

## HEPARIN (Systemic)

### Category

Anticoagulant.

### Indications

#### Accepted

Thrombosis, deep venous (prophylaxis and treatment) and

Thromboembolism, pulmonary (prophylaxis and treatment)<sup>3,4</sup>Heparin is indicated using a full-dose regimen in the treatment of patients with recent thrombosis or thrombophlebitis of the deep veins to prevent extension and embolization of the thrombus and to reduce the risk of pulmonary embolism or recurrent thrombus formation. In acute pulmonary embolism, full-dose heparin is indicated to decrease the risk of extension, recurrence, or death.

Heparin is also indicated using a low-dose regimen to prevent the development of venous thrombosis and pulmonary embolism following major abdominal or thoracic surgery in high-risk patients, such as patients with a history of thromboembolism and patients requiring prolonged immobilization following surgery, especially if they are 40 years of age or older. Low-dose heparin may be ineffective for this purpose in some patients, especially following hip surgery. Many clinicians question the validity of data showing the efficacy and safety of low-dose heparin prophylaxis.

[Low-dose heparin prophylaxis is also used to prevent thrombus formation in selected immobilized medical patients who are not at risk of hemorrhage.]

Heparin is also administered using an adjusted-dose regimen for prophylaxis against thromboembolic complications when low-dose heparin may not be effective, e.g., for general abdominal or thoracic surgery in very high-risk patients, high-risk orthopedic procedures such as elective hip surgery or knee reconstruction, and [the second half of the third trimester in pregnant women with a history of venous thrombosis or pulmonary embolism] \* 1, 2, 3, 4.

Adjusted-dose subcutaneous heparin is also recommended when long-term anticoagulation is required and use of a coumarin- or indandione-derivative anticoagulant is contraindicated or inadvisable (e.g., during pregnancy) 1, 2, 3, 4.

In addition, after the dosage of heparin has been stabilized (i.e., the desired level of anticoagulation has been achieved and maintained for a 2-week period without additional dosage adjustment) 6, further anticoagulant monitoring and dosage adjustment are not needed (except during pregnancy, when heparin requirements increase with the patient's blood volume as pregnancy progresses) 5, 6.

Therefore, this regimen can be utilized for the long-term treatment of nonpregnant patients when anticoagulant therapy cannot be monitored on a regular basis 1, 2, 3, 4.

Thromboembolism (prophylaxis)<sup>3,4</sup>Heparin is indicated prior to and during attempted cardioversion or surgery to prevent systemic thromboembolism that may occur in patients with chronic atrial fibrillation,

especially those with rheumatic mitral stenosis, congestive heart failure, left atrial enlargement, or cardiomyopathy.

Heparin is indicated as adjunctive therapy in acute myocardial infarction to reduce the risk of thromboembolic complications, especially in high-risk patients such as those with shock, congestive heart failure, prolonged arrhythmias (especially atrial fibrillation), previous myocardial infarction, or history of venous thrombosis or pulmonary embolism. Also, heparin may be administered to help prevent reocclusion following thrombolytic therapy in patients with acute myocardial infarction. 15

[Heparin is also used to prevent catheter-induced thromboembolism during coronary angiography and percutaneous transluminal angioplasty.] \*

Blood clotting (prophylaxis)¾Heparin is indicated to prevent blood clotting during extracorporeal circulation in cardiac surgery and dialysis procedures.

Heparin is indicated to prevent blood clotting during and following arterial surgery. It is administered systemically or by local intra-arterial injection.

Heparin is indicated to prevent blood clotting during blood transfusions and in blood sampling for laboratory purposes. However, heparinized blood should not be used for isoagglutinin, complement, or erythrocyte fragility tests, or for platelet counts. In addition, leukocyte counts should be performed within 2 hours after heparin is added to the blood sample.

Heparin is also available as a lock flush solution, which is not intended for anticoagulant therapy. This solution is used to maintain the patency of an indwelling intravascular device.

Coagulation, disseminated intravascular (treatment)¾Although heparin is indicated as a temporary measure in the treatment of disseminated intravascular coagulation, especially if there is clinical evidence of intravascular thrombosis, its use in this condition is controversial. The underlying cause of the condition must be determined and treated.

Thromboembolism, arterial (treatment)¾Heparin is indicated as adjunctive therapy for peripheral arterial embolism. It may prevent further thrombus formation when surgery must be delayed.

Thrombosis, cerebral (prophylaxis)¾Heparin is indicated to decrease the risk of cerebral thrombosis and death in patients with progressive stroke (stroke-in-evolution).

