Natrapharm

Rx

Pyrazinamide	Pyrazinamide	Rifampicin	Isoniazid + Pyridoxine HCl
Zcure® 250mg/5mL suspension	Zcure® 250mg/5mL suspension	Natricin® Forte 200mg/5mL suspension	Curazid® Forte 200mg/10mg per 5mL syrup

KIDZ KIT® 3

Pyrazinamide 250 mg/ 5 mL Suspension (Zcure)
Rifampicin 200 mg/ 5mL Suspension (Natricin Forte)
Isoniazid + Pyridoxine Hydrochloride 200 mg/10 mg per 5mL Syrup (Curazid Forte)
Antituberculosis

FORMULATION
Each 5ml of Zcure suspension contains:
Pyrazinamide.....250mg

Each 5ml of Natricin Forte suspension contains:
Rifampicin.....200mg

Each 5ml of Curazid Forte syrup contains:
Isoniazid.....200mg
Pyridoxine hydrochloride (Vit. B).....10mg

PRODUCT DESCRIPTION:
Zcure- White to off-white colored suspension. Banana/Vanilla flavored. Sweet fruit taste.

Natricin Forte- Red to brick-red to reddish-orange colored suspension. Strawberry flavored. Sweet fruit taste.

Curazid Forte- Clear Light yellow to yellowish syrup. Apple flavored. Sweet Fruit taste.

INDICATIONS
For the treatment of pulmonary and extrapulmonary tuberculosis.

PHARMACODYNAMICS
Zcure: Pyrazinamide has a bactericidal effect of *Mycobacterium tuberculosis* but appears to have no activity against other mycobacteria. The ph-dependent activity explains the clinical effectiveness of pyrazinamide.

Natricin Forte: Rifampicin is bactericidal against a wide range of microorganisms and interferes with their synthesis of nucleic acids by inhibiting deoxyribonucleic acid (DNA)-dependent ribonucleic acid (RNA) polymerase. It has the ability to kill intracellular organisms.

Curazid Forte: Isoniazid kills actively growing tubercle bacilli by inhibiting the mycolic acids which are the major components of the bacterial cell wall of *Mycobacterium tuberculosis.*

PHARMACOKINETICS
Zcure: Pyrazinamide is readily absorbed from the gastrointestinal tract. Peak serum concentrations occur about 2 hours after a dose by mouth and have been reported to be about 35 mcg/mL after 1.5 g and 66 mcg/mL after 3 g. Pyrazinamide is widely distributed in body fluids and tissues and diffuses into the CSF. The half-life (t½) has been reported to be about 9-10 hours. It is metabolised primarily in the liver by hydrolysis to the major active metabolite pyrazinoic acid which is subsequently hydroxylated to the major excretory product 5-hydropyrazinoic acid. It is excreted through the kidney mainly by glomerular filtration. About 70% of a dose appears in the urine within 24 hours mainly as metabolites and 4 to 14% as unchanged drug.
Pyrazinamide is removed by dialysis.

Natricin Forte: Rifampicin is readily absorbed from the gastrointestinal tract. Peak serum concentrations of the order of 10 μg/ml occur about 2 to 4 hours after a dose of 10 mg/kg body weight on an empty stomach. Absorption of rifampicin is reduced when the drug is ingested with food. The pharmacokinetics (oral and intravenous) in children is similar to adults.
In normal subjects the biological half-life of rifampicin in serum averages about 3 hours after a 600 mg dose and increases to 5.1 hours after a 900 mg dose. With repeated administration, the half-life decreases and reaches average values of approximately 2-3 hours. At a dose of up to 600 mg/day, it does not differ in patients with renal failure and consequently, no dosage adjustment is required.

Curazid Forte: Peak concentrations of about 3 to 8 pg per ml appear in blood 1 to 2 hours after a fasting dose of 300mg by mouth. The rate and extent of absorption of isoniazid is reduced by food. Isoniazid is not considered to be bound appreciably to plasma proteins and diffuses into all body tissues and fluids, including the CSF.

The plasma half-life for isoniazid ranges from about 1 to 6 hours, those who are fast acetylators having shorter half-lives. The primary metabolic route is the acetylation of isoniazid to acetylisoniazid by N-acetyltransferase found in the liver and small intestine. Acetylisoniazid is then hydrolyzed to isonicotinic acid and monoacetylhydrazine; isonicotinic acid is conjugated with glycine to isonicotinyl glycine (isonicotinuric acid) and monoacetylhydrazine is further acetylated to diethylhydrazine. Some unmetabolised isoniazid is conjugated to hydrazones. The metabolites of isoniazid have no tuberculo-static activity and apart from possibly monoacetylhydrazine they are also less toxic.

In patients with normal renal function, over 75% of a dose appears in the urine in 24 hours, mainly as metabolites. Small amounts of drug are also excreted in the feces. Isoniazid is removed by dialysis.

PRECAUTIONS
Pyrazinamide is contraindicated in patients with liver damage, but if treatment is necessary, the dosage must be reduced. Liver function should be assessed before and regularly during treatment. Pyrazinamide should not be given to patients with acute gout or hyperuricaemia and should be used with caution in patients with a history of gout. Caution should be observed in patients with impaired renal function. Increased difficulty has been reported in controlling diabetes mellitus when diabetics are given pyrazinamide.

