Summary of Product Characteristics

1. Name of the medicinal product

Streptomycin Sulphate for Injection 1g

2. Qualitative and quantitative composition

Each vial contains Streptomycin Sulphate equivalent to Streptomycin 1g.

3. Pharmaceutical form

Powder for Injection

White or almost white powder

4. Clinical particulars

4.1 Therapeutic indications

Streptomycin is indicated for the treatment of individuals with moderate to severe infections caused bysusceptible strains of microorganisms in the specific conditions listed below:

1.Mycobacterium tuberculosis: The Advisory Council for the Elimination of Tuberculosis, the American Thoracic Society, and the Center for Disease Control recommend that either streptomycin or ethambutol be added as a fourth drug in a regimen containing isoniazid (INH), rifampin and pyrazinamide for initial treatment of tuberculosis unless the likelihood of INH or rifampin resistance is very low. The need for a fourth drug should be reassessed when the results of susceptibility testing are known. In the past when the national rate of primary drug resistance to isoniazid was known to be less than 4% and was either stable or declining, therapy with two and three drug regimens was considered adequate. If community rates of INH resistance are currently less than 4%, an initial treatment regimen with less than four drugs may be considered.

Streptomycin is also indicated for therapy of tuberculosis when one or more of the above drugs is contraindicated because of toxicity or intolerance. The management of tuberculosis has become more complex as a consequence of increasing rates of drug resistance and concomitant HIV infection. Additional consultation from experts in the treatment of tuberculosis may be desirable in those settings.

2.non-tuberculosis infections: The use of streptomycin should be limited to the treatment of infections caused by bacteria which have been shown to be susceptible to the antibacterial effects of streptomycin and which are not amenable to therapy with less potentially toxic agents.

a. Pasteurella pestis (plague),

b. Francisella tularensis (tularemia),

c. Brucella,

d. Calymmatobacterium granulomatis (donovanosis, granuloma inguinale),

e. H. ducreyi (chancroid),

f. H. influenzae (in respiratory, endocardial, and meningeal infections - concomitantly with another antibacterial agent),

g. K. pneumoniae pneumonia (concomitantly with another antibacterial agent),

h. E.coli, Proteus, A. aerogenes, K. pneumoniae, and Enterococcus faecalis in urinary tract infections,

i. Streptococcus viridans, Enterococcus faecalis (in endocardial infections - concomitantly with penicillin),

j. Gram-negative bacillary bacteremia (concomitantly with another antibacterial agent).

To reduce the development of drug-resistant bacteria and maintain the effectiveness of streptomycin and other antibacterial drugs, streptomycin should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

4.2 Posology and method of administration

Intramuscular Route Only

Adults: The preferred site is the upper outer quadrant of the buttock, (i.e., gluteus maximus), or the mid-lateral thigh.

Children: It is recommended that intramuscular injections be given preferably in the mid-lateral muscles of the thigh. In infants and small children the periphery of the upper outer quadrant of the gluteal region should be used only when necessary, such as in burn patients, in order to minimize the possibility of damage to the sciatic nerve.

The deltoid area should be used only if well developed such as in certain adults and older children, and then only with caution to avoid radial nerve injury. Intramuscular injections should not be made into the lower and mid-third of the upper arm. As with all intramuscular injections, aspiration is necessary to help avoid inadvertent injection into a blood vessel.

Injection sites should be alternated. As higher doses or more prolonged therapy with streptomycin may be indicated for more severe or fulminating infections (endocarditis, meningitis, etc.), the physician should always take adequate measures to be immediately aware of any toxic signs or symptoms occurring in the patient as a result of streptomycin therapy.

1. TUBERCULOSIS: The standard regimen for the treatment of drug susceptible tuberculosis has been two months of INH, rifampin and pyrazinamide followed by four months of INH and

rifampin(patients with concomitant infection with tuberculosis and HIV may require treatment for a longer period).When streptomycin is added to this regimen because of suspected or proven drug resistance (see INDICATIONS AND USAGE section), the recommended dosing for streptomycin is as follows:

	Daily	Twice Weekly	Thrice Weekly
Children	20-40mg/kg Max 1 g	25-30 mg/kg Max 1.5 g	25-30 mg/kg Max 1.5 g
Adults	15 mg/kg Max 1 g	25-30 mg/kg Max 1.5 g	25-30 mg/kg Max 1.5 g

Streptomycin is usually administered daily as a single intramuscular injection. A total dose of not more than 120 g over the course of therapy should be given unless there are no other therapeutic options. In patients older than 60 years of age the drug should be used at a reduced dosage due to the risk of increased toxicity. Therapy with streptomycin may be terminated when toxic symptoms have appeared, when impending toxicity is feared, when organisms become resistant, or when full treatment effect has been obtained. The total period of drug treatment of tuberculosis is a minimum of 1 year; however, indications for terminating therapy with streptomycin may occur at any time as noted above.

