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Summary of the risk management plan (RMP) for Scenesse (afamelanotide)

This is a summary of the risk management plan (RMP) for Scenesse, which details the measures to be taken in order to ensure that Scenesse is used as safely as possible. For more information on RMP summaries, see here.

This RMP summary should be read in conjunction with the EPAR summary and the product information for Scenesse, which can be found on Scenesse's EPAR page.

Overview of disease epidemiology

Scenesse is used in patients with erythropoietic protoporphyria (EPP), a rare genetic disease that causes intolerance to light. Patients with this condition have a deficiency in one of the enzymes that produces haem (found in haemoglobin, the red pigment in blood). As a result, a substance known as protoporphyrin IX, a precursor of haem, accumulates in the body and it is this substance which causes the intolerance to light.

In the sun or under bright light, protoporphyrin IX absorbs the light through the exposed skin, causing symptoms such as severe pain, redness and swelling. The severity of the symptoms is such that patients generally avoid bright light exposure and have to spend most of their time in the dark.

EPP is a lifelong disease that affects approximately 650 people in the EU.

Summary of treatment benefits

Scenesse is an implant, inserted under the skin. It contains the active substance afamelanotide which is closely related to a hormone in the body known as alpha-melanocyte stimulating hormone that stimulates the production of a brown-black pigment in the skin that helps block the penetration of light. By stimulating the formation of this pigment, eumelanin, Scenesse prevents light from penetrating the skin, thus helping to reduce the painful reactions caused by light-activated protoporphyrin IX.

Scenesse has been shown in a study to lead to an increase in the amount of time patients can spend in sunlight. In the study involving 93 patients with EPP, patients were treated with either Scenesse or placebo (a dummy treatment) over a six month period. Daily records of exposure to sunlight between 10 am and 6 pm showed that patients treated with Scenesse spent on average 116 hours in sunlight without pain during the six month period compared with 61 hours for patients given placebo.

Unknowns relating to treatment benefits

The extra minutes a day that patients on Scenesse spent in sunlight appears to be small and its overall impact on patients' quality of life is not clear.

Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Change of pigmentary lesions (areas of skin becoming darker in colour)	Scenesse increases the level of pigment in the skin and makes the skin darker. When taking Scenesse the contrast between the colour of already darkened areas (such as freckles and sun spots) and the surrounding skin can become more pronounced. It is important to monitor these areas to make sure that any change observed is only a result of the drug's normal activity and that it does not mask more serious skin conditions. Any darkening of already darkened areas caused by Scenesse is reversible.	Doctors should carry out full body skin examinations of their patients twice a year to detect any abnormalities and seek specialist dermatology advice in case skin changes are detected that could develop into cancer. Patients should tell their doctors about changes in skin abnormalities such as in a mole.
Administration site reaction (side effects around the area where the implant is inserted)	Scenesse is inserted under the skin in the area above the hip using a large needle. It is therefore possible that some pain, discomfort or bruising will be experienced during or shortly after administration. These reactions normally resolve without the need for any treatment. They are believed to be due to the method of administration rather than the product itself.	Scenesse is available as a prescription only medicine and is only implanted and followed-up by trained and accredited specialists in porphyria centres. Patients should be observed for any allergic reaction for 30 minutes after Scenesse is given.

Important potential risks

Risk	What is known
Allergies and hypersensitivity (the body's immune system reacting to the product)	The body's immune system helps to fight infections by recognising unknown substances. However, sometimes the immune system can also respond to medicines and this reaction is known as an allergy or hypersensitivity. Scenesse has only been tested in a small number of patients. As with any medicine, some patients may experience an allergic reaction to the medicine or any of its components.
Off-label use in children	Scenesse has not been studied in children. Children up to 17 years of age suffering from EPP must not be given Scenesse as safety and effectiveness in children have not been demonstrated.
Off-label use in adults	Scenesse has not been fully evaluated in conditions other than EPP. Scenesse should not be used in other patient populations as safety and effectiveness in other patients have not been demonstrated.

Risk	What is known
Use during pregnancy and breastfeeding	Scenesse has not been evaluated during pregnancy or breastfeeding. The potential effect on the developing foetus or infant is not known.
Administration error	The implant is administered using a catheter needle; the risk of damage to the implant during the administration cannot be excluded.

