1. NAME OF THE MEDICINAL NEW CHEMICAL ENTITY (NCE)

The active pharmaceutical ingredient is:

CHLORIN-CHLOROPHYLL

The NCE consists of the active pharmaceutical ingredient in suspension

CHLORIN-CHLOROPHYLL FLUID 1 MG/ML IN LIPOSOMAL SUSPENSION

The medicine is a green liposomal suspension of chlorin-chlorophyll sensitiser available in three forms

a) Fluid for Infusion
b) Fluid to be added to a fatty drink such as chocolate milk
c) Gel for topical administration

The chlorin-chlorophyll sensitiser is activated by light.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

The suspension contains 1 mg of chlorin-chlorophyll per ml

Excipients make it a liposomal suspension. Chlorin-Chlorophyll is brought into a liposomal suspension with polyethylenic and phosphatidylcholine molecules, see section 6.1

3. PHARMACEUTICAL FORM

Green suspension for infusion, oral ingestion or topical application

4. CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATION

Chlorin-chlorophyll sensitiser is indicated for bulk reduction in patients with advanced cancer failing regular therapies or unlikely to be cured by regular therapies.

4.2 POSOLOGY AND METHOD OF ADMINISTRATION

The suspension must only be administered under expert supervision.

The chlorin-chlorophyll sensitiser must be activated by light.

POSOLOGY

The dose of sensitiser for intravenous and oral use is 1 mg/kg body weight. The dose for gel application is liberal.

The dose of light has not yet been defined

Paediatric population

There has been no reported experience in children

METHOD OF ADMINISTRATION

The green colour of the liposomal suspension is clear and that should be checked against a light for particulates. The suspension can be diluted in sodium chloride or other aqueous suspension. With topical application the chlorin-chlorophyll sensitiser is applied directly over the cancer to be absorbed by the cancer in about 20 minutes. The applicant should wear plastic gloves to protect administration to the hands.

For intravenous use the fluid should be warmed to 40^{o} Centigrade.

The medicine should be shielded from light.

4.3 CONTRAINDICATIONS

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Tumours known to be eroding into a major blood vessel.
- A planned surgical procedure within the next week.
- Pregnancy

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

At this date no patients have been treated with chlorin-chlorophyll for bulk reduction. Therefore, no safety profile is defined. However, in the process of scaling up from rodent experience a few humans have been treated with chlorin-chlorophyll. In contrast to available information on Chlorin-Chlorophyll that considers it to safe, we warn of the likelihood of very serious side effects that are hitherto unknown.

The chlorin-chlorophyll sensitiser on its own has no evidence of toxicity, but as soon as light is applied it initiates strong anti-cancer effects and strong side effects. Care should be exercised to avoid excessive tumour necrosis. The amount of sensitiser and light have a linear relationship with tumour necrosis. However, when necrosis is avoided there is a non-linear tumour response causing oedema. This effect will recur at intervals over many weeks, at least twelve. Late recurrences can be more severe that the initial response.

All patients will become temporarily photosensitive to sunlight for at least a week. Precautions must be taken to avoid exposure of skin and eyes to direct sunlight or bright indoor light as long as the treatment is ongoing. Skin photosensitivity reactions are caused by visible light; therefore, ultraviolet sunscreens provide no protection. As a precautionary measure, if prolonged outdoor activity is planned, the body should be protected by wearing some hat, long sleeved coloured shirt, and trousers. Be aware that most of the toxicities associated with are local effects seen as consequence of light-activation.

Unplanned or emergency surgical procedures must be undertaken when necessary. Precautions must be taken to avoid direct illumination of the patient with surgical lamps during these procedures. The use of headlamps is recommended instead. Some pulse oximeters may produce light of a wavelength close to that used for the photo-activation of the sensitiser. Oximeters must be repositioned at least every 10-15 minutes to avoid the risk of local skin burns. Pain occurs immediately after illumination and usually lasts a week. Illumination of airways may lead to local inflammation and oedema. The resulting complications (i.e. dyspnoea or even airway obstruction leading to, for instance, intubation or tracheotomy) should be anticipated. Prophylactic treatment with corticosteroids should be considered.

4.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

There is potential for exacerbation of skin photosensitivity if chlorin-chlorophyll sensitiser is used with other photosensitising active substances. No interactions have been observed.

