AUSTRALIAN PRODUCT INFORMATION – HYALASE® (HYALURONIDASE)

1 NAME OF THE MEDICINE

Hyaluronidase

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Hyalase is a purified and standardised preparation of the enzyme Hyaluronidase in the form of a sterile, freeze-dried powder.

Each ampoule contains 1,500 international units of hyaluronidase.

For the full list of excipients, see Section 6.1 List of excipients.

3 PHARMACEUTICAL FORM

White or pale yellowish white, sterile, freeze-dried powder for injection.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Hypodermoclysis

Obstetric anaesthesia

Prevention of post-partum haemorrhage (with ergometrine)

As an aid to local anaesthesia in ophthalmology

As an aid to local anaesthesia in fracture reduction

Subcutaneous administration of radiopaque substances in pyelography

4.2 DOSE AND METHOD OF ADMINISTRATION

Prior to use

Dissolve the freeze-dried powder in approximately 1mL of sterile pyrogen-free distilled water or directly in the solution with which the Hyalase has to be combined.

The solution should be used immediately after preparation. Hyalase is for one dose in one patient only. Discard any remaining contents.

Hypodermoclysis

An ordinary two-way subcutaneous infusion set is required with the fluid container supported about 1 metre above the patient. Suitable hypodermic needles (Record No.12) are attached to the connecting rubber tubes after any contained air has been expelled. The needles are then inserted into the subcutaneous tissues at selected sites and the fluid allowed to run in by gravity. The contents of one ampoule of Hyalase (1,500 international units), dissolved in 1mL of sterile distilled water, are injected through the rubber tubing about 2 to 3 cm from each needle, at the beginning of the infusion.

When this method is employed, approximately 200mL of fluid can be administered in 20 minutes.

The rate of administration can be further varied by raising or lowering the reservoir, but whenever greater speed is required, with possibly smaller volumes, the rate may be increased by injecting the fluid from a 20 or 50mL syringe, the appropriate amount of a solution of Hyalase being drawn into the syringe beforehand.

Repeated infusions may be given as required but it is advisable to change the site of injection. As solutions of the enzyme lose their activity in 12-24 hours, it is important that fresh solutions are prepared prior to each administration.

Injection may alternatively be given from a syringe directly into a site into which 1mL sterile distilled water containing 1,500 international units of Hyalase has previously been injected. The needle should be maintained in the site adopted throughout the procedure, which in this case, should not be unduly prolonged.

It is not advisable to raise the temperature of the fluid prior to infusion since this has been observed to reduce the rate of absorption.

Site of Injection

One of the great advantages of hypodermoclysis is that the possible sites of administration are numerous, irrespective of the position of the patient. Choice may be made, for example, from the axillae pectoral regions, subscapular and trunk areas, thighs and calves. The intramedullary route has also been used successfully (e.g. sternum and tibia).

In children, Gaisford and Evans consider the anterior abdominal wall presents the best site both from the point of view of maximal absorption and freedom from napkin contamination. In this case one needle is inserted on each side of and about 2 to 3 cm from the umbilicus and directed laterally. In general, 1,500 international units of Hyalase are sufficient for the administration of 500-1,000mL of most fluids. In the case of whole blood, however, 3,000 units may be required.

Obstetric anaesthesia

The anaesthetic mixture is prepared as follows:

Hyalase	1,500 international units.
Adrenaline hydrochloride	0.5mL of 1,000 dilution

Procaine hydrochloride 30mL of 1% solution

Heins' method is as follows:

The needle is passed horizontally to the ischial spine, and 5mL of the solution is deposited here to anaesthetise the pudendal nerve as it enters Alcock's canal. Next, 5mL of the mixture is infiltrated in the superior portion of the labia minora to anaesthetise the perineal branches of the iloinguinal nerve. The same procedure is carried out on both sides of the perineum.

Prevention of post-partum haemorrhage

When ergometrine is given intramuscularly, together with Hyalase, at the crowning of the foetal head, the oxytocic effect of the drug is apparent 3-4 minutes earlier than when ergometrine is given alone, and approximates to the effect seen after intravenous ergometrine. This technique is particularly useful when the doctor or midwife is working alone and the intravenous administration of ergometrine is impracticable. Extensive trials have shown that the routine use of intramuscular ergometrine Hyalase shortens the third stage of labour without increasing the danger of retained placenta, and produces a striking reduction in the incidence of post-partum haemorrhage.

The injection solution is made by dissolving the contents of one ampoule of Hyalase 1,500 international units in 1mL of ergometrine solution containing 0.5mg of ergometrine. This solution is prepared a little before it is needed and is held ready in the syringe: at the moment of the crowning or delivery of the foetal head it is injected intramuscularly into the thigh. Correct timing is most important.

As an aid to local anaesthesia in ophthalmology

The addition of 25 international units of Hyalase to each anaesthetic solution has been shown to give a better diffusion of the solution, a greater area of anaesthesia with less ballooning of the tissues, and more effective akinesia of the orbicularis and extra-ocular muscles. The injection of adrenaline, at a concentration not greater than 1 in 50,000 will maintain the duration of anaesthesia.

