NEW ZEALAND DATA SHEET

1. PRODUCT NAME

Heparinised Saline (Pfizer) Injection 50 IU/5mL Solution for Injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One ampoule contains heparin sodium 10 IU/mL, in 5mL ampoules.

Heparin sodium is a white or almost white powder, moderately hygroscopic, freely soluble in water.

Heparin sodium is a preparation containing the sodium salt of a sulfated glucosaminoglycan present in mammalian tissues. It is prepared from the intestinal mucosae of pigs.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection

Heparinised Saline Injection is a clear, colourless, sterile, preservative-free solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

- Maintenance of the patency of intravenous injection devices

4.2 Dose and method of administration

Dose

Heparinised Saline Injection contains no antimicrobial agent and is therefore intended for single use only.

To maintain the patency of intravenous injection devices and prevent clot formation, flush the catheter/cannula with 10 – 50 IU every four hours. The solution may be used following initial placement of the device in the vein, after each injection of a medication, or after withdrawal of blood for laboratory tests. If the drug to be administered is incompatible with Heparin (see section 4.5), the device must be flushed through with normal 0.9% Sodium chloride solution before and after the drug is administered. When heparin would interfere with or alter the results of blood tests, the heparin solution should be cleared from the device by aspirating and discarding it before withdrawing the blood sample. Consult the device manufacturer's instructions for specific details.

Note: Since repeated injections of small doses of heparin can alter tests for activated partial thromboplastin time (APTT), a baseline value for APTT should be obtained prior to insertion of an intravenous device.

4.3 Contraindications

- Known hypersensitivity to heparin or pork products,
- Heparinised saline should not be used for anticoagulant therapy,
- Severe thrombocytopenia,
- History of heparin-induced thrombocytopenia and heparin-induced thrombocytopenia and thrombosis,
- Heparin sodium should not be administered to patients in an uncontrollable active bleeding state (see section 4.4) except when this condition is the result of disseminated intravascular coagulation.

4.4 Special warnings and precautions for use

Heparin is not intended for intramuscular use.

- Heparinised Saline Injection is not recommended for use in neonates.
- In infants, the cumulative amounts of heparin received from frequent administration of Heparinised Saline Injection during a 24-hour period should be considered.
- Precautions must be exercised when drugs, which are incompatible with heparin, are administered through an indwelling intravenous catheter containing Heparinised Saline Injection (see sections 4.5 and 4.2).

Haemorrhage

Haemorrhage can occur at virtually any site in patients receiving heparin. An unexplained fall in haematocrit, a fall in blood pressure, or any other unexplained symptom warrants consideration of a haemorrhagic event. Heparin should be used with caution in conditions in which there is an increased risk of haemorrhage, such as:

Gastrointestinal: gastric or duodenal ulcers**,** continuous tube drainage of the stomach or small intestine, and oesophageal varices.

Cardiovascular: subacute bacterial endocarditis, severe hypertension.

Surgical: during and immediately after (a) spinal tap or spinal anaesthesia or (b) major surgery, especially those involving the brain, eye or spinal cord.

Haematological: actual or potential haemorrhagic states, such as haemophilia, thrombocytopenia, some vascular purpuras and cerebrovascular pathologies.

Other: menstruation, liver disease with impaired haemostasis and renal disease.

Thrombocytopenia

Thrombocytopenia has been reported to occur in patients receiving heparin with a reported incidence of 0% to 30%. The immuno-allergic effects of heparin manifest themselves between the 5th and 21st day of treatment. Platelet counts should be obtained at baseline and periodically during heparin administration. Mild thrombocytopenia (count greater than 100,000/mm^3) may remain stable or reverse even if heparin is continued. However, thrombocytopenia of any degree should be monitored closely. If the count falls below 100,000/mm^3 or if recurrent thrombosis develops (see **Heparin-induced Thrombocytopenia and Heparin-induced Thrombocytopenia and Thrombosis**), heparin should be discontinued, and if necessary, an alternative anticoagulant administered.

Heparin-induced Thrombocytopenia (HIT) and Heparin-induced Thrombocytopenia and Thrombosis (HITT)

Heparin-induced Thrombocytopenia (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 Thrombocytopenia and Thrombosis (HITT), the so-called "White-Clot Syndrome". Thrombotic events may also be the initial presentation for 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. Thrombocytopenia of any degree should be monitored closely. If the platelet count falls below 100,000/mm^3 or if recurrent thrombosis develops, the heparin product should be promptly discontinued and alternative anticoagulants considered if patients require continued anticoagulation.

