health
Department:
Health
REPUBLIC OF SOUTH AFRICA

Private Bag X828, PRETORIA, 0001 Dr AB Xuma Building1112 Voortrekker Road, Pretoria Townlands 351-JR, PRETORIA, 0187 Tel (012) 395 8000, Fax (012) 395 8918

Mr E van Zyl
Equity Pharmaceuticals (Pty) Ltd
100 Sovereign Road
Route 21 Corporate Park
Nellmapius Drive
Irene
Pretoria

Dear Mr van Zyl

Section 21 Authorization for STREPTOKINASE 1.5MU INJECTION

Attached, please find the Authorization for exemption under Section 21 of the Medicines and Related Substances Act by SAHPRA granted for:

- **Streptokinsae 1.5MU Injection**

The quantities for which approval was granted are only estimates based on procurement by provinces over the last 6 months. Please note that the National Department of Health (NDOH) cannot guarantee the procurement of these quantities, as NDOH has no control over orders being placed by provincial depots, and current stock holding might influence estimated quantities.

The following process will be followed to ensure the quality of the product being brought in:

1. Manufacturer will submit an assay and identification of every batch imported.
2. An additional assay of every batch will be done by a quality control laboratory.
3. A random sample will be assayed during the authorized period by a quality control laboratory.
4. Aggregate statistics to be submitted to NDOH in the first week of each month of all orders received and quantities supplied per province.
5. The NDOH needs to be advised of the quantities and date of arrival of stocks in terms of this authorization within 7 days after arrival.
6. The supplier will provide monthly reports, by the 7th of each month, using the attached format of orders received and issues done.
7. Participating Authorities (PAs) will provide a consolidated close out report of usage using the attached format on the date when an authorization lapses.

8. The full quantities imported in terms of this Section 21authorisation must be accounted for.
9. Note that this authorization DOES NOT cover supplies to the private sector.
10. Where this authorization is obtained to provide security of supply due to supply challenges from the contracted supplier, PAs are requested to buy out against contracted suppliers and ensure that related orders are cancelled accordingly to prevent over stocking once the contracted supplier gets back into stock.

It should be noted this authorization applies only for use of the product in the public sector with estimated usage quantities for a period of one month. The authorization is expected to expire on **19 March 2025**.

Table 1: Provincial estimates

Province	Six Months Estimate
Correctional Services	0
EC-MT	6
EC-PE	0
FS	40
GP	0
KZN	60
LP	0
MP	15
NC	0
NW	0
SAMHS	15
WC	550
Total	**686**

Yours sincerely

K Jamaloodien

KHADIJA JAMALOODIEN
CHIEF DIRECTOR: SECTOR WIDE PROCUREMENT
DATE: 20/9/2024

SAHPRA
SOUTH AFRICAN
HEALTH PRODUCTS
REGULATORY AUTHORITY

Section 21 Response Letter

9/19/2024 5:24 PM

Khadija Jamaloodien

National Department of Health
Dr AB Xuma Building
1112 Voortrekker Rd
Pretoria Townlands 351-JR
Pretoria
0187

Buhle.Mbongo@health.gov.za

Dear Khadija Jamaloodien,

REQUEST TO USE UNREGISTERED MEDICINE IN TERMS OF SECTION 21 OF THE MEDICINES AND RELATED SUBSTANCES ACT, 1965 (ACT 101 OF 1965):

Your application dated **9/18/2024 2:48 PM** refers

A. STATUS: Approved
B. APPLICANT: Khadija Jamaloodien
C. IMPORTING COMPANY: Equity Pharmaceuticals (Pty) Ltd
D. PATIENT/(S):
E. UNREGISTERED MEDICINES:

GENERIC NAME: Streptokinase

TRADE NAME: STPASE 1500000IU

F. QUANTITY: Streptokinase 1.5MU
Injection x 680 vials

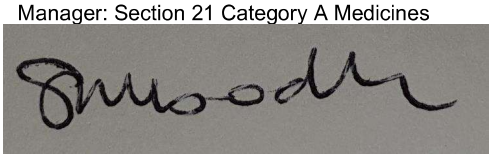
G. LETTER NUMBER: B-30657

Section 21 authorization letters are valid for a period of six months from the letter date, unless otherwise specified.

