175mm

123mm

concurrently with aminoglycosides during surgery or in the postoperative period)

Nephrotoxic medications, other or Ototoxic medications,

(concurrent or sequential use of these medications with aminoglycosides may increase the potential for ototoxicity or nephrotoxity; hearing loss may occur and may progress to deafness even after discontinuation of the drug and may be reversible, but usually is permanent; serial audiometric function determinations may be required; renal function determinations may be required).

(vancomycin and aminoglycosides must often be administered concurrently in the prophylaxis of bacterial endocarditis, in the treatment of endocarditis caused by streptococci and *Corynebacteria* species, in the treatment of resistant staphylococcal infections, or in penicillin-allergic patients; appropriate monitoring will help to reduce the risk of nephrotoxicity or ototoxicity; renal function determinations, serum aminoglycoside and vancomycin concentrations, dosage reductions, and/or dosage interval adjustments, or alternate antibacterials, may be required)

Neuromuscular blocking agents or medications with neuromuscular blocking activity, other

(concurrent use of medications with neuromuscular blocking activity, including halogenated hydrocarbon inhalation anesthetics, opioid analgesics, and massive transfusions with citrate anticoagulated blood, with aminoglycosides should be carefully monitored since neuromuscular blockade may be enhanced; caution is recommended when these medications and aminoglycosides are used concurrently during surgery or in the postoperative period, especially if there is a possibility of incomplete reversal of neuromuscular blockade postoperatively ; treatment with anticholinesterase agents or calcium salt may help reverse the blockade).

RECOMMENDED DOSAGE, DOSAGE SCHEDULE AND ROUTE OF ADMINISTRATION:

Usual adult and adolescent dose

Tuberculosis:

Intramuscular – In combination with other antimycobacterials, 1 gram (base) once a day. Dosage should be reduced to 1 gram two or three times a week as soon as clinically feasible.

Other infections:

Intramuscular – In combination with other antibacterials, 250 mg to 1 gram (base) every six hours; or 500 mg to 2 grams every twelve hours.

Note: Plague – Intramuscular: 500 mg to 1 gram (base) every six hours; or 1 to 2 grams every twelve hours.

Tularemia – Intramuscular: 250 to 500 mg (base) every six hours; or 500 mg to 2 grams every twelve hours for seven to ten days.

Usual adult prescribing limits:

Tuberculosis – 1 gram twice weekly to 2 grams (base) daily.

Other infections – Up to 4 grams (base) daily.

Usual pediatric dose

Tuberculosis:

Intramuscular – In combination with other antimycobacterials, 20 mg (base) per kg of body weight once a day. Maximum dose per day should not exceed 1 gram.

Other infections:

Intramuscular – In combination with other antibacterials, 5 to 10 mg (base) per kg of body weight every six hours; or 10 to 20 mg per kg of body weight every twelve hours.

Usual geriatric dose

Tuberculosis:

Intramuscular – In combination with other antimycobacterials; 500 to 740 mg (base) once a day.

Preparation of dosage form

For 1 g: To prepare initial dilution for intramuscular use, add 4.2 to 4.5 mL of 0.9% sodium chloride injection or sterile water for injection to each 1-gram vial, to provide a concentration of 200 mg (base)per mL or 3.2 to 3.5 mL of diluent to provide a concentration of 250 mg per mL.

SYMPTOMS AND TREATMENT FOR OVERDOSE AND ANTIDOTE(S):

Acute overdosage

Acute haemolytic anaemia and renal failure were reported in a 45-year-old man after he injected himself with streptomycin and ampicillin. He had been injecting himself repeatedly with streptomycin for a period of 15 years.

Specific treatment

Hemodialysis or peritoneal dialysis to remove aminoglycosides from the blood of patients with impaired renal function.

Anticholinesterase agents, calcium salts, or mechanical respiratory assistance to treat neuromuscular weakness and respiratory depression or paralysis (apnea),that may occur when two or more aminoglycosides are given concurrently.

Supportive care – Since there is no specific antidote, treatment of aminoglycoside overdose or toxic reactions should be symptomatic and supportive. Patients in whom intentional overdose is known or suspected should be referred for psychiatric consultation.

PACKING / PACK SIZES:

For 1 g: 1.36 g powder in transparent vial; 10, 25 and 50 vials in a carton.

STORAGE CONDITIONS, USER INSTRUCTIONS AND PHARMACEUTICAL PRECAUTIONS:

Store the powder below 30°C for 1gm . Protect from light. After reconstitution, the solution can be kept for up to 1 day in a cool place (below 30°C). Protect from light and freezing.

SHELF LIFE:

1 gm: 4 Years

MANUFACTURER AND PRODUCT REGISTRATION HOLDER:

SM PHARMACEUTICALS SDN BHD (218620-M)
Lot 88, Sungai Petani Industrial Estate
08000 Sungai Petani,
Kedah Darul Aman,
Malaysia.

12.10.2023

SM PHARMACEUTICALS SDN. BHD.

STREPTIN INJECTION 1 G

DESCRIPTION:

A white to pale yellow, odourless, sterile powder.

