

# NEW ZEALAND DATA SHEET

## 1 HEPARIN SODIUM (2U/mL solution for infusion)

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

### *Active substance*

Heparin sodium (2U/mL).

### *The biological origin of the active substance*

Heparin is a heterogenous mixture of variably sulphated polysaccharide chains composed of repeating units of disaccharides, *D*-glucosamine and *L*-iduronic acid or *D*-glucosamine and *D*-glucuronic acids. It is extracted from porcine intestinal mucosa.

Upon complete hydrolysis, it yields a mixture of *D*-glucosamine, *D*-glucuronic acid, *L*-iduronic acid, acetic acid and sulphuric acid.

Although others may be present, the main sugars occurring in heparin are: (1)  $\alpha$ -*L*-iduronic acid 2-sulfate, (2) 2-deoxy-2-sulfamino- $\alpha$ -*D*-glucose 6-sulfate, (3)  $\beta$ -*D*-glucuronic acid, (4) 2-acetamido-2-deoxy- $\alpha$ -*D*-glucose, and (5)  $\alpha$ -*L*-iduronic acid. These sugars are present in decreasing amounts, usually in the order (2) > (1) > (4) > (3) > (5), and are joined by glycosidic linkages, forming polymers of varying sizes.

### *Excipient with known effect*

Sodium chloride (0.9%).

For the full list of excipients, see Section 6.1.

## 3 PHARMACEUTICAL FORM

Solution for infusion.

**HEPARIN SODIUM** intravenous infusion is a clear, sterile, non-pyrogenic solution of heparin sodium standardised for use as an anticoagulant in 0.9% Sodium Chloride intravenous infusion buffered with 0.4mg citric acid monohydrate and 5.8mg dibasic sodium phosphate dodecahydrate ( $\text{Na}_2\text{HPO}_4 \cdot 12\text{H}_2\text{O}$ ) per mL to pH range of 5.5 - 8.0.

Heparin is strongly acidic because of its content of covalently linked sulphate and carboxylic acid groups. In heparin sodium, the acidic protons of the sulphate units are partially replaced by sodium ions.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic indications

**HEPARIN SODIUM** solution for intravenous infusion is indicated as an anticoagulant in extracorporeal circulation, dialysis procedures, and as an aid in the maintenance of catheter patency.

### 4.2 Dose and method of administration

Heparin sodium is not effective by oral administration and **HEPARIN SODIUM** solution for infusion should not be given orally.

Dosage, rate, and duration of administration are to be individualised and depend upon the indication for use, the patient's age, weight, clinical condition and concomitant treatment, and on the patient's clinical and laboratory response to the treatment.

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Carefully examine all presentations of heparin to confirm the correct formulation prior to administration of the drug.

Parenteral drug products should be inspected visually for particulate matter and discolouration prior to administration. Do not administer unless solution is clear and seal is intact. Use of a final filter is recommended during administration of all parenteral solutions, where possible.

### *Use in extracorporeal therapy*

The concentration of 2units/mL will suffice to prevent clotting on initiation of extracorporeal therapy by priming the devices with this solution. NOTE: A proper and effective heparinisation schedule must be initiated in the patient before and maintained throughout the procedures to prevent subsequent clotting and blood path obstruction. The particular manufacturer's directions for use of the dialyser or other extracorporeal apparatus must be referred to. The direction sheets for the use of therapeutic dosage forms of heparin must equally be referred to and adjusted to a given patients' condition and response to achieve sustained, effective anticoagulation within clinically safe parameters. Both intermittent and continuous infusion of 5 000, 10 000 or 20 000 units are employed for this purpose and are unrelated to the low dose heparin in this preparation that is directed at preparing the apparatus for initial use.

### *Maintenance of catheter patency*

Although the rate for infusion of the 2units/mL formulation is dependent upon age, weight, clinical condition of the patient and the procedure being employed, an infusion rate of 3mL/hour has been found to be satisfactory.