4.6 FERTILITY, PREGNANCY AND LACTATION

Pregnancy

There are no data from the use of chlorin-chlorophyll sensitiser in pregnant women. Chlorin-chlorophyll sensitiser should not be used during pregnancy unless the clinical condition of the woman requires treatment.
In the case of pregnancy and a tumour distant from the uterus, our hypothesis is that Chlorin-Chlorophyll, in conjunction with light is a potentially safe procedure for mother and unborn child.

Breast-feeding

A risk to the new-borns/infants cannot be excluded. The experimental status is posing an unnecessary risk when compared to bottle milk.

Fertility

The effects of chlorin-chlorophyll sensitiser on fertility in humans have not been studied. Our hypothesis is that Chlorin-Chlorophyll does not affect reproduction. Genotoxicity is not expected.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

On the basis of the pharmacodynamic profile, chlorin-chlorophyll sensitiser is presumed to be safe or unlikely to produce an effect on the ability to drive.

4.8 UNDESIRABLE EFFECTS

At this date no patients have been treated with chlorin-chlorophyll for bulk reduction. Therefore, no safety profile is defined. In the process of scaling up from rodent experience a few humans have been treated with chlorin-chlorophyll.

All patients who receive chlorin-chlorophyll sensitiser will become temporarily sensitive to light and must be instructed to observe precautions to avoid sunlight and bright indoor light.

4.9 OVERDOSE

In the event of an overdose of sensitiser, light will result in a more intense immune reaction than would be expected with the recommended dose. It is recommended that the patient is immediately admitted to a high tech intensive care unit.

5. PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group: Antineoplastic agents, other antineoplastic agents, ATC code: L01XD05. chlorin-chlorophyll is a sensitising agent used in the light-activated therapy of tumours. The pharmacodynamics is that the chlorin-chlorophyll emits reactive electrons after being illuminated by the light. The chlorin-chlorophyll attaches to the essential structures inside cancer cells. The electrons cause, among others, single and double strand breaks in the DNA of the cancer cells.

5.2 PHARMACOKINETIC PROPERTIES

Chlorin-chlorophyll liposomal suspension is a designed to circulate undisturbed for days. Pharmacokinetic studies show that the sensitiser is metabolised and cleared naturally within two to three days. However, the present formulation may leave the active ingredient circulating for weeks. In addition, it may remain absorbed in the cancer for months.

5.3 PRECLINICAL SAFETY DATA

In repeated dose toxicity studies in rodents, the main undesirable effects of chlorin-chlorophyll were phototoxicity and adverse injection site reactions. Local irritancy of chlorin-chlorophyll suspension for injection after intravenous administration occurred with all doses. No other signs of toxicity were found, while rodents were treated with doses exceeding those of humans. Genotoxicity has not been studied.

6. PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Polyethylenic Molecules; Phosphatidylcholine Molecules

6.2 INCOMPATIBILITIES

In the absence of compatibility studies, this NCE must not be mixed with other medicinal products. Chlorin-chlorophyll sensitiser can be diluted with aqueous suspensions.

6.3 SHELF LIFE

The shelf life has not been tested. Once opened, the suspension must be used immediately.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Do not store above 25^{o} C.

Store in the original package to protect from light.

6.5 NATURE AND CONTENTS OF CONTAINER

Bags are prepared for immediate use.

Type I amber glass vials with a bromobutyl elastomer stopper and aluminium seal for longer term storage. Each pack contains 1 vial.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL AND OTHER HANDLING

Appropriate precaution must be taken when handling this medicinal NCE. It has been shown that chlorin-chlorophyll sensitiser is non-irritant. Each vial represents a single dose and any unused suspension must be discarded.

Chlorin-chlorophyll sensitiser is photosensitive. Once removed from its packaging it must be administered immediately. Where delay is unavoidable, the suspension must be protected from light.

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

7. MARKETING AUTHORISATION HOLDER

Not applicable.

8. MARKETING AUTHORISATION NUMBER(S)

No market authorisation has been obtained

Intellectual properties of the NCE are owned by:

Hugo Intellectual Properties BV
The Netherlands

9. REGULATORY STATUS

The regulatory status is that chlorin-chlorophyll is registered in Russia.

10. DATE OF REVISION OF THE TEXT

24 April 2018