AA PHARMA MINOCYCLINE

Minocycline Hydrochloride Capsules USP 50 mg and 100 mg
Antibiotic

ACTIONS:
AA PHARMA MINOCYCLINE (minocycline hydrochloride) is a tetracycline with antibacterial activity against some Gram-negative and Gram-positive organisms. The action of AA PHARMA MINOCYCLINE is primarily bacteriostatic and is thought to exert its antimicrobial effect by the inhibition of protein synthesis.

INDICATION AND CLINICAL USES
AA PHARMA MINOCYCLINE (minocycline hydrochloride) may be indicated for the treatment of the following infections due to susceptible strains of the designated organisms:
Gallbladder infections caused by Escherichia coli;
Urinary tract infections: cystitis, gonorrhea, pyelonephritis caused by Escherichia coli, Proteus species, Klebsiella species, Enterobacter aerogens, Neisseria gonorrhoeae.
When penicillin is contraindicated, minocycline may be employed as an alternative drug in the treatment of anal and pharyngeal gonorrhea and syphilis.
Skin and soft tissue infections: Abscess cellulities, furunculosis, impetigo and pyoderma caused by: Staphylococcus epidermidis, Staphylococcus aureus, Streptococcus pyogenes, Proteus species, Escherichia coli.
Although tetracyclines are not the drugs of choice in any staphylococcal or streptococcal infection, minocycline could be useful in circumstances where these organisms are shown to be resistant to other agents but sensitive to minocycline. Bacterial evaluation of clinical cases involving proteus suggests a relatively lower success rate may be expected where these organisms are concerned.
Respiratory tract infections: bronchitis, pharyngitis, pneumonia, bronchopneumonia, sinusitis and tonsillitis caused by: Haemophilus Influenzae, Klebsiella species, Enterobacter species. Tetracyclines should not be prescribed for acute throat infections.

CONTRAINDICATIONS
History of hypersensitivity to minocycline or any other tetracyclines.

WARNINGS
Newborns, Infants and Children:
The use of tetracyclines, including minocycline, during tooth development (last half of pregnancy, infancy and childhood under the age of thirteen years) has been shown to cause permanent tooth discolouration (yellow-grey-brown). This is more common during long-term use, but has been observed following short-term courses. Enamel hypoplasia has also been reported. All tetracyclines including minocycline form a stable calcium complex in any bone-forming tissue. A decrease in the fibula growth rate has been observed in prematures given oral tetracycline in doses of 25 mg/kg every 6 hours. This appeared to be reversible when the drug was discontinued. Minocycline should not be used in such patients unless other drugs are ineffective or are contraindicated.
Pregnancy and Lactation:
Tetracyclines, including minocycline, are not recommended during pregnancy and lactation because of possible adverse effects on developing bones and teeth of the fetus and neonate. Results of animal studies indicate that tetracyclines cross the placenta, are found in fetal tissues and can have toxic effects on the developing fetus (often related to retardation of skeletal development). Evidence of embryo-toxicity has also been noted in animals treated early in pregnancy. The safety of minocycline for use during pregnancy has not been established.
Tetracyclines, including minocycline, are excreted in the milk of lactating women.
It is advisable to avoid giving minocycline in conjunction with penicillin since some bacteriostatic drugs may interfere with the bactericidal action of penicillin.
Minocycline should not be used for the treatment of streptococcal diseases unless the organism is demonstrated to be sensitive, since most streptococci have been found to be resistant to tetracycline drugs. If it is deemed necessary that infection due to Group A beta-hemolytic streptococci be treated with minocycline, then such treatment should be continued for at least ten days.
In the presence of significant renal impairment, usual oral doses may lead to excessive systemic accumulations of minocycline and possible liver toxicity. Under such conditions, lower than usual doses may be indicated. After initial therapy, and if therapy is prolonged, serum level determinations of the drug are advisable.
The anti-anabolic action of tetracyclines can also produce dose-related increased in BUN; consequently, in patients with significant renal impairment, elevated serum minocycline levels can lead to azotemia, hypophosphatemia and acidosis.
Minocycline is capable of aggravating the symptoms associated with lupus erythematosus. Therefore, caution should be taken when administering the drug to patients with this disease.
Minocycline has been shown to depress plasma prothrombin activity. Therefore patients who are on anticoagulant therapy should be monitored regularly and may require downward adjustment of their anticoagulant dosage.
Interference with vitamin K synthesis by micro-organisms in the gut has been reported.
Cross sensitization among the various tetracyclines is extremely common.
Pigmentation of skin, thyroid, bone and teeth have been reported occasionally in persons receiving minocycline usually for extended periods of time. The pigmentation may be irreversible.

