

MIMS Full Prescribing Information

Streptase

Company CSL

Primary Section: Cardiovascular System - Fibrinolytic agents

ARTG Registered medicine

MIMS revision date: 01 Nov 2011

Composition Streptokinase.

Description Streptase is highly purified streptokinase obtained from the culture filtrate of beta-haemolytic Streptococci of group C.

The various strengths of Streptase contain the following amounts of dry substance including pure lyophilised streptokinase and human albumin as stabilising agent:

250,000 IU streptokinase: 134 to 176 mg dried material;

1,500,000 IU streptokinase: 147 to 192 mg dried material.

Actions Pharmacology. Streptokinase acts with plasminogen to produce an activator complex that converts plasminogen to the proteolytic enzyme, plasmin. The more plasminogen bound within this complex, the less plasminogen is left to be converted into its enzymatically active form. Therefore, high doses of streptokinase are associated with a lower bleeding risk and low doses of streptokinase are associated with a higher bleeding risk. Due to the high degree of affinity and rapid reaction between streptokinase and antistreptokinase antibodies, which are possibly present in the patient's blood, low quantities of streptokinase are eliminated from the blood with a half-life of 18 minutes. The elimination half-life of streptokinase based on activator formation is about 80 minutes. The major part of streptokinase is degraded to peptides and eliminated by the intestines and kidneys. Plasmin degrades fibrin clots as well as fibrinogen and other plasma proteins. Plasmin is inactivated by circulating inhibitors such as alpha-2-plasmin inhibitor or alpha-2-macroglobulin. These inhibitors are rapidly consumed at high doses of streptokinase. Experimental studies have shown that Streptase induces lysis of the thrombus both superficially and also from within the thrombus.

Intravenous infusion of streptokinase is followed by increased fibrinolytic activity, which decreases plasma fibrinogen levels for 24 to 36 hours. The decrease in plasma fibrinogen is associated with decreases in plasma and blood viscosity and red blood cell aggregation. The hyperfibrinolytic effect disappears within a few hours after discontinuation, but a prolonged thrombin time may persist for up to 24 hours due to the decrease in plasma levels of fibrinogen and an increase in the amount of circulating fibrinogen degradation products (FDP).

Depending upon the dosage and duration of infusion of streptokinase, the thrombin time will decrease to less than twice the normal control value within four hours, and return to normal by 24 hours. Variable amounts of circulating antistreptokinase antibody are present in individuals as a result of recent streptococcal infections. The recommended dosage schedule usually obviates the need for antibody titration.

Two large, randomised, placebo controlled studies with a 60 minute intravenous infusion of Streptase 1,500,000 IU have reported a significant reduction both in acute mortality (five weeks) and after longer-term follow up (median 15 months). The overall reduction in mortality of patients treated with Streptase is of the order of 25%.

In the GISSI study¹, the reduction in mortality was time dependent; there was a 47% reduction in mortality among patients treated within one hour of the onset of chest pain, a 23% reduction among patients treated within three hours, and a 17% reduction among patients treated between three and six hours. There was also a reduction in mortality in patients treated between six and twelve hours from the onset of symptoms, but the reduction was not statistically significant.

In the ISIS II study², comparison of 8,592 patients allocated intravenous Streptase with 8,595 patients allocated placebo infusion, yielded a 25% reduction in five week mortality of the Streptase treated patients which was shown to be a highly significant result ($2p < 0.00001$). The reduction in mortality was also dependent on delay from time of onset of pain, with a significant difference from placebo observed up to 24 hours from pain onset, as follows.

0 to 4 hours: 35% reduction in odds of vascular death ($2p < 0.00001$);

5 to 12 hours: 16% reduction in odds of vascular death ($2p = 0.02$);

13 to 24 hours: 21% reduction in odds of vascular death ($2p = 0.08$).

In addition, left ventricular ejection fraction has been shown to be significantly higher in Streptase treated patients than in controls. The rate of reocclusion of the infarct related vessel has been reported to be approximately 20%.

The rate of reocclusion depends on dosage, additional anticoagulant therapy and residual stenosis.