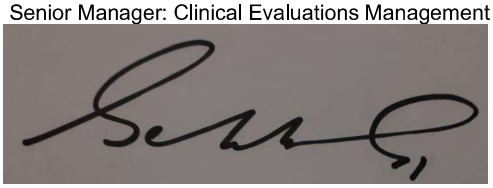
Comments:

Yours faithfully,

Dr S Munbodh
Manager: Section 21 Category A Medicines



T Sehloho
Senior Manager: Clinical Evaluations Management



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REQUEST FOR QUOTATION FORM

- **Instruction to complete this Request for Quotation (RFQ)**
  PLEASE PROVIDE A QUOTE FOR THE FOLLOWING PRODUCT(S).
  PLEASE QUOTE ON THIS RFQ FORM AND ATTACH YOUR QUOTE WITH THE REQUESTED DETAILS.
  THE SECTIONS HIGHLIGHTED IN YELLOW MUST BE COMPLETED BY THE SUPPLIER.
- **THIS DOES NOT CONSTITUTE ANY OBLIGATION TO PROCURE THE ITEM AS THIS WILL BE SUBMITTED FOR CONSIDERATION TO PROVINCIAL PROCUREMENT UNITS TO SERVE AS A BUY OUT AGAINST CURRENT NON-COMPLIANT SUPPLIERS.**

ONLY RESPONSES FROM DULY REGISTERED SUPPLIERS WILL BE EVALUATED

REFERENCE NUMBER:	NORMAL		SECTION 21	X	**S21RFQ138**
QUOTE ENQUIRY DATE	**19/08/2024**	QUOTE CLOSING DATE			**28/08/2024**
FOR CRITICAL DELIVERY, DELIVERY REQUESTED ON/BEFORE *(SCM Practitioner to Specify if applicable)*					

REQUESTING INSTITUTION CONTACT DETAILS

NAME OF REQUESTOR	Buhle Mbongo		
EMAIL ADDRESS	Buhle.Mbongo@health.gov.za		
PHONE No.	**012 395 9539**	FAX No.	**N/A**

PRODUCT INFORMATION

DESCRIPTION PER MPC	**Streptokinase 1.5MU Injection**		
TRADE DESCRIPTION	STPASE 1500000IU		
UNIT OF MEASURE	**1's**	PACK or BOX (*SIZE/ QUANTITY*)	**1's**
QUANTITY REQUIRED	**680 Vials/Ampoules**		

TO BE COMPLETED BY THE SUPPLIER/ SERVICE PROVIDER

SUPPLIER CONTACT DETAILS (as per CSD)

COMPANY NAME	Equity Pharmaceuticals (Pty) Ltd			
SUPPLIER NUMBER	MAAA007480			
SECURITY CODE				
SUPPLIER CODE (NDoH)				
CONTACT PERSON 1	NAME	**Ehrard van Zyl**		
	PHONE	**012 345 1747**	FAX	**012 345 1412**
	MOBILE	*072 040 8511*		
	E-MAIL	**ehrard@equitypharma.co.za**		
CONTACT PERSON 2	NAME	**Jaco Schoeman**		
	PHONE	**012 345 1747**		

	MOBILE	*076 734 0080*	
	E-MAIL	**jacos@equitypharma.co.za**	
QUOTE DETAILS			
PRICE PER UNIT (INCL. VAT)	R 476.10	TOTAL PRICE (INCL. DELIVERY & VAT)	R 323 747.00
VOLUMES AVAILABLE – 14DAYS	680		
VOLUMES AVAILABLE – 28DAYS			
VOLUMES AVAILABLE – 56DAYS			
VOLUMES AVAILABLE – 112DAYS			
QUOTE VALIDITY PERIOD	180 days		
NORMAL LEAD/DELIVERY TIME	3 days		
DEVIATION TO SPECIFICATION			
COMMENTS:			
DECLARATION BY SUPPLIER			
I hereby declare that in submitting this bid, there has been no consultation, communication, agreement or arrangement with any competitor/supplier regarding the price, quality, quantity, specifications and conditions or delivery particulars of the products or services to which this bid invitation relates.			
NAME	**Ehrard van Zyl**		
CAPACITY	**Business Unit Manager: Specialist Medicine**		
SIGNATURE *(OF A DULY AUTHORISED REPRESENTATIVE OF THE SUPPLIER)*			
DATE	**28/08/2024**		
Please submit quotations to Section21Quotes@health.gov.za			

