140mm

210mm

Trexate

Tablet/Injection

(Methotrexate)

ٹریکزیٹ

ٹیبلیٹ/انجیکشن

(میتھوٹریکزیٹ)

COMPOSITION:
Trexate Tablet 2.5mg
Each tablet contains:
Methotrexate.....2.5mg
(USP Specifications)
Trexate Tablet 10mg
Each tablet contains:
Methotrexate.....10mg
(USP Specifications
Trexate Injection 50mg/2ml
Each 2ml vial contains:
Methotrexate.....50mg
(USP Specifications)
Trexate Injection 1000mg/40ml
Each 40ml vial contains:
Methotrexate.....1000mg
(USP Specifications)

DESCRIPTION

Methotrexate (Trexate) is an antimetabolite used in the treatment of certain neoplastic diseases, severe psoriasis, and adult rheumatoid arthritis. Chemically Methotrexate (Trexate) is N-[4-[[(2,4-diamino-6-pteridinyl) methyl]methylamino]benzoyl]-Lglutamic acid. Molecular weight: 454.45 C20H22N8O5 Methotrexate (Trexate) Injection, USP is sterile and non-pyrogenic and may be given by the intramuscular, intravenous or intra-arterial route.

CLINICAL PHARMACOLOGY

Methotrexate (Trexate) inhibits dihydrofolic acid reductase. Dihydrofolate must be reduced to tetrahydrofolates by this enzyme before they can be utilized as carriers of one-carbon groups in the synthesis of purine nucleotides and thymidylate. Therefore, Methotrexate (Trexate) interferes with DNA synthesis, repair, and cellular replication. Actively proliferating tissues such as malignant cells, bone marrow, fetal cells, buccal and intestinal mucosa, and cells of the urinary bladder are in general more sensitive to this effect of Methotrexate (Trexate). When cellular proliferation in malignant tissues is greater than in most normal tissues, Methotrexate (Trexate) may impair malignant growth without irreversible damage to normal tissues.

Methotrexate (Trexate) in high doses, followed by leucovorin rescue, is used as a part of the treatment of patients with non-metastatic osteosarcoma. The original rationale for high dose Methotrexate (Trexate) therapy was based on the concept of selective rescue of normal tissues by leucovorin. More recent evidence suggests that high dose Methotrexate (Trexate) may also overcome Methotrexate (Trexate) resistance caused by impaired active transport, decreased affinity of dihydrofolic acid reductase for Methotrexate (Trexate), increased levels of dihydrofolic acid reductase resulting from gene amplification, or decreased polyglutamation of Methotrexate (Trexate). The actual mechanism of action is unknown.

PHARMACOKINETICS

Absorption

In doses of 0.1 mg (of methotrexate) per kg, methotrexate is completely absorbed from the G.I. tract; larger oral doses may be incompletely absorbed. Peak serum concentrations are achieved within 0.5 - 2 hours following I.V. / I.M. or intra-arterial administration. Serum concentrations following oral administration of methotrexate may be slightly lower than those following I.V. injection.

In adults, oral absorption appears to be dose dependent. Peak serum levels are reached within one to two hours. At doses of 30 mg/m2 or less, Methotrexate (Trexate) is generally well absorbed with a mean bioavailability of about 60%. The absorption of doses greater than 80 mg/m2 is significantly less, possibly due to a saturation effect.

Distribution

Methotrexate is actively transported across cell membranes. The drug is widely distributed into body tissues with highest concentrations in the kidneys, gall bladder, spleen, liver and skin. Methotrexate is retained for several weeks in the kidneys and for months in the liver. Sustained serum concentrations and tissue accumulation may result from repeated daily doses. Methotrexate crosses the placental barrier and is distributed into breast milk. Approximately 50% of the drug in the blood is bound to serum proteins.

After intravenous administration, the initial volume of distribution is approximately 0.18 L/kg (18% of body weight) and steady-state volume of distribution is approximately 0.4 to 0.8 L/kg (40 to 80% of body weight).