When the reinfarctions were evaluated in studies involving 8,800 streptokinase treated patients, the overall rate was 3.8% (range 2 to 15%). In over 8,500 control patients, the rate of reinfarction was 2.4%.

Indications Acute evolving myocardial infarction. For use in the management of acute myocardial infarction, for the lysis of intracoronary thrombi, for the improvement of ventricular function, and reduction of mortality when administered by either the intravenous or intracoronary route. Earlier administration of streptokinase is correlated with greater clinical benefit, the greatest benefit (in terms of mortality reduction) being seen when Streptase is administered within the first four hours after onset of symptoms. The treatment should always commence within six hours of the onset of pain.

Acute massive pulmonary embolism. For the lysis of objectively diagnosed (angiography or lung scan) pulmonary emboli, involving obstruction of blood flow to a lobe or multiple segments, with or without unstable haemodynamics.

Studies with thrombolytic therapy for pulmonary embolism show no significant difference in lung perfusion scan between the thrombolysis group and the heparin group at one year follow-up. However, measurements of pulmonary capillary blood volumes and diffusing capacities at two weeks and one year after therapy indicate that a more complete resolution of thrombotic obstruction and normalisation of pulmonary physiology was achieved with thrombolytic therapy, thus preventing the long-term sequelae of pulmonary hypertension and pulmonary failure.

Deep vein thrombosis. For the lysis of objectively diagnosed (preferably ascending venography), acute, extensive thrombi of the deep veins such as those involving the popliteal and more proximal vessels.

The long-term benefit of Streptase therapy for deep vein thrombosis (DVT) has been evaluated venographically. The combined results of five randomised studies show no residual thrombotic material in 60 to 75% of patients treated with streptokinase versus only 10% of those treated with heparin. Thrombolytic therapy also preserves venous valve function in a majority of cases, thus avoiding the pathologic venous changes that produce the clinical postphlebotic syndrome which occurs in 90% of the DVT patients treated with heparin.

Arterial thrombus or embolism. For the lysis of acute arterial thrombi and emboli.

There is a time related decrease in effectiveness. When administered three to ten days after onset of obstruction, rates of clearance of 50 to 75% were reported.

Occlusion of arteriovenous cannulae, including clotting in external arteriovenous shunts of patients on haemodialysis.

Contraindications Because thrombolytic therapy increases the risk of bleeding, Streptase, administered either systemically or locally, is contraindicated in the following situations.

Existing or recent haemorrhage and haemorrhagic diathesis (with the exception of consumption coagulopathy).

Potential for internal bleeding (e.g. peptic ulcer, ulcerative colitis, diverticulitis or visceral tumours).

All forms of reduced blood coagulability, in particular spontaneous fibrinolysis and extensive clotting disorders.

Recent (within two months) cerebrovascular accident, recent (within ten days) facial or head trauma, intracranial or intraspinal surgery, known intracranial neoplasm and all known neoplasms with risk of haemorrhage.

Invasive operations, e.g. recent organ biopsy, invasive diagnostic procedure, recent implantation of a vessel prosthesis, long-term traumatic closed chest massage or other recent surgery (until the sixth to tenth postoperative day, depending on the severity of surgical intervention).

Arteriovenous malformation or aneurysm.

Haemorrhagic diathesis including thrombocytopenia or pronounced hepatic or renal dysfunction.

Severe uncontrolled hypertension (systolic blood pressure > 200 mmHg, diastolic blood pressure > 100 mmHg, or hypertensive retinal changes grade III/IV), hypertonic fundus.

Severe liver or kidney damage.

Acute pancreatitis.

Simultaneous treatment with oral anticoagulants (international normalised ratio (INR) > 1.3).

Endocarditis or pericarditis (isolated cases of pericarditis, misdiagnosed as acute myocardial infarction and treated with Streptase, have resulted in pericardial effusions including tamponade).

Because of the danger of allergic anaphylactic reactions, Streptase is also contraindicated in the following situations.

Immediately after streptococcal infections which have produced a high antistreptokinase titre (e.g. acute rheumatic fever, acute glomerulonephritis).

