Like all medicines, Hyaluronidase may cause side-effects in some patients.

SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of Proprietary Medicinal Product
Hyaluronidase 1500 Ui. Powder for Solution for Injection/Infusion

2. Qualitative and Quantitative Composition
Each ampoule contains 1500 International Units of Hyaluronidase.

3. Pharmaceutical Form
Powder for solution for injection/infusion. A sterile freeze-dried powder for solution for injection or infusion.

4. Clinical Particulars
4.1 Therapeutic Indications
Hyaluronidase can be used to enhance permeation of subcutaneous or intramuscular injections, local anaesthetics and subcutaneous infusions and to promote resorption of excess fluids and blood in the tissues.

4.2 Posology and Method of Administration
Adults, children and the elderly:
With subcutaneous injection (hypodermoclysis): 1500ui of Hyaluronidase dissolved in 1ml of water for injections or normal saline injected into the skin, before the injection is set up, or injected into the tubing of the infusion set, about 2cm back from the needle, at the start of the infusion. 1500ui is sufficient for administration of 500-1000ml of most infusions. Refer to Section 4.4 for information on solutions for hypodermoclysis. Care should be taken in young children and the elderly to control the speed and total volume of fluid administered and to avoid over-hydration, especially in renal impairment.

With subcutaneous or Intramuscular injections: 1500ui of Hyaluronidase dissolved directly in the solution to be injected.

With local anaesthetics: 1500ui of Hyaluronidase is mixed with the quantity of local anaesthetic to be used. In ophthalmology, 15u of Hyaluronidase per ml is recommended.

Extravasation: Where dispersion rather than localisation is indicated, 1500ui of Hyaluronidase in 1ml of water for injections or normal saline infiltrated into the affected area as soon as possible after the extravasation is noted.

Haematoma: 1500ui of Hyaluronidase dissolved in 1ml water for injections or normal saline infiltrated into the affected area. Immediately before use dissolve the freeze-dried powder in approximately 1ml of water for injections or directly in the solution with which Hyaluronidase is to be mixed.

4.3 Contraindications
Hyaluronidase is haemostatically neutral. Not to be used for intravenous injections.

Not to be used to reduce the swelling of bites or stings or at sites where infection or malignancy is present.

Not to be used for anaesthetic procedures in cases of unexplained premature labour.

4.4 Special Warnings and Precautions for Use
Do not apply directly to the conjunctiva.

Not to be used to enhance the absorption and dispersion of dopamine and/or alpha agonist drugs.

Solutions for subcutaneous administration should be isotonic with extracellular fluid. Hyaluronidase is physically compatible with the commonly used infusion fluids. Use in hypodermoclysis has been reported with 0.3% sodium chloride, 0.18% sodium chloride with 4% glucose, 0.45% sodium chloride with 2.5% glucose and 5% glucose.

Potassium 34mmol/litre has been administered by hypodermoclysis in isotonic glucose or saline with 1500ui of Hyaluronidase.

Electrolyte-free fluids are less preferable than those containing electrolytes and should not be given too rapidly. Hyaluronidase has also been mixed with morphine, diamorphine, hydrocortisone, chlorpromazine, metoclopramide, promazine, domperidone, local anaesthetics and adrenaline (see 6.2 Incompatibilities).

4.5 Interactions with Other Medicaments products and Other Forms of Interaction
None stated.

4.6 Pregnancy and Lactation
It is not known whether the drug enters breast milk although it is unlikely to harm the breast-fed infant. Caution should be exercised in administering it to nursing mothers.

There is no evidence on the drug's safety in human pregnancy nor is there evidence from animal work that it is free from hazard. Avoid use in pregnancy unless there is no safer alternative.

4.7 Effects on Ability to Drive and to Use Machines
None known.
• Very rarely, severe allergic reactions to Hyaluronidase may occur, with difficulty breathing, rapid pulse and profuse sweating. If you develop any of these symptoms, contact your doctor or nurse immediately.
• Hyaluronidase has on rare occasions caused allergic reactions (itching, swelling around the eyes) or soreness, bleeding or bruising at the injection site.
• Local swelling may occur when Hyaluronidase is used with subcutaneous infusions.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting systems listed below:

United Kingdom:
Yellow Card Scheme
Website: http://www.mhra.gov.uk/yellows/card

Ireland:
HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517; Website: http://hpra.ie; e-mail: medsafety@hpra.ie;

Malta:
ADR Reporting, The Medicines Authority, Post-Licensing Directorate, 203 Level 3, Rue D’Argens, GZR-1368 Gzira; Website: www.medicinesauthority.gov.mt; e-mail: positionlicensing.medicinesauthority@gov.mt

By reporting side effects you can help provide more information on the safety of this medicine.

