AUSTRALIAN PRODUCT INFORMATION
MINIRIN®/OCTOSTIM® (desmopressin acetate) Injections

1. NAME OF THE MEDICINE

Desmopressin Acetate

2. QUANTITATIVE AND QUALITATIVE COMPOSITION

MINIRIN Injection contains desmopressin 4 micrograms/mL.
OCTOSTIM Injection contains desmopressin 15 micrograms/mL.

For the full list of excipients, see **Section 6.1 LIST OF EXCIPIENTS**.

3. PHARMACEUTICAL FORM

Solution for Injection.
Clear colourless solution.

4. CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Diabetes insipidus (MINIRIN Injection)

The treatment of ADH-sensitive cranial diabetes insipidus, including treatment of post-hypophysectomy polydipsia and polyuria.

Renal concentrating capacity (MINIRIN Injection)
By intramuscular administration to adults only, as a diagnostic test to establish renal concentrating capacity.

Mild and moderate haemophillia A and von Willebrand's disease (MINIRIN and OCTOSTIM Injections)
By intravenous infusion only, for the increase of factor VIII levels in patients undergoing dental or minor surgery. Not to be used in type IIB von Willebrand's disease since platelet aggregation may be induced.

Bleeding in patients with platelet dysfunction (MINIRIN and OCTOSTIM Injections)
Treatment of excessive bleeding in patients with congenital or acquired clinical conditions associated with platelet dysfunction which is characterised by a prolonged bleeding time except Glanzmann's thrombasthenia or platelet cyclo-oxygenase deficiency.

Examples are patients with uraemia, congenital or drug induced platelet dysfunction and patients undergoing cardiac surgery with cardiopulmonary bypass for prosthetic valve replacement or aorto-coronary bypass grafting especially when it is complicated by platelet function defects sufficient to prolong bleeding time despite relatively normal platelet cover. Desmopressin acetate offers no benefit as routine therapy in patients having an uncomplicated (simple) cardiopulmonary bypass procedure.

There is no definite evidence of efficacy in bleeding associated with cirrhosis of the liver and such use is not recommended.

4.2 DOSE AND METHOD OF ADMINISTRATION

MINIRIN Injection is normally administered intravenously but may, if needed, be given intramuscularly.
OCTOSTIM Injection is recommended for intravenous use only.

a. For ADH-sensitive cranial diabetes insipidus (MINIRIN Injection)

Adult
The average daily dose is 1 to 4 micrograms by injection.

Paediatric
Up to 0.4 micrograms (400 nanograms) daily.

The daily dose is usually given as two divided doses. The dosage must be determined for each individual patient and adjusted according to the diurnal pattern of response. Response should be estimated by two parameters: adequate duration of sleep and adequate, but not excessive, water turnover. In the event of signs of water retention/hyponatraemia, treatment should be interrupted and the dose adjusted. A single daily dose may be appropriate if it is tolerated and also satisfactorily controls the diabetes insipidus. About one third of patients may be controlled on a small daily dose. For immediate postoperative polyuria and polydipsia, the dose should be controlled by measurement of the urine osmolality. Monitoring in a high dependency setting is recommended. If there is doubt that a dose has been administered, a second dose should not be given until diuresis has occurred.

Mode of administration:
MINIRIN Injection may be administered intramuscularly or intravenously when the intranasal route is inconvenient.

When using doses of less than 4 micrograms the dose should be drawn up from the ampoule as a fraction of a millilitre using a diabetic syringe and not prepared by dilution or given by infusion. This is necessary because of the tendency of peptides to adhere to glass surfaces when in very dilute solutions.

