meto ject®

Metoject® PEN is a pre-filled autoinjector for automatic self-injection of methotrexate (MTX):

- The PEN is ready to use
- The device is designed to ensure a safe application by needle shield and childproof lock system
- It contains a MTX solution of 50 mg/ml and thus the smallest-possible injection volume
- Fast injection in max. 5 seconds

Indicated for

- Rheumatoid arthritis
- Psoriasis
- Psoriatic arthritis

Summary of the most important points

- Ready to use
- Easy to handle, especially for rheumatoid hands
- Safety through automatic needle shield protection and childproof lock
- Reduces injection pain[1]

7.5 mg | **10 mg** | **15 mg** | **20 mg** | **25 mg**

The different doses are colour-coded for an easy identification of the correct dosage.

medac

PRESCRIBING INFORMATION
(Please refer to the Summary of Product Characteristics before prescribing)
Metoject 7.5 mg / 10 mg / 15 mg / 20 mg / 25 mg solution for injection in pre-filled pen.
Therapeutic indications: Metoject is indicated for the treatment of: Active rheumatoid arthritis in adult patients, severe recalcitrant disabling psoriasis, which is not adequately responsive to other forms of therapy such as phototherapy, PUVA, and retinoids, and severe psoriatic arthritis in adult patients.
Posology and method of administration: Metoject should only be prescribed by physicians who are familiar with the various characteristics of the medicinal product and its mode of action. Patients must be educated to use the proper injection technique. The first injection of Metoject PEN should be performed under direct medical supervision. Metoject is injected **once weekly**. The patient must be explicitly informed about the fact that Metoject is administered **once a week only**. It is advisable to determine an appropriate fixed day of the week for the injection. Methotrexate elimination is reduced in patients with a third distribution space (ascites, pleural effusions). Such patients require especially careful monitoring for toxicity, and require dose reduction or, in some cases, discontinuation of methotrexate administration (reference section 5.2 and 4.4 of the SPC). *Adults, rheumatoid arthritis:* The recommended initial dose is 7.5 mg of Metoject once weekly, administered subcutaneously. Depending on the individual activity of the disease and tolerability, the dose may be increased gradually by 2.5 mg per week. A weekly dose of 25 mg should in general not be exceeded. Upon achieving the therapeutically desired result, the dose should be reduced gradually to the lowest possible effective maintenance dose. Use in children < 3 years of age is not recommended as insufficient data on efficacy and safety is available for this population (reference section 4.4 of the SPC). *Dosage in patients with psoriasis vulgaris, psoriatic arthritis:* It is recommended that a test dose of 5 – 10 mg should be administered parenterally, one week prior to therapy to detect idiosyncratic adverse reactions. The recommended initial dose is 7.5 mg of methotrexate once weekly, administered subcutaneously. The dose is to be increased gradually but should not, in general, exceed a weekly dose of 25 mg of methotrexate. The dose should be increased as necessary but should in general not exceed the maximum recommended weekly dose of 25 mg. Upon achieving the therapeutically desired result, the dose should be reduced gradually to the lowest possible effective maintenance dose. Maximum weekly dose. The dose should be increased as necessary but should in general not exceed the maximum recommended weekly dose of 25 mg. In a few exceptional cases a higher dose might be clinically justified, but should not exceed a maximum weekly dose of 30 mg of methotrexate as toxicity will markedly increase. Patients with renal impairment: Metoject should be used with caution in patients with impaired renal function (see section 4.3 of SPC for further information). Patients with hepatic impairment: Methotrexate should be administered with great caution, if at all, to patients with significant current or previous liver disease, especially if due to alcohol. If bilirubin is > 5 mg/dl (85.5 µmol/l), methotrexate is contraindicated. *Elderly:* Dose reduction should be considered due to reduced liver and kidney function as well as lower folate reserves. Use in patient with a third distribution space (pleural effusions, ascites): As the half-life of methotrexate can be prolonged to 4 times the normal length in patients who possess a third distribution space dose reduction or, in some cases, discontinuation of methotrexate administration may be required (see section 5.2 and 4.4 of the SPC). Instructions for subcutaneous use: If changing the oral application to parenteral administration a reduction of the dose may be required due to the variable bioavailability of methotrexate after oral administration.
Contraindications: Hypersensitivity to methotrexate or any of the excipients (reference section 6.1 of the SPC); severe liver impairment (reference section 4.2 of the SPC); alcohol abuse; severe renal impairment (creatinine clearance < 30 ml/min reference section 4.2 and section 4.4 of the SPC); pre-existing blood dyscrasias (bone marrow hypoplasia, leukopenia, thrombocytopenia, significant anaemia); serious, acute or chronic infections such as tuberculosis, HIV, other immunodeficiency syndromes; ulcers of the oral cavity and known active gastrointestinal ulcer disease; pregnancy, breast-feeding (reference section 4.6 of the SPC) ; concurrent vaccination with live vaccines.