Periodic platelet counts; hematocrits, and tests for occult blood in stool are recommended during the entire course of heparin therapy, regardless of the route of administration.

All injections in **VIAFLEX** plastic containers are intended for administration using sterile equipment. It is recommended that the intravenous administration apparatus be replaced at least every 24 hours.

## 4.3 Contraindications

**HEPARIN SODIUM** should not be used in the following patients:

- Who have had a diagnosis of heparin-induced thrombocytopenia (HIT) (with or without Thrombosis) within the previous 6 months, and while they test positive for HIT antibodies.
- With severe thrombocytopenia.
- In whom suitable blood coagulation tests - e.g. the whole-blood clotting time, partial thromboplastin time etc. - cannot be performed at appropriate intervals (this contraindication refers to full-dose heparin; there is usually no need to monitor coagulation parameters in patients receiving low dose heparin).
- With an uncontrollable active bleeding state (see Section 4.4), except when this is due to disseminated intravascular coagulation.
- With known hypersensitivity to heparin or porcine derivatives (see section 4.8) or to any ingredient in the formulation.

## 4.4 Special warnings and precautions for use

### *Hypersensitivity*

Hypersensitivity reactions with chills, fever and urticaria as the most usual manifestations, and also asthma, rhinitis, lacrimation, and anaphylactoid reactions have been reported.

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## *Vasospastic reactions*

Vasospastic reactions may develop independent of the origin of heparin, after the initiation of the therapy. The affected limb is painful, ischaemic and cyanosed. An artery to this limb may have been recently catheterised. After repeat injections, the reaction may gradually increase to include generalised vasospasm, with cyanosis, tachypnoea, feeling of oppression and headache.

## *Hyperkalaemia*

Heparin can suppress adrenal secretion of aldosterone leading to hyperkalaemia, particularly in patients with diabetes mellitus, chronic renal failure, pre-existing metabolic acidosis, a raised plasma potassium, or taking potassium sparing medicines. The risk of hyperkalaemia appears to increase with duration of therapy but is usually reversible upon discontinuation of heparin.

Plasma potassium should be measured in patients at risk of hyperkalaemia before starting heparin therapy and periodically in all patients on prolonged duration of treatment.

## *White Clot syndrome*

It has been reported that patients on heparin may develop new thrombus formation in association with thrombocytopenia resulting from irreversible aggregation of platelets induced by heparin, the so-called "white clot syndrome". The process may lead to severe thromboembolic complications like skin necrosis, gangrene of the extremities that may lead to amputation, myocardial infarction, pulmonary embolism, stroke and possible death. Therefore, heparin administration should be promptly discontinued if a patient develops new thrombosis in association with thrombocytopenia.

## *Spinal/Epidural haematomas*

When neuraxial anaesthesia (epidural/spinal anaesthesia) or spinal puncture is employed, patients anticoagulated or scheduled to be anticoagulated with unfractionated heparin or low molecular weight heparins/heparinoids for prevention of thromboembolic complications are at risk of developing an epidural or spinal haematoma which can result in long-term or permanent paralysis.

The risk of these events is increased by the use of indwelling epidural catheters for administration of analgesia or by the concomitant use of medicines affecting haemostasis such as non-steroidal anti-inflammatory drugs (NSAIDs), platelet inhibitors, or other anticoagulants. The risk also appears to be increased by traumatic or repeated epidural or spinal puncture.

Patients should be frequently monitored for signs and symptoms of neurological impairment. If neurological compromise is noted, urgent treatment is necessary. The physician should consider the potential benefit versus risk before neuraxial intervention in patient's anticoagulated or to be anticoagulated for thromboprophylaxis.

## *Heparin resistance*

Increased resistance to heparin is frequently encountered in patients with fever, thrombosis, thrombophlebitis, infections with thrombosing tendencies, myocardial infarction, cancer and in post-surgical patients. Monitor coagulation tests closely in such patients. It may be necessary to adjust the dose of heparin based on anti-Factor Xa levels (see section 4.8).