The parenteral daily doses are usually given as 2 divided doses separately adjusted if necessary.
A single daily dose may be appropriate if it is tolerated and also satisfactorily controls the diabetes insipidus.

b. As a diagnostic test of renal concentrating capacity (MINIRIN Injection) (see **Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE: In addition for renal concentrating capacity testing**)

Adults: Single dose of up to 4 micrograms by intramuscular injection
Paediatric: Due to lack of safety data, paediatric use is not recommended.

c. Mild to moderate haemophilia A and von Willebrand's disease (MINIRIN and OCTOSTIM Injections)

VIII: C assays should be undertaken regularly during treatment. Within 1/2 hour before surgery 0.4 micrograms desmopressin acetate/kg diluted to 10-100 mL in isotonic saline is given as slow intravenous infusion over 15-20 min. Before and 20 min after the infusion, VIII: C assays and in the case of von Willebrand's disease determination of VIIIR: Ag and bleeding time should also be carried out unless the patient's response is known from pretesting.
The critical haemostatic level for dentistry or surgery should be judged by the same

criteria as if the patient were being managed with blood products, except that the level may be expected to continue to rise for 1-2 hours after the infusion rather than beginning to fall immediately.
If a sufficient response was obtained with the initial dose of desmopressin acetate, further doses may be given at 12-hourly intervals so long as cover is required. VIII: C levels must be monitored regularly since some patients have shown a diminishing response to successive infusions.
If a sufficient level has not been reached to cover the intended surgical procedure, a supplementary dose of factor-VIII concentrate should be given to make up the deficit.

d. Treatment of bleeding in subjects with inherited and acquired platelet function defects

(MINIRIN and OCTOSTIM Injections)

Desmopressin acetate is given at a dose of 0.3 micrograms/kg diluted to 50 mL in isotonic saline as a slow intravenous infusion over 30 minutes. Further doses may be given at 12 hourly intervals as long as cover is required. In some patients a 12 hourly injection for 3-4 days may result in clinically significant fluid retention. In some studies combined therapy consisting of desmopressin acetate and a fibrinolytic inhibitor was used.

General surgery (except cardiac surgery)

Half an hour prior to surgery, desmopressin acetate is given as a slow intravenous infusion over 30 minutes.

Cardiac surgery

Desmopressin acetate is to be administered in patients with a prolonged bleeding time when cardiopulmonary bypass has been completed and immediately after protamine has been given to neutralise the effect of heparin or at any time thereafter.

Non-surgical use.

In patients with epistaxis, menorrhagia, or other bleeding episodes, desmopressin acetate is given as a slow intravenous infusion over 30 minutes. Red blood cell transfusion is of value in improving haemostasis in uraemic patients.

INSTRUCTIONS TO BE GIVEN TO PATIENTS:

Parenteral: Desmopressin acetate is not intended for self-administration.

4.3 CONTRAINDICATIONS

- Hypersensitivity to desmopressin acetate or any of the excipients.
- Habitual and psychogenic polydipsia (resulting in a urine production exceeding 40 mL/kg/24 hours)
- A history of unstable angina pectoris and/or known or suspected cardiac insufficiency and other conditions requiring treatment with diuretics
- Known hyponatraemia
- Syndrome of inappropriate ADH secretion (SIADH)
- von Willebrand's disease type IIB

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Desmopressin acetate is ineffective for the treatment of nephrogenic diabetes insipidus.

a. MINIRIN/OCTOSTIM Injections should be used with caution in patients at risk for increased intracranial pressure.

b. MINIRIN/OCTOSTIM Injections should be used with caution in patients with conditions characterised by fluid and/or electrolyte imbalance.

Desmopressin acetate should not be administered to dehydrated or overhydrated patients until water balance has been adequately restored. In haemophilia where high doses are given, extreme care must be paid to the water balance. Fluid intake should be restricted as much as possible and the patient should be weighed regularly.

Treatment with MINIRIN/OCTOSTIM Injections should be interrupted or carefully adjusted during acute intercurrent illnesses characterised by fluid and/or electrolyte imbalance (such as systemic infections, fever, gastroenteritis) as well as in excessive bleeding, and the fluid and electrolyte balance should be carefully monitored.

c. Hyponatraemia and hydration

Hyponatraemia in the context of the use of desmopressin is generally due to fluid overload, thus careful attention to fluid balance is needed. Other causes of hyponatraemia which may need excluding depending on the clinical situation include renal salt wasting due to central lesions, renal disorders or adrenal disorders.