Metabolism

After absorption, Methotrexate (Trexate) undergoes hepatic and intracellular metabolism to polyglutamated forms which can be converted back to Methotrexate (Trexate) by hydrolase enzymes. These polyglutamates act as inhibitors of dihydrofolate reductase and thymidylate synthetase. Small amounts of Methotrexate (Trexate) polyglutamates may remain in tissues for extended periods. The retention and prolonged drug action of these active metabolites vary among different cells, tissues and tumors. A small amount of metabolism to 7-hydroxyMethotrexate (Trexate) may occur at doses commonly prescribed. Accumulation of this metabolite may become significant at the high doses used in osteogenic sarcoma. The aqueous solubility of 7-hydroxyMethotrexate (Trexate) is 3 to 5 fold lower than the parent compound. Methotrexate (Trexate) is partially metabolized by intestinal flora after oral administration.

Half-Life

The terminal half-life reported for Methotrexate (Trexate) is approximately three to ten hours for patients receiving treatment for psoriasis, or rheumatoid arthritis or low dose antineoplastic therapy (less than 30 mg/m2). For patients receiving high doses of Methotrexate (Trexate), the terminal half-life is 8-15 hours.

Excretion

Renal excretion is the primary route of elimination and is dependent upon dosage and route of administration. With IV administration, 80% to 90% of the administered dose is excreted unchanged in the urine within 24 hours. There is limited biliary excretion amounting to 10% or less of the administered dose. Enterohepatic recirculation of Methotrexate (Trexate) has been proposed.

Renal excretion occurs by glomerular filtration and active tubular secretion. Nonlinear elimination due to saturation of renal tubular reabsorption has been observed in psoriatic patients at doses between 7.5 and 30 mg. Impaired renal function, as well as concurrent use of drugs such as weak organic acids that also undergo tubular secretion, can markedly increase Methotrexate (Trexate) serum levels. Excellent correlation has been reported between Methotrexate (Trexate) clearance and endogenous creatinine clearance.

INDICATIONS AND USAGE

Neoplastic Diseases

Methotrexate (Trexate) is indicated in the treatment of gestational choriocarcinoma, chorioadenoma destruens and hydatidiform mole. In acute lymphocytic leukemia, Methotrexate (Trexate) is indicated in the prophylaxis of meningeal leukemia and is used in maintenance therapy in combination with other chemotherapeutic agents. Methotrexate (Trexate) is also indicated in the treatment of meningeal leukemia. Methotrexate (Trexate) is used alone or in combination with other anticancer agents in the treatment of breast cancer, epidermoid cancers of the head and neck, advanced mycosis fungoides (cutaneous T cell lymphoma), and lung cancer, particularly squamous cell and small cell types. Methotrexate (Trexate) is also used in combination with other chemotherapeutic agents in the treatment of advanced stage non-Hodgkin's lymphomas. Methotrexate (Trexate) in high doses followed by leucovorin rescue in combination with other chemotherapeutic agents is effective in prolonging relapse-free survival in patients with nonmetastatic osteosarcoma who have undergone surgical resection or amputation for the primary tumor.

Psoriasis

Methotrexate (Trexate) is indicated in the symptomatic control of severe, recalcitrant, disabling psoriasis that is not adequately responsive to other forms of therapy, but only when the diagnosis has been established, as by biopsy and/or after dermatologic consultation. It is important to ensure that a psoriasis "flare" is not due to an undiagnosed concomitant disease affecting immune responses.

Rheumatoid Arthritis including Polyarticular-Course Juvenile Rheumatoid Arthritis

Methotrexate (Trexate) is indicated in the management of selected adults with severe, active rheumatoid arthritis (ACR criteria), or children with active polyarticular-course juvenile rheumatoid arthritis, who have had an insufficient therapeutic response to, or are intolerant of, an adequate trial of first-line therapy including full dose non-steroidal anti-inflammatory agents (NSAIDs).

