SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Paroven capsules 250 mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient: Oxerutins 250 mg

3 PHARMACEUTICAL FORM

Capsules

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Relief of symptoms of oedema associated with chronic venous insufficiency.

4.2 Posology and method of administration

Posology

Adults and elderly: 2 capsules (500mg) twice daily.

Patients with heart, renal or hepatic impairment

Patients who have oedema of the lower limbs due to heart, kidney or liver disease should not use Paroven because the effect of O-(beta- hydroxyethyl)-rutosides has not been shown in these indications.

Paediatric population

The safety and efficacy of Paroven in children and adolescents aged less than 18 years has not yet been established. No data are available.

Method of administration

Oral use.

4.3 Contraindications

Hypersensitivity to O-(beta-hydroxyethyl)-rutosides or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Patients with heart, renal or hepatic impairment

Treatment of leg oedema due to cardiac, renal or hepatic disease should be directed to the underlying cause; Paroven should not be used in these conditions. If leg pain and swelling do not improve, or get worse, the patient should consult their doctor.

4.5 Interaction with other medicinal products and other forms of interaction

None reported. Oxerutins have been shown not to interact with warfarin anticoagulants.

4.6 Fertility, Pregnancy and lactation

Pregnancy

Data on a limited number of exposed pregnancies indicate no adverse effects of O-(beta-hydroxyethyl)-rutosides on pregnancy or on the health of the fetus/new-born child. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/fetal development, parturition or postnatal development (see section 5.3 Preclinical safety data).

Nevertheless, according to generally accepted safety recommendations, HR should not be used during the first three months of pregnancy.

Breastfeeding

In animal studies, traces of HR were found in the fetuses and in the milk of breast-feeding dams. These minor amounts of HR are of no clinical significance.

Fertility

Animal studies did not indicate effects on fertility following administration of O-(ß-hydroxyethyl)-rutosides.

4.7 Effects on ability to drive and use machines

Paroven has no or negligible influence on the ability to drive and use machines.

In rare instances tiredness and dizziness have been reported in patients using this product. If affected, patients are advised not to drive or operate machines.

4.8 Undesirable effects

Paroven may cause in rare cases gastrointestinal side effects or skin reactions like

gastrointestinal disorder, flatulence, diarrhea, abdominal pain, stomach discomfort, dyspepsia, rash, pruritus or urticaria. Very rare is the occurrence of dizziness, headache, flushing, fatigue or hypersensitivity reactions like anaphylactoid 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 (can not to be

estimated from available data). Within each frequency grouping, adverse reactions are

presented in order of decreasing seriousness.

System Organ Class (SOC)	Adverse Reaction
Frequency	
Immune system disorders	
Very rare	Anaphylactoid reactions
	Hypersensitivity reactions
Nervous system disorders	

Very rare	Dizziness
Very rare	Headache
Vascular disorders	
Very rare	Flushing
Gastro-intestinal disorders	
Rare	Gastrointestinal disorder,
Rare	Flatulence
Rare	Diarrhea
Rare	Abdominal pain
Rare	Stomach discomfort
Dyspepsia	
Skin and subcutaneous tissue disorders	
Rare	Rash
Rare	Pruritus
Rare	Urticaria
Very Rare	Photosensitivity
Very Rare	Alopecia
General disorders and administration site conditions	
Very rare	Fatigue
Musculoskeletal, connective tissue and bone disorders	
Very Rare	Arthralgia

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medical 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 Yellow Card Scheme, www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

No cases of overdosage with symptoms have been reported. No specific antidotes are known.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Systemic vasoprotectors (bioflavonoid), ATC Code: C05CA51/rutoside combinations

Mechanism of action

The pharmacodynamic effects of HR have been demonstrated in different in vitro and in vivo studies. At the cellular level the capability of HR to protect the vascular wall from the oxidative attack of activated blood cells and its affinity to the endothelium of capillaries and venoles could be shown.

In studies in healthy individuals or in patients suffering from CVI the following pharmacodynamic effects of HR could be demonstrated:

- reduction of the capillary permeability

- restoration of the veno-arteriolar reflex

- increase of the venous refilling time

- increase of the transcutaneous oxygen tension.

All these effects are compatible with the primary effect of HR being on the microvascular endothelium, with a resultant diminution of oedema.

5.2 Pharmacokinetic properties

The standardised mixture of HR consists of mono-HR, di-HR, tri-HR, and tetra-HR, which differ in the number of their hydroxyethyl substituents.

Absorption

After oral administration of 14C-HR, peak plasma levels are detected after 2-9 hours.

Distribution

The plasma level declines progressively until 40 hours, after which the decline is very slow. This observation and the results obtained after i.v. application, indicate that HR may be distributed to tissues (especially the endothelium of vessels), from which it is progressively and slowly released back into the circulation.

Plasma protein binding is 27-29%.

Biotransformation

The main metabolic pathway of HR after oral administration is hepatic O-glucuronidation.

Elimination

HR and its metabolites are excreted by both the biliar and the renal route. Excretion via the renal pathway is complete after 48 hours. The mean terminal half-life of the main constituent of HR, the tri-HR, is 18.3 hours with a range of 13.5 to 25.7 hours.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of acute dose toxicity, repeated dose toxicity, genotoxicity and toxicity to reproduction.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Polyethylene glycol

Gelatin

Titanium dioxide E171

Yellow iron oxide E172

Black iron oxide E172

Shellac

6.2 Incompatibilities

None.

6.3 Shelf life

60 months.

6.4 Special precautions for storage

Protect from moisture.

6.5 Nature and contents of container

Blister pack composed of PVC blisters sealed with aluminium foil.

Blister pack composed of PVC/PE/PVDC blisters sealed with aluminium foil.

Pack sizes: 120 capsules.

6.6 Special precautions for disposal

Keep this medicine out of the sight and reach of children.

No special requirements for disposal.

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

7 MARKETING AUTHORISATION HOLDER

Thornton & Ross Ltd (‘trading as ‘STADA’),
Linthwaite,
Huddersfield,
HD7 5QH, UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 00240/0550

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

First authorisation: 19 July 1991

Date of renewal: 28 March 2011

10 DATE OF REVISION OF THE TEXT

22/10/2021