More than five days and less than twelve months since previous streptokinase therapy³.

Streptase should not be administered to patients who have experienced severe allergic reactions to the product.

Warnings Streptase will cause lysis of haemostatic fibrin deposits such as those occurring at sites of needle punctures, and bleeding may occur from such sites. In order to minimise the risk of bleeding during treatment with streptokinase, venepuncture and physical handling of the patient should be performed carefully and as infrequently as possible, and intramuscular injections must be avoided.

Should arterial puncture be necessary during intravenous therapy, upper extremity vessels are preferable. Pressure should be applied for at least 30 minutes, a pressure dressing applied, and the puncture site checked frequently for

evidence of bleeding.

In the following conditions, the risks of therapy (either systemically or locally administered) may be increased and should be weighed against the following anticipated benefits.

Obstetric delivery, abortion.

Previous puncture of noncompressible vessels, intramuscular injection.

Recent (within ten days) serious gastrointestinal bleeding and patients with gastrointestinal diseases or a history of chronic peptic ulcer.

Recent (within ten days) trauma including cardiopulmonary resuscitation.

Risk of severe local haemorrhage, e.g. due to translumbar aortography.

Patients with indwelling urethral catheter.

Invasive operations, e.g. recent intubation.

Diseases of the urogenital tract with tendency to haemorrhages.

Recent cavitating tuberculosis lesion in lungs (e.g. open tuberculosis) or severe bronchitis.

High likelihood of left heart thrombus, e.g. mitral stenosis with atrial fibrillation.

Haemostatic defects, including those secondary to severe hepatic or renal disease.

Pregnancy (see Precautions, Use in pregnancy).

Suspicion of severe atherosclerotic degeneration.

Cerebrovascular disease.

Known septic thrombotic disease or occluded arteriovenous cannula at seriously infected site.

Any other condition in which bleeding constitutes a significant hazard or would be particularly difficult to manage because of its location.

Should serious spontaneous bleeding (not controllable by local pressure) occur, the infusion of Streptase should be terminated immediately and treatment instituted as described under Adverse Effects.

Arrhythmias. Rapid lysis of coronary thrombi has been shown to cause reperfusion atrial or ventricular dysrhythmias requiring immediate treatment. Careful monitoring for arrhythmia is recommended during and immediately following administration of Streptase for acute myocardial infarction.

Hypotension. At the beginning of therapy, hypotension, tachycardia or bradycardia (reaching as far as shock in individual cases) are commonly observed. Patients should be monitored closely and, if symptomatic or alarming hypotension occurs, appropriate treatment administered. Corticosteroids can be administered prophylactically, and at the beginning of therapy the infusion should be performed slowly.

Other. Noncardiogenic pulmonary oedema has been reported rarely in patients treated with Streptase. The risk of this appears greatest in patients who have large myocardial infarctions and are undergoing thrombolytic therapy by the intracoronary route.

Rarely, polyneuropathy has been temporally related to the use of Streptase.

Should pulmonary embolism or recurrent pulmonary embolism occur during streptokinase therapy, the originally planned course of treatment should be completed in an attempt to lyse the embolus.

While pulmonary embolism may occasionally occur during Streptase treatment, the incidence is no greater than when patients are treated with heparin alone.

Precautions General. Because of the increased likelihood of resistance, due to antistreptokinase antibody, retreatment with Streptase or streptokinase containing products may not be effective if administered between five days and twelve months of prior streptokinase administration or streptococcal infections, such as streptococcal pharyngitis, acute rheumatic fever, or acute glomerulonephritis secondary to a streptococcal infection.

In principle, no thrombolytic treatment should be commenced before the tenth postoperative day. However, in cases of pulmonary embolism, the indication for earlier treatment may be very strong and after careful consideration of all the risks, Streptase may be given before the tenth postoperative day. The danger of bleeding from the operative area must, of course, be taken into account.