To obtain the required amount of Hyalase, dissolve the contents of one ampoule in 1.0mL of sterile distilled water or the local anaesthetic solution. Each 0.1mL of this Hyalase solution will contain 150 international units. The appropriate amount of this solution is added to the anaesthetic solution e.g. 6mL anaesthetic solution requires 0.1mL Hyalase solution.

As an aid to local anaesthesia in fracture reduction

The method described by Thorpe is as follows:

"Before injection the local anaesthetic agent (for Colles fracture 20mL of 1% procaine) is mixed with 1,500 international units of Hyalase. Two injections are made: the bulk of the solution is put directly into the fracture haematoma from the extensor aspect of the forearm and 2-3mL are infiltrated around the ulnar styloid process. The anaesthetic solution diffuses rapidly all around the injured areas and the fracture can be manipulated as soon as the needle is withdrawn"

For Pott's fracture - Thorpe recommends 40mL of 1% procaine and 1,500 international units of Hyalase.

Radiography

The following method for the subcutaneous administration of radiopaque substances with hyaluronidase in pyelography is that now generally adopted.

(a) The contents of one ampoule of Hyalase are dissolved in 1.0mL sterile distilled water (a fresh solution must be prepared on each occasion)

(b) 0.5mL of Hyalase solution is then added to 5.0mL of 35% diodone solution and made up to 15.0mL with sterile distilled water (This operation may be carried out in a 20mL syringe)

(c) 15mL of the mixture are injected subcutaneously in the scapular region and are followed immediately by a further 15.0mL at another site e.g. the contralateral scapular region.

(d) The area of injection is massaged vigorously to aid dispersion. Normally renal secretion commences five minutes after injection, adequate concentration is obtained in 24-25 minutes and is equal to that obtained by the intravenous method.

Note: The volumes stated are also applicable to children aged from a few weeks to five years provided that renal function is not grossly impaired.

4.3 CONTRAINDICATIONS

Hypersensitivity to hyaluronidase.

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.

Not to be used for intravenous injections because the enzyme is rapidly inactivated.

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

Not to be injected into or around an infected or acutely inflamed area because of the danger of spreading a localised infection.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Do not apply directly to the cornea.

Solutions for subcutaneous administration should be isotonic with extracellular fluid.

Physical incompatibility has been reported with heparin and adrenaline.

Furosemide, the benzodiazepines and phenytoin have been found to be incompatible with hyaluronidase.

Use in renal impairment

See Section 4.2 Dose and method of administration - Radiography.

Use in the elderly

No data available.

Paediatric use

See Section 4.2 Dose and method of administration - Site of Injection and Radiography.

Effects on laboratory tests

No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Physical incompatibility has been reported with heparin and adrenaline.

Furosemide, the benzodiazepines and phenytoin have been found to be incompatible with hyaluronidase.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

No data available.

Use in pregnancy

As there are no adequate and well-controlled studies conducted with Hyalase, it should be avoided in pregnancy.

Use in lactation

It is not known whether the drug enters breast milk. Caution should be exercised in administering it to breast-feeding mothers.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Oedema has been reported in association with hypodermoclysis.

Allergic reactions have included rare reports of orbital and / or periorbital oedema and / or periorbital inflammation occurring with the use of hyaluronidase in conjunction with local anaesthetics in ophthalmology.

Eye disorders such as conjunctival oedema (chemosis) and / or conjunctival inflammation, restricted eye movements, decreased visual acuity, blurred vision and exophthalmos (proptosis) have been reported.

Severe allergic reactions including anaphylaxis have been reported rarely.

Local irritation, infection, bleeding and bruising occur rarely.

Hyaluronidase has been reported to enhance the adverse events associated with co-administered drug products.

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration 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 at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

Symptoms of toxicity consist of local oedema or urticaria, erythema, chills, nausea, vomiting, dizziness, tachycardia and hypotension. The enzyme should be discontinued and supportive measures initiated immediately.

For information on the management of overdose, contact the Poisons Information Centre on 131126 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group: Enzymes, ATC code: B06AA03

Mechanism of action

Hyaluronidase has a temporary and reversible depolymerizing action on the polysaccharide hyaluronic acid which is present in the intercellular matrix of connective tissue. The intercellular "cement" is thereby made more permeable, permitting the rapid dispersal and absorption of injected substances; the reduction of tissue tension; and the rapid dispersal of extravascular fluid in joint and tissue damage.

Clinical trials

No data available.

5.2 PHARMACOKINETIC PROPERTIES

No data available.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No data available.

Carcinogenicity

No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Sodium hydroxide

6.2 INCOMPATIBILITIES

See Section 4.5 Interactions with other medicines and other forms of interactions.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 25ºC.

6.5 NATURE AND CONTENTS OF CONTAINER

1mL neutral glass ampoules. Available in packs of 5.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical structure

No data available.

CAS number

9001-54-1

7 MEDICINE SCHEDULE (POISONS STANDARD)

Unscheduled

8 SPONSOR

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9 DATE OF FIRST APPROVAL

Hyalase Product Information was Grandfathered and has not been evaluated by the TGA.

10 DATE OF REVISION

10 February 2026

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information

8	Sponsor address updated