SUMMARY OF PRODUCT CHRACTERISTICS

1. Name of the Medicinal Product

Brand Name: Tenectase
Generic Name: Recombinant Tissue Plasminogen Activator (TNK-tPA)/Tenecteplase Injection 20 mg

2. Quality and Quantitative Composition

Each vial contains:
Lyophilized Recombinant Tissue Plasminogen Activator (TNK-tPA) 20 mg
To be reconstituted with 10 ml of Sterile Water for
Injections I.P./BP/USP

For full list of excipients please refer section 6.1.

3. Pharmaceutical Form

Lyophilized Powder and solvent for solution for injection.

4. Clinical Particulars:

4.1 Therapeutic indications

TNK-tPA is indicated as thrombolytic agent for the treatment of acute ischemic stroke (AIS). Treatment should be initiated as soon as possible within 4.5 hours post onset of stroke symptoms.

4.2 Posology and method of administration Posology

The recommended total dose should not exceed 20mg and is based upon patient body weight. A single IV bolus dose of 0.2mg/kg should be administered over 5 to 10 seconds based on patient body weight. Treatment should be initiated as soon as possible after the onset of acute ischemic stroke symptoms.
The appropriate volume required to administer correct dose of TNK-tPA can be calculated in correspondence of patient body weight. The illustration calculation chart is given below:

Patient body weight (kg)	TNK-tPA dose (mg)	Volume (ml) of TNK-tPA to be administered at a dilution of 2 mg/ml	Patient body weight (kg)	TNK-tPA dose (mg)	Volume (ml) of TNK-tPA to be administered at a dilution of 2 mg/ml
60	12	6 mL	65	13	6.5 mL
70	14	7 mL	75	15	7.5 mL
80	16	8 mL	85	17	8.5 mL
90	18	9 mL	95	19	9.5 mL
≥100	20	10 mL			

Method of administration:

TNK-tPA is for intravenous administration only.

Replace the needle used for reconstitution with another pre-sterile needle provided in the kit for administration lo the patient. The product should be visually examined prior to administration for discoloration and particulate matter. TNK-tPA may be administered as reconstituted at 2mg/ml.

Precipitation may occur when TNK-tPA is administered in an IV line containing dextrose. Dextrose containing lines should be flushed with a saline containing solution prior to and following single bolus administration of TNK-tPA. Reconstituted TNK-tPA should be administered as a single IV bolus over 5 to 10 seconds. Because TNK-tPA contains no antibacterial preservatives, it should be reconstituted immediately before use. If the reconstituted TNK-tPA is not used immediately, refrigerate the TNK-tPA vial at 2-8°C (36-46F) and use within 4 hours.

Special Population

Elderly

The incidence of stroke and bleeding complications with TNK-tPA may be higher in elderly patients (age more than 80 years). In elderly patients, the benefits of TNK-tPA on mortality should be carefully weighed against the risk of increased adverse events, including bleeding.

Paediatric population

The safety and effectiveness of TNK-tPA in paediatric patients has not been established. TNK-tPA is not indicated for treatment of acute stroke in patients less than 18 years of age.

Renal and hepatic impairment

The effect of renal and hepatic dysfunction on tenecteplase has not been studied. However, caution may be necessary in such patients due to decrease in kidney and liver function.

Method of administration

The product should be visually inspected prior to administration for particulate matter and discoloration. Tenecteplase may be administered as reconstituted at 5mg/mL. Precipitation may occur when Tenecteplase is administered in an IV line containing dextrose. Dextrose-containing lines should be flushed with a saline-containing solution prior to and following single bolus administration of Tenecteplase.

Reconstituted Tenecteplase should be administered as a single IV bolus over 5 seconds. Because Tenecteplase contains no antibacterial preservatives, it should be reconstituted immediately before use. If the reconstituted Tenecteplase is not used immediately, refrigerate the Tenecteplase vial at 2 to 8°C (36–46°F) and use within 8 hours.

