**DESCRIPTION**

Heparin is a heterogenous group of straight-chain anionic mucopolysaccharides, called glycosaminoglycans, having anticoagulant properties. Although others may be present, the main sugars occurring in heparin are: (1) α-L-iduronic acid 2-sulfate, (2) 2-deoxy-2-sulfamino-α-D-glucose 6-sulfate, (3) β-D-glucuronic acid, (4) 2-acetamido-2-deoxy-α-D-glucose, and (5) α-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. Heparin is strongly acidic because of its content of covalently linked sulfate and carboxylic acid groups. In heparin sodium, the acidic protons of the sulfate units are partially replaced by sodium ions.

Its structural formula (representative subunits) is as follows:

![Heparin Structure](image)

Heparin Lock Flush Solution, USP, is a sterile solution of heparin sodium derived from porcine intestinal mucosa. Each mL contains either 10 or 100 USP heparin units in Water for Injection, benzyl alcohol 1% as a preservative, and sufficient sodium chloride to render the solution isotonic. The pH is adjusted between 5 to 7.5 with hydrochloric acid or sodium hydroxide.

**CLINICAL PHARMACOLOGY**

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 the conversion of fibrinogen to fibrin. Heparin also prevents the formation of a stable fibrin clot by inhibiting the activation of the fibrin stabilizing 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.

**INDICATIONS AND USAGE**

Heparin Lock Flush Solution is intended to maintain patency of an indwelling intravenous catheter designed for intermittent injection therapy or blood sampling. Heparin Lock Flush 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 analysis. See **DOSAGE AND ADMINISTRATION, Clearing Intermittent Infusion (Heparin Lock) Sets** for directions for use.

Heparin Lock Flush Solution is not to be used for anticoagulant therapy.
CONTRAINDICATIONS
Heparin sodium should NOT be used in patients with an uncontrollable active bleeding state (see WARNINGS), except when this is due to disseminated intravascular coagulation.

WARNINGS
Heparin Lock Flush Solution should be used with caution in infants with disease states in which there is an increased danger of hemorrhage.

    Neonatologists do not advise the use of the 100 units/mL concentration because of the risk of bleeding, especially in low birth weight infants.

    Heparin is not intended for intramuscular use.

Hypersensitivity. Patients with documented hypersensitivity to heparin should be given the drug only in clearly life-threatening situations. (See ADVERSE REACTIONS.)

Thrombocytopenia. Thrombocytopenia has been reported to occur in patients receiving heparin with a reported incidence of 0% to 30%. 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 PRECAUTIONS, White Clot Syndrome), the heparin product should be discontinued. If continued heparin therapy is essential, administration of heparin from a different organ source can be reinstituted with caution.

Miscellaneous. This product contains benzyl alcohol as a preservative. Benzyl alcohol has been reported to be associated with a fatal “Gasing Syndrome” in premature infants.

PRECAUTIONS
In infants, the cumulative amounts of heparin and benzyl alcohol received from the frequent administration of Heparin Lock Flush Solution during a 24-hour period must be considered.

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 possibly death. Therefore, heparin administration should be promptly discontinued if a patient develops new thrombosis in association with thrombocytopenia.

    Precautions must be exercised when drugs which are incompatible with heparin are administered through an indwelling intravenous catheter containing Heparin Lock Flush Solution. (See DOSAGE AND ADMINISTRATION.)

Carcinogenesis, Mutagenesis, Impairment of Fertility
No long-term studies in animals have been performed to evaluate the carcinogenic potential of heparin. Also, no reproduction studies in animals have been performed concerning mutagenesis or impairment of fertility.

Pregnancy
Pregnancy Category C
Teratogenic Effects: Animal reproduction studies have not been conducted with heparin sodium. It is also not known whether heparin sodium can cause fetal 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.

Nonteratogenic Effects: Heparin does not cross the placental barrier.

Nursing Mothers
Heparin is not excreted in human milk.
ADVERSE REACTIONS

Hemorrhage
Hemorrhage is the chief complication that may result from heparin. An overly prolonged clotting time or minor bleeding during therapy can usually be controlled by withdrawing the drug (see OVERDOSAGE).

Hypersensitivity
Generalized 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 side of the feet, may occur.