The danger of haemorrhage is increased by simultaneous or previous treatment with anticoagulants (e.g. heparin) or substances which inhibit platelet formation or function. If the patient is under active heparinisation, it should be neutralised by the administration of protamine sulfate before the start of thrombolytic therapy. The thrombin time (TT) should not be more than twice the normal control value before thrombolytic therapy is started. In patients who have been receiving coumarin derivatives, the international normalised ratio (INR) must be less than 1.3 before starting the streptokinase infusion.

Current data generally do not support the use of thrombolytic therapy in patients when the ECG shows only ST depression (with the exception of those patients with a true posterior infarct, as indicated by tall R waves and marked ST depression in leads V_1 to V_3).

Repeated administration. After administration of Streptase, the titre of antistreptokinase antibodies begins to rise after approximately one week, reaching a peak at two to three weeks and remains elevated for eight to twelve

months⁴. Because of the increased likelihood of resistance, Streptase may not be effective if given during this period.

Data on the risk of serious allergic and anaphylactic reactions on rechallenge and the relationship to antistreptokinase antibody titre are not available. (See Contraindications.)

Laboratory tests. *Intravenous or intracoronary infusion for myocardial infarction.* Intravenous administration of Streptase will cause marked decreases in plasminogen and fibrinogen and increases in thrombin time (TT), activated partial thromboplastin time (APTT) and prothrombin time (PTT). These changes may also occur in some patients with intracoronary administration of streptokinase.

Intravenous infusion for other indications. Before commencing thrombolytic therapy, it is desirable to obtain an APTT, PTT and TT, fibrinogen levels and a haematocrit and platelet count. If heparin has been given, it should be discontinued and the TT or APTT should be less than twice the normal control value before thrombolytic therapy is started. During the infusion, decreases in plasminogen and fibrinogen levels and an increase in the level of fibrin degradation products (FDP) (the latter two causing a prolongation in the clotting times of coagulation tests) will generally confirm the existence of a lytic state. Therefore, lytic therapy can be confirmed by performing the TT, APTT, PTT or fibrinogen levels approximately four hours after initiation of therapy. If heparin is to be reinstated following the Streptase infusion, the TT or APTT should be less than twice the normal value (see manufacturer's prescribing information for proper use of heparin).

Paediatric use. Safety and effectiveness in children have not been established.

Use in pregnancy (Category C)

While only minimal amounts of streptokinase cross the placenta, streptokinase specific antibodies are found in the fetal blood.

Animal reproduction studies have not been conducted with Streptase. It is also not known whether streptokinase can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Thrombolytic therapy within the first 18 weeks of pregnancy must be restricted to vital indications only, because of the risk of placental separation. Streptase should be given to a pregnant woman only if the benefit to the patient clearly outweighs the risk of treatment.

Use in lactation It is not known whether streptokinase is excreted in the breast milk, nor whether it has harmful effects on the newborn infant. In the absence of further information, it is recommended that breastfeeding be discontinued in a woman who is to receive Streptase.

Combination of Streptase with aspirin for treatment of myocardial infarction. The ISIS II study showed a significant benefit to patients treated with these two agents after acute myocardial infarction. Mortality (both short and longer-term) was reduced in these patients to a greater extent than in those treated with either agent alone.

Unless contraindicated, the concomitant use of aspirin, starting prior to Streptase infusion and continued for one month thereafter, may be instituted at the discretion of the doctor. The benefit of combination therapy should therefore be weighed against the risk of increased haemorrhage.

Anticoagulation treatment following Streptase. To prevent rethrombosis, it is recommended that long-term thrombolysis with Streptase should be followed by treatment with heparin or other fibrinolytics. The effect of streptokinase on TT and APTT will usually diminish within three to four hours after streptokinase therapy, and heparin therapy without a loading dose can be initiated when the TT or the APTT is less than twice the normal control value. (See Dosage and Administration.)

Following high dose (1.5 million IU), short-term treatment with Streptase for acute myocardial infarction, the use of subsequent anticoagulant treatment has not yet been shown to be of unequivocal benefit. Therefore, in this situation, the use of anticoagulants should be decided by the treating doctor.

Interactions The potential for an additive hypotensive effect should be borne in mind when Streptase therapy is combined with antihypertensive agents such as beta-blockers and glyceryl trinitrate. Until information regarding the interaction between Streptase and tissue plasminogen activator (tPA) is available, special care is required if such a combination is considered.