4.3 Contraindications

TNK-tPA therapy in patients with acute ischemic stroke is contraindicated in the following situations:

- Active internal bleeding
- Evidence of intracranial haemorrhage on CT scan
- Uncontrolled hypertension
- Intracranial or intraspinal surgery or intracranial trauma within 2 months
- History of cerebrovascular accident
- History of Arteriovenous malformation, intracranial neoplasm or aneurysm
- History of previous stroke or serious head trauma within last 3 months
- Major surgery or serious trauma within 14 days
- Myocardial infarction in past 30 days
- Rapidly improving or minor stroke caused by a blood clot in an artery of the brain (acute ischemic stroke symptoms)
- Clinically assessed severe stroke (NIHSS>25) preferably by CT scan or by appropriate imaging techniques
- Known bleeding diathesis
- Seizure at onset of stroke
- Blood Platelet count less than 100,000/ mm^3

- Administration of heparin within 48 hours preceding the onset of stroke with an elevated activated partial thromboplastin time at presentation
- Prior hypersensitivity to TNK-tPA

4.4 Special warning and precautions for use

If the patient is being administered with TNK-tPA, the patient should be evaluated for the possible benefits against the risks that may occur due to therapy. Bleeding either as internal bleeding or superficial or surface bleeding is one of the common complications observed on administration of TNK-tPA. The internal bleeding may occur at any site or any body cavity

e.g. in intracranial, the gastrointestinal, genitourinary or respiratory tracts. The superficial or surface bleeding is generally observed at sites of invasion through vascular puncture or at surgical sites.

In case of serious bleeding, which cannot be controlled by application of local pressure any concomitant anticoagulant treatment (anti-platelet agents or heparin and its derivatives) should be stopped immediately. It is advised that unnecessary invasive examination of the patients should be avoided for at least few hours after treatment with TNK-tPA.

It is predicted and evident from literature that the risk of thrombolytic therapy would be higher in patients with the following conditions:

- Pregnancy or lactating women
- Geriatrics
- Patients on anti-coagulants such as warfarin sodium, glycoprotein (GP) IIb/IIIa inhibitors
- Patients with severe hepatic dysfunction
- Patients having conditions such as left heart thrombus e.g. mitral stenosis with arterial fibrillation, acute pericarditis, Subacute bacterial endocarditis and Septic thrombophlebitis or occluded AV cannula, uncontrolled hypertension, Cerebrovascular disease, Diabetic hemorrhagic retinopathy or other hemorrhagic ophthalmic conditions, Hemostatic defects including those secondary to severe hepatic or renal disease
- Patients who have recently undergone major surgeries
- Patients with episodes of gastrointestinal or genitourinary bleeding

Precautions

General

Standard management of acute ischemic stroke should be implemented concomitantly with TNK-tPA treatment. In event of serious bleeding, anticoagulants should be discontinued immediately. If heparin has been administered, the effects can be reversed by protamine.

Readministration

The effect of re-administration of Tenectase in patients subjected prior to plasminogen activator therapy have not been systematically examined and should be avoided.

4.5 Interaction with other medicinal products and other forms of interactions Antiplatelet and anticoagulant drugs may increase the risk of bleeding if administered prior to, during or after TNK-tPA therapy. Formal interaction studies of TNK-tPA with other drugs have not been performed.

Drug/Laboratory Test Interactions

Presence of TNK-tPA therapy in blood in pharmacological concentrations is liable to interfere in laboratory tests as TNK-tPA remains active in *in-vitro* conditions. Hence, results of coagulation tests and/or measures of fibrinolytic activity may be unreliable unless specific precautions are observed to prevent *in-vitro* artifacts.

4.6 Fertility, Pregnancy and lactation Pregnancy (Category C)

Controlled studies have not been conducted in pregnant women and therefore, TNK-tPA should not be administered to pregnant women unless the anticipated benefits outweigh the potential risk associated with the foetus.

Lactation

It is not known whether TNK-tPA is excreted in human milk. It should be administered in a cautious manner to a nursing woman, as many drugs are excreted in human milk.

Fertility

Animal studies have not been performed to evaluate the effect on fertility.