2. TULAREMIA: One to 2 g daily in divided doses for 7 to 14 days until the patient is afebrile for 5 to 7 days.

3. PLAGUE: Two grams of streptomycin daily in two divided doses should be administered intramuscularly. A minimum of 10 days of therapy is recommended.

4. BACTERIAL ENDOCARDITIS:

Streptococcal endocarditis; in penicillin-sensitive alpha and non-hemolytic streptococcal endocarditis (penicillin MIC≤0.1 mcg/mL), streptomycin may be used for 2- week treatment concomitantly with penicillin. The streptomycin regimen is 1 g b.i.d. for the first week, and 500 mg b.i.d. for the second week. If the patient is over 60 years of age, the dosage should be 500 mg b.i.d. for the entire 2-week period.

b.Enterococcal endocarditis: Streptomycin in doses of 1 g b.i.d. for 2 weeks and 500mg b.i.d. for an additional 4 weeks is given in combination with penicillin. Ototoxicity may require termination of the streptomycin prior to completion of the 6-week course of treatment.

5.CONCOMITANT USE WITH OTHER AGENTS:

For concomitant use with other agents to which the infecting organism is also sensitive: Streptomycin is considered a second-line agent for the treatment of gram-negative bacillary bacteremia, meningitis, and pneumonia; brucellosis; granuloma inguinale; chancroid, and urinary tract infection.

For adults: 1 to 2 grams in divided doses every six to twelve hours for moderate to severe infections.

Doses should generally not exceed 2 grams per day.

For children: 20 to 40 mg/kg/day (8 to 20 mg/lb/day) in divided doses every 6 to 12 hours. (Particular care should be taken to avoid excessive dosage in children.)

4.3 Contraindications

A history of clinically significant hypersensitivity to streptomycin is a contraindication to its use. Clinically significant hypersensitivity to other aminoglycosides may contraindicate the use of streptomycin because of the known cross-sensitivity of patients to drugs in this class.

4.4 Special warnings and precautions for use

Ototoxicity: Both vestibular and auditory dysfunction can follow the administration of streptomycin. The degree of impairment is directly proportional to the dose and duration of streptomycin administration to the age of the patient, to the level of renal function and to the amount of underlying existing auditory dysfunction. The ototoxic effects of the aminoglycosides, including streptomycin, are potentiated by the co-administration of ethacrynic acid, mannitol, furosemide and possibly other diuretics.

The vestibulo-toxic potential of streptomycin exceeds that of its capacity for cochlear toxicity.

Vestibular damage is heralded by headache, nausea, vomiting and disequilibrium. Early cochlear injury is demonstrated by the loss of high frequency hearing. Appropriate monitoring and early discontinuation of the drug may permit recovery prior to irreversible damage to the sensorineural cells.

Pregnancy: Streptomycin can cause fetal harm when administered to a pregnant woman. Because streptomycin readily crosses the placental barrier, caution in use of the drug is important to prevent ototoxicity in the fetus. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus.

Precautions

General: Prescribing streptomycin in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Baseline and periodic caloric stimulation tests and audiometric tests are advisable with extended streptomycin therapy. Tinnitus, roaring noises, or a sense of fullness in the ears indicates need for audiometric examination or termination of streptomycin therapy or both.

Care should be taken by individuals handling Streptomycin for Injection to avoid skin sensitivity reactions. As with all intramuscular preparations, Streptomycin for Injection should be injected well within the body of a relatively large muscle and care should be taken to minimize the possibility of damage to

peripheral nerves. (See **DOSAGE AND ADMINISTRATION**.)

Extreme caution must be exercised in selecting a dosage regimen in the presence of preexisting renal insufficiency. In severely uremic patients a single dose may produce high blood levels for several days and the cumulative effect may produce ototoxic sequelae. When streptomycin must be given for prolonged periods of time alkalinization of the urine may minimize or prevent renal irritation.

A syndrome of apparent central nervous system depression, characterized by stupor and flaccidity, occasionally coma and deep respiratory depression, has been reported in very young infants in whom streptomycin dosage had exceeded the recommended limits.

Thus, infants should not receive streptomycin in excess of the recommended dosage.

In the treatment of venereal infections such as granuloma inguinale, and chancroid, if concomitant syphilis is suspected, suitable laboratory procedures such as a dark field examination should be performed before the start of treatment, and monthly serologic tests should be done for at least four months.

As with other antibiotics, use of this drug may result in overgrowth of non-susceptible organisms, including fungi. If superinfection occurs, appropriate therapy should be instituted.

Information for Patients: Patients should be counseled that antibacterial drugs including streptomycin should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold).When streptomycin is prescribed to treat a bacterial infection, patients should be told that although it is common to feel better early in the course of therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may (1) decrease the effectiveness of the immediate treatment and (2) increase the likelihood that bacteria will develop resistance and will not be treatable by streptomycin or other antibacterial drugs in the future.

