

For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory.

Streptokinase Injection I.P. **THROMBOFLUX™**

COMPOSITION :

Each vial contains :

Streptokinase I.P. 2,50,000 I.U. / 7,50,000 I.U. / 15,00,000 I.U.

Stabilizers :

Human albumin I.P. 0.17 mg / 1 lac I.U.

Polygeline 2.67 mg / 1 lac I.U.

DESCRIPTION :

THROMBOFLUX™ is a freeze-dried white powder containing Streptokinase. Streptokinase is a highly purified protein derived from the culture filtrate of beta haemolytic streptococci of Lancefield Group C. Streptokinase has the property of combining with human plasminogen to form plasminogen activator. One International unit is the quantity of Streptokinase that will lyse the standard blood clot completely in 10 minutes.

PHARMACOKINETICS :

Streptokinase of **THROMBOFLUX™** is rapidly cleared from the circulation following intravenous administration. Clearance is biphasic. Half life of 23 minutes has been reported for Streptokinase activator complex.

INDICATIONS :

Acute evolving transmural myocardial infarction.

Acute deep vein thrombosis.

Acute Pulmonary embolism.

Acute arterial thrombosis or embolism.

Occlusion of arterio-venous cannulae.

DOSAGE & ADMINISTRATION :

METHOD FOR RECONSTITUTION :

Sodium Chloride 0.9% (Physiological Saline) is the preferred diluent for **THROMBOFLUX™** although Dextrose 5% in water may be used.

1. Add 5 ml of the diluent slowly to the vial of **THROMBOFLUX™**, directing the needle point to the wall of the vial. Abolish residual vacuum by briefly loosening the needle from the syringe.

2. Tilt and roll the vial gently. Swirl the contents gently to effect dissolution. Do not shake to avoid foaming.

3. Once the powder is completely dissolved, transfer the content of the vial into 45 ml of the Physiological saline.

Do not add any other medication to THROMBOFLUX™ vials.

An intradermal skin test of 100 I.U. has been suggested to predict allergic response to THROMBOFLUX™. If positive reaction is not seen after 15 to 20 minutes, the therapeutic dose can be administered.

THROMBOFLUX™ is administered by intravenous, intra-arterial, or intracoronary infusion.

Acute evolving transmural myocardial infarction :

1. Intravenous infusion : 15,00,000 I.U. **THROMBOFLUX™** is made up in 100 ml of physiological saline or Dextrose solution and administered over 30 to 60 minutes.

Alternatively Intracoronary bolus doses of 10,000 to 30,000 I.U. have been administered in upto 20 ml infusion solution over 15 seconds to 2 minutes. Maintenance doses of 2000 to 4000 I.U. /min for 60 minutes by intracoronary infusion have been given.

2. Deep vein thrombosis, pulmonary embolism, arterial thrombosis or embolism :

A loading dose of 2,50,000 I.U. of **THROMBOFLUX™** in 100 to 300ml of physiological saline or Dextrose solution infused into a peripheral vein over 30 minutes has been found appropriate as a standard dose. Following the loading dose, a maintenance infusion of **THROMBOFLUX™** 1,00,000 I.U./hour is given for 24 to 72 hours.

3. Occlusion of arterio-venous cannulae :

THROMBOFLUX™ equivalent to 2,50,000 I.U. may be administered over 25 to 35 mins. in 2ml of solution to clear an occluded arterio-venous cannula. The drug is infused directly into the cannula which is then clamped for 2 hours, aspirated and flushed with physiological saline.

Local application in occluded haemodialysis shunts :

100 ml Physiological saline containing **THROMBOFLUX™** 1,00,000 I.U. :10,000 to 25,000 I.U. (10 to 25 ml) is deposited in the clotted portion of shunt. Which is then sealed on the venous side with forceps. A sterile single dose syringe is attached on the arterial side to form an air cushion against which the artery can pulsate. If required, the treatment may be repeated after 30 to 45 minutes.