4.7 Effects on ability to drive and use machines

Not applicable.

4.8 Undesirable effects

Bleeding is the most common adverse reaction reported with TNK-tPA therapy. On occurrence of serious bleeding, immediately discontinue heparin, anti-platelet therapy and other therapies associated with blood thinning. The other adverse reactions are generally sequelae of underlying diseases and disorders of patients and these events include intracranial haemorrhage like cerebral haemorrhage, cerebral haematoma, haemorrhagic stroke, haemorrhagic transformation of stroke, intracranial haematoma and subarachnoid haemorrhage. Symptomatic intracerebral haemorrhage represents the major adverse event. These events can be life-threatening.

Apart from intracranial haemorrhage (ICH) and stroke, following non-ICH bleedings may occur with TNK-tPA therapy: hematoma, gastrointestinal tract, urinary tract, puncture site (including catheterization site), retroperitoneal, respiratory tract and pharyngeal bleeding. Injection site haemorrhage, puncture site haemorrhage such as catheter haematoma and haemorrhage may also occur. The events increase with age and may also be life threatening.

Allergic Reactions

Allergic-type reactions (e.g., laryngeal edema, angioedema, rash, anaphylaxis and urticaria) have rarely been reported in patients treated with TNK-tPA. When such reactions occur, patients should be treated with conventional therapy.

Other Adverse Reactions

Nausea and/or vomiting, hypotension and fever have also been reported.

Reporting of side effects

Reporting suspected adverse reactions after Authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org/

4.9 Overdose

There is a minimal chance of overdose as this medicine is being given under the supervision of a neurologist. In the event of an overdose, there is an increased risk of bleeding which should be handled in an appropriate manner.

5. Pharmacological Properties

5.1 Pharmacodynamic Properties

Pharmacotherapeutic group: Antithrombotic agents, ATC code: B01AD11 Mechanism of action

Tenecteplase is a recombinant fibrin-specific plasminogen activator that is derived from native t-PA by modifications at three sites of the protein structure. It binds to the fibrin component of the thrombus (blood clot) and selectively converts thrombus-bound plasminogen to plasmin, which degrades the fibrin matrix of the thrombus. Tenecteplase has a higher fibrin specificity and greater resistance to inactivation by its endogenous inhibitor (PAI-1) compared to native t-PA.

Tenecteplase (0.2 mg/kg dose) has been approved in 28-July-2016 for acute ischemic stroke and Tenecteplase (0.5 mg/kg dose) was approved in 2006 for acute myocardial infarction (AMI) by Drugs Controller General India (DCGI).

Clinical Studies

Clinical Trials

Open label, multi-centric clinical studies were conducted in 104 acute ischemic stroke patients to assess the efficacy and safety of tenecteplase. Prior to the initiation of drug treatment, a cranial computerized tomography (CT) scan was performed to rule out the existence of intracranial haemorrhage in patients. Improvement of greater than 8 points or a score of 0 on the National Institute of Health Stroke Scale (NIHSS) score at 24 h was considered as primary efficacy variable. Secondary efficacy parameters were assessed by improvement in modified Rankin (mRS) scale and Barthel Index (BI). In patients treated with 0.2 mg/kg dose, 58.33% patients reported improvement of ≥4 points and 23.80% patients reported improvement of ≥8 points at 24 h. Modified Rankin severe disability score (4 or 5) showed statistical significant improvement from baseline to 1 month (77.38% vs. 15.0%, $p < 0.0001$). The Barthel Index median value (interquartile range) also showed improvement from 30 (11.25-50) at baseline to 60 (30-93.75) at day 7 ($p < 0.0001$) and to 80 (61.25-100) by 1 month.

The safety data of tenecteplase in clinical trials showed that only one patient suffered from symptomatic intracranial haemorrhage (sICH) within 36 h of treatment. Mortality occurred in 5 (4.81%) patients throughout the study. Only one death was associated with sICH whereas other deaths occurred due to other comorbidities.