4.5 Interaction with other medicinal products and other forms of interaction

Drug Interactions: The ototoxic effects of the aminoglycosides, including streptomycin, are potentiated by the co-administration of ethacrynic acid, furosemide, mannitol and possibly other diuretics.

4.6 Pregnancy and lactation

Pregnancy: Category D: See WARNINGS section.

Nursing Mothers: Because of the potential for serious adverse reactions in nursing infants from streptomycin, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

The following reactions are common: vestibular ototoxicity (nausea, vomiting, and vertigo); paresthesia of face; rash; fever; urticaria; angioneurotic edema; and eosinophilia.

The following reactions are less frequent: cochlear ototoxicity (deafness); exfoliative dermatitis; anaphylaxis; azotemia; leucopenia; thrombocytopenia; pancytopenia; hemolytic anemia; muscular weakness; and amblyopia.

Vestibular dysfunction resulting from the parenteral administration of streptomycin is cumulatively related to the total daily dose. When 1.8 to 2 g/day are given, symptoms are likely to develop in the large percentage of patients - especially in the elderly or patients with impaired renal function - within four weeks. Therefore, it is recommended that caloric and audiometric tests be done prior to, during, and following intensive therapy with streptomycin in order to facilitate detection of any vestibular dysfunction and/or impairment of hearing which may occur.

Vestibular symptoms generally appear early and usually are reversible with early detection and cessation of streptomycin administration. Two to three months after stopping the drug, gross vestibular symptoms usually disappear, except from the relative inability to walk in total darkness or on very rough terrain.

Although streptomycin is the least nephrotoxic of the aminoglycosides, nephrotoxicity does occur rarely.

Clinical judgment as to termination of therapy must be exercised when side effects occur

Reporting of suspected adverse reactions

Healthcare professionals are requested to report any suspected adverse reactions via pharmacy and poisons board, pharmacovigilance electronic reporting system, PVERs- https://pv.pharmacyboardkenya.org.

4.9 Overdose

Due to the lack of a specific antagonist, when this product is used in excess or toxicity reaction occurs, the main methods of treatment are symptomatic and supportive therapy, in the interim the patient should drink plenty of water. Hemodialysis or peritoneal dialysis facilitates to clear streptomycin from the blood.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Aminoglycoside antibacterial

ATC code: J01GA01

Streptomycin is an aminoglycoside antibiotic, and has a strong effect on mycobacterium tuberculosis, the

MIC is generally 0.5 μg/mL. Non M. tuberculosis bacteria is resistant to the product. It shows antibacterial activity against Gram-negative bacillus such as Escherichia coli, Klebsiella, Proteus mirabilis, Enterobacter, Salmonella, Shigella, Brucella, Pasteurellaceae etc. Neisseria meningitidis and Neisseria gonorrhoeae are hypersensitive to this product. Streptomycin has negligible anti-bacterial effects on the Staphylococcus and other Gram-positive bacillus. Streptococcus, Pseudomonas aeruginosa and anaerobic bacillus are resistant to this product.

Streptomycin inhibits protein synthesis by binding to 30S ribosomal subunits. The bacteria readily generate resistance when exposed to streptomycin. Use of streptomycin in conjunction with other antibacterial products or anti-tubercle bacillus drug may reduce or postpone generation of the resistance.

5.2 Pharmacokinetic properties

Absorption well after intramuscular injection. It distributes mainly through extracellular fluid, and appreciable concentrations are found in all organ tissues. The quantity found in cerebrospinal fluid, brain tissues and bronchus secreting fluid is less, while significant amounts have been found in bile, pleural fluid, ascites, tuberculous cavities and caseous tissue. Streptomycin can penetrate embryo tissue through the placenta. Protein binding rate is 20%~30%. The plasma elimination half-life (t1/2β) is 2.4~2.7 hours, it may be prolonged significantly if the kidney function declines. The product is not metabolized in the body, and excreted mainly by glomerular filtration. 80-98% of this product is excreted in the urine within 24 hours, about 1% is excreted in bile, and a little is excreted in the latex, saliva and sweat. Hemodialysis can clear considerable amounts of this product from the body.

5.3 Preclinical safety data

Not reported.

6. Pharmaceutical particulars

6.1 List of excipients

Not applicable

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Three years.

6.4 Special precautions for storage

Store below 30°C.

Do not freeze. Protect from light.

KEEP OUT OF REACH OF CHILDREN.

7.Marketing authorization holder

Name: Crown Healthcare

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Manufactured by:

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8. Marketing authorization number(s)- 2016/CTD4801/895

9. Date of first authorization/renewal of the authorization-16 Feb 2017

10. Date of revision of the test-02 March 2026