Thrombocytopenia has been reported to occur in patients receiving heparin with a reported incidence of 0% 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 possibly death. (See WARNINGS and PRECAUTIONS.)

Certain episodes of painful, ischemic, 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.

OVERDOSAGE

Symptoms. Bleeding is the chief sign of heparin overdose. 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. Neutralization of heparin effect.
When clinical circumstances (bleeding) require reversal of heparinization, protamine sulfate (1% injection) by slow infusion will neutralize heparin sodium. No more than 50 mg should be administered, very slowly, in any 10 minute period. Each mg of protamine sulfate neutralizes approximately 100 USP heparin units. The amount of protamine required decreases over time as heparin is metabolized. 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 1/2 hour after intravenous injection.

Administration of protamine sulfate 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 consult the labeling of Protamine Sulfate Injection, products.

DOSAGE AND ADMINISTRATION

PARENTERAL DRUG PRODUCTS SHOULD BE INSPECTED VISUALLY FOR PARTICULATE MATTER AND DISCOLORATION PRIOR TO ADMINISTRATION, WHENEVER SOLUTION AND CONTAINER PERMIT. SLIGHT DISCOLORATION DOES NOT ALTER POTENCY.

Clearing Intermittent Infusion (Heparin Lock) Sets
To prevent clot formation in a heparin lock set following its proper insertion, Heparin Lock Flush Solution is injected via the injection hub in a quantity sufficient to fill the entire set to the needle tip. This solution should be replaced each time the heparin lock is used. Aspirate before administering any solution via the lock in order to confirm patency and location of needle or catheter tip. If the drug to be administered is incompatible with heparin, the entire heparin lock set should be flushed with sterile water or normal saline before and after the medication is administered; following the second flush, Heparin Lock Flush Solution may be reinstalled into the set. The set manufacturer’s instructions should be consulted for specifics concerning the heparin lock set in use at a given time.
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 a heparin lock set.

Usually these dilute heparin solutions will maintain anticoagulation within the device for up to 4 hours.

Withdrawal of Blood Samples
Heparin Lock Flush Solution may also be used after each withdrawal of blood for laboratory tests. When heparin (or sodium chloride) 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.

HOW SUPPLIED
Heparin Lock Flush Solution, USP, is supplied as follows:

<table>
<thead>
<tr>
<th>NDC No.</th>
<th>Type Container</th>
<th>USP heparin Units/Fill</th>
<th>Quantity</th>
</tr>
</thead>
<tbody>
<tr>
<td>0409-1280-31</td>
<td>Carpuject™ with Luer Lock</td>
<td>10/1 mL</td>
<td>Bin of 50</td>
</tr>
<tr>
<td>0409-1280-32</td>
<td>Carpuject with Luer Lock</td>
<td>20/2 mL</td>
<td>Bin of 50</td>
</tr>
<tr>
<td>0409-1280-33</td>
<td>Carpuject with Luer Lock</td>
<td>30/3 mL</td>
<td>Bin of 25</td>
</tr>
<tr>
<td>0409-1280-35</td>
<td>Carpuject with Luer Lock</td>
<td>50/5 mL</td>
<td>Bin of 25</td>
</tr>
<tr>
<td>0409-1281-31</td>
<td>Carpuject™ with Luer Lock</td>
<td>100/1 mL</td>
<td>Bin of 50</td>
</tr>
<tr>
<td>0409-1281-32</td>
<td>Carpuject with Luer Lock</td>
<td>200/2 mL</td>
<td>Bin of 50</td>
</tr>
<tr>
<td>0409-1281-33</td>
<td>Carpuject with Luer Lock</td>
<td>300/3 mL</td>
<td>Bin of 25</td>
</tr>
<tr>
<td>0409-1281-35</td>
<td>Carpuject with Luer Lock</td>
<td>500/5 mL</td>
<td>Bin of 25</td>
</tr>
</tbody>
</table>

Store at 20 to 25°C (68 to 77°F). [See USP Controlled Room Temperature.] Do not freeze.
Caution: Federal (USA) law prohibits dispensing without prescription.

Revised: June, 2010

Printed in USA
Hospira, Inc., Lake Forest, IL 60045 USA