COMPOSITION:

Streptomycin Sulfate Sterile equivalent to Streptomycin 1 g.

ACTIONS AND MODE OR MECHANISMS OF ACTION:

Streptomycin is an aminoglycoside antibiotic which is particularly active against *mycobacterium tuberculosis* as well as against many Gram-negative bacteria, including *Yersinia, Brucella,* and *Francisella,* but not against *Pseudomonas aeruginosa.*

Like other aminoglycosides, streptomycin is actively transported across the bacterial cell membrane, irreversibly binds to one or more specific receptor proteins on the 30 S subunit of bacterial ribosomes, and interferes with an initiation complex between messenger RNA (mRNA) and the 30 S subunit. DNA may be misread, thus producing non-functional proteins; polyribosomes are split apart and are unable to synthesize protein. This results in accelerated aminoglycoside transport, increasing the disruption of bacterial cytoplasmic membranes, and eventual cell death.

Streptomycin is most active in an alkaline medium.

Note: Aminoglycosides are bactericidal, white most other antibiotics that interfere with protein synthesis are bacteriostatic.

PHARMACOLOGY (SUMMARY OF PHARMACODYNAMICS AND PHARMACOKINETICS):

Absorption

Rapidly and completely absorbed after intramuscular administration.

Distribution

Distributed to extracellular fluid, including serum, abscesses, ascitic, pericardial, pleural, synovial, lymphatic, and peritoneal fluids.

High concentrations found in urine.

Low concentrations found in bile, breast milk, aqueous humor, bronchial secretions, sputum and cerebral spinal fluid (CSF). In adults, does not cross the blood-brain barrier (BBB) in therapeutically adequate concentrations. Small improvement in penetration with inflamed meninges. Higher levels are achieved in the CSF of newborns than in adults.

Crosses the placenta.

Also distributed to all body tissues, where aminoglycosides accumulate intracellularly.

High concentrations found in highly perfused organs, such as the liver, lungs, and especially, the kidneys, where aminoglycosides accumulate in the renal cortex.

Lower concentrations are seen in muscle, fat and bone.

Protein binding

About one-third of streptomycin in the circulation is bound to plasma proteins.

Biotransformation

Not metabolised.

Half-life

Distribution half-life: 5 to 15 minutes

PM 02052/06-23

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Elimination half-life:
Adults –
Normal renal function: 2 to 4 hours
Impaired renal function: Varies with degree of dysfunction; up to 100 hours.
Cystic fibrosis patients: 1 to 2 hours.
Burn patients and febrile patients: May have a shorter half-life than average due to increased clearance of the drug.
Pediatrics –
Neonates: 5 to 8 hours
Children: 2.5 to 4 hours.
Time to peak concentration
Intramuscular: 0.5 to 2.0 hours.
Intravenous (time to post-distributional peak level): 30 minutes after end of 30-minute infusion, or 15 minutes after end of 1-hour infusion.
Peak serum concentrations
In adults with normal renal function –
Intramuscular – 1 gram: 25 to 50 mcg per mL.
Elimination
Renal; excreted unchanged by the glomerular filtration. 30 to 95% of aminoglycoside dose recovered in urine over 24 hours. Small amount excreted in bile.
Hemodialysis – Each 4 to 6 hour hemodialysis period decreases plasma aminoglycoside concentration by up to 50%.
Peritoneal dialysis – Less effective than hemodialysis. Removes approximately 25% of a dose in 48 to 72 hours.

INDICATIONS:
Tuberculosis, Plague and tularaemia, Bacterial endocarditis (only used in combination with penicillin G or ampicillin), Brucellosis (in conjunction with a tetracycline), Granuloma inguinale

CONTRAINDICATIONS:
Ear disease, pregnant women, myasthenia gravis, patients with a history of hypersensitivity to the ingredient of streptomycin sulfate, aminoglycoside antibiotics or bacitracin and impaired renal function.

