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

Urokinase For Injection

यु-फ्रॅग

U-FRAG™

LYOPHILIZED

COMPOSITION :
Each vial contains :
Urokinase I.P. ..... 2,50,000 I.U. / 5,00,000 I.U. / 7,50,000 I.U. / 10,00,000 I.U.

EXCIPIENTS :
Human Albumin I.P. 20mg
Sodium Citrate I.P. 24mg
Disodium Hydrogen Phosphate Dihydrate B.P. 7.8mg
Sodium Dihydrogen Phosphate Dihydrate I.P. 20mg

DESCRIPTION :
U-FRAG™ is a freeze-dried white powder containing Urokinase and excipients. Urokinase is an enzyme isolated from fresh human urine that activates plasminogen with the subsequent hydrolysis of fibrin and the dissolution of thrombin. Urokinase is a mixture of low (33,000) and high (54,000) molecular weight forms, the high molecular weight being predominant.

PHARMACOKINETICS :
Following intravenous infusion, Urokinase is cleared rapidly from the circulation by the liver. A plasma half-life of upto 20 minutes has been reported.

INDICATIONS :
Cerebral thrombosis, Cerebral infarction.
Acute Peripheral vascular thrombo-embolism.
Acute myocardial infarction.
Acute Pulmonary embolism.

DOSAGE & ADMINISTRATION :
Method for reconstitution :
Add 2 ml of Sterile Water for Injection slowly to the vial of **U-FRAG™**, directing the needle-point to the wall of the vial. Abolish residual vacuum by briefly loosening the needle from the syringe. Tilt and roll the vial gently. Swirl the contents gently to effect dissolution. Do not shake to avoid foaming. Once the powder is completely dissolved, the solution is further diluted with Physiological saline solution or 5% Dextrose solution prior to intravenous infusion.

Before administration of U-FRAG™, thrombin time, thrombinogen time and euglobulin solvent time are required to be determined and blood coagulation time should be monitored.

Do not add any other medication to U-FRAG™ vials. Administer the injection immediately after reconstitution without further storage.

U-FRAG™ may be infused intravenously by means of an infusion pump or it may be administered into an occluded coronary artery. For intravenous infusion, reconstituted solution is usually diluted further with 200ml normal Physiological saline or 5% Dextrose Injection. For intra-coronary administration, the reconstituted solution may be diluted further with 5% Dextrose Injection to provide a solution containing about 1,500 I.U./ml.

Cerebral thrombosis, Cerebral infarction :
The recommended daily dose of **U-FRAG™** is 6,000 - 3,00,000 I.U.

Acute peripheral vascular thrombo-embolism :
After the initial dose of 50,000 - 2,50,000 I.U. is administered, gradually reduce further doses for 7 days.

Acute myocardial infarction :
In the management of acute myocardial infarction infusion into the coronary arteries of **U-FRAG™** in a dose of 6,000 I.U. per minute, for upto 2 hours, has been recommended; coronary infusion should be preceded by intravenous heparin. Alternatively **U-FRAG™** has been given intravenously in usual dose of 2-3 million I.U. over 45 to 90 minutes.

Pulmonary embolism :
A initial dose of 4,400 I.U./Kg body weight of **U-FRAG™** is given over a period of 10 minutes. This is followed by a continuous infusion of 4,400 I.U. / Kg / hr of **U-FRAG™** for 12 hours. The dose may vary according to the patient's age, condition.

CAUTION :
Warning :
Severe haemorrhagic cerebral infarct has been reported. **U-FRAG™** should not be administered to patients with cerebral embolism to whom haemorrhagic cerebral infarction is likely to occur.

Contraindication :
Because thrombolytic therapy increases the risk of bleeding, **U-FRAG™** is contraindicated in the following cases -
Active internal bleeding.
History of cerebro-vascular accident.
Recent intra-cranial or intra-spinal surgery.
Intra-cranial neoplasm or in patient with aneurysm.
Known bleeding diathesis.
Severe uncontrolled hypertension.

Cautions :
U-FRAG™ should not be administered in the following patients but, if needed, must be carefully given in-patients with atrial fibrillation, infectious endocarditis, artificial cardiac valve and patients with neurogenic symptom.

The drug should be carefully administered in the following patients :
Haemorrhagic patients : Surgical treatment such as surgery (including liver or Kidney biopsy), haemorrhagic ophthalmologic disease such as diabetic haemorrhagic retinopathy, G.I. bleeding, urinary tract bleeding, pre-or post abortal and during menstruation.
Patients who are potentially bleeding: history of GI ulcer, colitis, severe hypertension, active tuberculosis, intra-cranial bleeding.
In-patients under anti-coagulant therapy.
In patients with severe hepatic and renal impairment.
In patients with condition of decline of haemostatic functions (coagulation factor deficiency, thrombocytopenia).
Geriatric patients.
In-patients with a history of hypersensitivity to Urokinase or tissue cultured Urokinase.

Adverse reaction :
Bleeding : It should be observed if cerebral bleeding, alimentary tract haemorrhage, haematuria, gingival bleeding occur during therapy. Treatment must be stopped when severe symptoms such as cerebral haemorrhage, GI bleeding occurs.
Hypersensitivity : Eruption, urticaria.
Liver : Rarely increase of AST, ALT may appear.
Others : Arrhythmia, hypotension, flush, chills, headache, and malaise.

General precautions :
When Urokinase therapy is first introduced, patients should be told what to do if bleeding occurs. During the therapy, blood coagulability (bleeding time, prothrombin time) through haematological test and clinical symptoms should be frequently monitored. If cerebral bleeding is suspected, the administration should be discontinued immediately. Generally, cerebral bleeding should be confirmed by computerized tomography. After the therapy is initiated, heart rupture may occur. Therefore the administration should be careful. For the treatment of coronary arterial embolism associated with myocardial infarction, haemodynamics should be monitored within 6 hour after the symptoms appear.

Drug interactions :
Bleeding tendency may be enhanced by the concomitant administration of the following drugs : anticoagulant agents (e.g. heparin, warfarin etc) antiplatelet drugs (e.g. aspirin, dipyridamole, Ticlopidine hydrochloride etc).

Use in pregnancy :
Thrombolytic therapy with **U-FRAG™** during the first stage of pregnancy should be used only when the expected benefits clearly outweigh the potential risks to the foetus, since there may be a risk of placental separation.

Use in children :
Safe use of **U-FRAG™** in children has not been established.

Use in the elderly :
U-FRAG™ should be carefully used because of increased danger of haemorrhage.

STORAGE :
Store at 2°C - 8°C. Protect from light.

PRESENTATION :
Vial packs of 2,50,000 I.U., 5,00,000 I.U., 7,50,000 I.U. and 10,00,000 I.U. in individual Cartons with Pack insert.

Manufactured in India by :
BHARAT SERUMS AND VACCINES LIMITED
Plot No. K-27, Additional M.I.D.C., Ambernath (E) - 421 501

IN90014D2