CONTRAINDICATIONS

Methotrexate (Trexate) can cause fetal death or teratogenic effects when administered to a pregnant woman. Methotrexate (Trexate) is contraindicated in pregnant women with psoriasis or rheumatoid arthritis and should be used in the treatment of neoplastic diseases only when the potential benefit outweighs the risk to the fetus. Women of childbearing potential should not be started on Methotrexate (Trexate) until pregnancy is excluded and should be fully counseled on the serious risk to the fetus should they become pregnant while undergoing treatment. Pregnancy should be avoided if either partner is receiving Methotrexate (Trexate); during and for a minimum of three months after therapy for male patients, and during and for at least one ovulatory cycle after therapy for female patients. Because of the potential for serious adverse reactions from Methotrexate (Trexate) in breast fed infants, it is contraindicated in nursing mothers. Patients with psoriasis or rheumatoid arthritis with alcoholism, alcoholic liver disease or other chronic liver disease should not receive Methotrexate (Trexate). Patients with psoriasis or rheumatoid arthritis who have overt or laboratory evidence of immunodeficiency syndromes should not receive Methotrexate (Trexate). Patients with psoriasis or rheumatoid arthritis who have preexisting blood dyscrasias, such as bone marrow hypoplasia, leukopenia, thrombocytopenia, or significant anemia, should not receive Methotrexate (Trexate). Patients with a known hypersensitivity to Methotrexate (Trexate) should not receive the drug.

BOXED WARNINGS.

Use caution when administering high-dose Methotrexate (Trexate) to patients receiving proton pump inhibitor (PPI) therapy. Case reports and published population pharmacokinetic studies suggest that concomitant use of some PPIs, such as omeprazole, esomeprazole, and pantoprazole, with Methotrexate (Trexate) (primarily at high dose), may elevate and prolong serum levels of Methotrexate (Trexate) and/or its metabolite hydroxyMethotrexate (Trexate), possibly leading to Methotrexate (Trexate) toxicities. In two of these cases, delayed Methotrexate (Trexate) elimination was observed when high-dose Methotrexate (Trexate) was co-administered with PPIs, but was not observed when Methotrexate (Trexate) was co-administered with ranitidine. However, no formal drug interaction studies of Methotrexate (Trexate) with ranitidine have been conducted.

PRECAUTIONS

General

Methotrexate (Trexate) has the potential for serious toxicity. Toxic effects may be related in frequency and severity to dose or frequency of administration but have been seen at all doses. Because they can occur at any time during therapy, it is necessary to follow patients on Methotrexate (Trexate) closely. Most adverse reactions are reversible if detected early. When such reactions do occur, the drug should be reduced in dosage or discontinued and appropriate corrective measures should be taken.

The clinical pharmacology of Methotrexate (Trexate) has not been well studied in older individuals. Due to diminished hepatic and renal function as well as decreased folate stores in this population, relatively low doses should be considered, and these patients should be closely monitored for early signs of toxicity.

Laboratory Tests

Patients undergoing Methotrexate (Trexate) therapy should be closely monitored so that toxic effects are detected promptly. Baseline assessment should include a complete blood count with differential and platelet counts, hepatic enzymes, renal function tests and a chest X-ray. During therapy of rheumatoid arthritis and psoriasis, monitoring of these parameters is recommended: hematology at least monthly, renal function and liver function every 1 to 2 months.