Observational study (Active Post Marketing Surveillance)

A total of 1015 subjects were recruited in a prospective, multicenter, open- label, observational, registry. Eligible patients presenting with symptoms of acute ischemic stroke were administered Tenectase®. Symptomatic intracerebral hemorrhage was considered as the primary safety outcome. The effectiveness was assessed using NIHSS, mRS and Barthel index. Six (0.6%) cases of symptomatic ICH and 12 serious adverse events occurred during the duration of the study. Of the 12 SAEs, 5 were related to Tenectase®. There were 10 (1%) deaths reported during the study. Of these 10 deaths, 3 were considered to be related to the treatment.

The early neurological improvement in patients was assessed by NIHSS score at 24 h and day 7/ day of discharge. Improvement on the NIHSS by ≥4 points or a score of 0 was observed in 348 (34.4%) patients at 24 h, and in 570 (56.3%) patients by day 7/ day of discharge. Similarly, improvement by ≥8 points or a score of 0 on NIHSS was observed in 146 (14.4%) patients and 269 (26.6%) patients at 24 h, and at day 7/ day of discharge respectively. At 3 months, mRS score 0-1 (excellent outcome) was observed in 541 (55.4%) patients, whereas functional independence (mRS 0- 2) was noted in 734 (75.1%) patients, indicating a long-term functional improvement. Barthel index score >50 was observed in 902 (93.3%) patients at 3 months.

Two clinical trials were performed by the MAH for the efficacy and safety of intravenous tenecteplase bolus in acute ischemic stroke.

Study I was an open-label, randomized study in which two doses of TNK-tPA (0.1 and 0.2 mg/kg) were compared. Study II was an open-label study in which TNK-tPA 0.2 mg/kg bolus was compared with historical controls. The primary endpoint for study I and study II was an improvement of ≥8 points or a score of 0 on the National Institutes of Health Stroke Scale (NIHSS) [major neurological improvement (MNI)] at 24 h. Secondary endpoints for both studies were neurological improvement as assessed using the NIHSS score, modified Rankin Scale (mRS) score and the Barthel Index (BI) on days 7, 30 and 90.

Minimal disability was defined as a mRS score of 0 or 1 and good functional recovery as a BI score of 50–90. Safety was assessed by the proportion of patients having sICH within 36 h and asymptomatic intracranial hemorrhage at 48 h after treatment.

In study I, 20 patients received 0.1 mg/kg and 30 received 0.2 mg/kg TNK-tPA. There was no significant difference in MNI at 24 h between 0.1 and 0.2 mg/kg TNK-tPA doses. The patients given 0.2 mg/kg TNK-tPA had a significantly better 3-month outcome (minimal disability, p = 0.007). There was no sICH in study I.

In study II, 62 patients (one lost to follow-up) received 0.2 mg/kg TNK-tPA. MNI was noted in ten patients (16.4%), 3-month minimal disability (excellent outcome) was noted in 37 patients (60.7%), and good functional recovery was seen in 33 patients (54.1%). sICH occurred in one patient, and four patients died. Pooled data of patients in study I and study II receiving 0.2 mg/kg TNK-tPA were compared with data from the historical National Institute of

Neurological Disorders and Stroke (NINDS) trial. For comparison, the primary endpoint of the NINDS trial (improvement on NIHSS of ≥4 points or a score of 0 at 24 h) was taken. The primary endpoint though was not significantly different (58.2% vs. 47%, p = 0.08), but with TNK-tPA, greater neurological improvement, minimal disability (70.3 vs. 39%, p<0.001) and good functional recovery (36.3 vs. 16%, p<0.001) was noted at 3 months. There was a lower incidence of sICH (1.1 vs. 6.4%, p = 0.05) and lower 3-month mortality (5.5 vs. 17%, p = 0.01) noted with TNK-tPA compared with alteplase. The data generated in these trials was in line with safety profile of tenecteplase.

