SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Procto-Glyvenol, 400 mg + 40 mg, suppository
Procto-Glyvenol, 5% + 2%, rectal cream

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

- One suppository (2 g) contains 400 mg of tribenoside and 40 mg of lidocaine.
- 1 g of rectal cream contains 50 mg of tribenoside and 20 mg of lidocaine hydrochloride.

Excipients with known effect:
Rectal cream: methyl parahydroxybenzoate, propyl parahydroxybenzoate, cetyl alcohol.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

- **Suppositories:** Yellowish-white, torpedo-shaped suppositories free from fissures, solid, slightly greasy.
- **Rectal cream:** White, homogeneous cream, with a mild characteristic odour.

4. CLINICAL PARTICULARS

4.1. THERAPEUTIC INDICATIONS

Local treatment of external and internal haemorrhoids.

4.2. POSOLOGY AND METHOD OF ADMINISTRATION

**Posology**

One suppository should be administered or the rectal cream applied morning and evening until acute symptoms have diminished, after which the dosage can be reduced to once a day.

**Paediatric population**

There is no clinical experience with tribenoside and lidocaine Rectal cream and Suppository in children.

4.3. CONTRAINDICATIONS

Hypersensitivity to the active substances or to any of the excipients of tribenoside and lidocaine Rectal cream and Suppository listed in section 6.1.

4.4. SPECIAL WARNINGS AND PRECAUTIONS FOR USE
Patients with hepatic impairment
Tribenoside and lidocaine Rectal cream and Suppository should be used with precaution in patients suffering from severe hepatic damage.

Paediatric population
There is no clinical experience with tribenoside and lidocaine Rectal cream and Suppository in children.

Information concerning excipients
Tribenoside and lidocaine rectal cream contains:
- cetyl alcohol which may cause local skin reactions (e.g. contact dermatitis).
- methyl parahydroxybenzoate and propyl parahydroxybenzoate which may cause allergic reactions (possibly delayed).

Contact with the eyes should be avoided.
The product must not be swallowed.

4.5. INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION
No interaction studies have been performed.

4.6. FERTILITY, PREGNANCY AND LACTATION
Pregnancy and breast-feeding
There are no controlled studies on the potential effects of tribenoside and lidocaine in pregnant or lactating women. As a precaution, tribenoside and lidocaine Rectal cream and Suppository should not be used during the first 3 months of pregnancy. Tribenoside and lidocaine Rectal cream and Suppository may be used as from the 4th month of pregnancy and during breast-feeding, however the recommended dosing should not be exceeded.

Fertility
Animal studies indicate that lidocaine does not have effects on fertility. No data is available on the potential effects of tribenoside on fertility.

4.7. EFFECTS ON ABILITY TO DRIVE AND USE MACHINES
Tribenoside and lidocaine Rectal cream and Suppository have no or negligible influence on the ability to drive and use machines.

4.8. UNDESIRABLE EFFECTS
Summary of the safety profile
Rare reported adverse reactions during treatment are local reactions like burning (application site pain), rash and pruritus which may spread beyond the application site. Beside these undesirable effects, the
administration of tribenoside and lidocaine Rectal cream and Suppository may trigger in very rare cases an anaphylactic reaction including possible symptoms (e.g. angioedema and face edema).

Tabulated list of adverse reactions

Adverse reactions are listed below by system organ class and frequency. 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), or not known (cannot be estimated from the available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

<table>
<thead>
<tr>
<th>System Organ Class (SOC)</th>
<th>Rare</th>
<th>Very rare</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immune system disorders</td>
<td></td>
<td>Anaphylactic reaction</td>
</tr>
<tr>
<td>Cardiac disorders</td>
<td></td>
<td>Cardiovascular disorder</td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastinal disorders</td>
<td></td>
<td>Bronchospasm</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td>Urticaria</td>
<td>Angioedema</td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
<td>Application site pruritus, application site rash, application site pain</td>
<td>Face edema</td>
</tr>
</tbody>
</table>

Description of selected adverse reactions

Anaphylactic reactions may very rarely occur, including angioneuronic edema, face edema, bronchospasm and cardiovascular disorders.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions is an important way to gather more information to continuously monitor of the benefit/risk balance of the medicinal product. Any suspected adverse reactions should be reported to Pharmaceutical Services, Ministry of Health, CY-1475, www.moh.gov.cy/phs, Fax: + 357 22608649.