Please ensure that you include the following as part of the Quotation:

- Delivery Time (Weeks)
- Price (Vat Inclusive)
- Generic Name
- Trade Name
- Central Supplier Database Summary Report (CSD)
- Medicine Registration Certificate (Only for Locally Registered Products)
- *Artwork/Labelling
- *Package Insert: (Please attach)
- *Manufacturer Certificate: (Please attach)
- *Country of Origin: (Please indicate)

*Additional items required when submitting a quote for a Section 21 Item (Unregistered Medicine)

All of the above is required to expedite the process in considering the quotation.

Please ***SUBMIT COMPLETED RFQ FORM AND QUOTATIONS ON AN OFFICIAL COMPANY LETTERHEAD***

***NB*:**

- The size of each individual attachment must not be more than 2MB (you may attach multiple files in one email but collectively they should not be more than 2MB in size).
- Please ensure that you provide all prescribed documentation that is outlined on page two of this RFQ.
- Kindly be advised that a picture format of an Artwork shall not be accepted. Artwork must be in pdf or word format only.
- All prices must please be submitted in two decimals.
- If submitting more than one quotation, please make sure that your subject line includes e.g., 1 of 2 or 1 of 3 etc.
- Any submission with missing documentation shall not be considered.
- Any submission with blurry relevant documents shall not be considered.
- The only electronic GMP Certificate considered is that from EUDRA.
- ***Email subject line for responses with quotes must be kept unchanged from the originally sent RFQ email.**

Please ***SUBMIT COMPLETED RFQ FORM AND QUOTATIONS ON AN OFFICIAL COMPANY LETTERHEAD***

28/08/2024

Equity Pharmaceuticals (Pty) Ltd.
1997/009942/07

+27 12 345 1747
+27 12 345 1412
equity@equitypharma.co.za

www.clinigengroup.com
www.equitypharma.co.za

QUOTATION # 20240828

TO: National Department of Health

TEL: 012 395 9539
FAX:
Email: Section21Quotes@health.gov.za

CONTACT PERSON / PATIENT: Buhle Mbongo

NB IMPORTED AND SUPPLIED UNDER SECTION 21 TERMS

PRODUCT CODE	DESCRIPTION	PACK SIZE	QUANTITY	PRICE EXCL	TOTAL INCL
	STPASE (Streptokinase) 1500000 IU	1's	1	R 414.00	R 476.10
			680	**R 281 520.00**	**R 323 748.00**
			680	**R 281 520.00**	**R 323 748.00**

Valid for 180 days

Employee Signature: _____

Date: 28/08/2024

Approved by: Ehrard van Zyl / Carel Bouwer

28/08/2024

Equity Pharmaceuticals (Pty) Ltd.
1997/009942/07

+27 12 345 1747
+27 12 345 1412
equity@equitypharma.co.za

www.clinigengroup.com
www.equitypharma.co.za

National Department of Health

Directorate: Affordable Medicines

E-mail: Section21Quotes@health.gov.za

Attention: Ms Buhle Mbongo

Dear Ms Mbongo

Re: Request for quotation – Streptokinase 1500000IU – Section 21 Supply

Trust you are well. Please find below our quotation for *Streptokinase* supplied under section 21 terms.

- Quantity: **680 vials**
- Delivery Time (Weeks): **1 week**
- Price (Vat Inclusive): **R 476.10**
- Generic Name: **Streptokinase**
- Trade Name: **STPASE 1500000IU**
- Packaging: **1 vial (10ml)**
- Specifications: **1500000IU**
- Shelf Life: **24 months**
- Package Insert: **Please find attached**
- Manufacturer: **Cadila Pharmaceuticals Ltd**
- Country of Origin: **India**

Please note that the immediate availability of the product is conditioned on the manufacturer receiving notice of our order as soon as possible. Unfortunately, the stock cannot be reserved for our purposes for too long.