Before starting long-term systemic lysis of deep vein thromboses and arterial occlusions with streptokinase, the effects of drugs which act upon platelet formation or function should be allowed to subside.

There is an increased risk of haemorrhage in patients simultaneously or previously receiving anticoagulants (such as heparin or coumarin derivatives), or drugs which inhibit platelet formation or function (e.g. platelet aggregation inhibitors, dextrans, phenylbutazone, dipyridamole, nonsteroidal anti-inflammatory drugs). The effect of heparin can, however, be neutralised rapidly by administration of protamine sulfate. The TT should not be more than twice the normal control value before thrombolytic therapy is started. In the case of prior treatment with coumarin derivatives, the INR must be less than 1.3 before starting a streptokinase infusion.

Adverse Reactions The following adverse reactions are based on experience from clinical trials and postmarketing. The following standard categories of frequency are used. Very common > 1/10; common > 1/100 and < 1/10; uncommon > 1/1,000 and < 1/100; rare 1/10,000 and < 1/1,000; very rare 1/10,000, including reported single cases.

Haemorrhage and bleeding. Common. Haemorrhages at invaded or disturbed sites, including the injection site, and ecchymoses. Gastrointestinal or genitourinary bleeding (including aggravation of menstrual bleeding), epistaxis. Uncommon. Intracranial haemorrhages with their complications and possible fatal outcome, retinal haemorrhages, severe haemorrhages (also with fatal outcome) including liver haemorrhages, retroperitoneal bleeding, splenic rupture. Blood transfusions are rarely required.

Very rare. Haemorrhages into the pericardium, including myocardial rupture during thrombolytic treatment of acute myocardial infarction.

In three studies in which anticoagulation was optimal following intravenous administration of Streptase for acute myocardial infarction, the incidence of major bleeding ranged from 0.3 to 6.2%. In 21 studies in which anticoagulation was compulsory, the incidence of major bleeding ranged from 0 to 16%. The overall incidence of major bleeding with high dose intravenous infusion is 1.2%.

Major bleed rates are difficult to determine for other dosages and patient populations because of the different dosing and intervals of infusions. The rates reported appear to be within the ranges reported for intravenous administration in acute myocardial infarction.

Haemorrhage is uncommon when the high dose, short-term lysis technique is used.² Slowing the rate of administration of streptokinase will not help correct bleeding and may make it worse. In severe haemorrhagic complications the Streptase therapy is discontinued and a proteinase inhibitor (e.g. aprotinin) administered in the following dosage: initially 500,000 KIU (kallikrein inactivator unit), if necessary up to 1 million KIU, followed by 50,000 KIU per hour by intravenous drip until the bleeding stops. In addition, combination with synthetic antifibrinolytics is recommended. If necessary, coagulation factors should be administered. Additional administration of synthetic antifibrinolytics was reported to be efficient in single cases of bleeding episodes.

Immune system disorders. Very common. Development of antistreptokinase antibodies (see Precautions).

Common. Allergic anaphylactic reactions such as rash, flushing, itching, urticaria, angioneurotic oedema, minor breathing difficulty, periorbital swelling, bronchospasm or hypotension.

Very rare. Delayed allergic reactions such as serum sickness, arthritis, arthralgia, vasculitis, interstitial nephritis and neuroallergic symptoms (polyneuropathy, e.g. Guillain-Barre syndrome), severe allergic reactions (up to shock, including respiratory arrest), renal insufficiency and uveitis.

Mild or moderate allergic reactions may be managed with concomitant antihistamine and/or corticosteroid therapy. If a severe allergic/ anaphylactic reaction occurs, the administration of Streptase has to be discontinued immediately and an appropriate treatment should be initiated. The current medical standards for shock treatment should be observed. Lysis therapy should be continued with homologous fibrinolytics.

Nervous system disorders. Rare. Neurological symptoms (e.g. dizziness, confusion, paralysis, hemiparesis, agitation or convulsion) in the context of cerebral haemorrhages or cardiovascular disorders with hypoperfusion of the brain.

