been reported with prolonged therapy. Nephrotoxicity, ototoxicity and neuromuscular blockade have been reported (see boxed WARNINGS and PRECAUTIONS sections).

OVERDOSAGE: Because of low absorption, it is unlikely that acute overdosage would occur with oral neomycin sulfate. However, prolonged administration could result in sufficient systemic drug levels to produce neurotoxicity, ototoxicity and/or nephrotoxicity. Hemodialysis will remove neomycin sulfate from the blood.

DOSEAGE AND ADMINISTRATION: To minimize the risk of toxicity, use the lowest possible dose and the shortest possible treatment period to control the condition. Treatment for periods longer than two weeks is not recommended.

Hepatic coma: For use as an adjunct in the management of hepatic coma, the recommended dose is 4 to 12 grams per day given in the following regimen:
2. Give supportive therapy, including blood products, as indicated.
3. Give Neomycin Sulfate Tablets in doses of 4 to 12 grams of neomycin sulfate per day (right to 24 tablets) in divided doses. Treatment should be continued over a period of five to six days, during which time protein should be returned incrementally to the diet.
4. If less potent orally drugs cannot be used for chronic hepatic insufficiency, neomycin in doses of up to four grams daily (eight tablets per day) may be necessary. The risk for the development of neomycin induced toxicity progressively increases when treatment must be extended to preserve the life of a patient with hepatic encephalopathy who has failed to fully respond. Frequent periodic monitoring of these patients to ascertain the presence of drug toxicity is mandatory (see PRECAUTIONS). Also, neomycin serum concentrations should be monitored to avoid potentially toxic levels. The benefits to the patient should be weighed against the risks of nephrotoxicity, permanent ototoxicity and neurotoxicity following the accumulation of neomycin in the tissues.

Preoperative Prophylaxis for Elective Colorectal Surgery
Listed below is an example of a recommended bowel preparation regimen. A proposed surgery time of 8:00 a.m. has been used.

Pre-op Day 3: Minimum residue or clear liquid diet. Bisacodyl, 1 tablet orally at 6:00 p.m.

Pre-op Day 2: Minimum residue or clear liquid diet. Magnesium sulfate, 30 mL, 50% solution (15 g) orally at 10:00 a.m., 2:00 p.m., and 6:00 p.m. Enema at 7:00 p.m. and 8:00 p.m.

Pre-op Day 1: Clear liquid diet. Supplemental (IV) fluids as needed. Magnesium sulfate, 30 mL, 50% solution (15 g) orally at 10:00 a.m. and 2:00 p.m. Neomycin sulfate (1 g) and erythromycin base (1 g) orally at 1:00 p.m., 2:00 p.m. and 11:00 p.m. No enema.

Day of Operation: Patient evacuates rectum at 6:30 a.m. for scheduled operation at 8:00 a.m.

HOW SUPPLIED: Neomycin Sulfate Tablets, USP, 500 mg (equivalent to 350 mg of neomycin base per tablet) are available as round, off-white, unscored tablets, debossed “500” and “PT”.

Supplied as: NDC 39822-0310-9 as Unit Dose blister packages of packages of 100 tablets (10 strips of 10 tablets each).

Store at 20°-25°C (68°-77°F) (see USP Controlled Room Temperature).

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NST-PI-02

Manufactured for:
XGEN
Pharmaceuticals, Inc.
Big Flats, NY 14814
Neomycin Sulfate Tablets, USP 500 mg

To reduce the development of drug-resistant bacteria and maintain the effectiveness of neomycin sulfate tablets and other antibacterial drugs, neomycin sulfate tablets should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria.

**WARNINGS:** SYSTEMIC ABSORPTION OF NEOMYCIN OCCURS FOLLOWING ORAL ADMINISTRATION AND TOXIC REACTIONS MAY OCCUR. Patients treated with neomycin should be under close clinical observation because of the possibility of systemic absorption. NEOMYCIN SULFATE IS NOT A SUBSTITUTE FOR ANTI-BODY ABSORPTION THERAPY AND NEOMYCIN SULFATE IS NOT THERAPEUTICLY EQUIVALENT TO NEUROTOXICITY (INCLUDING OTITIS EXTERNA) AND NEUROTOXICITY FOLLOWING THE ORAL USE OF NEOMYCIN SULFATE HAVE BEEN REPORTED, EVEN WHEN USED IN RECOMMENDED DOSES. THE POTENTIAL FOR NEUROTOXICITY, PERMANENT BILATERAL AUDITORY TOXICITY AND SOMETIMES VESTIBULAR TOXICITY IS PRESENT IN PATIENTS WITH NORMAL RENAL FUNCTION WHEN TREATED WITH HIGHER DOSES OF NEOMYCIN AND/OR FOR LONGER PERIODS THAN RECOMMENDED. Serial, vestibular and audiometric tests, as well as tests of renal function, should be performed in high-risk patients. THE RISK OF NEUROTOXICITY AND OTITIS EXTERNA IS GREATER IN PATIENTS WITH IMPAIRED RENAL FUNCTION. Patients with impaired renal function who develop coelomic damage will not have symptoms during therapy to warn them of developing eighth nerve destruction and total or partial deafness may occur long after neomycin has been discontinued.