Special warnings and precautions for use: Patients must be clearly informed that the therapy has to be administered **once a week,** not every day. Patients undergoing therapy should be subject to appropriate supervision so that signs of possible toxic effects or adverse reactions may be detected and evaluated with minimal delay. Therefore treatment with methotrexate should only be initiated and supervised by physicians whose knowledge and experience includes the use of antimetabolite therapy. Because of the possibility of severe or even fatal toxic reactions, the patient should be fully informed by the physician of the risks involved and the recommended safety measures. Recommended examinations and safety measures: Before beginning or reinstituting methotrexate therapy after a rest period: Complete blood count with differential blood count and platelets, liver enzymes, bilirubin, serum albumin, chest x-ray and renal function tests. If clinically indicated, exclude tuberculosis and hepatitis, see section 4.4 of the SPC for further information). During therapy (at least once a month during the first six months and every three months thereafter): An increased monitoring frequency should be considered also when the dose is increased, see section 4.4 of the SPC for further information).
Sodium: This medicinal product contains less than 1 mmol sodium (23 mg) per dose, i.e. essentially "sodium-free".**Interactions with other medicines:** Special care should be taken with Methotrexate and Alcohol, hepatotoxic medicinal products, haematotoxic medicinal products, oral antibiotics, antibiotics, medicinal products with high plasma protein binding, probenecid, weak organic acids, pyrazoles, non-steroidal anti-inflammatory agents, medicinal products with adverse reactions on the bone marrow, medical products which cause folate deficiency, folic acid, other antirheumatic medicinal products, sulphasalazine, mercaptopurine, proton-pump inhibitors, theophylline, caffeine or theophylline-containing beverages. **Fertility, pregnancy and lactation:** Methotrexate is contraindicated during pregnancy and is excreted in breast milk and there is a risk for the infant. Methotrexate can be genotoxic, all women are advised to consult a genetic counselling centre, if possible, already prior to therapy. Men should seek advice about the possibility of sperm preservation before starting therapy. **Effects on ability to drive and use machines:** Central nervous symptoms such as tiredness and dizziness can occur during treatment, Metoject has minor or moderate influence on the ability to drive and use machines. **Undesirable effects**: The following headings are used to organise the undesirable effects in order of frequency: Very common (≥1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1,000 to < 1/100), rare (≥1/10,000 to < 1/1,000), very rare (<1/10,000), not known (cannot be estimated from the available data) The most relevant undesirable effects are suppression of the haematopoietic system and gastrointestinal disorders. **Very common:** Gastrointestinal disorders (Stomatitis, dyspepsia, nausea, loss of appetite, **abdominal pain) and Hepatobiliary disorders (Abnormal liver function tests (increased ALAT, ASAT, alkaline phosphatase and bilirubin). Common**: Blood and lymphatic system disorders (Leukopenia, anaemia, thrombopenia). **Uncommon**: Infections and infestations (Pharyngitis), Blood and lymphatic system disorders (Pancytopenia), Metabolism and nutrition disorders (Precipitation of diabetes mellitus), Psychiatric disorders (Depression, Confusion). Nervous System Disorders (dizziness) and Gastrointestinal disorders (Gastrointestinal ulcers and bleeding, enteritis, vomiting, pancreatitis), Hepatobiliary disorders (Cirrhosis, fibrosis and fatty degeneration of the liver, decrease in serum albumin), Skin and subcutaneous tissue disorders (Photosensitisation, loss of hair, increase in rheumatic nodules, skin ulcer, herpes zoster, vasculitis, herpetiform eruptions of the skin, urticarial), Musculoskeletal and connective tissue disorders (Arthralgia, myalgia, osteoporosis), Renal and urinary disorders (Inflammation and ulceration of the urinary bladder, renal impairment, disturbed micturition) and Reproductive system and breast disorders (Inflammation and ulceration of the vagina). **Rare:** Infections and infestations (Infection (incl. reactivation of inactive chronic infection), sepsis, Pneumocystis jirovecii pneumonia, conjunctivitis), Immune system disorders (Allergic reactions, anaphylactic shock, hypogammaglobulinaemia), Psychiatric disorders (Mood alterations), Eye disorders (visual disturbances), Cardiac disorders (Pericarditis, pericardial effusion, pericardial tamponade), VASCULAR DISORDERS (Hypotension, thromboembolic events), Respiratory, thoracic and mediastinal disorders (Pulmonary fibrosis, shortness of breath and bronchial asthma, pleural effusion), Gastrointestinal disorders (Gingivitis), Hepatobiliary disorders (acute hepatitis), Skin and subcutaneous tissue disorders (Increased pigmentation, acne, petechiae, ecchymosis, allergic vasculitis), Musculoskeletal and connective tissue disorders (stress fracture), Renal and urinary disorders (Renal failure, oliguria, anuria, electrolyte disturbances), General disorders and administration site conditions (Fever, wound-healing impairment). See Section 4.8 of the SPC for very rare and unknown undesirable effects.
Overdose: Calcium folinate is the specific antidote for neutralising the toxic undesirable effects of methotrexate.
Legal classification: POM. **Marketing authorisation holder:** Medac Gesellschaft für klinische Spezialpräparate mbH
Theaterstrasse 6, 22880 Wedel, Germany. **Marketing authorisation Number:** PA0623/014/002, PA0623/014/003, PA0623/014/004, PA0623/014/005, PA0623/014/006 **Date of revision of text:** June 2018.

For a copy of the SmPC or further medical information, please contact medical@dccvital.com .
Adverse events should be reported to Fannin Ltd, Pharmacovigilance at +353 (0)86 839 4447 or medical@dccvital.com.
Reporting of suspected adverse reactions: Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Health care professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Earlsfort Terrace, IRL-Dublin 2; Tel: +353 (0) 1 676 4971; Fax:+353 (0)1 676 2517. Website: www.hpra.ie; Email: medsafety@hpra.ie.

Additional information available on request.

References: 1. Hattesohl et al. German Society Rheumatology 2017 doi: 10.3205/17dgrh244.

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