We look forward to your response.

Please contact me if you require any additional information.

Kind Regards

Ehrard van Zyl

These ranged in severity from minor breathing difficulty to bronchospasm, periorbital swelling or angioneurotic edema.

Fever: Although streptokinase is nonpyrogenic in standard animal tests, approximately 33% of patients treated with streptokinase have shown increases in body temperature of >0.83°C. Symptomatic treatment is usually sufficient to alleviate discomfort.

Symptoms And Treatment Of Overdose:
Minor bleeding complications with streptokinase are usually overcome by decreasing the dosage. Should serious uncontrollable bleeding occur as a result of overdosage, the infusion of streptokinase and any other concomitant anticoagulant should be discontinued immediately. If necessary, blood loss and reversal of the bleeding tendency can be effectively managed with whole blood (fresh blood preferable), packed red cells and cryoprecipitate or fresh frozen plasma.

Dosage And Administration:
Streptokinase should be administered by volumetric infusion pump. Do not use drop-counting infusion methods since streptokinase may alter droplet size.

Acute Myocardial Infarction: Streptokinase treatment of coronary thrombosis should be instituted as soon as possible after the onset of symptoms of acute myocardial infarction. The greatest benefit in mortality reduction was observed when streptokinase was administered within 4 hours, but statistically significant benefit has been reported when administered up to 24 hours .

I.V. Administration: With the above regimen, 1 500 000 IU within 60 minutes, no coagulation tests are necessary to monitor streptokinase therapy. Unless contraindicated, the concomitant use of ASA at a dose of 160 mg/day orally, starting prior to streptokinase infusion and continued for 1 month is recommended.

Deep Vein Thrombosis, Pulmonary or Arterial Embolism or Arterial Thrombosis: Streptokinase treatment should be instituted as soon as possible after onset of thrombotic event, preferably within 7 days. Any delay in instituting lytic therapy to evaluate the effect of heparin therapy decreases the potential for optimal efficacy, although slight enhancement of clot lysis has been shown with initiation of thrombolytic therapy up to 2 weeks after the onset of symptoms of deep vein thrombosis.

Directions for Preparation of the solution :
STPase should be reconstituted by adding 5 ml Water for Injections or isotonic saline to a 750000 IU or 1500000 IU vial. For dissolution gently swirl the vial. Avoid shaking to prevent foaming. The concentrated solution must not be injected undiluted.

The reconstituted solution is transferred to an infusion bottle or a PVC bag containing either isotonic saline or dextrose 5%. The diluted solution is intended for intravenous or intracoronary administration.

Presentation : Flint Vial of 10 ml

Storage : Store between 2°C to 8°C. Protect from light.

"Based on Technology developed by
IMTECH, Chandigarh, India.
A Constituent Establishment of CSIR"

Manufactured by :
CADILA

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

STREPTOKINASE INJECTION IP

(Fibrinolytic Agent)

STPase

STPase 1500000 IU
Each vial contains
Streptokinase IP 1500000 IU

STPase 750000 IU
Each vial contains
Streptokinase IP 750000 IU

Clinical Pharmacology:
Streptokinase acts with plasminogen (or plasmin) to produce an "activator complex" that converts residual plasminogen into the proteolytic enzyme, plasmin. Plasmin is capable of hydrolysing fibrin into polypeptides; it also hydrolyses fibrinogen and other plasma proteins. Since plasminogen is present in the thrombus/embolus, activation by streptokinase occurs within the thrombus/embolus as well as on its surface. The activity of streptokinase is expressed in International Units (IU) and is a measure of its ability to cause lysis of a fibrin clot via the plasmin system in vitro. The effect on coagulation after i.v. administration may persist for 12 to 24 hours after discontinuation due to a decrease in plasma levels of fibrinogen and an increase in the amount of circulating fibrin(ogen) degradation products (FDP).