9. HOW TO STORE HYALURONIDASE

Keep out of the sight and reach of children.
• Hyaluronidase should not be stored above 25°C. Store the ampoules in the package container in which they were dispensed.
• The injection must be used immediately after preparation. Any portion of the contents not used at once should be discarded.
• Hyaluronidase should not be given if the powder shows signs of discoloration (it should be white).
• Hyaluronidase should not be used after the expiry date on the label. The expiry date refers to the last day of the month.
Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help protect the environment.

6. FURTHER INFORMATION

What Hyaluronidase looks like and contents of the pack
Hyaluronidase is a sterile, freeze-dried powder in 1 ml neutral glass ampoule, containing 1500 international units of the active ingredient (hyaluronidase).
The registered pack size is 10 x 1ml glass ampoules.
Other formats
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0800 198 5000 (UK only)
Other formats
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Please be ready to give the following information:

<table>
<thead>
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<th>Product Name</th>
<th>Reference Number</th>
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<tr>
<td>Hyaluronidase 1500 U, Powder for Solution for Injection/Infusion</td>
<td>PL 29831/0113</td>
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Marketing Authorisation Holder and Manufacturer
Marketing Authorisation Holder:
Wockhardt UK Ltd, Ash Road North, Wrexham, LL13 9UF, UK.

Manufacturers:
CP Pharmaceuticals Ltd, Ash Road North, Wrexham, LL13 9UF, UK.

Leaflet prepared: December 2014

4.8 Undesirable Effects
Oedema has been reported in association with hyperdromoclysis. Allergic reactions have included rare reports of periorbital oedema occurring with the use of hyaluronidase in conjunction with local anaesthetics in ophthalmology. Severe allergic reactions including anaphylaxis have been reported rarely. Local irritation, infection, bleeding and bruising occur rarely.

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:

United Kingdom:
Yellow Card Scheme
Website: http://www.mhra.gov.uk/yellows/ card

Ireland:
HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517; Website: http://hpra.ie; e-mail: medsafety@hpra.ie;

Malta:
ADR Reporting, The Medicines Authority, Post-Licensing Directorate, 203 Level 3, Rue D’Argens, GZR-1368 Gzira; Website: www.medicinesauthority.gov.mt; e-mail: positionlicensing.medicinesauthority@gov.mt

4.9 Overdose
No cases of overdose appear to have been reported.

5. Pharmacological Properties

5.1 Pharmacodynamic Properties
Hyaluronidase is an enzyme that has a temporary and reversible depolymerising effect on the polysaccharide hyaluronic acid, which is present in the intercellular matrix of connective tissue.

5.2 Pharmacokinetic Properties
Not applicable

5.3 Preclinical Safety Data
There are no additional pre-clinical data of relevance to the prescriber.

6. Pharmaceutical Properties

6.1 List of Excipients
None.

6.2 Incompatibilities
Physical incompatibility has been reported with haptan and adrenalin, although in clinical practice very low concentrations of adrenalin are combined with hyaluronidase without problems. Furthermore, the benzodiazepines and phenytoin have been found to be incompatible with hyaluronidase.

6.3 Shelf Life
U nopenned 3 years.
Once opened use immediately and discard any unused contents.

6.4 Special Precautions for Storage
Do not store above 25°C.

6.5 Nature and Contents of Container
1ml neutral glass ampoule containing a plug of white freeze-dried powder.

6.6 Instructions for Use/Handling
The solution should be used immediately after preparation. The appearance of the solution is clear and not more than faintly yellow. For detailed instructions on preparation and administration, see section 4.2. For single use only. Discard any unused contents.

7. Marketing Authorisation Holder
Wockhardt UK Ltd
Ash Road North
Wrexham
LL13 9UF

8. Marketing Authorisation Number
Ireland: IR 15381/11
UK: PL 29831/0113
Malta: M.1540/1701

9. Date of First Authorisation/Renewal of Authorisation
April 2006

10. Date of Revision of Text
10/2015/3

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