Cardiac complication and vascular disorders. Common. At the beginning of therapy, hypotension, tachycardia or bradycardia (see Precautions).

Very rare. Cholesterol embolism.

In the setting of fibrinolytic therapy with Streptase in patients with myocardial infarction, the following events have been reported as complications of myocardial infarction and/or symptoms of reperfusion.

Very common. Hypotension, heart rate and rhythm disorders, angina pectoris.

Common. Recurrent ischaemia, heart failure, reinfarction, cardiogenic shock, pericarditis, pulmonary oedema.

Uncommon. Cardiac arrest (leading to respiratory arrest), mitral insufficiency, pericardial effusion, cardiac tamponade, myocardial rupture, pulmonary or distal embolism.

These cardiovascular complications can be life threatening and may lead to death. During local lysis of peripheral arteries, distal embolisation cannot be excluded.

Respiratory disorders. Very rare. Noncardiogenic pulmonary oedema after intracoronary thrombolytic therapy in patients with extensive myocardial infarction.

Gastrointestinal disorders. Common. Nausea, diarrhoea, epigastric pain and vomiting.

General disorders. Common. Headache and back pain, muscle pain (including myalgia), chills and/or fever as well as asthenia/ malaise. Symptomatic treatment of fever is usually sufficient to alleviate discomfort and prophylactic administration of corticosteroids should prevent fever.

Laboratory investigations. Common. Transient elevations of serum transaminase as well as bilirubin (in individual cases sometimes leading to jaundice).

Dosage and Administration (See Tables 1 and 2.) Streptase should be given either by intravenous infusion or by injection close to the site of occlusion (intra-arterially). The route of administration, dosage and duration of therapy will depend on the indication. When thrombolytic therapy is necessary and a high antibody concentration against streptokinase is present or recent streptokinase therapy has been given (more than five days and less than one year previously), homologous fibrinolytics should be used (see also Contraindications and Precautions).

Acute evolving myocardial infarction. Streptase should be given as soon as possible after the onset of symptoms. The greatest benefit in terms of mortality reduction is observed when the high dose, short-term lysis treatment is instituted within four hours of onset of symptoms. The agent should not be administered to patients with symptoms of greater than six hours duration of myocardial pain or transmural ischaemia.

Pulmonary embolism, deep vein thrombosis, arterial thrombus or embolism. Streptase treatment should be instituted as soon as possible after onset of the thrombotic event, preferably within seven days. Any delay in instituting lytic therapy to evaluate the effect of heparin therapy decreases the potential for optimal efficacy. Since human exposure to Streptococci is common, antibodies to streptokinase are prevalent. Thus, a loading dose of streptokinase sufficient to neutralise these antibodies is required. A dose of streptokinase 250,000 IU infused into a peripheral vein over 30 minutes has been found appropriate in over 90% of patients. However, if the thrombin time or any other parameter of lysis after four hours of treatment is less than approximately 1.5 times the normal control value, discontinue streptokinase, as excessive resistance to streptokinase is present.

Arteriovenous cannulae occlusion. Before using Streptase, an attempt should be made to clear the cannula by careful syringe technique, using heparinised saline solution. If adequate flow is not re-established, streptokinase may be employed. Allow the effect of any pretreatment anticoagulants to diminish. Instil streptokinase 250,000 IU in 2 mL of solution into each occluded limb of the cannula slowly.

Clamp off cannula limb(s) for two hours. Observe the patient closely for possible adverse effects. After treatment, aspirate contents of infused cannula limb(s), flush with saline, reconnect cannula.

Refer to Table 1.