## *Haemorrhage*

Haemorrhage can occur at virtually any site in patients receiving heparin (e.g., gastrointestinal bleeding with haematemesis and melaena, or haematuria). Fatal haemorrhages have occurred. An unexplained fall in blood pressure, anaemia and fall in haematocrit or any other unexplained symptom should lead to serious consideration of haemorrhagic event. Haematocrit testing and tests for occult blood in stools should be performed periodically during heparin administration.

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**HEPARIN SODIUM** solution for infusion should be used with extreme caution in disease states in which there is increased danger of haemorrhage. Some of the conditions in which increased danger of haemorrhage exists are:

- *Cardiovascular*: Subacute bacterial endocarditis; severe hypertension.
- *Surgical*: During and immediately following
  - (a) spinal tap or spinal anaesthesia or
  - (b) major surgery, especially involving the brain, spinal cord or eye.
- *Haematologic*: Conditions associated with increased bleeding tendencies, such as haemophilia, thrombocytopaenia, and some vascular purpuras.
- *Gastrointestinal*: Ulcerative lesions and continuous tube drainage of the stomach or small intestine. It should be appreciated that gastrointestinal or urinary tract bleeding during anticoagulant therapy may indicate the presence of an underlying occult lesion.
- Patients with hereditary antithrombin III deficiency receiving concurrent antithrombin III therapy (see section 4.5).
- *hepatic*: Liver disease with impaired haemostasis.
- *Other*: Menstruation, and in patients with indwelling catheters.

### *Coagulation testing*

When heparin is administered in therapeutic amounts, its dosage should be regulated by frequent blood coagulation tests. If the coagulation test is unduly prolonged or if haemorrhage occurs, **HEPARIN SODIUM** solution for infusion should be discontinued promptly (see Section 4.9).

### *Thrombocytopaenia*

Thrombocytopaenia has been reported to occur in patients receiving heparin with a reported incidence of up to 30%. Platelet counts should be obtained at baseline and periodically during heparin administration. Mild thrombocytopaenia (count greater than 100,000/mm<sup>3</sup>) may remain stable or reverse even if heparin is continued. However, thrombocytopaenia of any degree should be monitored closely. If the count falls below 100,000/mm<sup>3</sup> or if recurrent thrombosis develops (see *HIT and HITT* below), the heparin product should be discontinued and, if necessary, an alternative anticoagulant administered. If continued heparin therapy is essential, administration of heparin from a different organ source can be reinstated with caution.

### *Heparin-induced Thrombocytopaenia (HIT) and Heparin-induced Thrombocytopaenia and Thrombosis (HITT)*

Heparin-induced Thrombocytopaenia (HIT) is a serious antibody-mediated reaction resulting from irreversible aggregation of platelets. HIT may progress to the development of venous and arterial thromboses, a condition referred to as Heparin-induced Thrombocytopaenia and Thrombosis (HITT). Thrombotic events may also be the initial presentation of HITT. These serious thromboembolic events include deep vein thrombosis, pulmonary embolism, cerebral vein thrombosis, limb ischemia, stroke, myocardial infarction, mesenteric thrombosis, renal arterial thrombosis, skin necrosis, gangrene of the extremities that may lead to amputation, and possibly death.

Once HIT or HITT is diagnosed or strongly suspected, all heparin sodium sources (including heparin flushes) should be discontinued and an alternative anticoagulant used. Future use of heparin sodium, especially within 3 to 6 months following the diagnosis of HIT or HITT, and while patients test positive for HIT antibodies, should be avoided.

Immune-mediated HIT is diagnosed based on clinical findings supplemented by laboratory test confirming the presence of antibodies to heparin sodium, or platelet activation induced by heparin sodium. Platelet counts should be obtained at baseline and periodically during heparin

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administration. A drop in platelet count greater than 50% from baseline is considered indicative of HIT. Platelet counts begin to fall 5 to 10 days after exposure to heparin sodium in heparin-naïve individuals, and reach a threshold by days 7 to 14. In contrast, 'rapid onset' HIT can occur very quickly (within 24 hours following heparin sodium initiation), especially in patients with a recent exposure to heparin sodium (i.e. previous 3 months). Thrombosis development shortly after documenting thrombocytopenia is a characteristic finding in almost half of all patients with HIT.