PRECAUTIONS
The administration of AA PHARMA MINOCYCLINE (minocycline hydrochloride) to children under 13 years of age is not recommended.
Bulging fontanels have been reported in young infants following full therapeutic dosage of tetracyclines including minocycline.
Benign intracranial hypertension (or pseudotumour cerebri) has very rarely been reported in adults. These signs disappeared rapidly when the drug was discontinued.
Administration of isotretinoin or other systemic retinoids or retinol should be avoided shortly before, during, and shortly after minocycline therapy. Each of these agents used alone has been associated with benign intracranial hypertension.
Patients should be warned to avoid exposure to direct sunlight and/or ultraviolet light while under treatment with minocycline or other tetracycline drugs, and treatment should be discontinued at the first evidence of skin erythema or discomfort. Photosensitivity manifested by an exaggerated sunburn reaction has been observed in some individuals taking tetracyclines. Studies to date indicated that photosensitivity is rarely reported with minocycline.
Patients treated with minocycline may suffer from headaches, light-headedness, dizziness or vertigo. Administration of minocycline in excess of the recommended dosage can increase the frequency and severity of these CNS symptoms. Patients should be cautioned about driving vehicles or using hazardous machinery while on minocycline therapy. These symptoms may disappear during therapy and usually disappear rapidly when the drug is discontinued.
As with other antibiotics, minocycline therapy may result in overgrowth of non-susceptible organisms (including fungi). If super-infection occurs, minocycline should be discontinued and appropriate therapy instituted.
The development of cross-resistance to many antibiotics can develop rapidly in several species of microorganisms. The clinician should bear this in mind if therapy with minocycline is not achieving expected results.
The frequency of resistance to minocycline in hemolytic streptococci is highest in strains from infections of the ear, wounds and skin. Culture and sensitivity studies should be performed whenever feasible and routinely in suspected streptococcal infections.
Since sensitivity reactions are more likely to occur in persons with a history of allergy, asthma, hay fever, or urticarial, minocycline should be used with caution in such individuals.
Before treating patients with gonorrhea, a darkfield examination should be made from any lesion suggestive of concurrent syphilis. Serological tests for syphilis should be repeated monthly for at least 4 months.
Minocycline should be used with caution in patients with hepatic dysfunction and in conjunction with alcohol or other hepatotoxic drugs.
In long-term therapy with minocycline, periodic laboratory evaluation of organ systems, including hematopoietic, renal and hepatic studies should be performed.
Minocycline has been shown to depress plasma prothrombin activity. Therefore, patients who are on anticoagulant therapy should be monitored regularly and may require downward adjustment of their anticoagulant dosage. Interference with vitamin K synthesis by microorganisms in the gut has been reported.
Antacids containing aluminum, calcium or magnesium and oral iron preparations impair absorption and should not be given to patients taking oral minocycline.
Dairy products can delay absorption. Studies to date have indicated that the absorption of minocycline is not notably influenced by foods.