Neuromuscular blocking and respiratory paralysis have been reported following the oral use of neomycin. The possibility of the occurrence of neuromuscular blocking and respiratory paralysis should be considered if neomycin is administered, especially to patients receiving neuromuscular blocking agents such as tubocurarine, succinylcholine, decamethonium, or in patients receiving massive transfusions of citrate anticoagulated blood. Blockage may occur, causing tissue anoxia but mechanical respiratory assistance may be necessary.

Concurrent and/or sequential systemic, oral or topical use of other aminoglycosides, including paromomycin and other potentially nephrotoxic and/or neurotoxic drugs such as bacitracin, cephalosporins, ampicillin, polymyxin, colistin, and neomycin should be avoided because the toxicity may be additive. Other factors which increase the risk of toxicity are advanced age and dehydration.

The concurrent use of neomycin with potent diuretics such as ethacrynic acid or furosemide should be avoided, since diuretics by themselves may cause toxicity. In addition, when administered intravenously, diuretics may enhance neomycin toxicity by altering the antibiotic concentration in serum and tissue.

**DESCRIPTION:** Neomycin Sulfate Tablets, USP, for oral administration, contain an average of 500 mg of neomycin sulfate which is derived from the metabolic products of the actinomycete Streptomyces fradiae. Structurally, neomycin sulfate may be represented as follows:

\[
\text{Neomycin B Sulfate, } \text{C}_{46}\text{H}_{64}\text{N}_{12}\text{O}_{15}\text{S}_{2} \cdot \text{H}_{2}\text{O}
\]

Chemically, it is 0-2, 6-diamino-2, 6-dideoxy-D-glucopyranosyl

(1-4)-2-deoxy-D-glucopyranosyl

(1-4)-2-deoxy-D-glucopyranosyl

(1-4)-2-deoxy-D-glucopyranosyl residue in the neobiosome moiety of 1-p-D-ribofuranosyl.

Inactive Ingredients: Calcium Stearate, Povidone.

**CLINICAL PHARMACOLOGY:** Neomycin sulfate is poorly absorbed from the normal gastrointestinal tract. The small absorbed fraction is rapidly distributed in the tissues and is excreted by the kidney in keeping with the degree of kidney function. The unabsorbed portion of the drug (approximately 97%) is eliminated unchanged in the feces.

Growth of most intestinal bacteria is rapidly suppressed following oral administration of neomycin sulfate, with the suppression persisting for 48-72 hours. Neutrophilic yeast and occasionally resistant strains of Enterobacter aerogenes (formerly Aerobacter aerogenes) replace the intestinal bacteria.

As with other aminoglycosides, the amount of systemically absorbed neomycin increases cumulatively with each repeated dose administered until a steady state is achieved. The kidney functions as the primary excretory pathway as well as the tissue binding site, with the highest concentration found in the renal cortex. With repeated dosings, progressive accumulation also occurs in the inner ear. Release of tissue-bound neomycin occurs slowly over a period of several weeks after dosing has been discontinued.

The potential for severe tissue damage increases with each repeated dose administered until a steady state is achieved. The kidney functions as the primary excretory pathway as well as the tissue binding site, with the highest concentration found in the renal cortex. With repeated dosings, progressive accumulation also occurs in the inner ear. Release of tissue-bound neomycin occurs slowly over a period of several weeks after dosing has been discontinued.

Microbiology: In vitro tests have demonstrated that neomycin is bactericidal and acts by inhibiting the synthesis of protein in susceptible bacterial cells. It is effective primarily against aerobic and anaerobic gram-negative bacteria (other than gonococci and pneumococci). Neomycin is active in vitro against Escherichia coli and the Klebsiella-Enterobacter group. Neomycin is not active against anaerobic bowel flora.

If susceptibility testing is needed, using a 30 mg/dl organism, producing zones of 16 mm or greater are considered susceptible. Resistant organisms produce zones of 13 mm or less. Zones greater than 13 mm and less than 16 mm indicate intermediate susceptibility.

**INDICATIONS AND USAGE:** To reduce the development of drug-resistant bacteria and maintain the effectiveness of neomycin sulfate tablets and other antibacterial drugs, neomycin sulfate tablets 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.

**Suppression of intestinal bacteria:** Neomycin sulfate tablets are indicated as adjunctive therapy as part of a regimen for the suppression of the normal bacterial flora in patients (children and adults) who are predisposed to infection (e.g., the cancer patient). When neomycin sulfate tablets are prescribed to treat a bacterial infection, patients should be told that although the symptoms can 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 drug, (2) cause the pathogen to become resistant to the antibiotic, (3) make it more difficult to treat the next infection, and (4) spread germs to other people.