Drug Interactions

Concomitant administration of some NSAIDs with high dose Methotrexate (Trexate) therapy has been reported to elevate and prolong serum Methotrexate (Trexate) levels, resulting in deaths from severe hematologic and gastrointestinal toxicity. Methotrexate (Trexate) is partially bound to serum albumin, and toxicity may be increased because of displacement by certain drugs, such as salicylates, phenylbutazone, phenytoin, and sulfonamides. Renal tubular transport is also diminished by probenecid; use of Methotrexate (Trexate) with this drug should be carefully monitored. In the treatment of patients with osteosarcoma, caution must be exercised if high-dose Methotrexate (Trexate) is administered in combination with a potentially nephrotoxic chemotherapeutic agent (e.g., cisplatin). Methotrexate (Trexate) increases the plasma levels of mercaptopurine. The combination of Methotrexate (Trexate) and mercaptopurine may therefore require dose adjustment. Oral antibiotics such as tetracycline, chloramphenicol, and no absorbable broad spectrum antibiotics, may decrease intestinal absorption of Methotrexate (Trexate) or interfere with the enterohepatic circulation by inhibiting bowel flora and suppressing metabolism of the drug by bacteria. Penicillins may reduce the renal clearance of Methotrexate (Trexate); increased serum concentrations of Methotrexate (Trexate) with concomitant hematologic and gastrointestinal toxicity have been observed with high and low dose Methotrexate (Trexate). Use of Methotrexate (Trexate) with penicillins should be carefully monitored. Methotrexate (Trexate) may decrease the clearance of theophylline; theophylline levels should be monitored when used concurrently with Methotrexate (Trexate). Vitamin preparations containing folic acid or its derivatives may decrease responses to systemically administered Methotrexate (Trexate).

Carcinogenesis, Mutagenesis, Impairment of Fertility

No controlled human data exist regarding the risk of neoplasia with Methotrexate (Trexate). Methotrexate (Trexate) has been evaluated in a number of animal studies for carcinogenic potential with inconclusive results. Although there is evidence that Methotrexate (Trexate) causes chromosomal damage to animal somatic cells and human bone marrow cells, the clinical significance remains uncertain. NonHodgkin's lymphoma and other tumors have been reported in patients receiving low-dose oral Methotrexate (Trexate).

Pregnancy

Psoriasis and rheumatoid arthritis: Methotrexate (Trexate) is in Pregnancy Category X.

Pediatric

Use Safety and effectiveness in pediatric patients have been established only in cancer chemotherapy and in polyarticular-course juvenile rheumatoid arthritis. Methotrexate (Trexate) injectable formulations containing the preservative benzyl alcohol are not recommended for use in neonates.

Geriatric Use

Clinical studies of Methotrexate (Trexate) did not include sufficient numbers of subjects age 65 and over to determine whether they respond differently from younger subjects. In general, dose selection for an elderly patient should be cautious reflecting the greater frequency of

decreased hepatic and renal function, decreased folate stores, concomitant disease or other drug therapy (i.e., that interfere with renal function, Methotrexate (Trexate) or folate metabolism) in this population.

Organ System Toxicity

Gastrointestinal:

If vomiting, diarrhea, or stomatitis occur, which may result in dehydration, Methotrexate (Trexate) should be discontinued until recovery occurs. Methotrexate (Trexate) should be used with extreme caution in the presence of peptic ulcer disease or ulcerative colitis.

Hematologic:

Methotrexate (Trexate) can suppress hematopoiesis and cause anemia, aplastic anemia, pancytopenia, leukopenia, neutropenia, and/or thrombocytopenia. In patients with malignancy and preexisting hematopoietic impairment, the drug should be used with caution, if at all. In controlled clinical trials in rheumatoid arthritis (n=128), leukopenia (WBC 3000/mm3) was seen in 2 patients, thrombocytopenia (platelets <100,000/mm3) in 6 patients, and pancytopenia in 2 patients. In psoriasis and rheumatoid arthritis, Methotrexate (Trexate) should be stopped immediately if there is significant drop in blood counts. In the treatment of neoplastic diseases, Methotrexate (Trexate) should be continued only if the potential benefit warrants the risk of severe myelosuppression. Patients with profound granulocytopenia and fever should be evaluated immediately and usually require parenteral broad-spectrum antibiotic therapy.