Delayed Onset of HIT and HITT

Heparin-induced Thrombocytopenia and Heparin-induced Thrombocytopenia and Thrombosis 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.

Hyperkalaemia

Heparin sodium suppresses the secretion of aldosterone by the adrenal gland with possible consequent hyperkalaemia, particularly in patients with diabetes mellitus, chronic kidney failure, positive anamnesis for metabolic acidosis, increased potassium plasma levels, or in patients being treated with potassium-sparing drugs. The risk of hyperkalaemia seems to increase with the duration of treatment but is normally reversible. Serum electrolytes must be measured in at-risk patients before starting heparin therapy and must then be monitored regularly, particularly when treatment is prolonged for more than 7 days.

Skin Necrosis

Cases of skin necrosis have been reported, sometimes preceded by purpura or painful erythematous lesions, when heparin was administered subcutaneously. In these cases, it is advisable to stop the treatment immediately.

Anaesthesia

Caution is required in the prophylaxis and heparin treatment of patients undergoing spinal anaesthesia or epidural and/or lumbar puncture. In patients who have received anaesthesia by epidural or spinal administration, or by lumbar puncture, the prophylactic use of heparin was, in very rare cases, associated with epidural or spinal haematomas with resulting prolonged or permanent paralysis. The risk is higher when using epidural or spinal catheters for anaesthesia while simultaneously using drugs that affect clotting, such as non-steroidal anti-inflammatory drugs (NSAIDs), which are anticoagulant or inhibit platelet aggregation, and in the case of traumatic or repeated punctures.

When deciding the interval between the administration of heparin at prophylactic dosages and the placement or removal of the spinal or epidural catheter, both the characteristics of the medicinal product and the patient's clinical profile shall be evaluated. In the case of non-fractioned heparin, it is recommended to administer the pre-operative dose of heparin at least 1 hour after placing the catheter for anaesthesia, to remove the catheter at least 4 hours after the last dose of heparin and administer the first dose of post-operative heparin at least 1 hour after removal of the catheter.

If a decision is made to administer an anticoagulant treatment during the spinal or epidural anaesthesia, the patient must be closely monitored to identify early signs or symptoms of neurological impairment such as lumbar pain, motor-sensory deficits (torpor and weakness of the lower limbs), dysfunction of the intestine or bladder. The staff must be prepared to identify such signs and symptoms. Furthermore, the patients must be told to immediately inform the doctor or nurse if they experience the above-mentioned symptoms.

In the event of signs or symptoms indicative of suspected spinal or epidural haematoma, diagnostic tests must be performed urgently and, if indicated, spinal decompression (laminectomy) must be performed promptly (within 6-12 hours).

Hypersensitivity

As heparin is derived from animal tissues it should be used with caution in patients with a history of allergy as hypersensitivity reactions may occur.

Laboratory Tests

Periodic platelet counts, haematocrits and tests for occult blood in stools are recommended during the entire course of heparin use.

Effect on Laboratory Tests

Hyperaminotransferasemia: Significant elevations of aminotransferase [serum glutamic oxaloacetic transaminase (SGOT) and serum glutamic pyruvic transaminase (SGPT)] levels have occurred in a high percentage of patients (and healthy subjects) who have received heparin therapy, although the low dose of Heparinised Saline would not normally evoke this.

Use in the Elderly

Elderly patients (patients over 60 years of age), particularly women, appear to have a higher risk of haemorrhage and should be carefully monitored.

Paediatric Population

Heparinised Saline Injection is not recommended for use in neonates.

4.5 Interaction with other medicines and other forms of interaction

Protamine sulphate, a heparin antidote, inhibits the anticoagulant action.

Platelet Inhibitors: Drugs such as acetylsalicylic acid, NSAIDs, dextran, ibuprofen, indomethacin, dipyridamole, hydroxychloroquine, glucocorticoids 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.

Other Interactions: Digoxin, tetracyclines, nicotine, or antihistamines may partially counteract the anticoagulant action of heparin sodium.

Other medicines which may potentiate the effect of heparin include probenecid, etacrynic acid, vitamin K antagonists, alprostadil, cytostatic agents, cefamandole, valproic acid and propylthiouracil. High doses of penicillins, some contrast media, asparaginase and epoprostenol may also affect the coagulation process of heparin sodium.

Heavy alcohol drinkers are at greater risk of major heparin associated bleeding than moderate or non-drinkers.

Experimental evidence suggests that heparin may antagonise the actions of ACTH, corticosteroids and insulin.