Liver functions should be checked before treatment with rifampicin and special care should be taken in alcoholic patients or those with pre-existing liver disease who require monitoring during therapy. When other liver function tests are within normal limits, hyperbilirubinaemia in the first weeks or moderately elevated alkaline phosphatase are not indications to withdraw rifampicin. However, dose adjustment is necessary when there is over evidence of hepatic impairment and treatment should be suspended when there is evidence of more serious liver toxicity. It is contraindicated in patients with jaundice or hypersensitivity with rifampicin.

Isoniazid should be administered with caution to patients with convulsive disorders, a history of tic or renal dysfunction. Patients who are at risk of neuropathy or pyridoxine deficiency, including those who are diabetic, alcoholic, malnourished, uraemic, pregnant or infected with HIV, should receive pyridoxine usually in a dose of 10mg daily, although some have suggested using 50mg daily. If symptoms of hepatitis such as malaise, fatigue, anorexia and nausea develop isoniazid should be discontinued pending evaluation.

Periodic eye examinations during isoniazid treatment have been suggested. Liver function should be assessed before and regularly during treatment of these anti-tuberculosis drugs.

WARNING
Hypersensitivity: Stop all drugs and evaluate at the first sign of a hypersensitivity reaction. Careful monitoring of hepatic function is recommended with the concurrent use of Pyrazinamide, Rifampicin and Isoniazid.

INTERACTIONS
Pyrazinamide: The use of pyrazinamide is contraindicated in patients with severe liver damage. Pyrazinamide may cause hepatocellular injury, particularly in patients with underlying liver disease and during co-administration with other hepatotoxic agents including other anti-tuberculosis drugs such as isoniazid and rifampin. Therapy with pyrazinamide should be administered cautiously and under strict medical supervision in patients with liver disease or a history of alcoholism.

Rifampicin: The blood concentrations of methadone, oral hypoglycemic agents, digitalis derivatives, corticosteroids and anticoagulants may be affected if rifampicin is given simultaneously. Dosage adjustment is recommended in such cases.

Isoniazid: Inhibits the metabolism of the following drugs: anticonvulsants (i.e Carbamazepine, phenytoin, primidone, and valproic acid), benzodiazepines, haloperidol, ketoconazole, theophylline and warfarin.
Concomitant antacid administration may reduce the absorption of Isoniazid.
Corticosteroids may decrease the serum concentration of Isoniazid by increasing acetylation rate and/or renal clearance.

ADVERSE EFFECTS
Hepatoxicily is the most serious side-effect of pyrazinamide therapy and its frequency appears to be dose-related. However, in currently recommended dose, when given with isoniazid and rifampicin, the incidence of hepatitis has been reported to be less than 3%. Hyperuricaemia commonly occurs and may lead to attacks of gout.

Rifampicin is usually well tolerated. Adverse effects are more common during intermittent therapy or after restarting interrupted treatment. Gastrointestinal adverse effects include nausea, vomiting, anorexia and epigastric distress. Administration on an empty stomach is recommended for maximal absorption, but this has to be balanced against administration after a meal to minimize gastrointestinal intolerance. Pseudomembranous colitis has been reported. Rifampicin produces transient abnormalities in liver functions. Rifampicin causes a harmless orange-red discoloration of the urine and other body fluids.

Isoniazid is generally well tolerated at currently recommended doses. Patients who are slow acetylators of isoniazid appear to have a higher incidence of some adverse effects. Also patients whose nutrition is poor are at risk of peripheral neuritis which is one of the commonest adverse effects of isoniazid. Other neurological adverse effects include psychotic reactions and convulsions. Pyridoxine may be given to prevent or treat these adverse effects. Optic neuritis has also been reported.
Haematological effects reported following use of isoniazid include various anaemias, agranulocytosis, thrombocytopenia and eosinophilia.

For suspected adverse drug reaction, report to the FDA: www.fda.gov.ph

NATRICIN FORTE SUSPENSION DOES NOT CONTAIN SODIUM METABISULFITE

CAUTION
Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

DOSAGE AND ADMINISTRATION
Kidz Kit 3 is indicated for the initial 8 - week (2 months) phase of short course anti-tuberculosis treatment.

Usual dose for both children and adult:
- Pyrazinamide (Zcure) suspension: 25mg per kg bodyweight daily maximum daily dose is 3g
- Rifampicin (Natricin Forte) suspension: 10mg per kg body weight once a day with a daily maximum dose of 600mg
- Isoniazid + Pyridoxine Hydrochloride (Curazid Forte) syrup : 5mg per kg bodyweight with a daily maximum dose of 300mg

OVERDOSAGE
Do not take more than prescribed dose. Taking more medication will not improve yoursymptoms; rather they may cause poisoning or serious side-effects. If you suspect that you or anyone else who may have overdosed of Kidz Kit 3 Suspension, please go to the emergency department of the closest hospital or nursing home. Do not give your medicines to other people even if you know that they have the same condition or it seems that they may have similar conditions. Please consult your physician or pharmacist for more information.

AVAILABILITY
Each kit contains:
2- 120ml bottle of Pyrazinamide 250mg/5ml (Zcure) suspension
1- 120ml bottle of Rifampicin 200mg/5ml (Natricin Forte) suspension
1- 120ml bottle of Isoniazid + Pyridoxine 200mg/10mg/5ml (Curazid Forte) syrup

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STORE AT TEMPERATURES NOT EXCEEDING 300C

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