Indications And Clinical Uses:
Acute Myocardial Infarction: For use in the management of suspected acute myocardial infarction, for the lysis of acute thrombi obstructing coronary arteries associated with evolving transmural myocardial infarction, for the improvement of ventricular function, and for the reduction of infarct size and mortality associated with acute myocardial infarction, when administered by the i.v. or intracoronary route, as well as for the reduction of congestive heart failure associated with AMI when administered by the i.v. route.
Thrombolysis following i.v. streptokinase is usually achieved within less than 1 hour. Early administration is correlated with greater clinical benefit.

Pulmonary Embolism:
In adults for the lysis of acute massive pulmonary emboli, defined as obstruction or significant filling defects involving 2 or more lobar pulmonary arteries or an equivalent amount of emboli in other vessels. It is also indicated for embolization accompanied by unstable hemodynamics i.e., failure to maintain blood pressure without supportive measures. The diagnosis should be confirmed by objective means, preferably by pulmonary arteriography via an upper extremity vein, or non-invasive procedures such as lung scanning.

Deep Vein Thrombosis:
For lysis of acute, extensive thrombi of the deep veins in adults such as those involving the popliteal and more proximal vessels. Diagnosis should be confirmed by ascending venography or other equally objective methods. Studies have demonstrated a better salvage of valvular function and prevention of postphlebitic syndrome by the combined usage of streptokinase and heparin than by heparin alone.

Arterial Thrombosis and Embolism:
For the lysis of acute arterial thrombi and for the lysis of arterial emboli. However, the use of streptokinase in arterial emboli originating from the left side of the heart (e.g. in mitral stenosis accompanied by atrial fibrillation) should be avoided due to the danger of new embolic phenomena including those to cerebral vessels.

Arteriovenous Cannula Occlusion:
For clearing of totally or partially occluded arteriovenous cannulae as an alternative to surgical intervention when acceptable flow cannot otherwise be achieved.

Contraindications:
Because thrombolytic therapy increases the risk of bleeding, streptokinase is contraindicated in the following conditions: active internal bleeding; recent (within 2 months) cerebrovascular accident, intracranial or intraspinal surgery

(see Warnings); intracranial neoplasm; severe uncontrollable hypertension; uncontrollable clotting disorders.

Streptokinase should not be administered to patients having experienced severe allergic reaction to the product.

Warnings : Bleeding:

The aim of streptokinase therapy is the production of sufficient amounts of plasmin for the lysis of intravascular deposits of fibrin; however, fibrin deposits which provide hemostasis, for example at sites of needle punctures, are also lysed and bleeding from such sites may occur.

Following i.v. high-dose brief-duration streptokinase therapy (1,500,000 IU over 60 minutes), in acute myocardial infarction, severe bleeding complications requiring transfusion are extremely rare (0.3 to 0.5%), and combined therapy with low-dose ASA (160 mg/day over a period of 1 month) does not appear to increase the risk of major bleeding. The addition of ASA to streptokinase may cause a slight increase in the risk of minor bleeding (3.1% without ASA vs 3.9% with ASA).

I.M. injections and nonessential handling of the patient must be avoided during treatment with streptokinase. Venipunctures should be performed carefully and as infrequently as possible.

Should an arterial puncture be necessary, 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. When internal bleeding occurs, it may be more difficult to manage than that which occurs with conventional anticoagulant therapy.

Arrhythmias:

Rapid lysis of coronary thrombi may cause reperfusion atrial or ventricular dysrhythmia requiring immediate treatment. Careful monitoring for arrhythmia should be maintained during and immediately following administration of streptokinase.

Hypotension :

Hypotension, sometimes severe, not secondary to bleeding or anaphylaxis has been observed during i.v. streptokinase infusion in 1 to 10% of patients. Patients should be monitored closely and should symptomatic or alarming hypotension occur, appropriate treatment should be administered. This treatment may include a decrease in the i.v. streptokinase infusion rate. Smaller hypotensive effects are common and have not required treatment.

Precautions : General :

Streptokinase should be used in hospitals where the recommended diagnostic and monitoring techniques are available.

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

Repeated Administration:

Because of the increased likelihood of resistance due to antistreptokinase antibody, streptokinase may not be effective if administered between 5 days and 6 months of a prior streptokinase administration or streptococcal infection (e.g., streptococcal pharyngitis, acute rheumatic fever or acute glomerulonephritis secondary to a streptococcal infection).

