musculoskeletal and connective tissue disorders		Back pain	Arthralgia Myalgia Pain in extremity Muscle spasm Musculoskeletal pain Musculoskeletal stiffness Joint stiffness Groin pain Sensation of heaviness
Renal and urinary disorders			Cystitis
Reproductive system and breast disorders			Menorrhagia Dysmenorrhoea Breast tenderness Menstruation irregular Vaginal discharge Libido decreased
General disorders and administration site conditions		Implant site hypersensitivity Implant site reaction Implant site pain Implant site haematoma Implant site erythema Implant site irritation Asthenia Fatigue Implant site discolouration Feeling hot	Oedema peripheral Oedema mucosal Pain Implant site oedema Pyrexia Chills Injection site haematoma Injection site irritation Implant site hypertrophy Implant site pruritus Device expulsion Application site discolouration Hangover Influenza like illness
Investigations		Blood creatine phosphokinase increased	Alanine aminotransferase increased Aspartate aminotransferase increased Liver function test abnormal Transaminases increased Transferrin saturation decreased

System Organ Class	Very common	Common	Uncommon
			Blood cholesterol increased Blood glucose increased Blood iron decreased Blood pressure diastolic increased Blood urine present Biopsy skin
Injury, poisoning and procedural complications			Wound complication Open wound Fall Procedural nausea

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 α-melanocyte stimulating hormone (α-MSH). Afamelanotide is a melanocortin receptor agonist and binds predominantly to the melanocortin-1 receptor (MC1R). Its binding lasts longer than that of α-MSH. This results in part from afamelanotide's resistance to immediate degradation by serum or proteolytic enzymes (half-life approximately 30 min). 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 broad band 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

It has been demonstrated that EPP patients receiving SCENESSE 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; SCENESSE arithmetic mean: 115.6 h, median 69.4h; placebo mean 60.6h, median 40.8h).

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.

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). 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.

Data on possible interactions or effects in special populations, e.g. in patient 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
D04 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

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 responsible for batch release

Catalent Germany Schorndorf GmbH
Steinbeisstrasse 1-2
73614 Schorndorf
Germany

Catalent UK Packaging Ltd
Lancaster Way
Wingates Industrial Estate
Westhoughton, Bolton
Lancashire BL5 3XX
United Kingdom

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

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**

The marketing authorisation holder shall submit the first periodic safety update report for this product within 6 months following authorisation. Subsequently, the marketing authorisation holder shall submit periodic safety update reports for this product in accordance with the requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and 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 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

If the dates for submission of a PSUR and the update of a RMP coincide, they can be submitted at the same time.

- **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.

- **Obligation to conduct post-authorisation measures**

The MAH shall complete, within the stated timeframe, the below measures:

Description	**Due date**
Retrospective chart review study The MAH shall conduct a retrospective study comparing long term safety data and outcome endpoints in patients receiving and not receiving SCENESSE, or having discontinued SCENESSE use. The second primary objective of the study should be the assessment of the compliance with risk minimization recommendations and the controlled access program for patients receiving SCENESSE.	Draft protocol to be submitted 2 months after notification of the European Commission decision Intermediate reports: annual submission. Final report: 6 years after approval.

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

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

Description	Due date
Disease registry 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.

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.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

CLINUVEL EUROPE LIMITED
10 Earlsfort Terrace
Dublin 2
D04 T380
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/969/001

13. BATCH NUMBER

BN

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC:
SN:
NN:

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

SCENESSE 16 mg implant
afamelanotide
Subcutaneous use

2. METHOD OF ADMINISTRATION

Read the package leaflet before use.

3. EXPIRY DATE

EXP

4. BATCH NUMBER

BN

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 implant

6. OTHER

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 is a medicine that contains the active substance afamelanotide. Afamelanotide is a synthetic form of a body hormone called alpha-melanocyte stimulating hormone (α-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 use 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 using SCENESSE if you have or have ever had:
- heart problems (including an irregular heart beat) or severe breathing problems (such as asthma or bronchitis)
- 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 using 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 between the ages of 0 and under 18 years 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 during the spring and summer months. Three implants per year are recommended, depending on the length of effect required. However, this number should not exceed more than 4 per year.

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; reactions at the implant site including pain, redness, itching, bruising and changes to colour of overlying skin.

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

General changes to the skin including freckles and skin darkening; migraine (a severe headache); back pain; abdominal (tummy) pain, diarrhoea and vomiting, decreased appetite; fatigue (tiredness), dizziness, drowsiness and weakness; hot flushes; upper respiratory tract infections (colds).

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

- Infected hair follicle, fungal infection, urinary tract infection

- Chills, fever, flu, flu-like illness, blocked nose, blocked sinuses, inflamed nose and throat, nose inflammation

- Depression, inability to sleep, poor quality sleep, fainting, fainting sensation, fall, hangover, weakness, inability to get legs comfortable, increased sensitivity to touch, headache following injury, burning sensation, abnormal taste sensation

- Swollen eye lids, red eyes, dry eye, difficulty focusing on close objects, ringing in ears

- Palpitations, fast heart rate, bruising, high blood pressure, difficulty to make some sounds

- Inflamed lips, lip swelling, colouration on lip, gum pain, toothache, discoloured gums, reduced sense of touch in mouth, lip discolouration, tongue discolouration

- Increased hunger, nausea following implant insertion, indigestion, infection in stomach and intestines, inflamed stomach and intestines, heartburn ,inflamed stomach, irregular bowel movements, wind, bloated tummy, tummy pain

- Irregularity of skin, rash with small blisters, itch, rash, red rash, red swelling on skin, rash with small bumps, itchy rash, skin irritation, lighter skin patches, acne, eczema, secretions on skin, skin peeling, skin with loss of colour, hair colour changes, excessive sweating

- Joint pain, muscle pain, pain in arms and legs, sudden muscle contraction, pain in muscles and bones, stiffness of muscles and bones, joint stiffness, groin pain, feeling of heaviness, swelling in lower limbs

- Heavy and prolonged period, abnormal period, breast tenderness, irregular periods, discharge from vagina, decreased sex drive

- Pain, swelling around site of implantation, bruising at injection site, irritation at injection site, enlargement at implant site, itching at implant site, implant falling out, change in colour of skin at implant site

- Decrease white blood cells, abnormal liver function tests, decreased iron binding, increased cholesterol, increased sugar level, decreased blood iron level, increased blood pressure, blood in urine

- Wound complication, open wound

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.
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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This leaflet was last revised in

This medicine has been authorised under 'exceptional circumstances'. This means that because of the rarity of this disease 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.

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.