CAUTIONS :

1. THROMBOFLUX™ is contraindicated in the following conditions :

- Invasive or traumatic procedures within the previous 10 days including the following : surgery, biopsy.
- Hypertension (treated or untreated), hypertension or diabetic retinopathy, cerebral apoplexy within 2 months, transient ischaemic attacks.
- Active internal bleeding including history of peptic ulceration, ulcerative colitis, diverticulitis or other bleeding, gastrointestinal lesions. Potential haemorrhage including : thrombocytopenia, severe hepatic or renal impairment.
- Potential for cardiac thrombo-emboli including : active or recent infective endocarditis, atrial valve disease with atrial fibrillation.
- Previous streptokinase therapy, more than 5 days and up to 6 months previously or recent streptococcal infection, since an elevated titre of antistreptokinase antibody may render the treatment ineffective.
- Increased risk of pulmonary haemorrhage including : active tuberculosis and deformity.
- Coma.

2. Adverse reaction :

Adverse effects occurred in about 18% of patient with acute myocardial infarction when a high dose of streptokinase was administered for a short time. The most of hangover effects are hypotension (about 10%). The other side effects are allergic reaction and bleedings (respectively 4%), or excessive haemorrhage (0.5%).

In a long-term treatment with other diseases (deep vein thrombosis, Pulmonary embolism), side effects occurred up to 50%.

Occasionally occurred : (over 1% of patients)

Allergic reaction, a slight to moderate elevation in body temperature, hypotensive bradycardia.

Extremely rarely occurred :

Anaphylactic shock, Arthralgia, Arthritis, Vasculitis.

- In therapy for acute myocardial infarction, hypotension may occur due to fast rate of infusion. There may be severe haemorrhage, in which case administration of streptokinase must be discontinued. If necessary, tranexamic acid should be given immediately by slow intravenous injection.

- Streptokinase administration has been associated with back pain. It may be appropriate to discontinue the infusion.
- There have been a few reports of polyradiculoneuropathy (Gullian-Barre syndrome) following treatment with streptokinase.

3. General Precautions:

- It is recommended that I.M. injection be avoided for the first 24 hours.
- Streptokinase infusion may cause hypotension as a result of rapid rate of infusion.
- On termination of Streptokinase treatment, the patient should be given anticoagulants in an attempt to prevent re-thrombosis. Preferably heparin should be given, starting four hours after the end of thrombolysis and then an oral anticoagulant may be introduced after 24 hours of streptokinase discontinuation.
- Following 7 to 10 days of treatment with streptokinase, the patient's anti-streptokinase antibodies titre increases considerably and returns to normal only after up to 6 months. Normally a second treatment with streptokinase should not be considered within 6 months of the first. If a second treatment is considered necessary within 6 months the loading dose should be individually determined. The titrated initial dose should be calculated determining the smallest quantity of streptokinase required.
- If heparin or oral anticoagulants have been given before commencing streptokinase therapy, further administration should be stopped. The streptokinase infusion can then be started after 4 hour.

4. Drug interactions:

- A dose of streptokinase, in combination with heparin is not recommended, because concomitant dose of the drugs may cause bleeding complications.
- Drugs which affect blood platelet function, such as salicylic acid preparations, pyrazolone or indole derivatives, should not be administered concurrently with streptokinase since the risk of bleeding will be increased.

5. Others:

- Thrombolytic therapy with streptokinase during the first 18 weeks of pregnancy should be avoided, since there may be a risk of placental separation.
- It is not known whether this drug is excreted in human milk.
- Geriatric patients 75 years of age and older may be at increased risk of cerebral hemorrhage during streptokinase therapy.

STORAGE:

Store at 2°C to 8°C. Protect from light.

PRESENTATION :

Vial packs of 2,50,000 I.U., 7,50,000 I.U. and 15,00,000 I.U. packed individually in cartons.

Manufactured in India by :

BHARAT SERUMS AND VACCINES LIMITED

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