ADVERSE REACTIONS
The following adverse reactions have been reported with the tetracycline analogues including minocycline:

a. Central Nervous System: increased intracranial pressure, headaches, light-headedness, dizziness or vertigo and, rarely, fainting spells have been reported with a variable but overall incidence of approximately 7% in patients treated with minocycline. These symptoms usually disappear rapidly when the drug is discontinued.
b. Gastrointestinal System: anorexia, nausea, vomiting, diarrhea, stomatitis, glossitis, enterocolitis, pruritis ani, constipation, dysphagia and inflammatory lesions (with monilial overgrowth) in the anogenital region.
c. Teeth and bone: dental staining (yellow-gray-brown) has been reported in children of mothers given tetracyclines, including minocycline, during the latter half of pregnancy, and in children given the drug during the neonatal period, infancy and childhood to age of 13 years. Enamel hypoplasia has also been reported. Discolouration of bones and teeth has been documented to occur rarely in adolescents and adults upon extended treatment with minocycline. The effects may be irreversible. At present the mechanism of staining, although not completely elucidated, appears to be mediated by the formation of stable iron complex.
d. Renal: rise in BUN has been reported and is apparently dose-related. Increased excretion of nitrogen and sodium has also been reported.
e. Skin: maculopapular and erythematous rashes. Rarely reported – exfoliative dermatitis, onycholysis, discolouration of the nails, pigmentation of the skin and mucous membrane, erythema multiforme, Stevens-Johnson syndrome.
f. Hypersensitivity reactions: urticarial, angioneurotic edema, anaphylaxis, anaphylactoid purpura, pericarditis and exacerbation of systemic lupus erythematosus.
g. Agranulocytosis.
h. Other: elevated SGOT or SGPT values, hepatic cholestasis, hemolytic anemia, neutropenia, thrombocytopenia and eosinophilia. When given over prolonged periods, minocycline, like other tetracyclines, has been reported to produce brown-black microscopic discolouration of the thyroid gland. Abnormalities of thyroid function have not been shown to date. If adverse reactions or idiosyncrasy occur, the administration of minocycline should be discontinued and appropriate alternate therapy instituted.

SYMPTOMS AND TREATMENT OF OVERDOSAGE
Symptoms and Signs:
Dizziness, nausea, vomiting, abdominal pain, intestinal hemorrhage, hypotension, lethargy, coma, acidosis, azotemia without a concomitant rise in creatinine.
Treatment:
Specific antidote: none.
General antidotes: Antacids (e.g., calcium carbonate or lactate, milk of magnesia, aluminum hydroxide) which form relatively insoluble complexes with minocycline. (Calcium Solution 5%: 50 g calcium carbonate or lactate dissolved in 1000 mL water, yields a 5% solution). Gastric lavage, if necessary.

DOSAGE AND ADMINISTRATION
Children 13 Years of Age or Older:
The usual dosage of AA PHARMA MINOCYCLINE (minocycline hydrochloride) is 4 mg/kg initially followed by 2 mg/kg every 12 hours. Tetracyclines are not recommended in children under 13 years of age (see Warnings).
Adults:
The usual oral dosage of AA PHARMA MINOCYCLINE is 100 mg or 200 mg initially, followed by 100 mg every 12 hours. Alternatively, if more frequent doses are preferred, two or four 50 mg doses may be given initially, followed by one 50 mg dose every 6 hours. Therapy should be continued for 1 or 2 days beyond the time when characteristic symptoms or fever have subsided.
For treatment of syphilis, AA PHARMA MINOCYCLINE therapy should be administered over a period of 10 or 15 days. Close follow-up, including laboratory tests, is recommended. Concomitant therapy: Antacids containing aluminum, calcium or magnesium and/or iron preparations impair absorption and should not be given to patients taking minocycline.

AVAILABILITY OF DOSAGE FORMS
AA PHARMA MINOCYCLINE 50 mg Capsules
Each orange capsule, imprinted “APO 50”, contains minocycline hydrochloride equivalent to 50 mg minocycline. Available in bottles of 100, 500 and 1000 and in unit dose packages of 30’s and 100’s.
Not all pack sizes may be available.
AA PHARMA MINOCYCLINE 100 mg Capsules
Each orange and purple capsule, imprinted “APO 100”, contains minocycline hydrochloride equivalent to 100 mg minocycline. Available in bottles of 100, 500 and 1000 and in unit dose packages of 30’s and 100’s.
Not all pack sizes may be available.