Streptase**Table 1**

Dosage schedule: part A

IV administration	Initial dose	Maintenance dose	Long-term control/ anticoagulant therapy
High dose, short-term lysis for acute myocardial infarction	Single dose of 1,500,000 IU over 30-60 min. Aspirin may also be instituted at the discretion of the physician (see Precautions, Combination of streptase with aspirin for treatment of myocardial infarction)	If reocclusion occurs within 5 days of initial dose a second dose may be given	No laboratory tests are necessary before or during streptase therapy. Aspirin may be continued at the discretion of the physician. Additional anticoagulant therapy may be given at the discretion of the treating physician
Long-term lysis for deep vein thrombosis, arterial thrombus, pulmonary embolism	250,000 IU over 30 min	100,000 IU/hour for 24-120 hours depending on location, extent of occlusion and clinical improvement	PTT should be tested from the 16th hour after commencement of streptase infusion. Adequate anticoagulation protection is achieved if PTT is 2 to 4 times normal If PTT is < twice normal, give heparin at a rate of 500 to 800 IU/hour (see manufacturer's instructions for proper use of heparin) If PTT is > 2 to 4 times normal, double the dose of streptase for several hours. If dose regulation fails at greatly prolonged PTT, discontinue streptase If PTT shows tendency towards normal values, give heparin 500-800 IU/hour simultaneously with continued maintenance dose of streptase. Continue heparin until PTT is within the normal therapeutic range

Refer to Table 2.

Streptase**Table 2**

Dosage schedule: part B

Local administration	Initial dose	Maintenance dose	Long-term control/ anticoagulant therapy
Intracoronary infusion for acute myocardial infarction	20,000 IU bolus (up to 200,000 IU has been given as an initial bolus)	2 to 4,000 IU/minute for 30-90 minutes (average 60 minutes)	-
Other intra-arterial application	1 to 2,000 IU at 3 to 5 minute intervals up to 3 hours	-	Heparin treatment is recommended after streptokinase therapy to prevent rethrombosis
Arteriovenous cannulae occlusion	Instil 250,000 IU in 2 mL solution slowly into occluded limb, clamp off cannula limbs for 2 hours	-	After treatment, aspirate contents of infused cannulae limb(s), flush with saline and reconnect cannulae

Reconstitution. Streptase is a lyophilised injection which should be reconstituted in sterile normal saline for injection or Haemacel (plasma volume substitute derived from degraded gelatine). Initially 5 mL of solution should be added to the vial and mixed. The entire contents of the vial should then be withdrawn and diluted as required. The reconstituted solution should be used immediately or stored in a refrigerator (2 to 8deg. C) for up to 24 hours. Parenteral solutions should be inspected visually for particulate matter and discolouration prior to administration. (Note that the human albumin constituent may impart a slightly yellow colour to the solution.) The stability of Streptase in solution is dependent not only on the temperature and concentration, but also on the pH of the diluent which should not be lower than 6.5. It has been shown that the best stability is achieved when Haemacel is used.

Overdosage If severe uncontrollable bleeding occurs as a result of overdosage, Streptase infusion should be ceased immediately. Bleeding can be reversed and blood loss managed effectively with appropriate replacement therapy. Administration of aminocaproic acid or aprotinin may be useful (see Adverse Effects, Haemorrhage and bleeding).

Presentation Powder for reconstitution (sterile, lyophilised): 250,000 IU, 1,500,000 IU.

Storage Store at 2 to 25deg. C. Shelf life: 3 years.

References 1. Long-term effects of intravenous thrombolysis in acute myocardial infarction: final report of the GISSI Study. Gruppo Italiano per lo Studio Della Streptochinasi nell 'Infarto Miocardico (GISSI). Lancet 1987; 8564: 871-874.

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3. Transmural, haemorrhagic myocardial infarction after intracoronary streptokinase. Clinical, angiographic and necropsy findings. Mathey, D.G., Schofer, J., Kuck, K-H., Beil, U., Kloppel, G et al. British Heart Journal, 1982; 48: 546-351.

4. Antistreptokinase titres after intravenous streptokinase. Jalihal, S., Morris, G.K. Lancet 1990; 335: 184-185.

Poisons Schedule S4.

Date of TGA approval or last amendment 16/02/2011

This information can also be found online at: https://www-mimsonline-com-au.cknservices.dotsec.com/Search/FullPI.aspx?ModuleName=Product%20Info&searchKeyword=Streptokinase&PreviousPage=~/Search/QuickSearch.aspx&SearchType=&ID=3350001_2