Drugs Antagonising Effects of Heparin

The concomitant administration of intravenous nitroglycerin may reduce the anticoagulant effect of heparin with a rebound effect on discontinuation of the nitroglycerin. Therefore, in the case of concomitant administration, it is recommended to closely monitor clotting and any adjustment of the heparin dosage.

The concomitant use of heparin with andexanet alfa may reduce the effectiveness of heparin. Andexanet alfa, a recombinant modified human coagulation factor Xa used for reversal of anticoagulation with apixaban or rivaroxaban, has been shown to bind to heparin-bound antithrombin III (ATIII) and may reduce the anticoagulant effect of heparin.

4.6 Fertility, pregnancy and lactation

Pregnancy - Category C

Animal reproduction studies have not been conducted with heparin sodium. It is also not known whether heparin sodium can cause foetal harm when administered to a pregnant woman or can affect reproduction capacity. Heparin sodium should be given to a pregnant woman only if clearly needed.

Breast-feeding

Heparin is not excreted in the breast milk.

Fertility

Also, no reproduction studies in animals have been performed concerning impairment of fertility.

4.7 Effects on ability to drive and use machinery

Heparin does not affect the ability to drive or use machines.

4.8 Undesirable effects

Haematological: Haemorrhage is the major risk associated with heparin therapy although the low dose of Heparinised Saline would not normally evoke this. An overly prolonged clotting time or minor bleeding during therapy can usually be controlled by withdrawing the drug.

Spinal and Epidural Haematoma: In patients treated with heparin for prophylaxis and who have undergone epidural or spinal anaesthesia or spinal puncture. These haematomas have caused various degrees of neurological impairment, which have included prolonged or permanent paralysis.

Hypersensitivity: Heparin in therapeutic and prophylactic doses is essentially non-toxic but may cause allergic reactions and possibly anaphylactic reactions in susceptible patients. Generalised hypersensitivity reactions have been reported, with chills, fever, and urticaria as the most common manifestations; asthma, rhinitis, lacrimation, headache, nausea and vomiting, and anaphylactoid reactions (including shock) have occurred more rarely. Dyspnoea, bronchospasm, oedema of the glottis have also been observed with anaphylactic or hypersensitivity reactions. Itching and burning, especially on the plantar site of the feet, may occur.

Thrombocytopenia, Heparin-induced Thrombocytopenia (HIT) and Heparin-induced Thrombocytopenia and Thrombosis (HITT) and Delayed Onset of HIT and HITT: Thrombocytopenia induced by heparin may be of two types. The first is an acute, but usually mild, fall in platelet count occurring within 1 to 4 days of initiation of therapy and which may resolve without cessation of treatment. A direct effect of heparin on platelet aggregation appears to be responsible. The second type is a delayed onset thrombocytopenia, which has an immunological basis, and is more serious. It usually occurs after 7 to 11 days of heparin and drug withdrawal is indicated. Thrombocytopenia of any degree should be monitored closely (see section 4.4).

Local Irritation: Skin necrosis at the injection site has been reported and is thought to be a local manifestation of heparin induced platelet aggregation and thrombosis. This should be taken as a warning sign in patients who develop it and heparin therapy should be immediately discontinued. Local irritation and erythema have been also been reported.

Hyperaldosteronism and Hyperkalaemia: hyperkalaemia most frequently occurs in patients with chronic renal decompensation or diabetes mellitus, or patients already being treated with drugs that induce hyperkalaemia.

Other: Osteoporosis, alopecia and increased transaminase levels.

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://pophealth.my.site.com/carmreportnz/s/.

4.9 Overdose

Symptoms

The usual sign of overdosage is bleeding or haemorrhage. Nosebleeds, blood in urine or tarry stools may be noted as the first sign of bleeding. Easy bruising or petechial formations may precede frank bleeding.

Treatment

The drug should be withdrawn and clotting time and platelet count should be determined. Prolonged clotting time will indicate that there is an anticoagulant effect requiring neutralisation and in this case, protamine sulfate should be administered. The dose should be calculated by titration of the individual patient's requirements but as a general guide, approximately 1 mg of protamine sulfate neutralises 100 IU of heparin (mucous) that has been injected in the previous 15 minutes. No more than 50 mg should be administered, very slowly, in any 10 minute period. Since heparin is being continuously eliminated the dose should be reduced as time elapses. 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 half an hour after intravenous injection.