[Thromboembolism, cerebral, recurrence (prophylaxis)] \*¾Heparin is also used in the treatment of patients with recent cerebral embolism to decrease the risk of recurrence and death; however, this use is controversial. Although administration of an anticoagulant too soon after a cerebral embolism may increase the risk of cerebral hemorrhage, recent studies have indicated that the risk of early recurrence may be greater than the risk of anticoagulant therapy. It is recommended that heparin therapy be initiated only if the patient is not hypertensive and a computerized tomographic (CT) scan performed 24 hours or longer following the onset of the stroke shows no evidence of hemorrhagic transformation. If severe hypertension is present, or the embolic stroke is large, there is a risk of late hemorrhagic transformation and anticoagulant therapy should be delayed for several days. If hemorrhagic transformation is documented, anticoagulant therapy should be postponed for at least 8 to 10 days. Long-term anticoagulation is recommended. 1, 2

## Precautions to Consider

### Cross-sensitivity and/or related problems

Patients with a history of allergies, especially those who are allergic to swine, beef, or other animal proteins, may be allergic to this medication also (depending on heparin source).

### Pregnancy/Reproduction

Pregnancy% Heparin does not cross the placenta and is the anticoagulant of choice for use during pregnancy because it does not affect blood clotting mechanisms in the fetus. Although heparin has not been reported to cause birth defects, use during pregnancy has been reported to increase the risk of stillbirth or prematurity. However, the underlying condition, rather than heparin itself, may have been responsible. Also, the reported incidence (13 to 22%) of these complications is lower than that reported with coumarin-derivative anticoagulants (31%). In addition, caution is recommended when heparin is used during the last trimester of pregnancy or during the postpartum period because of the increased risk of maternal bleeding.

Especially careful monitoring of the patient and attention to dosage are recommended during pregnancy. Heparin requirements increase, because of expansion of the patient's blood volume, as pregnancy progresses 5, 6, 7.

Readjustment of heparin dosage may be needed following delivery 7.

### FDA Pregnancy Category C.

### Breast-feeding

Heparin is not distributed into breast milk. However, administration to lactating women has rarely been reported to cause rapid (within 2 to 4 weeks) development of severe osteoporosis and vertebral collapse.

### Pediatrics

Appropriate studies performed to date have not demonstrated pediatrics-specific problems that would limit the usefulness of heparin in children. However, heparin injections that contain benzyl alcohol should not be administered to premature neonates because the preservative has been associated with a fatal "gasping syndrome" in these patients.

### Geriatrics

Patients 60 years of age or older, especially females, may be more susceptible to hemorrhaging during heparin therapy. Also, elderly patients are more likely to have age-related renal function impairment, which may increase the risk of bleeding in patients receiving anticoagulants.

### Dental

Bleeding from gingival tissue may be a symptom of heparin overdose.

Heparin therapy increases the risk of localized hemorrhage during and following oral surgical procedures. Consultation with the prescribing physician may be advisable prior to oral surgery, to determine whether a temporary dosage reduction or withdrawal of heparin therapy is feasible. Also, local measures to minimize bleeding should be used at the time of surgery.

#### Drug interactions and/or related problems

The following drug interactions and/or related problems have been selected on the basis of their potential clinical significance (possible mechanism in parentheses where appropriate) %not necessarily inclusive (>> = major clinical significance):

Note: Combinations containing any of the following medications, depending on the amount present, may also interact with this medication.

Interactions listed below may not apply to short-term use of heparin followed by protamine reversal, as in cardiovascular surgery.

In addition to the documented interactions listed below, the possibility should be considered that multiple effects leading to further impairment of blood clotting and/or increased risk of bleeding may occur if heparin is administered to a patient receiving any medication having a significant potential for causing hypoprothrombinemia, thrombocytopenia, or gastrointestinal ulceration or hemorrhage.

Acid citrate dextrose (ACD)-converted blood %blood collected in heparin and later converted to ACD blood

#### Medical considerations/Contraindications

The medical considerations/contraindications included have been selected on the basis of their potential clinical significance (reasons given in parentheses where appropriate) % not necessarily inclusive (>> = major clinical significance).

Except under special circumstances, this medication should not be used when the following medical problems exist

>> Abortion, threatened or

>> Aneurysm, cerebral or dissecting aorta, except in conjunction with corrective surgery or

>> Cerebrovascular hemorrhage, confirmed or suspected

(increased risk of uncontrollable hemorrhage)

>> Hemorrhage, active uncontrollable, except in disseminated intravascular coagulation

>> Hypertension, severe uncontrolled

(increased risk of cerebral hemorrhage)

>> Thrombocytopenia, severe, heparin-induced, within past several months

(risk of recurrence, which may cause resistance to heparin and new thromboembolic complications)

(must be performed at periodic intervals during full-dose therapy as a guide to dosage, efficacy, and safety)

(PTT tests are used to establish dosage requirements during the initial phase of adjusted-dose therapy; they are also required at periodic intervals throughout adjusted-dose therapy, as a guide to dosage and efficacy, if the patient is pregnant)