Nordimet® (methotrexate) Solution for injection in pre-filled pen

Please refer to the Summary of Product Characteristics (SmPC) for full prescribing information

Presentation: Pre-filled pen containing 7.5 mg (in 0.3 ml), 10 mg (in 0.4 ml), 12.5 mg (in 0.5 ml), 15 mg (in 0.6 ml), 17.5 mg (in 0.7 ml), 20 mg (in 0.8 ml), 22.5 mg (in 0.9 ml) and 25 mg (in 1.0 ml) methotrexate in solution for injection. **Indications**: Active rheumatoid arthritis in adult patients. Polyarthritic forms of severe, active juvenile idiopathic arthritis, when the response to non-steroidal anti-inflammatory drugs (NSAIDs) has been inadequate. Severe recalcitrant disabling psoriasis, which is not adequately responsive to other forms of therapy such as phototherapy, PUVA and retinoids. Severe psoriatic arthritis in adult patients. Induction of remission in moderate steroid-dependent Crohn's disease in adult patients, in combination with corticosteroids and for maintenance of remission, as monotherapy, in patients who have responded to methotrexate. **Dosage and administration**: Nordimet should only be prescribed by physicians with expertise in the use of methotrexate and a full understanding of the risks of methotrexate therapy. Nordimet is injected once weekly, administered subcutaneously. Patients must be educated and trained in the proper injection technique when self-administering methotrexate. The first injection of Nordimet should be performed under direct medical supervision.

Important warning about the dosage of Nordimet
In the treatment of rheumatoid arthritis, active juvenile idiopathic arthritis, psoriasis, psoriatic arthritis and Crohn's disease requiring dosing once a week, Nordimet **must only be used once a week.** Dosage errors or incorrect administration of Nordimet can result in serious adverse reactions, including death. Healthcare professionals and patients should be clearly instructed. Please read this section of the SmPC very carefully.