Infants, elderly and patients with serum sodium levels in the lower range of normal may have an increased risk of hyponatraemia.

Central diabetes insipidus

- The aim of fluid therapy is to replace urinary fluid loss.
- Children, patients with cognitive impairment, and patients with inadequate thirst sensation need close monitoring of fluid intake.
- Regular monitoring of serum and urinary sodium and osmolality is recommended at the discretion of the clinician.

In addition for renal concentrating capacity testing:

- When used for diagnostic purposes the fluid intake must be limited to a maximum of 0.5 L to satisfy thirst from 1 hour before until at least 8 hours after administration. Renal concentrating capacity testing in children below the age of 1 year should only be performed under carefully supervised conditions in hospital.

In addition for haemostatic use:

- Measures to prevent fluid overload must be taken in patients requiring treatment with diuretic agents.

d. Special attention must be paid to the risk of fluid retention/hyponatraemia. The fluid intake should be restricted to the least possible and the body weight should be checked regularly. Should there be a gradual increase of the body weight, decrease of serum sodium to below 130 mmol/L or plasma osmolality to below 270 mOsm/kg body weight, the fluid intake must be reduced drastically and the administration of MINIRIN/OCTOSTIM Injections interrupted.

e. Risks of thrombosis and Cardiovascular Events

- Due to risk of development of tachyphylaxis following repeated dosing with desmopressin, alternative haemostatic therapies, other than desmopressin, should be considered in situations where long-term haemostasis is required (active bleeding for more than 2-4 days), including active postoperative bleeding and variceal bleeding in patients with cirrhosis.
- Myocardial ischaemia. Desmopressin acetate should be used with caution in patients with cardiovascular disease and the elderly.
- Due to post-marketing reports of deep vein thrombosis, cerebrovascular accident and disorder (stroke), cerebral thrombosis, myocardial infarction, angina pectoris and chest

pain in relation to MINIRIN/OCTOSTIM injections used for the haematological indications, considerations should be taken before using MINIRIN/OCTOSTIM injection in patients with risk factors for or a history of thrombosis, atherosclerotic cardiovascular disease, atherosclerotic cerebrovascular disease or angioplasty.

- Special attention should be given when desmopressin is co-administered with other drugs affecting water and/or sodium homeostasis (see **Section 4.5 INTERACTION WITH OTHER MEDICINES and OTHER FORMS OF INTERACTIONS**). In patients with chronic therapy with drug(s) affecting water and/or sodium homeostasis, MINIRIN/OCTOSTIM Injections should be administered after confirmation of normal baseline sodium.

f. Post-operative use.

In a context of the management of diabetes insipidus, the use of desmopressin in a post-operative setting should only occur after the diagnosis of diabetes insipidus has been confirmed. Small doses should be administered with strict fluid balance and regular clinical assessment.

g. In patients with platelet dysfunction. Skin bleeding time should be monitored: i. before surgery with marked prolongation indicating high risk of increased blood loss. ii. during treatment with desmopressin acetate.

h. MINIRlN/OCTOSTIM Injections do not reduce prolonged bleeding time in thrombocytopenia.

i. MINIRIN/OCTOSTIM Injections should be used with caution in patients with cystic fibrosis because of impaired water handling and increased risk of hyponatraemia.

j. Severe bladder dysfunction and outlet obstruction should be considered before starting treatment for central diabetes insipidus.

Paediatrics use

MINIRIN/OCTOSTIM injections should be used with caution in very young patients.

Use in the elderly

MINIRIN/OCTOSTIM Injections should be used with caution in elderly patients, particularly those with other risk factor for thrombotic disease.

Use in renal impairment

MINIRIN/OCTOSTIM Injections should be used with caution in patients with moderate and severe renal insufficiency (creatinine clearance below 50 mL/min) (see **Section 5.2 PHARMACOKINETIC PROPERTIES**).

