SUMMARY OF PRODUCT CHARACTERISTICS

Procto-Glyvenol Suppositories
Procto-Glyvenol Cream

Composition
Active ingredients: tribenoside, lidocaine hydrochloride/ lidocaine.

Excipients
Suppositories: Hard fat #2 (Witepsol W35), Hard fat #1 (Witepsol E85)
Cream: Purified water, Paraffin, liquid, Stearic acid, Sorbitol liquid (non crystallizing), Cetyl Alcohol, Macrogol cetostearyl ether (Cetomacrogol-1000), Isopropyl Palmitate, Sorbitan stearate (Arlacel-60), Methyl parahydroxybenzoate, Propyl parahydroxybenzoate,

Pharmaceutical forms and quantity of active ingredient per unit
1 suppository (2 g) contains 400 mg of tribenoside and 40 mg of lidocaine.
Yellowish-white and torpedo-shaped suppositories.
1 g of cream contains 50 mg of tribenoside and 21.2 mg of lidocaine hydrochloride. White and homogenous cream.

Indications/Possible uses
Suppositories: Local relief of haemorrhoids.
Cream: External & internal haemorrhoids.

Posology/Method of administration
Adults: During the acute phase of the disorder, apply the cream or suppository in the morning and evening; subsequently, reduce to one application of cream or one suppository a day.

30g of cream (1 tube) are enough for approximately 20-30 applications.
Avoid contact with the eyes.

Intended for adult use only; not suitable for children.

Using the cream:
• clean the area concerned with a suitable cloth,
• dry thoroughly (with a soft cloth or a towel) before applying the cream.
For external use (without applicator):
Apply the cream around the anus with a clean finger.
For use in the anal canal (with applicator):
• after removing the seal from the tube, screw the supplied applicator on to the tube,
• remove the protective cap from the applicator,

• carefully insert the applicator into the anus, not too deeply, and gently press on the tube,
• after each use, clean the outside of the applicator with a moistened cloth or moistened cotton and replace the protective cap.
Wash hands thoroughly with soap and water after use.

Using the suppositories:
• wash hands thoroughly before and after use,
• detach 1 suppository from the strip and remove the wrapping,
• before inserting the suppository, clean the area concerned with a soft cloth or a towel and gently dry,
• carefully insert the suppository into the anus so that it does not protrude,
• do not use aids, such as petroleum jelly or oils, to facilitate insertion.

Contraindications
Hypersensitivity to the active substances, lidocaine or tribenoside, or any of the excipients listed under Composition.

Warnings and precautions
When there is anal bleeding, suspected blood in the stool, or when other unusual symptoms occur, a medical examination is indicated.

When the symptoms occur for the first time, self-medication must not last for more than 7 days. Repeated treatments will only take place after a confirmed diagnosis has been made by a doctor.

Procto-Glyvenol should be used with caution in patients with severel liver function disorders.

There is no clinical experience available with regard to use in children.

Avoid any contact with the eyes and do not swallow the preparation.

Procto-Glyvenol cream contains *cetyl alcohol*, which may cause local skin reactions (e.g. contact dermatitis).
The cream also contains *methyl parahydroxybenzoate and propyl parahydroxybenzoate*; these substances may trigger allergic reactions,as well as delayed reactions.

Interactions
No interaction studies have been performed.

Lidocaine should be used with caution in patients taking beta blockers or other antiarrhythmic drugs, as the potential toxic effects (e.g. myocardial depression) are additive.

Pregnancy/Breastfeeding
Insufficient data available on use in pregnant patients.

There are no animal studies on tribenoside or on the combination of tribenoside and lidocaine. Similarly, it is not known if tribenoside crosses the placenta. Lidocaine shows some embryotoxicity. Under these conditions, Procto-Glyvenol should not be used during pregnancy, particularly in the first three months, except where absolutely necessary.

Lidocaine may pass into breast milk. The benefits for the mother should be weighed against the risks for the child. As a precaution treatment of breastfeeding should be stopped.

Effect on ability to drive and to operate machinery
No corresponding studies have been performed.

Undesirable effects
The following adverse reactions are arranged based on system organ class and frequency. Frequencies are defined: 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), not known (cannot be estimated from the available data).