Rheumatoid arthritis: The recommended initial dose is 7.5 mg of methotrexate once weekly. Depending on the individual activity of the disease and patient tolerability, the initial dose may be increased. A weekly dose of 25 mg should in general not be exceeded. Doses exceeding 20 mg/week can be associated with significant increase in toxicity, especially bone marrow suppression. Once the desired therapeutic result has been achieved, the dose should be reduced gradually to the lowest possible effective maintenance dose. Polyarthritic forms of severe, active juvenile idiopathic arthritis: The recommended dose is 10-15 mg/m² BSA per week. In therapy-refractory cases, the weekly dose may be increased up to 20 mg/m² BSA per week. Use in children < 3 years of age is not recommended. Psoriasis vulgaris and psoriatic arthritis: A test dose of 5-10 mg subcutaneously administered one week prior to initiation of therapy is recommended. The recommended initial dose is 7.5 mg methotrexate once weekly. Dose is to be increased gradually but should not, in general, exceed a weekly dose of 25 mg of methotrexate. Doses exceeding 20 mg per week can be associated with significant increase in toxicity, especially bone marrow suppression. Once the desired therapeutic result has been achieved, the dose should be reduced gradually to the lowest possible effective maintenance dose. The dose should be increased as necessary but should in general not exceed the maximum recommended weekly dose of 25 mg; exceptional cases > 25 mg might be clinically justified, but should not exceed a maximum weekly dose of 30 mg. Crohn's disease: Induction treatment: 25 mg/week administered subcutaneously. Once patients have adequately responded to combination therapy, the corticosteroids should be tapered. Response to treatment can be expected after 8 to 12 weeks. Maintenance treatment: 15 mg/week administered subcutaneously, as monotherapy, if the patient has entered remission. Renal impairment, hepatic impairment, elderly patients, patients with a third distribution space (pleural effusions, ascites) or paediatric population: Please refer to the SmPC. Note: When switching from oral to subcutaneous use, a reduction in the dose may be required, due to the variable bioavailability of methotrexate after oral administration. **Contraindications:** Hypersensitivity to methotrexate or to any of the excipients. Severe hepatic impairment, if serum bilirubin is > 5 mg/dl (85.5 µmol/l). Alcohol abuse. Severe renal impairment (creatinine clearance < 30 ml/min). Pre-existing blood dyscrasias (e.g., bone marrow hypoplasia, leukopenia, thrombocytopenia or significant anaemia). Immunodeficiency. Serious, acute or chronic infections such as tuberculosis and HIV. Stomatitis. Ulcers of the oral cavity and known active gastrointestinal ulcer disease. Pregnancy. Breast-feeding. Concurrent vaccination with live vaccines. **Special warnings and precautions:** Patients must be clearly advised that the therapy is to be administered once a week, and not every day. Patients receiving therapy should be appropriately monitored before and during treatment; see SmPC for full details of blood tests and other investigations including hepatic, renal and respiratory monitoring. The possible risks of effects on reproduction, pregnancy loss and congenital malformations should be discussed with male and female patients of childbearing potential. The absence of pregnancy must be confirmed before Nordimet is used. Male and female patients treated with Nordimet should use effective contraception during treatment and for at least six months after. Methotrexate contact with skin and mucosal membranes is to be avoided; in cases of contamination rinse the area with plenty of water. Particular caution should be exercised in the presence of inactive, chronic infections (e.g., herpes zoster, tuberculosis, hepatitis B or C) due to possible activation. Malignant lymphomas may occur in patients receiving low-dose methotrexate; in which case, methotrexate must be discontinued. In patients with pathological accumulation of liquid in body cavities ("third space"), such as ascites or pleural effusions, the plasma elimination half-life of methotrexate is prolonged. Pleural effusions and ascites should be drained prior to initiation of methotrexate treatment. Conditions leading to dehydration such as emesis, diarrhoea or stomatitis, can increase the toxicity of methotrexate due to elevated levels of the active substance. In these cases use of methotrexate should be interrupted until the symptoms cease. Diarrhoea and ulcerative stomatitis can be toxic effects and require interruption of therapy, otherwise haemorrhagic enteritis and death from intestinal perforation may occur. If haematemesis, black discolouration of the stool or blood in stool occur, therapy is to be interrupted. Cases of progressive multifocal leukoencephalopathy have been reported in patients receiving methotrexate, PML can be fatal and should be considered in the differential diagnosis in immunosuppressed patients with new onset or worsening neurological symptoms. Encephalopathy/Leukoencephalopathy have been reported in oncologic patients receiving methotrexate therapy and cannot be excluded for methotrexate therapy in non-oncologic indications. Vitamin preparations or other products containing folic acid, folinic acid or their derivatives may decrease the effectiveness of methotrexate. Radiation induced dermatitis and sun-burn can reappear under methotrexate therapy (recall-reaction). Psoriatic lesions can exacerbate during UV-irradiation and simultaneous administration of methotrexate. Concomitant administration of folate antagonists such as trimethoprim/sulphamethoxazole has been reported to cause an acute megaloblastic pancytopenia in rare instances. Photosensitivity manifested by an exaggerated sunburn reaction has been observed in some individuals taking methotrexate. Exposure to intense sunlight or to UV rays should be avoided. Patients should use a sun- protection product with a high protection factor. **For drug interactions and additional information on fertility, pregnancy and lactation information please see SmPC. Undesirable effects: See SmPC for full list of undesirable effects.** Very common: Stomatitis. Dyspepsia. Appetite loss. Abdominal pain. Nausea. Abnormal liver function tests. Common: Leukopenia. Anaemia. Thrombopenia. Headache. Tiredness. Drowsiness. Pneumonia. Interstitial alveolitis/pneumonitis. Oral ulcers. Diarrhoea. Exanthema. Erythema. Pruritus. Uncommon: Pharyngitis. Pancytopenia. Precipitation of diabetes mellitus. Depression. Confusion. Dizziness. Enteritis. Vomiting. Pancreatitis. Gastrointestinal ulceration and bleeding. Cirrhosis, fibrosis and fatty degeneration of liver. Decrease in serum albumin. Herpes Zoster. Vasculitis. Arthralgia. Osteoporosis. Inflammation and ulceration of bladder. Renal impairment. Rare: Infection. Conjunctivitis. Sepsis. Allergic reactions. Anaphylactic shock. Hypogammaglobulinaemia. Visual disturbances. Pericarditis. Pericardial effusion. Pericardial tamponade. Hypotension. Thromboembolic events. Pulmonary fibrosis. Pneumocystis jiroveci pneumonia. Shortness of breath and bronchial asthma. Pleural effusion. Acute hepatitis. Allergic vasculitis. Stress fracture. Renal failure. Oliguria. Anuria. Very rare: Lymphoma. Agranulocytosis. Lymphoproliferative disorders. Severe courses of bone marrow depression. Acute aseptic meningitis. Convulsions. Paralysis. Impaired vision. Retinopathy. Haematemesis. Haematorrhoea. Toxic megacolon. Hepatic failure. Stevens-Johnson syndrome. Toxic epidermal necrolysis. Paraesthesia/Hypoaesthesia. Loss of libido. Impotence. Gynaecomastia. Oligospermia. Not known: Eosinophilia. Encephalopathy/Leukoencephalopathy. Jaw osteonecrosis (secondary to lymphoproliferative disorders). Epistaxis. Pulmonary alveolar haemorrhage. Injection site necrosis. Oedema. Skin exfoliation/dermatitis exfoliative. **Cost (for single Nordimet Pen)**: 7.5 mg: £13.37, 10 mg: £13.77, 12.5 mg: £14.85, 15 mg: £14.92, 17.5 mg: £15.75, 20 mg: £16.06. 22.5 mg: £16.61 and 25 mg: £16.64 **Legal classification**: POM. **MA numbers: Nordimet**: PLGB 40621/0024 – 0031 & EU/1/16/1124/001 – 008. **Further information available from**: Nordic Pharma Ltd., Building 1410, Arlington Business Park, Theale, Reading, RG7 4SA. **Date of revision**: February 2024. **Item code:** UK-PEN-2400051.

Adverse events should be reported. Reporting forms and information can be found at yellowcard.mhra.gov.uk or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Nordic Pharma at medinfo.uk@nordicpharma.com