

# Protamine Indication And Dosage

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Clinical pharmacy team

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WHAT?



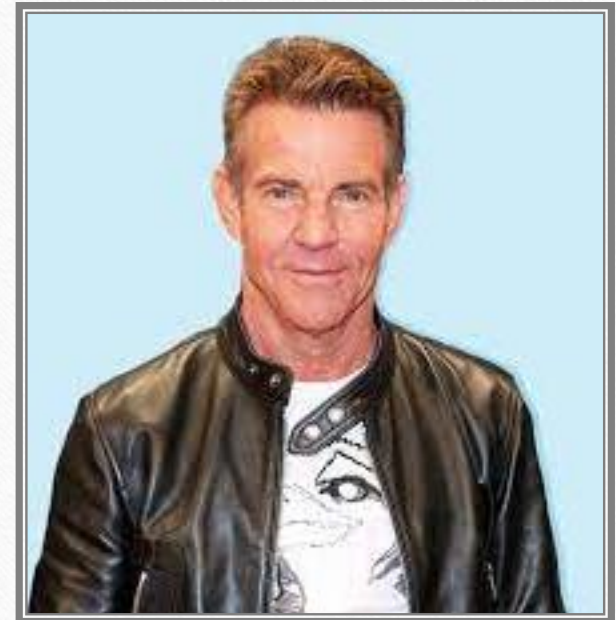
WHY?

# Heparine anticoagulant

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- Prophylaxis and treatment of thromboembolic disorders and
- Anticoagulant for blood transfusions, and central-lines patency .

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- In 2007, the newborn twins of American actor Denis Quaid received a **massive overdose** of heparin at Cedars-Sinai Hospital in Los Angeles.



# Magnitude of overdosing

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- In 2007, According US Pharmacopeia, during the past 18 months there have been roughly 250.
- Between 2001-2006 there over 16,000 heparin errors blamed on incorrect dosing in Los Angeles.

# Contributing Factors to the Heparin Medication Errors

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- 1) Failure to carefully and accurately **read the label** on the medication vial prior to administering the drug to the patient;
- 2) Inaccurate filling of syringes (substituting 10,000 units/mL 1-mL vials for 10 units/mL 1-ml vials);
- 3) Non-distinct “look-alike” labels on the heparin vials;
- 4) Similar size of the heparin vials as both were 1-mL vials.
- 5) **Dilution errors**

# Management protocol

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- 10,000 units/mL heparin solutions were removed from the formulary.
- All heparin flush solutions (10 units/mL and 100 units/mL) supplied by the pharmacy in automated drug-dispensing machines were changed to pre-filled syringes.
- Addition of protamine sulphate to the formulary.

# Protamine

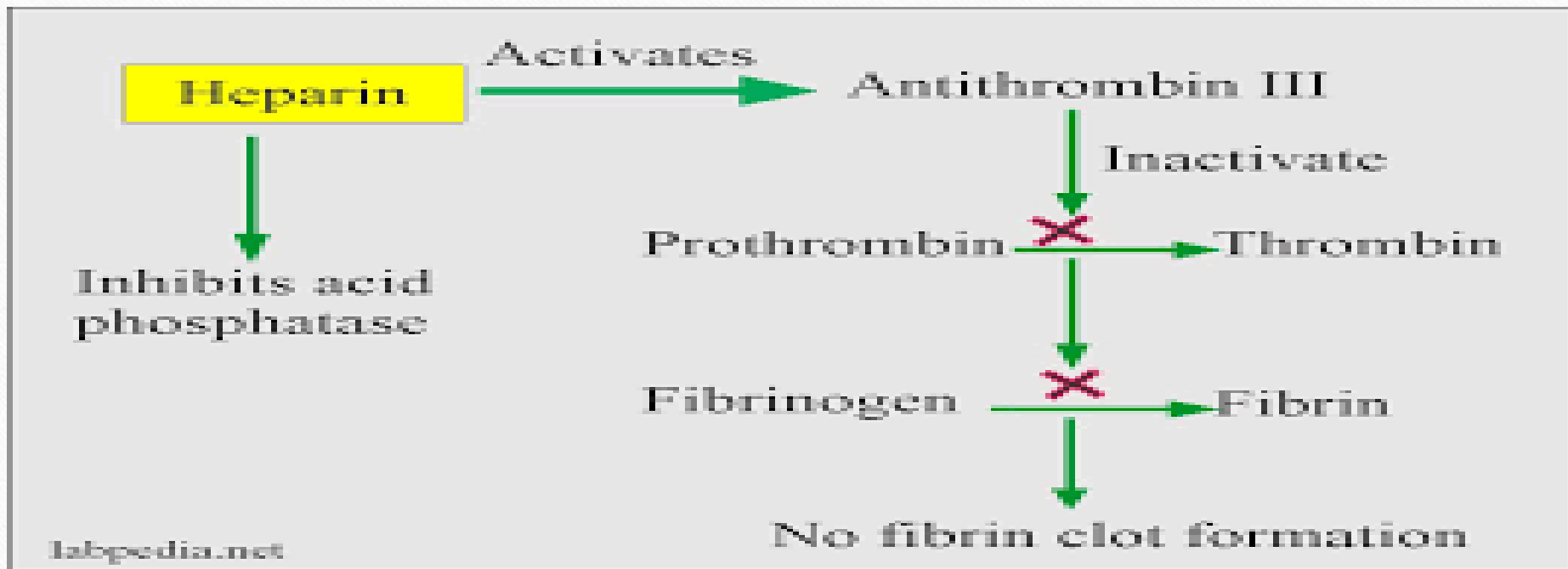
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Heparine antidote