ADVERSE REACTIONS

IN GENERAL, THE INCIDENCE AND SEVERITY OF ACUTE SIDE EFFECTS ARE RELATED TO DOSE AND FREQUENCY OF ADMINISTRATION. THE MOST SERIOUS REACTIONS ARE DISCUSSED ABOVE UNDER ORGAN SYSTEM TOXICITY IN THE PRECAUTION SECTION. THAT SECTION SHOULD ALSO BE CONSULTED WHEN LOOKING FOR INFORMATION ABOUT ADVERSE REACTIONS WITH METHOTREXATE (TREXATE). The most frequently reported adverse reactions include ulcerative stomatitis, leukopenia, nausea, and abdominal distress. Other frequently reported adverse effects are malaise, undue fatigue, chills and fever, dizziness and decreased resistance to infection. Other adverse reactions that have been reported with Methotrexate (Trexate) are listed below by organ system. In the oncology setting, concomitant treatment and the underlying disease make specific attribution of a reaction to Methotrexate (Trexate) difficult.

Alimentary System:

Gingivitis, pharyngitis, stomatitis, anorexia, nausea, vomiting, diarrhea, hematemesis, melena, gastrointestinal ulceration and bleeding, enteritis, pancreatitis.

Blood and Lymphatic System Disorders:

Suppressed hematopoiesis, anemia, aplastic anemia, pancytopenia, leukopenia, neutropenia, thrombocytopenia, agranulocytosis, eosinophilia, lymphadenopathy and lymphoproliferative disorders (including reversible). Hypogammaglobulinemia has been reported rarely.

Cardiovascular:

Pericarditis, pericardial effusion, hypotension, and thromboembolic events (including arterial thrombosis, cerebral thrombosis, deep vein thrombosis, retinal vein thrombosis, thrombophlebitis, and pulmonary embolus).

Central Nervous System:

Headaches, drowsiness, blurred vision, transient blindness, speech impairment including dysarthria and aphasia, hemiparesis, paresis and convulsions have also occurred following administration of Methotrexate (Trexate). Following low doses, there have been occasional reports of transient subtle cognitive dysfunction, mood alteration or unusual cranial sensations, leukoencephalopathy, or encephalopathy.

Hepatobiliary Disorders:

Hepatotoxicity, acute hepatitis, chronic fibrosis and cirrhosis, hepatic failure, decrease in serum albumin, liver enzyme elevations.

Musculoskeletal System:

Stress fracture. Ophthalmic: conjunctivitis, serious visual changes of unknown etiology.

Pulmonary System:

Respiratory fibrosis, respiratory failure, alveolitis, interstitial pneumonitis deaths have been reported, and chronic interstitial obstructive pulmonary disease has occasionally occurred.

Skin:

Erythematous rashes, pruritus, urticaria, photosensitivity, pigmentary changes, alopecia, ecchymosis, telangiectasia, acne, furunculosis, erythema multiforme, toxic epidermal necrolysis, Stevens-Johnson syndrome, skin necrosis, skin ulceration and exfoliative dermatitis

Hepatic:

Methotrexate (Trexate) has the potential for acute (elevated transaminases) and chronic (fibrosis and cirrhosis) hepatotoxicity. Chronic toxicity is potentially fatal; it generally has occurred after prolonged use (generally two years or more) and after a total dose of at least 1.5 grams. In studies in psoriatic patients, hepatotoxicity appeared to be a function of total cumulative dose and appeared to be enhanced by alcoholism, obesity, diabetes and advanced age. An accurate incidence rate has not been determined; the rate of progression and reversibility of lesions is not known. Special caution is indicated in the presence of preexisting liver damage or impaired hepatic function.

OVERDOSAGE

Leucovorin is indicated to diminish the toxicity and counteract the effect of inadvertently administered Overdosages of Methotrexate (Trexate). Leucovorin administration should begin as promptly as possible. As the time interval between Methotrexate (Trexate) administration and leucovorin initiation increases, the effectiveness of leucovorin in counteracting toxicity decreases. Monitoring of the serum Methotrexate (Trexate) concentration is essential in determining the optimal dose and duration of treatment with leucovorin.