Thrombocytopenia of any degree should be monitored closely. If the platelet counts fall below 100,000/mm<sup>3</sup> or if recurrent thrombosis develops, the heparin product should be promptly discontinued and alternative anticoagulant considered if patients require continued anticoagulation.

### *Delayed onset of HIT and HITT*

HIT and HITT can occur up to several weeks after the discontinuation of heparin therapy. Patients presenting with thrombocytopenia or thrombosis after discontinuation of heparin should be evaluated for HIT and HITT.

### *Other*

Solutions containing sodium ions should be used with great care in patients with congestive heart failure, severe renal insufficiency, and in clinical states in which there exists oedema with sodium retention. These solutions should also be used with caution in patients receiving corticosteroids or corticotropin.

The intravenous administration of solutions can cause fluid and/or solute overloading resulting in dilution of serum electrolyte concentrations, over-hydration, congested states or pulmonary oedema. The risk of dilutional states is inversely proportional to the electrolyte concentrations and volume of the infusion. The risk of solute overload causing congested states with peripheral and pulmonary oedema is directly proportional to the electrolyte concentrations and volume of the infusion.

Clinical evaluation and periodic laboratory determinations are necessary to monitor changes in fluid balance and electrolyte concentration and acid base balance during prolonged parenteral therapy or whenever the condition of the patient warrants such an evaluation.

Excessive administration of potassium free solutions may result insignificant hypokalaemia.

### *Use in renal impairment*

Heparin sodium should be used with caution in the patients with renal disease. In patients with diminished renal function, administration of heparin may result in sodium retention.

### *Use in hepatic impairment*

Heparin sodium should be used with caution in the patients with hepatic disease.

### *Use in elderly*

A higher incidence of bleeding has been reported in patients, particularly women, over 60 years of age (see Section 4.4/Haemorrhage). Clinical studies indicate that lower doses of heparin may be indicated in these patients.

### *Paediatric use*

Safety and effectiveness in paediatric patients has not been established.

### *Effects on laboratory tests*

Periodic platelet counts; hematocrits, and tests for occult blood in stool are recommended during the entire course of heparin therapy, regardless of the route of administration (see Section 4.2).

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## 4.5 Interaction with other medicines and other forms of interaction

### *Oral anticoagulants*

Heparin sodium may prolong the one-stage prothrombin time. Therefore, when heparin sodium is given with dicumarol or warfarin sodium, a period of at least 5 hours after the last intravenous dose, or 24 hours after the last subcutaneous dose should elapse before blood is drawn if a valid prothrombin time is to be obtained.

### *Platelet inhibitors*

Medicines such as NSAIDs (e.g., acetylsalicylic acid, ibuprofen, indomethacin), dextran, phenylbutazone, dipyridamole, hydroxychloroquine, epoprostenol, clopidogrel, thienopyridines, glycoprotein IIb/IIIa antagonists, and others that interfere with platelet aggregation reactions (the main haemostatic defence of heparinised patients) may induce bleeding and should be used with caution in patients receiving heparin sodium. To reduce the risk of bleeding, a reduction in the dose of antiplatelet agent or heparin is recommended.

### *Antithrombin III (human)*

The anticoagulant effect of heparin is enhanced by concurrent treatment with antithrombin III (human) in patients with hereditary antithrombin III deficiency. To reduce the risk of bleeding, a reduction in the dose of heparin is recommended during treatment with antithrombin III (human).

### *Other interactions*

Digitalis, tetracyclines, nicotine or antihistamines may partially counteract the anticoagulant action of heparin sodium.

Tobacco smoke and nicotine may decrease the anticoagulant effects of heparin. Increased doses of heparin may be required in smokers.

