Iruxol® Ointment

For the enzymatic wounds & burn debridement

Each 1 gm of Ointment contains 0.6 units of clostridiopeptidase A (EC3.4.24.3) in a lipophilic anhydrous ointment base.

PRODUCT DESCRIPTION
Iruxol® Ointment contains:
Collagenase is a holoprotein from the purified culture filtrate of Clostridium histolyticum.
The active constituent is the collagenase clostridiopeptidase A (EC3.4.24.3) with associated proteases. The enzyme is a proteolytic enzyme with a high specificity for native and denatured collagen used as a debriding agent.

Iruxol® Ointment, is a brown, lipophilic ointment with a faint characteristic odor.

Protects collagenase from proteases as an active ingredient

INDICATIONS
Iruxol® Ointment is indicated for the enzymatic debridement of necrotizing wounds, including leg and decubitus ulcers.
- In ulcers & necroses, such as leg ulcers, decubitus, gangrene of the extremities, especially diabetic gangrene, frostbite; in poorly healing wounds due to wounds after operations, radiotherapy, and accidents.

DOSAGE AND ADMINISTRATION:

For topical administration:

If not otherwise prescribed by physician:

- 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 with the wound surface should be ensured. Occasionally, twice daily use may be required.

- It is unnecessary to apply too great 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 collagenase ointment will be usefully supplemented by a pressure bandage and in arteriosclerotic disorders, ulcers of diabetic or neurologic etiology, by appropriate drug treatment.

- Necrotic material which has separated should be removed when dressing is changed.

- To ensure a successful enzymatic wound treatment with Iruxol® ointment, sufficient moisture must be present in the wound area during therapy. In dry wounds, the base must therefore be moisturized with normal saline (0.9% NaCl) or other solutions which are well tolerated by the tissue (e.g. 5% glucose). Dry and hard crusts should first be softened by applying a moist dressing.

- Treatment with Iruxol® ointment 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, frumycetin, bacitracin, gentamycin, polymyxin B, and penicillin, e.g., erythromycin, have been shown to be compatible with Iruxol® ointment.

CONTRAINdications:

- Hypersensitivity to the active substance(s) or to any of the inactive ingredients.
- It is also contraindicated in patients with major burns.

WARNINGS AND PRECAUTIONS

Contact with eyes and mucosa should be avoided.

In diabetic patients, dry gangrene should be moisturized with caution in order to avoid conversion to a necrotic tissue, which cannot be dissolved by enzymes.

If no improvement is seen in the wound after 14 days, treatment with Iruxol® ointment should be discontinued.

Collagenase should be used cautiously in debilitated patients because of the increased risk of bacteremia and/or bacterial sepsis.

Collagenase is optimally effective at a pH of 6 to 8.

DRUG INTERACTIONS

Iruxol ointment 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® ointment.

PREGNANCY AND LACTATION

Although no evidence of any teratogenic effect has been reported, since studies have not been performed in pregnant women, Iruxol ointment should only be administered during the first three months of pregnancy when strictly indicated.

Nursing Mothers: Since Iruxol ointment does not enter the systemic circulation, excretion into breast milk is unlikely.

ADVERSE REACTIONS

Reactions during Clinical Trials

Collagenase ointment was generally well tolerated during clinical trials in 775 patients with the single ingredient product. In cases of severe side effects, discontinuation of treatment should be considered.

There were no serious adverse events causally attributed to collagenase during the clinical trials.

The following table describes adverse events reported with collagenase ointment during the clinical trials. Within each system organ class, the reactions are ranked under headings of frequency, using the following convention:
- common (>1/1000, <1/100)
- uncommon (>1/1000, <1/100)
- very rare (<1/10000)
- not reported

<table>
<thead>
<tr>
<th>Body System</th>
<th>Frequency</th>
<th>Preferred Term</th>
</tr>
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<tbody>
<tr>
<td>Nervous System Disorders</td>
<td>Common</td>
<td>Burning sensation</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td>Uncommon</td>
<td>Erythema, Pruritus</td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
<td>Common</td>
<td>Pain</td>
</tr>
</tbody>
</table>

* Source: 1998 Clinical Expert report. Sec. 5.1 Supportive therapy on collagenase. Frequency data does not consider causality to collagenase.

OVERDOSE:

Accidental ingestion of the drug is unlikely.

CLINICAL PHARMACOLOGY

Pharmacodynamic Properties

The 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. Iruxol ointment is indicated for the enzymatic treatment of wounds, where necrotic tissue is to be digested and removed, thus promoting the wound-healing process.

Necrotic tissue is anchored to the wound surface by strands of native collagen, and it can only be removed enzymatically after the native collagen strands have been digested. Collagenases are the only proteolytic enzymes capable of digesting strands of native collagen. They attack the apolar region of the collagen fibers which consist of several successive triplets with the specific amino acid sequence, glycine, proline, and hydroxyproline or another amino acid. By splitting the apolar region, the collagen fiber is broken down into high molecular weight peptides, which can then be completely digested by collagen peptides 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 the protein components of the wound, thus intensifying the wound cleansing effect.

Toxicology:

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

Pharmacokinetic Properties:

The optimal effect of Iruxol ointment is seen about 6 to 12 hours post application and lasts up to 24 hours. Neither antibodies to collagenase were detected in the blood of patients with skin lesions (venous leg ulcer, etc.) treated topically with collagenase for up to nine weeks.

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

The systemic absorption and absorption in the gastrointestinal tract is unlikely. Consequently, 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 ointment become part of the endogenous peptide and amino acid pool.

STORAGE:

- Store at room temperature, don’t store above 25°C for a long period.
- Out of the reach of children.
- Only, for topical administration.

How supplied:

- Aluminium tube, coated inside, plastic cap, cardboard outer carton with insert.
- Pack of 15 g ointment.

List #: N120

CDS92060108.doc Signed copy on file
02 / 20 / 2008
Authorization Date: 22 December 2008
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