Missing information

Risk	What is known
Use in older patients (over 70 years of age)	Scenesse has not been studied in patients older than 70 years of age.
Use in patients with other illnesses such as clinically significant kidney, liver or heart impairment	Scenesse has not been studied in patients with other, potentially serious illnesses, such as patients who suffer from liver, kidney or heart disease. There is an increased risk of side effects in these patients.
Long-term safety data	Scenesse has only been used for a limited time in controlled clinical trials. The safety of Scenesse has not been evaluated in clinical trials of duration longer than 2 years. These data support safe use of up to 4 consecutive implants.
Pharmacokinetic data (data on how the medicine is absorbed, distributed, metabolised and excreted from the body)	Dose-finding studies have not been conducted and the pharmacokinetics of afamelanotide or any of its metabolites have not yet been fully characterised. Data of possible interactions or effects in special populations, e.g. patients with liver or kidney impairment are not available.

Summary of risk minimisation measures by safety concern

All medicines have a summary of product characteristics (SmPC) which provides physicians, pharmacists and other healthcare professionals with details on how to use the medicine, and also describes the risks and recommendations for minimising them. Information for patients is available in lay language in the package leaflet. The measures listed in these documents are known as 'routine risk minimisation measures'.

The SmPC and the package leaflet are part of the medicine's product information. The product information for Scenesse can be found on Scenesse's EPAR page.

This medicine has special conditions and restrictions for its safe and effective use (additional risk minimisation measures). Full details on these conditions and the key elements of any educational material can be found in Annex II of the product information which is published on Scenesse's EPAR

page; how they are implemented in each country however will depend upon agreement between the marketing authorisation holder and the national authorities.

These additional risk minimisation measures are for the following risks:

Side effects around the area where the implant is inserted (administration site reactions) and administration error

Risk minimisation measure:
Objective and rationale: To minimise the risk of discomfort or injury during administration of Scenesse.
Description: Educational material for healthcare professionals that detail the correct administration procedure for the Scenesse implant. This will include the SmPC and an educational video. The educational material will be provided prior to prescription.

Off-label use in adults

Risk minimisation measure:
Objective and rationale: To ensure that Scenesse is not used in non-EPP adult patients.
Description: Controlled access programme to limit the use of Scenesse to designated porphyria centres.

Planned post-authorisation development plan

List of studies in post-authorisation development plan

Study / activity (including study number)	**Objectives**	**Safety concerns / efficacy issue addressed**	**Status**	**Planned date for submission of (interim and) final results**
Retrospective chart review (study to measure the effectiveness of risk minimisation measures)	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 will be the	Safety parameters: • Changes of pigmentary lesions • Administration site reactions • Allergy and hypersensitivity • Off-label use in paediatric	Protocol submission	Study to start 6 months after study protocol approval Intermediate reports will be submitted annually. Final report: 6years after protocol approval

Study / activity (including study number)	Objectives	Safety concerns / efficacy issue addressed	Status	Planned date for submission of (interim and) final results
	assessment of the compliance with risk minimization recommendations and the controlled access program for patients receiving Scenesse.	patients • Off-label use in adults • Use in pregnancy and lactation • Administration error		
Disease registry	Registry will gather long term safety data and outcome endpoints in patients with EPP. The registry will collect data from both patients and physicians	Safety parameters: • Changes of pigmentary lesions • Administration site reactions • Allergy and hypersensitivity • Administration error	Protocol submission	Study to start immediately after study protocol approval Intermediate reports will be submitted annually
Pharmacokinetic study in EPP patients (CUV052)	Scenesse PK profile in EPP patients Determine the PK profile in at least 12 EPP patients after administration of implant 1 on Day 1 and implant 2 on Day 60.	Safety parameter: pharmacokinetic data	Started	Study to finish 3Q 2015 Final study report: December 2015

Studies which are a condition of the marketing authorisation

The disease registry and the retrospective chart review (study to measure the effectiveness of risk minimisation measures) are conditions of the marketing authorisation.

Summary of changes to the risk management plan over time

Not applicable

This summary was last updated in 10-2014