**Contraindications:** Neomycin sulfate oral preparations are contraindicated in patients with a history of hypersensitivity to neomycin. Neomycin is contraindicated in patients with hepatic insufficiency or who are debilitated, elderly, or otherwise unable to tolerate diarrhea. Neomycin should not be used in patients with severe hepatic or renal insufficiency or both.

**Precautions:** General: Prescribing neomycin sulfate tablets in the absence of a proven or strongly suspected bacterial infection or prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria. As with other antibiotics, use of oral neomycin may result in overgrowth of non- susceptible organisms, particularly fungi. If this occurs, appropriate therapy should be instituted.

Neomycin is quickly and almost totally absorbed from body surfaces (except the urinary bladder) after local irrigation and when applied topically in association with surgical procedures. Delayed-onset irreversible deafness, renal failure and death due to excretory blockade (regardless of the status of renal function) have been reported following irrigation of both small and large surgical fields with minute quantities of neomycin. Therefore, patients with renal impairment should be considered if neomycin is administered, especially to patients whose mothers received neomycin during pregnancy. Although various side effects such as deafness and neuritis have not been reported in the treatment of pregnant women with other aminoglycosides, the potential for harm exists. Animal reproduction studies of neomycin have not been conducted. If neomycin 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 neomycin sulfate tablets in the absence of a proven or strongly suspected bacterial infection or prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria. As with other antibiotics, use of oral neomycin may result in overgrowth of non-susceptible organisms, particularly fungi. If this occurs, appropriate therapy should be instituted.

Neomycin is quickly and almost totally absorbed from body surfaces (except the urinary bladder) after local irrigation and when applied topically in association with surgical procedures. Delayed-onset irreversible deafness, renal failure and death due to excretory blockade (regardless of the status of renal function) have been reported following irrigation of both small and large surgical fields with minute quantities of neomycin. Future studies should be performed to determine the effect of neomycin on auditory function.

**Adverse Reactions:** The most common adverse reactions to oral neomycin sulfate are nausea, vomiting, and diarrhea. The "Malabsorption Syndrome" characterized by increased fecal bile acid excretion and reduces intestinal lactase activity.

**WARNINGS:** Systemic absorption of neomycin occurs following oral administration and toxic reactions may occur. Patients treated with neomycin should be under close clinical observation because of the possibility of systemic absorption. Neomycin sulfate is not a substitute for anti-body absorption therapy and neomycin sulfate is not therapeutically equivalent to neurotoxicity (including otitis externa) and neurotoxicity following the oral use of neomycin sulfate have been reported, even when used in recommended doses. The potential for neurotoxicity, permanent bilateral auditory toxicity and sometimes vestibular toxicity is present in patients with normal renal function when treated with higher doses of neomycin and/or for longer periods than recommended. Serial, vestibular and audiometric tests, as well as tests of renal function, should be performed in high-risk patients. The risk of neurotoxicity and otitis externa is greater in patients with impaired renal function.

Neuromuscular blocking and respiratory paralysis have been reported following the oral use of neomycin. The possibility of the occurrence of neuromuscular blocking and respiratory paralysis should be considered if neomycin is administered, especially to patients receiving neuromuscular blocking agents such as tubocurarine, succinylcholine, decamethonium, or in patients receiving massive transfusions of citrate anticoagulated blood. Blockage may occur, causing tissue anoxia but mechanical respiratory assistance may be necessary.

Concurrent and/or sequential systemic, oral or topical use of other aminoglycosides, including paromomycin and other potentially nephrotoxic and/or neurotoxic drugs such as bacitracin, cephalosporins, ampicillin, polymyxin, colistin, and neomycin should be avoided because the toxicity may be additive.

Other factors which increase the risk of toxicity are advanced age and dehydration.

The concurrent use of neomycin with potent diuretics such as ethacrynic acid or furosemide should be avoided, since diuretics by themselves may cause toxicity. In addition, when administered intravenously, diuretics may enhance neomycin toxicity by altering the antibiotic concentration in serum and tissue.

**HOSTILE MICROORGANISMS:** It is not known whether neomycin is excreted in human milk, but it has been shown to be excreted in cow milk following a single intramuscular injection. Other aminoglycosides have been shown to be excreted in human milk. Because many antimicrobial agents are excreted in human milk, a decision should be made whether to discontinue nursing or to continue the drug, taking into account the importance of the drug to the mother.

**Pediatric Use:** The safety and efficacy of oral neomycin sulfate in patients less than 18 years of age is necessary. Neomycin should be used with caution and the period of treatment should not exceed two weeks because of absorption from the gastrointestinal tract.

**ADVERSE REACTIONS:** The most common adverse reactions to oral neomycin sulfate are nausea, vomiting, and diarrhea. The "Malabsorption Syndrome" characterized by increased fecal bile acid excretion and reduces intestinal lactase activity.