

CLINICAL POLICIES AND PROCEDURES

**NEWBORN USE ONLY
GIVEN ON DOCTORS ORDER ONLY****TISSUE PLASMINOGEN ACTIVATOR
ALTEPLASE**

IMPORTANT NOTE	The drug should be not be used without the approval of consultant neonatologist. The benefits of therapy should be weighed against its dangers of intraventricular bleed or with low platelets in sick, preterm babies. While the drug can be effective in the thrombolysis, it is associated with low margin of safety and an unknown risk-benefit ratio.
DESCRIPTION	Recombinant tissue plasminogen activator (rt-PA). It has the property of fibrin enhanced conversion of plasminogen to plasmin. Actilyse is fibrin dependent. When introduced into the systemic circulation Actilyse binds to fibrin in a thrombus and converts entrapped plasminogen to plasmin. This initiates local fibrinolysis and clot dissolution but with minimal systemic effects. Rt-PA is better than streptokinase because its short half-life, non-antigenic properties and local specific action on plasminogen bound fibrin. In studies, it has been shown to have an overall patency (clot dissolution) rate of 94%.
USE	<ol style="list-style-type: none">1. Arterial and venous thrombosis2. Central venous catheter occlusions3. Renal vein thrombosis4. Intracardiac thrombus secondary to cvcs5. Vegetations from infective endocarditis not responding to conventional antibiotic therapy
CONTRAINDICATION	Major surgery during the last 10 days, history of severe bleeding such as intracranial, pulmonary or gastrointestinal haemorrhage. Correct the following before starting r-TPA: platelets<100,000, low fibrinogen<100g/l, severe coagulation factor deficiencies.
PHARMACOKINETICS	Actilyse is cleared rapidly from plasma primarily by the liver. Half-life is about 5 minutes.
PRESENTATION	50mg/vial with 50ml solvent and transfer cannula
DOSE	Before starting therapy get baseline investigations including FBC and Coagulation studies(PT, APTT, Fibrinogen)
OCCLUDED CENTRAL LINE	Instill 1mg/ml solution of rt-PA into CVC in an amount equal to CVC lumen capacity (0.1-2ml) plus an additional 10%. After 20 minutes check for CVC lumen patency, and if necessary, a second rt-PA instillation can be performed. With this dosing regime, it's effects are local with little or minimal systemic side effects. If possible, infuse the drug into or close to thrombus.

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SYSTEMIC THROMBOLYSIS

1. **High dose regime** Loading dose of 0.7mg/kg over 30-60 minutes followed by a continuous infusion of 0.2mg/kg/hr (dose range 0.1-0.3mg/kg/hr) of rt-PA ± heparin 4-10U/kg/hr. **This is the preferred regime.** The infusion dose of rt-PA depends on the success of thrombolytic treatment, complications and coagulation status.
Review therapy after every 6-12 hours. Infusion is stopped in case of total or partial clot lysis with only minor clot residue after 5 days of treatment and complications, such as general or significant local bleeding. Total duration of treatment is determined by the response (improvement in circulation and clot dissolution) and the overall assessment of risk.
2. **Low dose regime** Loading dose of 0.7mg/kg over 30-60 minutes, followed by a continuous infusion of 0.02–0.04mg/kg/hr of rt-PA. Choose this dosing regime if the risk of intracerebral haemorrhage is considered very high such as sick ELBW infants with cerebral echodensities and/or low fibrinogen levels and/or low platelets.
3. **Follow-up treatment** After successful systemic thrombolysis with low dose 2-6U/kg/hr heparin should be considered as long as central venous lines are required.

RECONSTITUTION

Add 50ml of solvent aseptically to the 50mg of Actilyse by the use of transfer cannula supplied to make a 1mg/ml solution.

Do not use water for injection available in the unit.

The transfer cannula must always be introduced vertically into the stopper and through the mark at its centre. As an alternative to transfer cannula, we can use large bore needle directing the stream of solvent into the drug cake. Slight foaming is not unusual. Standing the vial undisturbed for a few minutes will allow dissipation of any large bubbles. Avoid excessive or vigorous shaking.

FURTHER DILUTE 10ml(10mg) of reconstituted solution with 40ml of 0.9% sodium chloride to give a 0.2mg/ml solution.

STORAGE

Solution can be stored up to 24 hours in refrigerator (2-8°C).

MONITORING

6-12hourly monitoring of platelets, PT, APTT, Fibrinogen

Preferred coagulation test values under treatment with systemic rt-PA are: PT 30-40sec, APTT 50-60sec, Fibrinogen ≥150g/l

PRECAUTION

Avoid frequent venepunctures and arterial punctures while on therapy!

ADVERSE EFFECT

local and systemic bleeding intracranial haemorrhage, allergic reaction

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