Use in hepatic impairment

No dose adjustment is needed for patients with hepatic impairment (see **Section 5.2 PHARMACOKINETIC PROPERTIES**).

Effects on laboratory tests

No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Special attention should be given when desmopressin is co-administered with other drugs affecting water and/or sodium homeostasis, e.g. opioids, selective serotonin reuptake inhibitors, tricyclic antidepressants, nonsteroidal anti-inflammatory drugs, chlorpromazine, carbamazepine and some antidiabetics of the sulfonylurea group since concurrent use can lead to an increased risk of fluid retention/hyponatraemia (see **Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE**).

It is unlikely that desmopressin will interact with drugs affecting hepatic metabolism, since desmopressin has been shown not to undergo significant liver metabolism in *in vitro* studies with human microsomes. However, formal *in vivo* interaction studies have not been performed.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

Studies with desmopressin in animals have shown no impairment of fertility in male and female rats.

Use in pregnancy (Category B1)

Caution should be exercised when prescribing to pregnant women.

Data on a limited number (n=53) of exposed pregnancies in women with diabetes insipidus as well as data on a limited number of exposed pregnancies in women with bleeding complications (n=216) indicate no adverse effects of desmopressin on pregnancy or on the health of the foetus/newborn child. To date, no other relevant epidemiological data are available. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonic/foetal development, parturition or postnatal development.

Embryofoetal development studies performed with desmopressin in rats and rabbits given subcutaneous doses up to 50 ng/kg/day and 200 µg/kg/day, respectively, and in rats given intravenous doses up to 241 µg/kg/day, revealed no evidence for a harmful effect on the foetus.

Animal reproduction studies have shown no clinically relevant effects on parents and offspring. In vitro analysis of human cotyledon models have shown that there is no transplacental transport of desmopressin when administered at therapeutic concentration corresponding to recommended dose.

Use in lactation

Subtherapeutic levels of desmopressin acetate have been detected in the breast milk of lactating women. Until further evidence of its safe use during lactation is available, it is not to be administered to lactating women.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

MINIRIN and OCTOSTIM Injections have no or negligible influence on the ability to drive and use machines.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Summary of the safety profile

The most frequently reported adverse reaction with MINIRIN Injection during post-marketing is hyponatraemia. Hyponatraemia may cause headache, nausea, vomiting, water intoxication, weight increase, malaise, abdominal pain, muscle cramps, dizziness, confusion, decreased consciousness, generalised or local oedemas (peripheral, face), and in severe cases brain oedema, hyponatraemic encephalopathy, convulsions, and coma (see **Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE**).

Rare cases of serious hypersensitivity reactions including anaphylactoid shock and reaction have been reported in association with MINIRIN/OCTOSTIM Injections (see **Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE**).

Tabulated list of adverse reactions

The table below (**Table 1**) is based on the frequency of adverse drug reactions reported in clinical trials with MINIRIN Injection conducted in adults for treatment of central diabetes insipidus and haematological indications (N=53) and OCTOSTIM injections (N=76), combined with the post-marketing experience for MINIRIN/OCTOSTIM Injections. Reactions only seen in post-marketing or in other desmopressin formulations have been added in the 'Frequency not known' table (**Table 2**). Table 1 and 2 shows the frequencies of adverse reactions reported. Adverse reactions are classified according to frequency and system organ class. Frequency categories are defined according to the following convention: 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) and Frequency not known (cannot be estimated from the available data).

Table 1. Frequency of adverse drug reactions reported (clinical trials, spontaneous reports including the literature)

MedDRA Organ Class	Common (≥1/100 to <1/10)	Rare (≥1/10,000 to <1/1,000)	Very rare (<1/10,000)
Metabolism and nutrition disorders			Hyponatraemia
Nervous system disorders	Headache	Dizziness	
Cardiac disorders	Tachycardia[1]		
Vascular disorders	Flushing[1], Hypotension[1]		
Gastrointestinal disorders	Nausea, Abdominal pain		
General disorders and administration site conditions	Fatigue		

[1)] At high doses, transient fall in blood pressure with a reflex tachycardia and facial flushing at the time of administration.