DOSAGE AND ADMINISTRATION

Oral Dose

This medicine should be taken once a week.

Do not exceed the weekly dose of this medicine due to toxicity hazards in psoriasis and rheumatoid arthritis.

The prescriber may specify the day of intake on the prescription.

Psoriasis

Before starting treatment it is advisable to give the patient a test dose of 2.5-5.0 mg to exclude unexpected toxic effects. If, one week later, appropriate laboratory tests are normal, treatment may be initiated. The usual dose is 5-25 mg taken once weekly, starting with a low dose and increasing as necessary. The planned weekly dose may be administered in three divided doses at 12 hour intervals over 24 hours. The prescriber should specify the day of intake on the prescription. The patient should be fully informed of the risks involved and the clinician should pay particular attention to the appearance of liver toxicity by carrying out liver function tests before starting methotrexate treatment, and repeating these at 2 to 4 month intervals during therapy. The aim of therapy should be to reduce the dose to the lowest possible level with the longest possible rest period. The use of methotrexate may permit the return to conventional topical therapy which should be encouraged.

Rheumatoid Arthritis

The usual dose is 7.5 - 15 mg once weekly. The planned weekly dose may be administered in three divided doses at 12 hour intervals over 24 hours. The schedule may be adjusted gradually to achieve an optimal response but should not exceed a total weekly dose of 20 mg. The prescriber should specify the day of intake on the prescription.

Injection Dose

Neoplastic Diseases

Oral administration in tablet form is often preferred when low doses are being administered since absorption is rapid and effective serum levels are obtained. Methotrexate (Trexate) injection may be given by the intramuscular, intravenous or intra-arterial route. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

Choriocarcinoma and similar trophoblastic diseases:

Methotrexate (Trexate) is administered orally or intramuscularly in doses of 15 to 30 mg daily for a five-day course. Such courses are usually repeated for 3 to 5 times as required, with rest periods of one or more weeks interposed between courses, until any manifesting toxic symptoms subside.

Leukemias:

When used for induction, Methotrexate (Trexate) in doses of 3.3 mg/m2 in combination with 60 mg/m2 of prednisone, given daily, produced remissions in 50% of patients treated, usually within a period of 4 to 6 weeks. Methotrexate (Trexate) is administered 2 times weekly either by mouth or intramuscularly in total weekly doses of 30 mg/m2. It has also been given in doses of 2.5 mg/kg intravenously every 14 days.

Meningeal Leukemia:

In the treatment of prophylaxis of meningeal leukemia, Methotrexate (Trexate) must be administered intrathecally. Preservative free Methotrexate (Trexate) is diluted to a concentration of 1 mg/mL in an appropriate sterile, preservative free medium such as 0.9% Sodium Chloride Injection, USP. The cerebrospinal fluid volume is dependent on age and not on body surface area. The CSF is at 40% of the adult volume at birth and reaches the adult volume in several years. Intrathecal Methotrexate (Trexate) administration at a dose of 12 mg/m2 (maximum 15 mg) has been reported to result in low CSF Methotrexate (Trexate) concentrations and reduced efficacy in pediatric patients and high concentrations and neurotoxicity in adults.

