METORAX® 10mg

Methotrexate BP

Methotrexate is a folate antagonist that occupies a special place in antineoplastic chemotherapy like remission in leukemia and the cure of a solid tumor and choriocarcinoma. High dose regimens of Methotrexate are useful for tumors such as osteogenic sarcoma. Methotrexate has also been used with benefit in the treatment of psoriasis .

Now-a-days, Methotrexate is widely used as a disease modifying antirheumatic drug (DMARD) that is suitable for moderate to severe rheumatoid arthritis. Methotrexate inhibits the enzyme dihydrofolate reductase, essential for the synthesis of purines and pyrimidines and thus DNA and RNA synthesis are interrupted. Folate antagonists kill cells during the S phase of the cell cycle.

Methotrexate is readily absorbed from the gastro-intestinal tract at doses of less than 25 mg/m^2. A direct relationship exists between dose and plasma concentrations. Approximately 35% of methotreaxate is bound to plasma proteins . 40 to 50% of a small dose (2.5-15 µg/kg) and 90% of a larger dose (150 µg/kg) is excreted unchanged in the urine within 48 hours , mostly within the first 8 hours . A small amount of methotrexate is also excreted in the stool, probably through the biliary tract.

PRESENTATION

Each film- coated tablet contains Methotrexate BP 10 mg.

INDICATION & USES

Methrotrexate is indicated in moderate to severe rheumatoid arthritis , malignant disease and psoriasis. Methotrexate is indicated for the treatment of breast carcinoma, gestational choriocarcinoma and in patients with chorioadenoma destruens and hydatidiform mole. Methotrexate is also indicated for palliation of acute and subacute lymphocytic and meningeal leukaemia. Greatest effect has been observed in palliation of acute lymphoblastic (stem-cell) leukaemias. In combination with corticosteroids methotrexate has been used to induce remissions, but is now commonly used to maintain induced remissions. Methotrexate is also effective in the treatment of advanced stages (III and IV Peters Staging System) of lymphosarcoma, particularly in those cases in children; and in advanced cases of mycosis fungoides.

DOSAGE & ADMINISTRATION

Leukaemia in children (maintenance): By mouth, 15 mg/m^2 body surface weekly in combination with other drugs.

Maintenance therapy of acute lymphoblastic leukaemia: A common dose of 15 - 30 mg/m^2 body surface, once or twice weekly by mouth with other agents .

Choriocarcinoma: Treated with doses of 15 - 30 mg daily by mouth for 5 days at intervals of 1 - 2 weeks for 3 - 5 courses. Doses of 10 - 16 mg/m^2 have also been employed in the treatment of breast cancer, often in combination with Cyclophosphamide & Fluorouracil.

In the treatment of rheumatoid arthritis : By mouth, 7.5-10 mg once weekly as a single dose or divided into 3 doses of 2.5 mg given at intervals of 12 hours, adjusted according to response; maximum total weekly dose 20 mg.

In the treatment of psoriasis : Single weekly doses of 10 - 25 mg may be given by mouth, adjusted according to response; ELDERLY: consider dose reduction with extreme caution; CHILD: not recommended.

CONTRAINDICATIONS

Pregnant psoriatic patients should not receive methotrexate. Psoriatic patients with severe renal or hepatic disorders should not receive methotrexate. Psoriatic patients with pre-existing blood dyscrasias, such as marrow hypoplasia, leukopenia, thrombocytopenia or anaemia, should not receive methotrexate. Overt or laboratory evidence of immunodeficiency syndrome.
Hypersensitivity to methotrexate.

PRECAUTIONS

It should be used with caution in hepatic & renal impairment and porphyria. Full blood counts (including differential white cell count and platelet count), renal and liver function tests are required before starting treatment and repeated weekly until therapy stabilized, thereafter patients should be monitored every 2-3 months . Extreme caution should be exercised in blood disorders (avoid if severe), peptic ulceration, ulcerative colitis , diarrhoea, ulcerative stomatitis (withdraw if stomatitis develops) and porphyria. It should be avoided if a significant pleural effusion or ascites is present because it tends to accumulate in these fluids , and its subsequent return to the circulation will be associated with myelosuppression.

SIDE EFFECTS

The most common side effects of methotrexate are on the bone marrow and gastrointestinal epithelium. Bone marrow depression can occur abruptly and leucopenia, thrombocytopenia & anaemia may also occur. Megaloblastic anaemia has also been reported. Gingivitis, pharyngitis, stomatitis, anorexia, vomiting, diarrhoea, haematemesis, melaena, gastrointestinal ulceration and bleeding, enteritis, hepatic toxicity resulting in acute liver atrophy, necrosis, fatty metamorphosis, periportal fibrosis, or hepatic cirrhosis. The effect of methotrexate on the intestinal mucosa has led to malabsorption and, in rare cases, to toxic megacolon. Stomatitis & diarrhoea are signs for which treatment should be interrupted, otherwise haemorrhagic enteritis , intestinal perforation and death may follow. Methotrexate therapy is associated with liver damage, both acute (notably after high doses) and more seriously, chronic (generally after long term administration). Other adverse effects include renal failure and tubular necrosis following high doses , pulmonary reactions including life threatening interstitial lung disease, skin reactions ,alopecia, osteoporosis , arthralgia, myalgia, ocular irritation & precipitation of diabetics .

PREGNANCY AND LACTATION

Methotrexate should be avoided during pregnancy. It is teratogenic and fertility may be reduced during therapy but this may be reversible. Following administration to a woman or a man, avoid conception for at least 3 months after stopping.Breast-feeding should be discontinued.

DRUG INTERACTIONS

Analgesics : Excretion of methotrexate probably reduced by NSAIDs (increased risk of toxicity); excretion also reduced by aspirin and azapoprazone (avoid concomitant use).

Antibacterials : Excretion of methotrexate possibly reduced by ciprofloxacin (possibly increased risk of toxicity); Antifolate effect of methotrexate increased by sulfamethoxazole (as cotrimoxazole) and sulphonamides (as trimethoprim) - avoid concomitant use; risk of methotrexate toxicity increased by sulphonamides, doxycycline or tetracycline; excretion of methotrexate reduced by penicillins (increased risk of toxicity).

Antiepileptics : Antifolate effect of methotrexate increased by phenytoin; cytotoxics reduce absorption of phenytoin.

Antimalarials : Antifolate effect increased by pyrimethamine.

Cyclosporin : Increased toxicity.

Corticosteroids : Increased risk of haematological toxicity.

Uricosurics : Excretion of methotrexate reduced by probenecid (increased risk of toxicity).

Retinoids : Plasma concentration of methotrexate increased by acitretin (also increased risk of hepatotoxicity)- avoid concomitant use.

Ulcer-Healing drugs : Excretion of methotrexate possibly reduced by omeprazole (possibly increased risk of toxicity).

PACKAGING

Metorax 10mg : Each Box Containing 3 x 10 tablets in alu-pvc pack.

PHARMACEUTICAL PRECAUTION

Keep in a dry (below 30°C.) place away from light and heat.

WARNING

Keep out of the reach of children.

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