4.9. OVERDOSE

There is no experience of overdosage with tribenoside and lidocaine Rectal cream and Suppository. In case of accidental oral ingestion gastric lavage is recommended together with symptomatic treatment and general supportive measures.

5. PHARMACOLOGICAL PROPERTIES

5.1. PHARMACODYNAMIC PROPERTIES
Pharmacotherapeutic group: Antihemorrhoidals for topical use. ATC code: C05A D Products containing local anaesthetics.

Mechanism of action

Tribenoside reduces capillary permeability and improves vascular tone. It also has anti-inflammatory properties and exerts an antagonistic action on a number of endogenous substances, which play a role as mediators in the development of inflammation and pain.

Lidocaine is a local anaesthetic, which relieves itching, smarting and pain caused by haemorrhoids.

5.2 PHARMACOKINETIC PROPERTIES

Absorption

The systemic bioavailability of tribenoside from suppositories amounts to only 30% of that attained when the substance is given orally or intravenously. Between 2-20% of the tribenoside contained in the cream is absorbed through the skin. Peak plasma concentrations of 1 microgram/ml (tribenoside & metabolites) were recorded 2 hours after rectal administration of 1 suppository (400 mg tribenoside).

Lidocaine is absorbed readily from mucous membranes and poorly from intact skin. Its bioavailability is about 50% after rectal administration. Peak plasma concentrations of only 0.70 microgram/ml were recorded 112 minutes after administration of 1 suppository of as much as 300 mg lidocaine.

Distribution

Lidocaine is markedly bound to alpha1-acid glycoprotein.

Biotransformation

Tribenoside is extensively metabolized in the body. Lidocaine is rapidly metabolized in the liver.

Elimination

Tribenoside: 20-27% of the dose administered by suppository is excreted in the urine in the form of metabolites.

Lidocaine metabolites are excreted in the urine with less than 10% of unchanged lidocaine.

5.3 PRECLINICAL SAFETY DATA

Tribenoside:
Non-clinical acute and repeated dose toxicity studies with tribenoside showed the product to be practically non-toxic by oral administration. Reproduction toxicity studies are not available. Rectal application produces effective local concentrations with minimal systemic exposure and is, therefore, not expected to produce a toxicological profile different from oral tribenoside.

Lidocaine:
In animal studies the toxicity noted after overdosage of lidocaine consisted of effects on the central nervous and cardiovascular systems. No drug-related adverse effects were seen in reproduction toxicity studies, neither did lidocaine show a mutagenic potential in either in vitro or in vivo mutagenicity tests.
6. PHARMACEUTICAL PARTICULARS

6.1. LIST OF EXCIPIENTS

- **Suppository**: Hard fat N°1 (Witepsol E85), Hard fat N° 2 (Witepsol W35)
- **Rectal Cream**: Macrogol cetostearyl ether (Cetomacrogol 1000), Cetyl alcohol, Isopropyl palmitate, Liquid paraffin, Methyl parahydroxybenzoate, Propyl parahydroxybenzoate, Sorbitan stearate (Arlacel 60), Sorbitol liquid (non crystallising), Stearic acid, Purified water.

6.2. INCOMPATIBILITIES

Not applicable.

6.3. SHELF LIFE

- **Suppository**: 5 years
- **Rectal cream**: 5 years

6.4. SPECIAL PRECAUTIONS FOR STORAGE

Do not store above 30°C.
Store in the original package.

6.5. NATURE AND CONTENTS OF CONTAINER

- **Suppository**: box of 10, sealed in polyethylene and polypropylene laminated aluminium foil.
- **Rectal cream**: 30 g, aluminium tube with an inner coating made of epoxy-phenol resin lacquer, a polyethylene cap, a latex joint and a polyethylene nozzle.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL AND OTHER HANDLING

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Recordati Hellas Pharmaceuticals SA.
7, Zooodochou Pigis Street 15231,
K. Chalandri, Athens,
Greece

8. MARKETING AUTHORISATION NUMBER(S)

Cream: 17441
Suppositories: 18327

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

Cream: 13 November 1997/ 20 June 2008
Suppositories: 24 August 1999/ 20 June 2008
10. DATE OF REVISION OF THE TEXT

6 October 2015