Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Iruxol Mono 1.2U/g Ointment

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram of ointment contains not less than 1.2 units of clostridiopeptidase A and not less than 0.24 units of associated proteases.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Ointment.
A brown, lipophilic ointment with a faint characteristic odour.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Iruxol Mono is indicated for the enzymatic debridement of necrotising wounds, including leg and decubital ulcers.

4.2 Posology and method of administration

For topical administration.

A layer of approximately 2 mm of ointment should be applied to the dressing or directly to the slightly moistened area to be treated once daily. Close contact to the wound surface should be assured. Occasionally, twice daily use may be required.

It is unnecessary to apply too great an amount of the product to the wound. With this, the cleaning process is not improved.

In general, it will suffice to change the dressing once daily. An increase of activity may possibly be obtained by applying the ointment twice daily.

The treatment of varicose ulcers with Iruxol Mono ointment will be usefully supplemented by a pressure bandage and in arterial circulatory disorders, ulcers of diabetic or neurologic etiology, by appropriate drug treatment.

To ensure successful enzymatic wound treatment with Iruxol Mono ointment, sufficient moisture must be present in the wound area during therapy.

In dry wounds, the wound base must therefore be moistened with physiological saline (0.9% NaCl) or other solutions which are well tolerated by the tissue (e.g. glucose). Dry and hard crusts should first be softened by applying a moist dressing.

Treatment with Iruxol Mono should be discontinued when the whole surface of the wound is clean.

Whenever infection is present, an appropriate antibiotic treatment should be considered.

Chloramphenicol, neomycin, framycetin, bacitracin, gentamicin, polymyxin B and macrolides, e.g. erythromycin, have been shown to be compatible with Iruxol Mono.

As is common clinical practice, the wound edges and healthy skin should be protected in order to avoid irritation.

4.3 Contraindications

Iruxol Mono is contra-indicated in patients hypersensitive to any of the ingredients.

4.4 Special warnings and precautions for use

Contact with eyes and mucosa should be avoided.

In diabetic patients, dry gangrenes should be moistened with caution in order to avoid conversion to moist gangrene.

If a reduction in necrotic tissue is not observed within 14 days of commencing treatment with Iruxol Mono, discontinue treatment and replace with an alternative method of debridement.

4.5 Interaction with other medicinal products and other forms of interaction

Iruxol Mono should not be used in the presence of antiseptics, heavy metals, detergents and soaps because the activity of collagenase will be inhibited.

Tyrothricin, gramicidin and tetracyclines should not be used locally with Iruxol Mono.

Silver and silver sulfadiazine products can however be used with Iruxol Mono, without affecting the activity of the collagenase enzymes.

4.6 Fertility, pregnancy and lactation

Although no evidence of any teratogenic effect has been reported, Iruxol Mono should only be administered during the first three months of pregnancy when strictly indicated. Since collagenase does not enter the systemic circulation, excretion into breast milk is unlikely.

4.7 Effects on ability to drive and use machines

Iruxol Mono is not likely to have an effect on the ability to drive and use machines.

4.8 Undesirable effects

Iruxol Mono ointment is generally well tolerated.

Side effects include local pain, pruritus, burning and erythema. In severe cases, discontinuation of treatment should be considered.

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 HPRA Pharmacovigilance, Website: www.hpra.ie

4.9 Overdose

Inadvertent intake of the drug is unlikely, but if it occurs, it should be removed from the stomach (vomiting or gastrolavage, if required).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

The active ingredient of Iruxol Mono is the enzyme preparation, collagenase. ATC Code D03BA02.

The wound healing is speeded up if the wound base is free from necrotic tissue. There are different methods of wound cleaning.

The topical application of hydrolytic enzymes is an atraumatic method. Enzymatic debridement, however, is not invariably successful since, apart from denatured collagen, native collagen is also to be found in wounds. Collagenases are the only

proteolytic enzymes capable of digesting strands of native collagen. They attack the apolar region of the collagen fibres which consist of several successive tripeptides with the specific amino acid sequence, glycine, proline and hydroxyproline or another amino acid. By splitting the apolar region, the collagen fibre is broken down into high molecular weight peptides, which can then be completely digested by collagen peptidases and non-specific proteases.

Due to its substrate specificity, the effect of collagenase alone is not sufficient for the debridement of wounds, since it does not affect fibrous or globular proteins. The combined action of collagenase and its associated proteases ensures the digestion of all protein components of the wound, thus intensifying the wound cleansing effect.

Stimulatory effects on cells involved in the wound healing process, particularly fibroblasts, endothelial cells, monocytes and keratinocytes have been demonstrated in vitro, following application of collagenase N to cells grown on collagen plates. In particular, there is evidence that collagenase N induces a reorganisation of endothelial cells in a dose-dependent manner, to form 3 dimensional capillary like tubules, indicative of the first stages of angiogenesis.

5.2 Pharmacokinetic properties

Neither anti-collagenase antibodies or collagenase were detected in the blood of patients with skin lesions (venous leg ulcer, etc.) treated topically with Iruxol Mono for up to 9 weeks.

Clinical investigators who treated patients with an enzyme preparation of *Clostridium histolyticum* in ointment form reported the same results. Moreover, there has been no evidence suggesting collagenase absorption in a 4-week study in monkeys (*Macaca arctoides*) with standard dermal traumas. Nor did the serum samples of these animals reveal anti-collagenase precipitin-type antibodies.

Hence collagenase is not absorbed through inflamed necrotic skin; it even appears to be inactivated and digested in the necrotic area itself. It is likely that the degradation products of the enzyme mixture contained in Iruxol Mono ointment become part of the endogenous peptide and amino acid pool.

5.3 Preclinical safety data

From the toxicological point of view, Iruxol Mono is well tolerated. There is hardly any acute toxicity and healthy mucosa or skin are not significantly affected. No signs of allergic potential or systemic intolerability reactions were observed after topical application to intact or scarified skin.

According to the results of immunological studies, there is no evidence of systemic absorption of Iruxol Mono after application either to intact skin or areas of ulceration. Therefore extensive toxicological studies, e.g. reproduction, mutagenicity, carcinogenicity studies, are not required.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Liquid paraffin
White soft paraffin

6.2 Incompatibilities

None.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store below 25°C.

6.5 Nature and contents of container

Aluminium tubes contains 10 g and 20 g of ointment.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Smith & Nephew GmbH
Friesenweg 30
22763 Hamburg
Germany

8 MARKETING AUTHORISATION NUMBER

PA22696/001/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 3rd September 1990

Date of last renewal: 3rd September 2010

10 DATE OF REVISION OF THE TEXT

August 2022