5.2 Pharmacokinetic Properties

(Following details are referenced from tenecteplase studies in AMI indication)

Absorption and distribution

Tenecteplase is an intravenously administered, recombinant protein that activates plasminogen. Following intravenous bolus administration of 30 mg tenecteplase in patients with acute myocardial infarction, the initially estimated tenecteplase plasma concentration was 6.45 ± 3.60 µg/mL (mean ± SD). The distribution phase represents 31% ± 22% to 69% ± 15% (mean ± SD) of the total AUC following the administration of doses ranges from 5 to 50 mg.

Data on tissue distribution were obtained in studies with radioactively labelled tenecteplase in rats. The main organ to which tenecteplase distributed was the liver. It is not known whether and to which extent tenecteplase binds to plasma proteins in humans. The mean residence time (MRT) in the body is approximately 1 h and the mean (± SD) volume of distribution at the steady-state (Vss) ranged from 6.3 ± 2 L to 15 ± 7 L.

Biotransformation

Tenecteplase is cleared from circulation by binding to specific receptors in the liver followed by catabolism to small peptides. Binding to hepatic receptors is, however, reduced compared to native t-PA, resulting in a prolonged half-life.

Elimination

After single intravenous bolus injection of tenecteplase in patients with acute myocardial infarction, tenecteplase antigen exhibits biphasic elimination from plasma. There is no dose dependence of tenecteplase clearance in the therapeutic dose range. The initial, dominant half-life is 24 ± 5.5 (mean ±SD) min, which is 5 times longer than native t-PA. The terminal half-life is 129 ± 87 min, and plasma clearance is 119 ± 49 ml/min.

Increasing body weight resulted in a moderate increase of tenecteplase clearance, and increasing age resulted in a slight decrease of clearance. Women exhibit in general lower clearance than men, but this can be explained by the generally lower body weight of women. Linearity/Non-Linearity

The dose linearity analysis based on AUC suggested that tenecteplase exhibits non-linear pharmacokinetics in the dose range studied, i.e. 5 to 50 mg.

Renal and hepatic impairment

Because elimination of tenecteplase is through the liver, it is not expected that renal dysfunction will affect its the pharmacokinetics. This is also supported by animal data. However, the effect of renal and hepatic dysfunction on pharmacokinetics of tenecteplase in humans has not been specifically investigated.

5.3 Preclinical Safety Data

Acute Toxicity Studies:

1) Acute Intravenous Toxicity Study in Sprague Dawley Rats:

Reduced locomotor activity and ataxic gait were observed in animals treated at the dose level of 100 mg/kg body weight. All animals survived through the study period of 14 days. Body weight gain of male and female treated animals was found to be normal on day 7 and on day 14. Gross pathological examination did not reveal any abnormalities attributable to the treatment. It was concluded that the acute lethal intravenous dose in Sprague Dawley rats is greater than 100 mg/kg body weight.

2) Acute Intravenous Toxicity Study in Swiss Albino Mice:

Reduced locomotor activity and ataxic gait were observed in animals treated at the dose level of 100 mg/kg body weight. All animals survived through the study period of 14 days. Body weight gain of male and female treated animals was found to be normal on day 7 and on day 14. Gross pathological examination did not reveal any abnormalities attributable to the treatment. It was concluded that the acute lethal intravenous dose in Swiss Albino mice is greater than 100 mg/kg body weight.

3) Acute Intravenous Toxicity Study in New Zealand White Rabbits:

Reduced locomotor activity was observed in male and female animals from 50 mg/kg dose group during the study period of 14 days. Discoloration at the site of injection was observed in animals treated at the dose levels of 25 mg/kg and 50 mg/kg body weight. Animals treated at the dose level of 12.5 mg/kg did not reveal any signs of intoxication during the study period. All animals treated at different dose levels survived through the study period of 14 days. Body weight gain of male and female treated animals was found to be normal on day 7 and on day 14. Gross examination revealed internal bleeding in the abdominal cavity in one male animal from 50 mg/kg dose group. It was concluded that the acute lethal intravenous dose in New Zealand White rabbits is greater than 50 mg/kg body weight.