Intravenous nitroglycerin administered to patients receiving heparin may result in a decrease of the partial thromboplastin time with subsequent rebound effect upon discontinuation of nitroglycerin. Careful monitoring of partial thromboplastin time and adjustment of heparin dosage are recommended during coadministration of heparin and intravenous nitroglycerin.

The use of ACE inhibitors and angiotensin-II antagonists in conjunction with heparin increase the risk of hyperkalaemia.

When administering **HEPARIN SODIUM** solution for infusion concomitantly with medicines listed above monitor coagulation tests frequently and adjust dose as necessary.

### *Drug/Laboratory tests interactions*

*Hyperaminotransferasaemia:* Significant elevations of aminotransferase (SGOT [S-AST] and SGPT [S-ALT]) levels have occurred in a high percentage of patients (and healthy subjects) who have received heparin. Since aminotransferase determinations are important in the differential diagnosis of myocardial infarction, liver disease, and pulmonary emboli, elevation of these enzymes in patients that might be caused by medicines (like heparin) should be interpreted with caution.

## 4.6 Fertility, pregnancy and lactation

### *Fertility*

Animal reproduction studies have not been conducted with heparin sodium. No reproduction studies in animals have been performed concerning mutagenesis or impairment of fertility. It is not known whether heparin sodium can affect reproduction capacity.

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## *Pregnancy (Category C)*

Heparin does not cross the placental barrier. There are no adequate data from the use of **HEPARIN SODIUM** solution for infusion in pregnant women. It is not known whether heparin sodium can cause foetal harm when administered to a pregnant woman. Physicians should carefully consider the potential risks and benefits for each patient before prescribing **HEPARIN SODIUM** solution for infusion. Heparin sodium should be given to pregnant women only if clearly needed.

## *Breast-feeding*

Heparin is not excreted in human milk. There are no adequate data from the use of **HEPARIN SODIUM** solution for infusion in lactating women. Physicians should carefully consider the potential risks and benefits for each patient before prescribing **HEPARIN SODIUM** solution for infusion.

## 4.7 Effects on ability to drive and use machines

Not applicable.

## 4.8 Undesirable effects

The following adverse reactions have been reported in the post-marketing experience, listed by MedDRA System Organ Class (SOC), then, where feasible, by Preferred Term in order of severity:

- **VASCULAR DISORDERS:** Haemorrhage, Gastrointestinal haemorrhage, Adrenal haemorrhage, Retroperitoneal haemorrhage, Epistaxis, Contusion, Vasospastic reactions.  
Haemorrhage is the chief complication that may result from heparin therapy (see Section 4.4). An overly prolonged clotting time or minor bleeding during therapy can usually be controlled by withdrawing the drug (see Section 4.9). **It should be appreciated that gastrointestinal or urinary tract bleeding during anticoagulant therapy may indicate the presence of an underlying occult lesion.** Bleeding can occur at any site but certain specific haemorrhage complications may be difficult to detect:
  - a) Adrenal haemorrhage, with resultant acute adrenal insufficiency, has occurred during anticoagulant therapy. Therefore, such treatment should be discontinued in patients who develop signs and symptoms of acute adrenal haemorrhage and insufficiency. Initiation of corrective therapy should not depend on laboratory confirmation of the diagnosis, since any delay in an acute situation may result in a patient's death.
  - b) Ovarian (corpus luteum) haemorrhage developed in a number of women of reproductive age receiving short or long-term anticoagulant therapy. This complication, if unrecognised, may be fatal.
  - c) Retroperitoneal haemorrhage.
- **BLOOD AND LYMPHATIC SYSTEM DISORDERS:** Thrombocytopenia, Heparin-Induced Thrombocytopenia (with or without Thrombosis).  
Thrombocytopenia has been reported to occur in patients receiving heparin with a reported incidence of up to 30%. While often mild and of no obvious clinical significance, such thrombocytopenia can be accompanied by severe thromboembolic complications such as skin necrosis, gangrene of the extremities that may lead to amputation, myocardial infarction, pulmonary embolism, stroke and possible death (see Section 4.4/Thrombocytopenia, Heparin-induced Thrombocytopenia(HIT) and Heparin-induced Thrombocytopenia and Thrombosis (HITT)).