Immune system disorders
Very rare: anaphylactic reactions (angioedema)

Cardiac disorders
Very rare: Cardiovascular disorders

Respiratory, thoracic and mediastinal organs
Very rare: bronchospasm

Skin and subcutaneous tissue disorders
Rare: urticaria

General disorders and administration site conditions
Rare: pruritus, eruption, pain.

Reporting suspected adverse reactions after authorisation of the medicinal product is important.

It allows continued monitoring of the benefit/risk balance of the medicinal product.

Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form https://sideeffects.health.gov.il/

Additionally, please also report to GSK Israel (il.safety@gsk.com)

Overdose
No cases of overdosing have been reported.

The systemic toxicity of lidocaine can affect the central nervous system and the cardiovascular system.
In the event of accidental ingestion, symptomatic treatment and general support measures are recommended.

Properties/Effects
ATC Code: C05AD01
The effect of tribenoside is based on reducing capillary permeability and increasing vascular tonicity, and on its local properties as an anti-inflammatory and antagonistic properties with regard to a range of endogenous substances that play an important role as mediators in the onset of inflammation and in the origin of pain.

Lidocaine is a local anaesthetic agent and relieves the pain, burning sensation and itching caused by haemorrhoids.

Pharmacokinetics
Absorption
The systemic bioavailability of tribenoside in suppository form is only 30% in comparison with oral administration (capsules). When Procto-Glyvenol cream is applied, approximately 2-20% of tribenoside is absorbed percutaneously. Two hours after insertion of a suppository (400 mg of tribenoside) into the rectum, maximum plasma concentrations of tribenoside of 1µg/ml and its metabolites are observed.

Lidocaine is readily absorbed by the mucous membranes, but only moderately from intact skin. Following rectal administration, the bioavailability of lidocaine is approximately 50%. The maximum plasma concentrations of 0.70 µg/ml is reached 122 minutes after insertion of a suppository of 300 mg lidocaine.

Distribution

Lidocaine binds variably to plasma proteins in a concetration-dependent manner, primarily to alpha 1-acid glycoproteins(approximately 60-80% for concentrations of 1-4 µg/mL).

Metabolism

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

Elimination

Tribenoside: After insertion of a suppository 20-27% of the dose is excreted in the urine in the form of metabolites.

Lidocaine: Less than 10% is excreted unchanged; the metabolites are excreted in the urine.

Preclinical data

There are no relevant preclinical data on tribenoside or the combination of tribenoside and lidocaine.

Mutagenicity studies on lidocaine have yielded negative results. However, there is evidence to suggest that the lidocaine metabolite, 2, 6–xylidine, has mutagenic effects in rats and possibly also in humans. These indications come from in vitro tests using this metabolite at very high, almost toxic, concentrations. There are no data to suggest that the parent substance, lidocaine, is equally mutagenic. Moreover, 2, 6 -xylidine showed tumorigenic potential in a carcinogenicity study carried in rats with transplacental exposure and post-natal treatment of the animals for 2 years. In this highly sensitive test system, malignant and benign tumours were observed at very high doses, particularily in the nasal cavity (ethmoturbinals). As the significance of these findings for humans can not be ruled out with sufficient certainty, high doses of lidocaine should not be administered for a prolonged period.

Reproduction toxicity studies conducted with lidocaine have not shown any evidence to suggest teratogenicity but embryotoxicity has been observed (reduced foetal weight). Behavioural changes have been reported in the descendents of that received a dose of lidocaine during pregnancy corresponding to almost the maximum recommended dose in humans.

Specific comments

Stability

The medication must not be used after the date following the wording “EXP” on the packaging.

Comments regarding storage

Store Procto-Glyvenol Suppositories and Procto-Glyvenol cream out of the reach of children

Store Procto-Glyvenol Suppositories and Procto-Glyvenol below 25ºC.

Manufacturer

GSK Consumer Health SA , Switzerland
Route De I’Etraz 1260 Nyon, Switzerland

Packs
Suppositories: 10 suppositories. Sealed polyethylene and polypropylene aluminium foil.
Cream: 30 g. Aluminium tube with a protective inner coating, a cap and a nozzle.

Registration Holder:
GSK Consumer Healthcare Israel Ltd.,
P.O.B. 3256, Petach-Tikva

Registration numbers:
Cream: 044-65-23919
Suppositories: 067-40-23920

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ProGly DR V3