Protamine may cause anaphylactoid reactions that may be life threatening. (See the protamine label for additional information). Hence the drug should be given only when resuscitation techniques and treatment of anaphylactoid shock are readily available.

For risk assessment and advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group**:** Anticoagulant.

ATC Code: B01AB01

Heparin is a heterogeneous group of straight-chain anionic mucopolysaccharides, called glycosaminoglycans, possessing anticoagulant properties. It is composed of polymers of alternating derivations of α-D-glucosamido (*N*-sulfated *O*-sulfated or *N*-acetylated) and *O*-sulfated uronic acid (α-L-iduronic acid or β-D-glucuronic acid).

Heparin CAS Registry Number is 9005-49-6.

Mechanism of Action

Heparin is a naturally occurring mucopolysaccharide with *in vitro* and *in vivo* anticoagulant activity. Heparin acts at multiple sites in the normal coagulation systems. 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, which in turn prevents the conversion of fibrinogen to fibrin. Under normal conditions an equilibrium between fibrinogen deposition and lysis keeps the vascular system free of thrombi. Under abnormal conditions of trauma, surgery or circulatory collapse, the equilibrium shifts towards clot formation. The action of heparin is to shift the equilibrium back towards normal thereby reducing clot formation.

5.2 Pharmacokinetic properties

Heparin is extensively bound to plasma proteins. It does not cross the placenta and is not excreted in breast milk. The exact route of metabolism of heparin is unknown and well defined renal elimination of the drug has not been identified. In the absence of evidence for a conventional route of elimination, transfer to an extravascular space such as the reticuloendothelial system has been postulated.

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.

Log linear plots of heparin plasma concentrations with time for a wide range of dose levels are linear, which suggests the absence of zero order processes. Liver and the reticuloendothelial system are the sites of biotransformation. The biphasic elimination curve, a rapidly declining alpha phase ($t_{1/2}$ = 10minutes) and, after the age of 40, a slower beta phase indicate uptake in organs. The absence of a relationship between anticoagulant half-life and concentration half-life may reflect factors such as protein binding of heparin.

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

5.3 Preclinical safety data

Genotoxicity

No reproduction studies in animals have been performed concerning mutagenesis.

Carcinogenicity

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

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hydrochloric acid,
Sodium hydroxide,

Sodium chloride,
Water for injections.

6.2 Incompatibilities

Heparinised Saline Injection is incompatible with certain substances in solution. Specialised literature should be consulted to verify with which substances incompatibilities have been noted. The following incompatibilities have been reported: amikacin sulfate, erythromycin lactobionate, gentamicin sulfate, kanamycin sulfate, tetracycline sulfate, tobramycin sulfate, vancomycin hydrochloride, hydrocortisone sodium succinate, doxorubicin, droperidol, ciprofloxacin, mitozantrone, morphine sulfate, haloperidol lactate, promethazine hydrochloride, codeine phosphate, hyaluronidase, benzylpenicillin sodium, methadone hydrochloride, pethidine hydrochloride, reteplase, methicillin sodium, levorphanol bitartrate, alteplase, amiodarone hydrochloride, ampicillin sodium, aprotinin, cephalothin sodium, cytarabine, dacarbazine, daunorubicin hydrochloride, diazepam, dobutamine hydrochloride, netilmicin sulfate, oxytetracycline hydrochloride, polymyxin B sulfate, streptomycin sulfate, some phenothiazines vinblastine sulfate and colistin.

Heparin sodium has also been reported to be incompatible with cisatracurium besilate, labetalol hydrochloride and nicardipine hydrochloride. Admixture with glucose can have variable effects. Incompatibility has been reported between heparin and fat emulsion.

6.3 Shelf life

20 months

6.4 Special precautions for storage

Store at or below 25°C.

6.5 Nature and contents of container

Heparinised Saline Injection 50 IU/5mL (sterile) Steriluer® plastic ampoule (50s)

6.6 Special precautions for disposal

Single use only. Discard unused portion.

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

7. MEDICINE SCHEDULE

Prescription medicine

8. SPONSOR

Pfizer New Zealand Limited
P O Box 3998

Auckland, New Zealand
Toll Free Number: 0800 736 363
www.pfizermedicalinformation.co.nz

9. DATE OF FIRST APPROVAL

27 August 2009

10. DATE OF REVISION OF THE TEXT

05 September 2025

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SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
Throughout	Minor editorial changes.
4.5	Update to include a drug-drug interaction between heparin and andexanet alfa.
4.8, 4.9	DS Template change: changed reporting URL and added risk assessment wording.
8	New website information.