SIDE EFFECTS / ADVERSE REACTIONS:
Clinically Significant: 8th Nerve Disorders: Damage to the 8th nerve, causing such symptoms as hearing loss, tinnitus and vertigo (mainly vestibular dysfunction) may occur; therefore, sufficient observation should be performed. It is advisable to discontinue administration if these symptoms appear. Particular care should be taken when use of streptomycin is unavoidable.
Acute Renal Failure: Rarely, severe renal disorders, eg acute renal failure may occur, sufficient observation including periodical tests should be made. If abnormalities appear, streptomycin should be stopped and suitable measures should be performed.
Shock: Rarely, shock symptoms occur, sufficient observation is needed. When such symptoms as palpitation, perspiration, chill, headache, general malaise, etc. occur, administration should be discontinued and appropriate treatment should be given.
Mucocutaneo-Ocular Syndrome (Stevens-Johnson Syndrome) and Toxic Epidermal Necrosis (Lyell Syndrome): Rarely, Stevens-Johnson syndrome, and Lyell syndrome may appear. Close observation is therefore needed, and streptomycin should be discontinued and suitable measures should be taken if these symptoms appear.
Interstitial Pneumonia: Rarely, interstitial pneumonia accompanied by fever, coughing, dyspnea, abnormal chest x-ray, eosinophilia, etc. may develop. Close observation should therefore be made, and streptomycin should be discontinued and suitable measures including administration of steroids should be taken if these symptoms appear.
Other Adverse Reactions: Renal: Rarely edema, proteinuria, hematuria and abnormality in electrolytes, eg potassium may occur.
Hepatic: Since hepatic disorders, eg increases in GOT and GPT may infrequently occur, monitor the patient carefully and, if any abnormality is detected, take suitable measures including stopping administration.
Hematologic: Rarely, such haematological disorders as haemolytic anemia and granulocytopenia may develop, sufficient observation including haematological tests, is needed. If any abnormality is seen, administration of streptomycin should be discontinued.
Hypersensitivity: If fever, eruption, etc appears, administration of streptomycin should be discontinued. In cases where re-administration is necessary, eg in the case of tuberculosis, desensitisation should be done.
Dermatologic: Lichen planus-type eruption may appear. Close observation is therefore needed and streptomycin should be discontinued if such symptom appears.
Avitaminosis: Rarely, vitamin K deficiency symptoms (hypoprothrombinemia, hemorrhagic tendency, etc) and vitamin B group deficiency symptoms (glossitis, stomatitis, anorexia, neuritis, etc) may occur.
Others: Such symptoms as numbness of the lips and formication may develop

PRECAUTIONS / WARNINGS:
Breast milk.
The drug enters breast milk but not in sufficient quantities to harm the infant, but the risk of possible sensitisation should be remembered.
Children
The drug may be given to children in appropriate doses. CNS depression, characterized by stupor, flaccidity, coma, or deep respiratory depression, has been reported in very young infants receiving streptomycin at doses that exceeded the maximum recommended amount. However, all aminoglycosides have this potential to cause neuromuscular blockade.
Pregnant women
The drug should be avoided because of the risk of eighth nerve toxicity in the fetus. In addition, streptomycin has been reported to cause total irreversible, bilateral congenital deafness in children whose mothers received aminoglycosides during pregnancy.
The elderly
Streptomycin should be used with caution in the elderly because of the risk of ototoxicity. Also, elderly patients are more likely to have an age-related decrease in renal function. Recommended doses should not be exceeded, and the patient's renal function should be carefully monitored during therapy. Geriatric patients may require smaller daily doses of aminoglycosides in accordance with their increased age, decreased renal function, and possibly, decreased weight.

Concurrent disease
The drug should be avoided in patients with impaired renal function or a normal dose should be given at intervals such that the trough serum concentration does not exceed 4mg/l.
Cross-sensitivity and/or related problems.
Patients hypersensitive to one aminoglycoside may be hypersensitive to other aminoglycosides also.
Pain and tenderness at the site of injection
Patients may experience pain and tenderness at the site of injection

DRUG INTERACTIONS:
Potentially hazardous interactions
Streptomycin is incompatible with acids and alkalis.
Potentially useful interactions
Streptomycin and benzylpenicillin act synergistically against Streptococcus faecalis. They should not be given together unless the preparation is freshly made, because the combination rapidly becomes less active on storage.
The following drug interactions and/or related problems have been selected on the basis of their potential clinical significance.
Note: Combinations containing any of the following medications, depending on the amount present, may also interact with this medication.
Aminoglycosides, two or more concurrently or Capreomycin
(concurrent and/or sequential use of 2 or more aminoglycosides by any route or concurrent use of capreomycin with aminoglycosides should be avoided since the potential for ototoxicity, nephrotoxicity, and neuromuscular blockade may be increased; hearing loss may occur and may progress even after discontinuation of the drug; loss of hearing may be reversible, but usually is permanent; neuromuscular blockade may result in skeletal muscle weakness and respiratory depression or paralysis [apnea] . Also, concurrent use of 2 or more aminoglycosides may result in reduced bacterial uptake of each one since the medications compete for the same uptake mechanism)
Antimyasthenics
(concurrent use of medications with neuromuscular blocking action may antagonize the effect of antimyasthenics on skeletal muscle; temporary dosage adjustments of antimyasthenics may be necessary to control symptoms of myasthenia gravis during and following use of medications with neuromuscular blocking action)
Beta-lactam antibiotics
(aminoglycosides can be inactivated by many beta-lactam antibiotics [cephalosporins, penicillins] *in vitro* and *in vivo* in patients with significant renal failure.
Indomethacin, intravenous
(when aminoglycosides are administered concurrently with intravenous indomethacin in the premature neonate, renal clearance of aminoglycosides may be decreased, leading to increased plasma concentrations, elimination half-lives, and risk of aminoglycoside toxicity; dosage adjustment of aminoglycosides based on measurement of plasma concentrations and/or evidence of toxicity may also be required).
Methoxyflurane or Polymyxins, parenteral
(concurrent and/or sequential use of these medications with aminoglycosides should be avoided since the potential for nephrotoxicity and/or neuromuscular blockade may be increased; caution is also recommended when methoxyflurane or polymyxins are used

PM 02052/06-23