Description of selected adverse reactions

During post-marketing the most frequently reported adverse reaction with MINIRIN/OCTOSTIM is hyponatraemia. Hyponatraemia may cause headache, nausea, vomiting, water intoxication, weight increase, malaise, abdominal pain, muscle cramps, dizziness, confusional state, decreased consciousness, generalised or local oedemas (peripheral, face), and in severe cases brain oedema, hyponatraemic encephalopathy, convulsions, and coma. Nausea, vomiting, headache and dizziness have been reported without registered hyponatraemia. The hyponatraemia is a result of the antidiuretic effect, arising from increased water reabsorption by the renal tubules and osmotic dilution of plasma. Special attention should be paid to the precautions addressed in **Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE**.

Hyponatraemia is reversible. Treatment should be individualised, and rapid overcorrection should be avoided to reduce the risk of further complications (see **Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE**).

Post-marketing hypersensitivity reactions including local allergic reactions such as dyspnoea, erythema, generalized or local oedemas (peripheral, face), pruritus, rash, rash macular, rash maculopapular, rash erythematous, skin plaque and urticaria, have been reported in association with MINIRIN/OCTOSTIM Injections. More serious hypersensitivity reactions including

anaphylactic shock and reaction, and anaphylactoid shock and reaction have also been reported in association with MINIRIN/OCTOSTIM Injections. Allergic reactions usually occur rapidly after drug administration and may occur during first time usage or after repeated exposure of MINIRIN/OCTOSTIM Injections.

Table 2. The table below lists adverse events from post-marketing experience via spontaneous case reports and literature cases:

These reactions are reported voluntarily from a population of uncertain size, as it is not possible to reliably estimate their frequency which is therefore categorised as not known.

MedDRA Organ Class	**Frequency not known**
Immune system disorders	Hypersensitivity, anaphylactic reaction, anaphylactoid reaction and other serious allergic conditions
Metabolism and nutrition disorders	Water intoxication[1] Weight increased[1]
Psychiatric disorders	Confusional state[1]
Nervous system disorders	Ischemic stroke[4] Coma[1] Loss of consciousness[1,3] Hyponatraemic encephalopathy[1] Brain oedema[1,3] Convulsions[1]
Cardiac disorders	Acute myocardial infarction[4] Angina pectoris[3] Chest pain[3]
Vascular disorders	Deep vein thrombosis[3] Cerebrovascular accident and disorder (stroke)[3] Cerebral thrombosis[3] Hypertension[3]
Respiratory, thoracic and mediastinal disorders	Dyspnoea Pulmonary embolism[3]
Gastrointestinal disorders	Vomiting[2]
Skin and subcutaneous tissue disorders	Rash maculo-papular Rash erythematous Rash macular Urticaria Erythema Pruritus Rash
General disorders and administration site conditions	Generalised or local oedemas[2] (peripheral, face) Injection/infusion site reactions including swelling, pain, extravasation, erythema, bruising and nodules Chills[3] Malaise[1]

1) Reported with hyponatraemia.
2) Reported with or without hyponatraemia
3) Reported mainly for the haematological indications (high dose)

4) Only for the haematological indications (high dose) and only in patients with known history of, or risk factors for, thrombosis, atherosclerotic cardiovascular/cerebrovascular disease, or a history of angioplasty.

Rare post-marketing cases of deep vein thrombosis, cerebrovascular accident/disorder (stroke), cerebral thrombosis, pulmonary embolism, myocardial infarction, angina pectoris and chest pain have been reported in patients treated with desmopressin. Due to confounding factors and/or missing information, a causal relationship with MINIRIN/OCTOSTIM Injections has not been established/confirmed.