Certain episodes of painful, ischaemic, and cyanosed limbs have in the past been attributed to allergic vasospastic reactions. Whether these are in fact identical to the thrombocytopenia-associated complications remains to be determined.

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- RENAL AND URINARY DISORDERS: Haematuria.
- ENDOCRINE DISORDERS: Hypoaldosteronism, suppression of aldosterone synthesis.
- SKIN AND SUBCUTANEOUS TISSUE DISORDERS: Skin/Cutaneous necrosis, delayed transient alopecia.
- MUSCULOSKELETAL, CONNECTIVE TISSUE AND BONE DISORDERS: Osteoporosis (following long term administration of high doses of heparin).
- IMMUNE SYSTEM DISORDERS: General hypersensitivity reactions have been reported, with chills, fever and urticaria as the most usual manifestations, and asthma, rhinitis, lacrimation, headache, nausea and vomiting, and anaphylactoid reactions, including shock, occurring more rarely. Itching and burning, especially on the plantar site of the feet, may occur.
- METABOLISM AND NUTRITION DISORDERS: Hyperkalaemia, Hyperlipidaemia. Rebound hyperlipidaemia on discontinuation of heparin sodium have also been reported.
- REPRODUCTIVE SYSTEM AND BREAST DISORDERS: Priapism, Ovarian cyst.
- GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS: Injection site reaction, local irritation, erythema, mild pain, haematoma or ulceration may follow deep subcutaneous (intrafat) injection of heparin sodium. These complications are much more common after intramuscular use, and such use is not recommended.
- INVESTIGATIONS: Significant elevations of aspartate aminotransferase (SGOT [S-AST]) and alanine aminotransferase (SGPT [S-ALT]) levels have occurred in a high percentage of patients (and healthy subjects) who have received heparin.

### *Reporting of suspected adverse reactions*

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions <https://nzphvc.otago.ac.nz/reporting/>

## 4.9 Overdose

### *Symptoms*

An overdose requires immediate medical attention and treatment. Bleeding is the primary sign of heparin overdose. Easy bruising, petechial formations, nosebleeds, blood in urine or tarry stools may be the first signs or symptoms of a heparin overdose.

### *Treatment*

**Neutralization of heparin effect:** When clinical circumstances (bleeding) require reversal of heparinisation, protamine sulphate (1% solution) by slow infusion will neutralise heparin sodium. No more than 50mg should be administered, very slowly in any 10-minute period. Each mg of protamine sulphate neutralises approximately 100 USP heparin units. Ideally, the dose required to neutralise the action of heparin should be guided by blood coagulation tests or calculated from a protamine neutralisation test. The amount of protamine required decreases over time as heparin is metabolised. Although the metabolism of heparin is complex, it may, for the purpose of choosing a protamine dose, be assumed to have a half-life of about 30 minutes after intravenous injection.



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Administration of protamine sulphate can cause severe hypotensive and anaphylactoid reactions. Because fatal reactions often resembling anaphylaxis have been reported, the drug should be given only when resuscitation techniques and treatment of anaphylactoid shock are readily available. For additional information, the labelling of protamine sulphate products should be consulted.

Blood or plasma transfusions may be necessary; these dilute but do not neutralise heparin.

For advice on the management of overdose please contact the National Poisons Centre on phone number: 0800 764 766 [0800 POISON] in New Zealand (or 131126 in Australia).