4) Acute Intramuscular Toxicity Study in Sprague Dawley Rats:

Reduced locomotor activity and ataxic gait were observed in animals treated at the dose level of 100 mg/kg body weight. All animals survived through the study period of 14 days.

Body weight gain of male and female treated animals was found to be normal on day 7 and on day 14. Gross pathological examination did not reveal any abnormalities attributable to the treatment. It was concluded that the acute lethal intramuscular dose in Sprague Dawley is greater than 100 mg/kg body weight.

5) Acute Intramuscular Toxicity Study in Swiss albino mice:

Reduced locomotor activity and ataxic gait were observed in animals treated at the dose level of 100 mg/kg body weight. All animals survived through the study period of 14 days. Body weight gain of male and female treated animals was found to be normal on day 7 and on day 14. Gross pathological examination did not reveal any abnormalities attributable to the treatment. It was concluded that the acute lethal intramuscular dose in Swiss Albino mice is greater than 100 mg/kg body weight.

6) Acute Intramuscular toxicity study in New Zealand White rabbits:

No signs of intoxication were observed in animals treated at different dose levels. All animals survived through the study period of 14 days. Body weight gain of male and female treated animals was found to be normal on day 7 and on day 14. Gross examination revealed internal bleeding in the abdominal cavity in two female animals from 50 mg/kg dose group. It was concluded that the acute lethal intramuscular dose in New Zealand White rabbits is greater than 50 mg/kg body weight.

7) Sub-Chronic Intravenous Toxicity Study (7 day) in Sprague Dawley Rat:

The Sub chronic intravenous toxicity study was designed and conducted to determine the toxicity profile of Recombinant Human TNK-tPA when administered daily for 7 days in Sprague Dawley rats. Recombinant Human TNK-tPA diluted with water for injection was administered to animals at the dose levels 2.5 mg/kg, 5 mg/kg and 10 mg/kg body weight. Two additional dose levels were added to the study as 0 mg/kg (Rev.) and 10 mg/kg (Rev.), in order to study the reversibility or delayed occurrence of symptoms, if any. The control animals were administered with vehicle only.

8) Sub-Chronic Intravenous Toxicity Study (7 day) in Swiss Albino Mice:

The Sub-Chronic intravenous toxicity study was designed and conducted to determine the toxicity profile of Tenecteplase when administered daily for 7 days in Swiss Albino mice. Tenecteplase diluted with water for injection was administered to animals at the dose levels 2.5 mg/kg, 5 mg/kg and 10 mg/kg body weight. Two additional dose levels were added to the study as 0 mg/kg (Rev.) and 10 mg/kg (Rev.), in order to study the reversibility or delayed occurrence of symptoms, if any. The control animals were administered with vehicle only.

9) Sub-Chronic Intravenous Toxicity Study in Pregnant Sprague Dawley Rat:

The toxicity study was designed and conducted to determine the developmental toxicity profile of Recombinant Human TNK-tPA when administered intravenously daily from 10 to 12 days of gestation to pregnant Sprague Dawley rats. Recombinant Human TNK-tPA dissolved in water for injection was administered to rats via intravenous route at the dose level of 0 mg/kg and 5 mg/kg/day body weight. On gestation day 20, all surviving pregnant rats were sacrificed. Total, live and dead foetuses were examined and recorded.

10) Sub-Chronic Intravenous Toxicity Study (7 day) in New Zealand White Rabbit:

The Sub-Chronic intravenous toxicity study was designed and conducted to determine the toxicity profile of TNK-tPA when administered daily for 7 days to New Zealand White Rabbit. TNK-tPA diluted with water for injection was administered to rabbits via intravenous route at the dose levels ranging from 0 mg/kg, 2.5 mg/kg, 5mg/kg and 10 mg/kg body weight. The control animals were administered with vehicle only. All the male and female animals from control and all the treated dose groups up to 10 mg/kg survived throughout the dosing period of 7 days. Animals treated at the dose level of 10 mg/kg, exhibited reduced locomotor activity during the dosing period of 7 days. Animals from 2.5 mg/kg and 5 mg/kg dose groups exhibited no signs of intoxication throughout the dosing period of 7 days. Male and female animals from all the treated dose groups exhibited normal body weight gain at the end of the dosing period of 7 days. Food consumption of control and treated animals was found to be comparable throughout the dosing of 7 days.