Paediatric population

Adverse reaction data from clinical trials in children is very limited.

Other special populations

Elderly and patients with serum sodium levels in the lower range of normal may have an increased risk of developing hyponatraemia (see **Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE**).

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

Overdose of MINIRIN/OCTOSTIM Injections leads to a prolonged duration of action with an increased risk of water retention and hyponatraemia.

Treatment: The treatment of hyponatraemia should be individualised and can include discontinuation of MINIRIN treatment, fluid restriction and symptomatic treatment.

For information on the management of overdose, contact the Poison Information Centre on 13 11 26 (Australia).

5. PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group: vasopressin and analogues.

ATC code: H01B A02

MINIRIN Injection 4 micrograms/mL and OCTOSTIM Injection 15 micrograms/mL, contain desmopressin, a structural analogue of the natural pituitary hormone arginine vasopressin, also known as antidiuretic hormone (ADH). Early treatment of central diabetes insipidus used a more or less purified extract from bovine or porcine posterior pituitaries. These caused unpleasant complications of use. When vasopressin became known, two forms were found - arginine vasopressin (found in humans) and lysine vasopressin (found in pig pituitaries).

Two chemical changes have been made to the natural hormone to form desmopressin:
a. deamination of the N-terminal of cysteine-1
b. substitution of 8-D-arginine for 8-L-arginine

According to results from antidiuretic and pressor tests in rats these changes increase antidiuretic activity three to five fold, while pressor activity is reduced to 0.1% of that of ADH.

Mechanism of action

The actions of desmopressin can be summarised as follows:

Antidiuretic action
Desmopressin acts at a receptor site in the renal collecting tubule to increase permeability to water reabsorption.

Effect on factor-VIII
High doses (0.3 micrograms/kg intravenously) of desmopressin acetate produce marked and sustained increases of factor-VIII coagulant activity (VIII: C) as well as of the von Willebrand factor (vWF). At the same time plasminogen activator is released.

Effect on bleeding time
At doses of 0.3-0.4 micrograms/kg intravenously, desmopressin results in a normalisation of, or marked reduction in, the prolonged skin (template) bleeding time. The exact mechanism of this effect is not known.
It is not known whether the effects of desmopressin are direct or act through a mediator or second messenger.
There is a temporal correlation between a reduction in bleeding time and the presence in plasma of high molecular weight monomers of the von Willebrand factor which are thought to be released from storage sites. It is thought likely that desmopressin exerts its effect through its V_2-receptor agonist activity.

Other Effects:

Oxytocic effect
A slight in vitro oxytocic effect has been reported in animals. A slight stimulatory effect on uterine activity in non-pregnant women has been noted at doses of 15 and 20 micrograms intranasally (see **Section 4.6 FERTILITY, PREGNANCY AND LACTATION: Use in Pregnancy**).

Vasodilator effect
At doses used to treat bleeding, desmopressin has a vasodilatory effect, causing a minor decrease in diastolic or systolic blood pressure.

Clinical trials

No data available.

5.2 PHARMACOKINETIC PROPERTIES

Absorption

Using intravenous (IV) doses, 100% of desmopressin is systematically available.
The bioavailability following subcutaneous injection compared with intravenous administration is about 85%. Maximal plasma concentration after 0.3 µg/kg given as a subcutaneous injection is achieved after approximately 60 minutes and in average it amounts to 600 ng/mL.

Distribution

No information is available on protein binding. The distribution of desmopressin is best described by a two-compartment distribution model, with a volume of distribution during the elimination phase of 0.3-0.5 L/kg.

Metabolism

It is thought that the presence of the D-isomer in position eight prolongs the antidiuretic effect compared to ADH.
The *in-vivo* metabolism of desmopressin has not been studied. *In vitro* human liver microsome metabolism studies of desmopressin have shown that no significant amount is metabolised in the liver by the cytochrome P450 system, and thus human liver metabolism *in vivo* by the cytochrome P450 system is unlikely to occur. The effect of desmopressin on the pharmacokinetics of other drugs is likely to be minimal due to its lack of inhibition of the cytochrome P450 drug metabolising system.