## 5 PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

<i>Pharmacotherapeutic groups:</i>	Blood and blood forming organs, Antithrombotic agents
<i>ATC codes:</i>	B01AB001

#### *Mechanism of action*

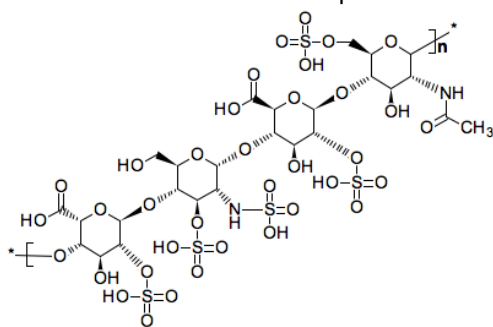
Heparin inhibits reactions that lead to the clotting of blood and the formation of fibrin clots both *in vitro* and *in vivo*. Heparin acts at multiple sites in the normal coagulation system. Small amounts of heparin in combination with Antithrombin III (heparin cofactor) can inhibit thrombosis by inactivating activated Factor X and inhibiting the conversion of prothrombin to thrombin. Once active thrombosis has developed, larger amounts of heparin can inhibit further coagulation by inactivating thrombin and preventing conversion of fibrinogen to fibrin. Heparin also prevents the formation of a stable fibrin clot by inhibiting the activation of the fibrin stabilising factor.

Bleeding time is usually unaffected by heparin. Clotting time is prolonged by full therapeutic doses of heparin; in most cases it is not measurably affected by low doses of heparin.

Heparin does not have fibrinolytic activity; therefore it will not lyse existing clots.

Clinical trials have not demonstrated the superiority of heparin in the maintenance of catheter patency over fluid not containing anticoagulant medication (e.g. normal saline).

#### *Chemical structure: Sodium heparin*



*Molecular formula:* C<sub>26</sub>H<sub>41</sub>NO<sub>34</sub>S<sub>4</sub>

*Molecular weight:* 1039.83

*Appearance:* white or almost off-white powder, odorless, hygroscopic.

*Solubility:* soluble in water; insoluble in ethanol, acetone and other organic solvents.

*CAS number:* 9041-08-1.

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## 5.2 Pharmacokinetic properties

No data available.

## 5.3 Preclinical safety data

### *Genotoxicity*

No reproduction studies in animals have been performed concerning mutagenesis or impairment of fertility.

### *Carcinogenicity*

No long-term studies in animals have been performed to evaluate carcinogenic potential of heparin.

## 6 PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

#### *Inactive ingredients*

Sodium chloride, citric acid monohydrate, dibasic sodium phosphate dodecahydrate and water for injections.

### 6.2 Incompatibilities

Do not add other drugs to Heparin Sodium in 0.9% Sodium Chloride Intravenous Infusion.

### 6.3 Shelf life

24 months from date of manufacture.

### 6.4 Special precautions for storage

Store at or below 30°C.

### 6.5 Nature and contents of container

**HEPARIN SODIUM** is supplied in single dose **VIAFLEX** plastic bag containers for intravenous administration in the following sizes and concentrations.

<b>HEPARIN SODIUM</b> solution for infusion preparations:				
Code No.	Composition (name and quantity of ingredients)	Osmolality (mOsmol/kg)	ARTG TT50-	Pack size
AHB0944A	<b>HEPARIN SODIUM</b> , 2 IU/mL in Viaflex IV Bag <u>Active:</u> Heparin sodium (2000IU) <u>Excipients:</u> Sodium chloride 9g (154mmol); Citric acid monohydrate 0.4g (1.9mmol); Dibasic sodium phosphate dodecahydrate 5.8g (16.2mmol) and Water for injections to 1000mL.	350	19435, TT50-3874	1000mL x 12
AHB0953A	<b>HEPARIN SODIUM</b> , 2 IU/mL in Viaflex IV Bag <u>Active:</u> Heparin sodium (1000IU) <u>Excipients:</u> Sodium chloride 4.5g (77mmol); Citric acid monohydrate 0.2g (0.95mmol); Dibasic sodium phosphate dodecahydrate 2.9g (8.1mmol) and Water for injections to 500mL.	350	19434, TT50-3874	500mL x 18

Not all pack sizes may be marketed.

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## 6.6 Special precautions for disposal and other handling

Any unused medicine or waste material should be disposed of in accordance with local requirements.