Pregnancy:

Experience in pregnant women has not shown that streptokinase increases the risk of fetal abnormalities if administered during pregnancy. If this drug is used during pregnancy, the possibility of fetal harm appears remote. Because studies cannot rule out the possibility of harm, however, streptokinase should be used during pregnancy only if clearly needed.

Children:

Safety and effectiveness in children have not been established.

Lactation:

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

Drug Interactions:

The potential for an additive hypotensive effect should be borne in mind when streptokinase therapy is combined with

There is an increased risk of hemorrhage in:

Patients previously receiving heparin or coumarin derivatives.

The effect of heparin can, however, be rapidly neutralized by administering protamine sulfate. In the case of prior treatment with coumarin derivatives, the Quick value must be more than 50% before the beginning of lysis.

Patients receiving simultaneous treatment with platelet-aggregation inhibitors, e.g., ASA (see below also), phenylbutazone, dipyridamole and nonsteroidal anti-inflammatory drugs (NSAIDS).

Patients receiving simultaneous or previous treatment with dextrans.

Combination of Streptokinase with ASA for Treatment of Myocardial Infarction:

In the treatment of acute myocardial infarction with i.v. streptokinase (1 500 000 IU over 1 hour) combined with enteric-coated ASA (160 mg/day for 1 month), it was shown that the combined treatment results in a further reduction in mortality rate, as well as a decreased risk of reinfarction and stroke in comparison to treatment with each of the drugs alone. The addition of ASA to streptokinase may cause a slight increase in the risk of minor bleeding, but does not appear to increase the incidence of major bleeding. Unless contraindicated, concomitant administration of ASA is recommended.

Anticoagulation Treatment Following Streptokinase:

Anticoagulation Following Treatment for Myocardial Infarction: The use of anticoagulants following administration of streptokinase treatment for acute myocardial infarction increases the risk of bleeding, and has not been shown to be of unequivocal clinical benefit. Therefore, their use should be decided upon at the discretion of the treating physician.

Patient Monitoring:

I.V. or Intracoronary Artery Infusion for Myocardial Infarction: I.V. administration of streptokinase will cause marked decreases in plasminogen and fibrinogen levels and increases in thrombin time (TT), activated partial thromboplastin time (APTT), and prothrombin time (PT), which usually normalize within 12 to 24 hours. These changes may also occur in some patients with intracoronary administration of the drug.

I.V. Infusion for Other Indications:

Before commencing thrombolytic therapy, it is desirable to obtain a thrombin time (TT), activated partial thromboplastin time (APTT), prothrombin time (PT), and hematocrit and platelet count to obtain hemostatic status of the patient.

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 the plasminogen and fibrinogen levels and an increase in the level of FDP (the latter two serving to prolong the clotting times of coagulation tests) will generally confirm the existence of a lytic state. Therefore, therapy can be monitored by performing the TT, or APTT or PT, approximately 4 hours after initiation of therapy.

Adverse Reactions:

The following adverse reactions have been frequently associated with i.v. therapy but may also occur with intracoronary artery infusion.

Bleeding:

The reported incidence of bleeding (major or minor) has varied widely depending on the indication, dose, route and duration of administration and concomitant therapy.

Severe internal bleeding involving gastrointestinal, genitourinary, retroperitoneal or intracerebral sites, may occur. Intracerebral bleeding in connection with the treatment of myocardial infarction has been reported with an incidence of 0.1 to 0.3%.

Several fatalities due to cerebral and other serious internal hemorrhage have occurred during thrombolytic therapy.

In the treatment of acute myocardial infarction with i.v. streptokinase, the GISSI and ISIS-2 studies reported a rate of major bleeding (requiring transfusion) of 0.3 to 0.5%. In the TIMI study, which required both invasive techniques and administration of anticoagulants, a frequency of 15.6% for major bleeding (intracranial, or decrease in hemoglobin>5 g/dl, or decrease in hematocrit>15%) was reported.

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STREPTOKINASE
INJECTION IP

STPase

1500000 IU

"Based on Technology