Excretion

The excretion of desmopressin is similar to that of ADH but considerably slower. The total clearance of desmopressin has been calculated to 7.6 L/hr. In healthy subjects the fraction excreted unchanged was 52% (44-60%). Plasma half- life varies between 3 and 4 hours. The duration of the haemostatic effect depends on the half-life for factor-VIII coagulant activity (VIII: C), which is about 8-12 hours.

Characteristics in specific groups of patients

Renal impairment

Table 3. Single Dose Pharmacokinetics after Intravenous Administration of Desmopressin in Healthy Volunteers and Patients with Mild, Moderate and Severe Renal Impairment (Geometric Data)

	AUC (h*pg/ml)	C_{max} (pg/ml)	CL (L/h)	$t_{1/2}$ (h)#
Healthy	186.1	108.4	10.75	2.77
Mild	280.8	127.5	7.12	3.99
Moderate	453.3	111.3	4.41	6.57
Severe	681.5	116.4	2.93	8.74

Harmonic mean data

* Geometric mean

CLINICAL IMPLICATIONS OF PHARMACOKINETIC DATA

Desmopressin is thought to be resistant to the inactivation that occurs with ADH. Intravenous or intramuscular doses should be about one tenth the intranasal dose for equivalent efficacy. In some patients, the duration of effect may be sufficiently long to permit once daily dosage if the single dose can be tolerated.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

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

Carcinogenicity

No studies of the carcinogenic potential have been performed.

6. PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

MINIRIN and OCTOSTIM Injections also contain sodium chloride, hydrochloric acid and water for injections.

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

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 at 2 to 8°C. Refrigerate. Do not freeze. Protect from light.

6.5 NATURE AND CONTENTS OF CONTAINER

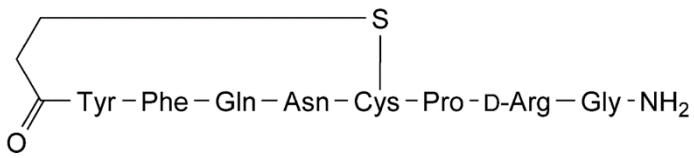
Parenteral:
MINIRIN Injection **4 micrograms/mL**: Box of 10 ampoules of 1 mL.
OCTOSTIM Injection **15 micrograms/mL** (for intravenous administration only): Box of 10 ampoules of 1 mL.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical structure



Synonyms of desmopressin
DDAVP
1-desamino-8-D-Arginine vasopressin.
Desamino-cys-1-D-Arginine-8 vasopressin.

Molecular weights

Desmopressin base	1069.22
Desmopressin acetate	1183.34

Desmopressin is a white, fluffy powder, soluble in water, alcohol and glacial acetic acid.

CAS Numbers

Desmopressin base	16679-58-6
Desmopressin acetate	62288-83-9

7. MEDICINE SCHEDULE (POISONS STANDARD)

Prescription Only Medicine (S4)

8. SPONSOR

Ferring Pharmaceuticals Pty Ltd
Suite 2, Level 1, Building 1
20 Bridge Street
Pymble NSW 2073
Australia

For the most current approved PI, please refer to https://www.ebs.tga.gov.au/ or http://www.ferring.com.au/

9. DATE OF FIRST APPROVAL

21/08/1992 (MINIRIN 4 µg/mL Injection)
15/02/1994 (OCTOSTIM 15 µg/mL Injection)

10. DATE OF REVISION

29 July 2024

Summary Table of Changes

Section Changed	Summary of new information
4.4	Updated warning regarding repeated dosing with desmopressin leading to tachyphylaxis. Updated warning for patients with risk of, or known history of atherosclerotic diseases.
4.8	The following AEs have been added in the Not Known frequency category: ➢ Anaphylactoid reaction, ischemic stroke
All	Minor editorial changes throughout the PI.