### *Directions for use of Viaflex plastic container*

Do not use plastic containers in series connections. Such use could result in air-embolism due to residual air being drawn from the primary container before administration of the fluid from the secondary container is completed.

Pressurising intravenous solutions contained in flexible plastic containers to increase flow rates can result in air embolism if the residual air in the container is not fully evacuated prior to administration.

Use of a vented intravenous administration set with the vent in the open position could result in air embolism. Vented intravenous administration sets with the vent in the open position should not be used with flexible plastic containers.

### *To Open*

Tear over pouch down side at slit and remove solution container. Some opacity of the plastic due to moisture absorption during the sterilisation process may be observed. This is normal and does not affect the solution quality or safety. The opacity will diminish gradually. Check for minute leaks by squeezing inner bag firmly. If leaks are found discard solution as sterility may be impaired. **Do not add supplementary medication.**

Because dosages of this drug are titrated to response, no additives should be made to **HEPARIN SODIUM** Injection.

### *Preparation for administration*

**HEPARIN SODIUM** Injection is a sterile preparation. Thus, aseptic technique must be applied throughout the administration.

1. Suspend container from eyelet support.
2. Remove plastic protector from outlet port at bottom of container.
3. Attach administration set. Refer to complete directions accompanying set.

For single use only. Discard any unused portion.

Do not reconnect partially used bags.

## 7 MEDICINE SCHEDULE

Prescription Medicine.

## 8 SPONSOR

**HEPARIN SODIUM** is distributed in New Zealand by:

Baxter Healthcare Ltd  
33 Vestey Drive  
Mt Wellington  
Auckland 1060

Baxter Healthcare Ltd  
PO Box 14 062  
Panmure  
Auckland 1741

Phone (09) 574 2400.

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**HEPARIN SODIUM** is distributed in Australia by:

Baxter Healthcare Pty Ltd  
1 Baxter Drive  
Old Toongabbie, NSW 2146.

## 9 DATE OF FIRST APPROVAL

Date of publication in the New Zealand Gazette of consent to distribute the medicine:  
13 March 1986.

## 10 DATE OF REVISION OF THE TEXT

19 January 2022.

## SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
All	Correct and consistent use of trade name and dosage form.
3	Clarification of appearance.
4.2	Inclusion of safety information (from CCSI) confirming patient individualisation, and recommending examination of product to confirm formulation.
4.3	Inclusion of safety information (from CCSI) relating to contraindication with diagnoses of HIT.
4.4	Inclusion of safety information (from CCSI) relating to: Hypersensitivity, Vasospastic reactions, Hyperkalaemia, Heparin resistance and coagulation test monitoring, Haemorrhage, Thrombocytopenia, HIT and HITT, and Other, Use in renal impairment, Use in hepatic impairment.
4.5	Inclusion of safety information (from CCSI) relating to: Platelet inhibitors, Antithrombin III, Other interactions.
4.6	Clarification and inclusion of safety information (from CCSI) relating to: Fertility, Pregnancy and Breast-feeding.
4.8	Standard statement included and additional safety information (from CCSI) relating to: Vascular disorders, Renal and urinary disorders, Endocrine disorders, Skin and subcutaneous tissue disorders, Musculoskeletal connective tissue and bone disorders, Metabolism and nutrition disorders, reproductive system and breast disorders, and Investigations.
4.9	Inclusion of safety information (from CCSI) relating to: Symptoms and Treatment of overdose.
5.1	Updated Chemical structure and inclusion of Pharmacodynamic properties.
5.3	Genotoxicity statement updated.
6.5	Table: correction of osmolality and clarification of excipient names and units of measure.
6.6	Inclusion of safety information (from CCSI) relating to potential of embolism. Preparation for administration updated.

*Based on Australian PI approved on 15 December 2021 and CCSI 459 2021APR20.*

*Please refer to the Medsafe website ([www.medsafe.govt.nz](http://www.medsafe.govt.nz)) for most recent data sheet.*

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