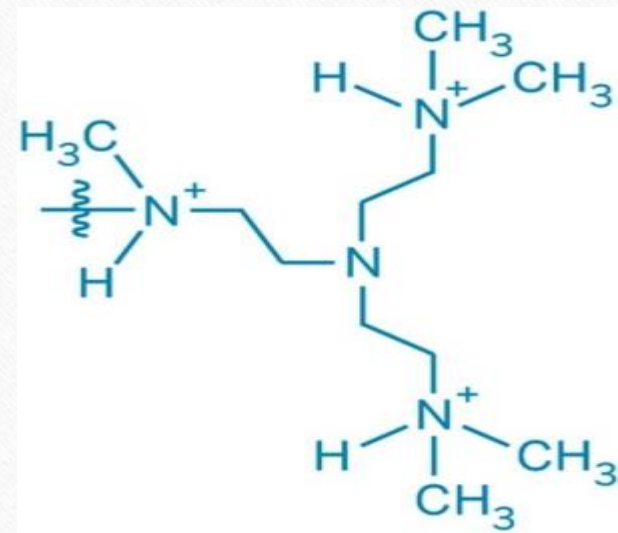
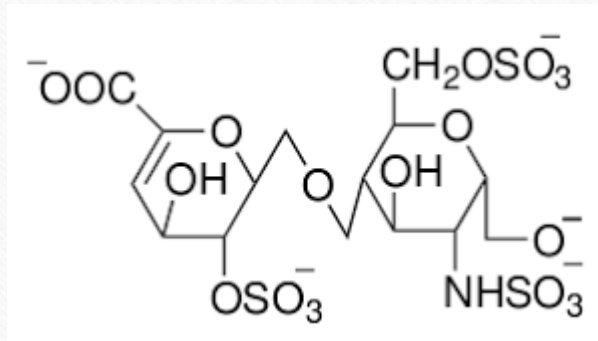




# Mechanism of action



# Mechanism of action



**Heparin-binding group**

# Mechanism of action

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- Protamine is a highly positively charged peptide consisting of about 32 amino acids and neutralises the effect of heparin through electrostatic binding between the cationic arginine groups of protamine and the anionic heparin in a 1:1 ratio resulting in neutral protamine-heparin salt.
- In parallel, the binding of protamine to heparin dissociates the anti-thrombin/heparin complex, leading to the recovery of the original anti-thrombin activity.

# Dosage regimen

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- Protamine dosage is determined by the most recent dosage of heparin or low molecular weight heparin.
- 1 mg of protamine sulfate neutralizes ~100 units of heparin or 1 mg of enoxaparin.

## Dosage regimen

- Neonatal
  - Heparin concentrations decrease rapidly after heparin administration, adjust the protamine dosage depending upon the duration of time since heparin administration as follows:

Time Since Last Heparin Dose (min)	Dose of Protamine (mg) to Neutralize 100 units of Heparin IV
<30	1
30 to 60	0.5 to 0.75
60 to 120	0.375 to 0.5
>120	0.25 to 0.375

# Dosage regimen

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- **Enoxaparin overdose:**

**Note:** Anti-Xa activity is never completely neutralized (maximum: ~60% to 75%). Excessive protamine doses may worsen bleeding potential.

- Enoxaparin last administered in  $\leq 8$  hours: IV: Dose of protamine sulfate should equal the dose of enoxaparin administered; therefore, 1 mg protamine neutralizes 1 mg enoxaparin.
- *Enoxaparin last administered in  $> 8$  hours or second dose of protamine is required : IV: 0.5 mg protamine per 1 mg enoxaparin.*

# Dosage regimen

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- Pediatrics:
  - IV heparin: as neonatal dose
  - SC heparine: 1 to 1.5 mg protamine per 100 units heparin, administering a portion of the protamine dose slowly IV followed by the remaining portion as a continuous infusion over 8 to 16 hours (the expected absorption time of the SubQ heparin dose)
  - Enoxapaine: as neonatal dose

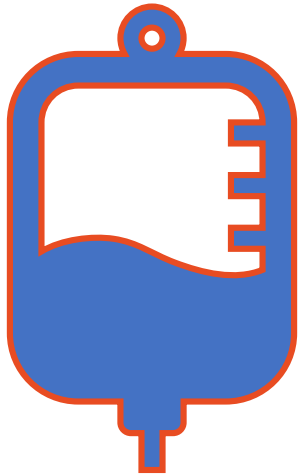
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- Renal & hepatic adjustment : not needed





# Administration:

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- Parenteral: IV: Administer undiluted with slow rate not to exceed 5 mg/minute (50 mg in any 10-minute period);
- Caution: rapid IV infusion causes hypotension

# Adverse Reactions

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- Cardiovascular: Bradycardia, flushing, hypotension, sudden decrease of blood pressure
- Central nervous system: Lassitude
- Gastrointestinal: Nausea, vomiting
- Hematologic & oncologic: Hemorrhage
- Hypersensitivity: Hypersensitivity reaction
- Respiratory: Dyspnea, pulmonary hypertension

# Precautions

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- Cardiac surgery patients: May be ineffective in some patients following cardiac surgery despite adequate doses

## Storage/Stability

- Store at 20°C to 25°C. Do not freeze. Diluted solutions should not be stored.

THANK  
YOU

A decorative illustration of a branch with red and pink leaves and small dark berries, framing the text 'THANK YOU'. The leaves are rendered in various shades of red and pink, with some showing detailed vein patterns. The berries are small, dark, and clustered together. The text 'THANK YOU' is written in a black, serif font, with 'THANK' on the top line and 'YOU' on the bottom line. The entire illustration is set against a light, textured background.