Haematological analysis and Biochemical analysis revealed no abnormalities attributable to the treatment.

Gross pathological examination revealed minimal to massive blood clots in the peritoneal cavity indicative of internal bleeding in all male and female animals from 5 mg/kg and 10 mg/kg dose groups. Histopathological examination revealed marked focal haemorrhagic necrosis with multifocal early degenerative changes in the hepatic parenchyma, intraluminal mild to marked haemorrhages in the distal convoluted tubules of the kidneys and mild focal subserosal haemorrhages in the urinary bladder in one male animal from 10 mg/kg dose group. Based on these findings the no observed effect level (NOEL) of TNK-tPA, when administered to New Zealand White Rabbits via intravenous route, over a period of 7 days was found to be 2.5 mg/kg in male and female animals.

6. Pharmaceutical Particulars

6.1 List of excipients

Arginine
Phosphoric
Acid
Polysorbate 20

6.2 Incompatibilities

Tenecteplase shows incompatibility with dextrose containing IV line. Hence dextrose containing lines should be flushed with saline solutions prior to and following single bolus administration of TNK-tPA.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store lyophilized TNK-tPA at 2 to 8°C. Do not use beyond the expiration date stamped on the vial.
If the reconstituted Tenecteplase is not used immediately, refrigerate the TNK-tPA vial at 2 to 8°C (36–46F) and use within 4 hours.

6.5 Nature and contents of container

Each combi-kit contains one Tenectase vial, one vial of Sterile Water for Injections I.P. 10 ml, Three Alcohol Swabs of isopropyl Alcohol 70%v/v, one 10 ml Sterile Disposable Syringe with Needle, one additional Pre-sterile Needle (21G) along with Package Insert packed in plastic tray in a Mono Carton.

6.6 Special precautions for disposal and other handling

Reconstitution

Withdraw 10 ml of Sterile Water for Injection (SWFI) from the supplied vial and inject the entire contents of the syringe into the vial containing 20 mg of tenecteplase, directing the SWFI stream into the powder. Slight foaming upon reconstitution is not unusual; any large bubbles will dissipate if the product is allowed to stand undisturbed for several minutes. Gently swirl until contents are completely dissolved. DO NOT SHAKE. The reconstituted preparation results in a colorless to pale yellow transparent solution containing TNK-tPA. The reconstituted preparation contains TNK-tPA in a concentration of 2mg/ml. Determine the appropriate dose of TNK-tPA and withdraw this volume (in milliliters) from the reconstituted vial with the syringe. Any unused solution should be discarded.

Administration

Replace the needle used for reconstitution with another pre-sterile needle provided in the Kit for administration to the patient. The product should be visually examined prior to administration for discoloration and particulate matter. TNK-tPAmay be administered as reconstituted at 2 mg/mL. Precipitation may occur when TNK-tPAis administered in an IV line containing dextrose. Dextrose containing lines should be flushed with a saline-containing solution prior to and following single bolus administration of TNK-tPA. Reconstituted TNK-tPA should be administered as a single IV bolus over 5 to 10 seconds. Because TNK-tPA contains no antibacterial preservatives, it should be reconstituted immediately before use. If the reconstituted TNK-tPA is not used immediately, refrigerate the TNK-tPAvial at 2°C - 8°C (36°F-46°F) and use within 4 hours.

7. Marketing Authorization Holder

Manufacturer:
Gennova Biopharmaceuticals Limited
Block-1, Plot No, P-1 & P-2, ITBT Park, Phase II, MIDC, Hinjawadi,
Pune-411057 Maharashtra INDIA

Marketed by:
EMCURE PHARMACEUTICALS LIMITED

8. Marketing Authorization Numbers

H2025/CTD12101/26095

9. Date of first authorization/renewal of the authorization

August 2016

10. Date of revision of the text

21/08/2026