SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Prednisolon Unimedic 31.25 mg rectal solution.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

125 ml contains 31.25 mg prednisolone sodium phosphate equivalent to 23.25 mg prednisolone.

Excipients with known effect
Methyl parahydroxybenzoate (E218) and propyl parahydroxybenzoate (E216).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Rectal solution.
Clear solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Ulcerative proctosigmoiditis.

4.2 Posology and method of administration

Posology

125 ml solution is administered rectally once daily preferably before going to bed, with the patient lying on their left side. After the application, the patient should lie on their stomach for at least 3 to 5 minutes. The dose should stay in the rectum as long as possible, preferably overnight. The duration of treatment is usually 1 to 4 weeks but prolonged treatment may also be necessary. Treatment results should be monitored clinically and when needed, by endoscopy.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
Local viral, fungal and bacterial infections, e.g. tuberculosis or gonorrhoea.

4.4 Special warnings and precautions for use

In connection with continuous use, the risk of systemic effects should be considered. Particular caution is required when treating patients who switch from oral steroids, as disturbances of the endogenous cortisol balance (HPA axis) can be expected.

Visual disturbance
Visual disturbance may be reported with systemic and topical use of corticosteroids. If patients experience symptoms, such as blurred vision or other visual disturbances, referral to an ophthalmologist should be considered to assess the possible causes. These may include cataract, glaucoma or rare diseases, such as central serous chorioretinopathy (CSCR), which have been reported after the use of systemic and topical corticosteroids.

4.5 Interaction with other medicinal products and other forms of interaction

The following combinations involving Prednisolon Unimedic may require dose adjustment:

Phenobarbital, phenytoin and carbamazepine
Phenobarbital (also a metabolite of primidone), phenytoin and carbamazepine, either alone or combined, induce the metabolism of hydrocortisone, prednisolone and methylprednisolone (shown in children with asthma), resulting in an increased dose requirement. This interaction probably applies to the entire group of glucocorticoids.

Rifampicin
Rifampicin induces the microsomal oxidation of glucocorticoids (hydrocortisone, prednisolone and methylprednisolone). This results in an increased need of steroids during treatment with rifampicin and in a decreased need for steroids after such treatment.

Prednisolone also interacts with:

Ketoconazole
Ketoconazole inhibits the enzyme CYP3A4. In one study, increased prednisolone concentrations were reported as a result but, in another study, no interaction could be shown.

Itraconazole
Itraconazole increases the AUC of prednisolone after an oral single dose by 24%. This indicates that the metabolism of prednisolone is influenced by CYP3A4 inhibitors to an essentially lesser extent than that of methylprednisolone.

4.6 Fertility, pregnancy and lactation

Pregnancy
Studies in animals have shown reproductive toxicity with corticosteroids (see section 5.3). The relevance in humans is not known.
After peroral long-term treatment, reduced placental and birth weight has been observed in humans and animals. Long-term treatment is associated with a risk of suppression of the adrenal cortex in neonates. Therefore, corticosteroids should only be used during pregnancy after careful consideration.

Breastfeeding
Prednisolone is excreted into breast milk, but an effect on the child appears unlikely at therapeutic doses.

Fertility
Studies in animals have shown that corticosteroids impair fertility (see section 5.3).

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

The most common adverse effect is nausea (3%). Prednisolone is absorbed to some extent and may cause systemic effects, such as decrease in plasma cortisol.

The frequency categories are based on the following convention:
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).

Eye disorders
Not known: Blurred vision (see also section 4.4)

Gastrointestinal disorders
Common: Nausea

Investigations
Rare: Decrease in plasma cortisol

Reporting of suspected adverse reactions
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. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

Toxicity and symptoms: Acute toxicity, also at massive doses, does not usually cause any clinical problems.
Acute overdose may possibly aggravate pre-existing medical conditions, such as ulcer, electrolyte imbalance, infections or oedema. Repeated high doses of methylprednisolone have caused hepatic necrosis and increases in amylase. Bradyarrhythmia, ventricular arrhythmia and cardiac arrest have been observed in connection with intravenous administration of high doses of methylprednisolone and dexamethasone.
Treatment: Not usually required. Gastric evacuation and charcoal as appropriate. Symptomatic treatment.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: water-soluble glucocorticoids acting locally, ATC code: A07EA01

Prednisolon Unimedic is stable aqueous solution of prednisolone 21-disodium phosphate for intrarectal treatment of ulcerative proctosigmoiditis. Prednisolone 21-disodium phosphate has a considerably more potent anti-inflammatory, antiallergic and immunosuppressive effect than cortisone or hydrocortisone but has a lesser effect on electrolyte balance.

5.2 Pharmacokinetic properties

After a single dose of Prednisolon Unimedic, up to 40% of the prednisolone dose is absorbed.

5.3 Preclinical safety data

Animal studies have shown that corticosteroids may cause malformations of different kinds (palatoschisis, skeletal malformations). After long-term treatment, reduced placental and birth weight has been observed in animals.

It has been shown that corticosteroids impair fertility when administered to rats.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Purified water, sodium chloride, ethanol (96 %), nicotinamide, methyl parahydroxybenzoate (E218), propyl parahydroxybenzoate (E216), sodium citrate, disodium phosphate dihydrate, sodium hydroxide, citric acid

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

1 year

6.4 Special precautions for storage

Keep in the outer carton in order to protect from light.
Do not store above 25 °C.

6.5 Nature and contents of container

Each pack contains 6 soft plastic bottles à 125 ml with a nozzle and a protective cap.

6.6 Special precautions for disposal and other handling

A plastic bag is used for hand protection.

7. MARKETING AUTHORISATION HOLDER

[To be completed nationally]

8. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: {DD month YYYY}

10. DATE OF REVISION OF THE TEXT

04 February 2020