GUIDELINES FOR METHOTREXATE (TREXATE) THERAPY WITH LEUCOVORIN RESCUE

1. Administration of Methotrexate (Trexate) should be delayed until recovery of the WBC count is less than 1500/microliter
2. The neutrophil count is less than 200/microliter
3. The platelet count is less than 75,000/microliter
4. The serum bilirubin level is greater than 1.2 mg/dL
5. The SGPT level is greater than 450 U
6. Mucositis is present, until there is evidence of healing
7. Persistent pleural effusion is present; this should be drained dry prior to infusion.
8. Adequate renal function must be documented. a. Serum creatinine must be normal, and creatinine clearance must be greater than 60 mL/min, before initiation of therapy. b. Serum creatinine must be measured prior to each subsequent course of therapy. If serum creatinine has increased by 50% or more compared to a prior value, the creatinine clearance must be measured and documented to be greater than 60 mL/min (even if the serum creatinine is still within the normal range).
9. Patients must be well hydrated, and must be treated with sodium bicarbonate for urinary alkalinization. a. Administer 1,000 mL/m2 of intravenous fluid over 6 hours prior to initiation of the Methotrexate (Trexate) infusion. Continue hydration at 125 mL/m2 /hr (3 liters/m2 /day) during the Methotrexate (Trexate) infusion, and for 2 days after the infusion has been completed. b. Alkalinize urine to maintain pH above 7.0 during Methotrexate (Trexate) infusion and leucovorin calcium therapy. This can be accomplished by the administration of sodium bicarbonate orally or by incorporation into a separate intravenous solution.
10. Repeat serum creatinine and serum Methotrexate (Trexate) 24 hours after starting Methotrexate (Trexate) and at least once daily until the Methotrexate (Trexate) level is below 5 x 10-8 mol/L (0.05 micromolar).
11. The table below provides guidelines for leucovorin calcium dosage based upon serum Methotrexate (Trexate) levels. Patients who experience delayed early Methotrexate (Trexate) elimination are likely to develop nonreversible oliguric renal failure. In addition to appropriate leucovorin therapy, these patients require continuing hydration and urinary alkalinization, and close monitoring of fluid and electrolyte status, until the serum Methotrexate (Trexate) level has fallen to below 0.05 micromolar and the renal failure has resolved. If necessary, acute, intermittent hemodialysis with a high-flux dialyzer may also be beneficial in these patients.

12. Some patients will have abnormalities in Methotrexate (Trexate) elimination, or abnormalities in renal function following Methotrexate (Trexate) administration, which are significant but less severe than the abnormalities described in the table below. These abnormalities may or may not be associated with significant clinical toxicity. If significant toxicity is observed, leucovorin rescue should be extended for an additional 24 hours (total 14 doses over 84 hours) in subsequent courses of therapy. The possibility that the patient is taking other medications which interact with Methotrexate (Trexate) (e.g., medications which may interfere with Methotrexate (Trexate) binding to serum albumin, or elimination) should always be reconsidered when laboratory abnormalities or clinical toxicities are observed.

CAUTION: DO NOT ADMINISTER LEUCOVORIN INTRATHECALLY.

DILUTION INSTRUCTIONS FOR LIQUID METHOTREXATE (TREXATE) INJECTION PRODUCT

Methotrexate (Trexate) Injection USP, the solution may be further diluted with a compatible medium such as Sodium Chloride Injection, USP. Storage for 24 hours at a temperature of 21° to 25°C results in a product which is within 90% of label potency.

STORAGE AND INSTRUCTIONS

Store at controlled room temperature, 20° to 25°C (68° to 77°F).Protect from sunlight, heat and moisture. Keep out of the reach of children.

To be sold on the prescription of a registered oncologist or on demand from cancer hospitals, institutions and oncologists only.

HOW SUPPLIED

Trexate Tablet 2.5mg
30's, 100's tablets.
Trexate Tablet 10mg
100's tablets.
Trexate Injection 50mg/2ml
1 vial
Trexate Injection 1000mg/40ml
1 vial

خوراک وطریقہ استعمال:

سرطان کے ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

ہدایات:

دوا کو ۲۰- ۲۵ ڈگری سینٹی گریڈ کے درمیان محفوظ کریں۔

دھوپ، گرمی، نمی سے محفوظ رکھیں اور بچوں کی پہنچ سے دور رکھیں۔

صرف مستند اونکولوجسٹ یا کینسر ہسپتال کے نسخے پر فروخت کریں۔

Manufactured by:
PHARMASOL
PRIVATE LIMITED
Plot # 549,Sundar Industrial Estate,
Lahore, Pakistan.