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metoject®/metex® –
THE METHOTREXATE AUTOINJECTOR

Efficacy and use of subcutaneous methotrexate in psoriasis therapy

medac

Content

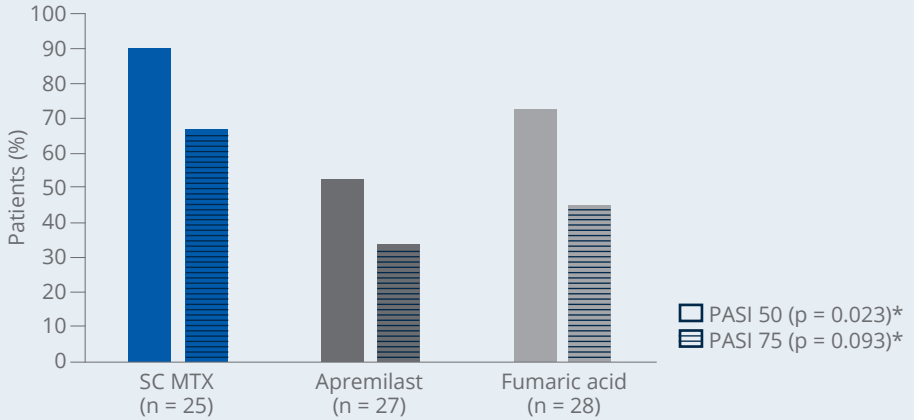
Why chose SC MTX for first-line therapy?

Current European guidelines recommend the subcutaneous administration for firstline MTX therapy[1].

Subcutaneous methotrexate (SC MTX) was compared to apremilast and fumaric acid in a prospective, multiarm study of patients (n = 80) with plaque psoriasis. In a real-world clinical setting, patient-reported and clinical outcomes were examined during the first 6 months of treatment[2].

HIGH CLINICAL RESPONSE IN PATIENTS TREATED WITH SC MTX

More patients treated with SC MTX showed a PASI-50/75 response at week 24 than patients treated with apremilast or fumaric acid esters. 2 of 3 patients in the MTX group (66.7%) achieved a 75% reduction from baseline (PASI 75) at week 24.

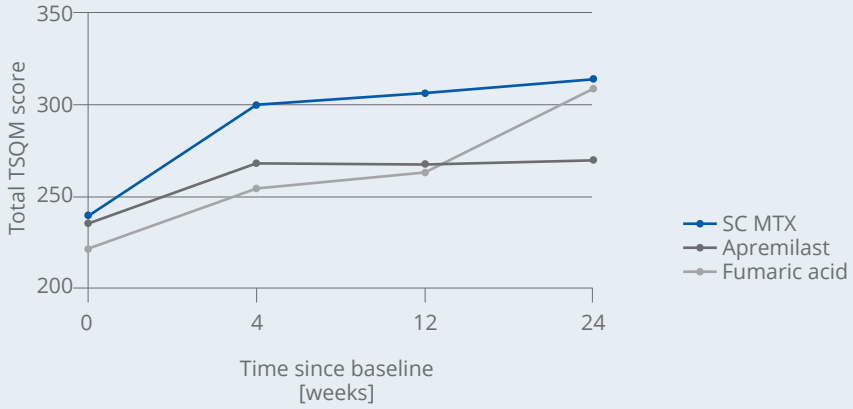


*Comparison between the three groups

Most patients achieve a high clinical response with SC MTX compared to apremilast or fumaric acid.

HIGHEST TREATMENT SATISFACTION WITH SC MTX OVER TIME

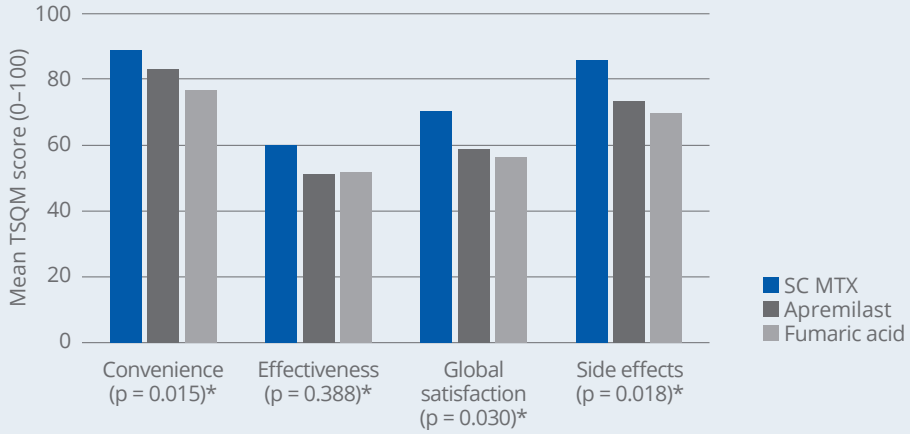
Compared to oral apremilast and fumaric acid, patients receiving SC MTX assigned the highest treatment satisfaction levels in all four domains (convenience, effectiveness, global satisfaction, side-effects), already beginning at week 4, in the total Treatment Satisfaction Questionnaire for Medication (TSQM) score (306.3 ± 50.9, p = 0.05).



After only 4 weeks, the highest treatment satisfaction level was seen with SC MTX, against drugs applied as tablets.

SC MTX SCORES HIGH IN ALL AREAS OF PATIENTS' TREATMENT SATISFACTION

Patients treated with SC MTX showed higher satisfaction compared to the oral drugs according to the TSQM scores in all 4 domains: convenience, side effects, global satisfaction and effectiveness. TSQM score ranges from 0 (extremely dissatisfied) to 100 (extremely satisfied). A person's total TSQM score was calculated by taking the mean of the TSQM points across all available visits.



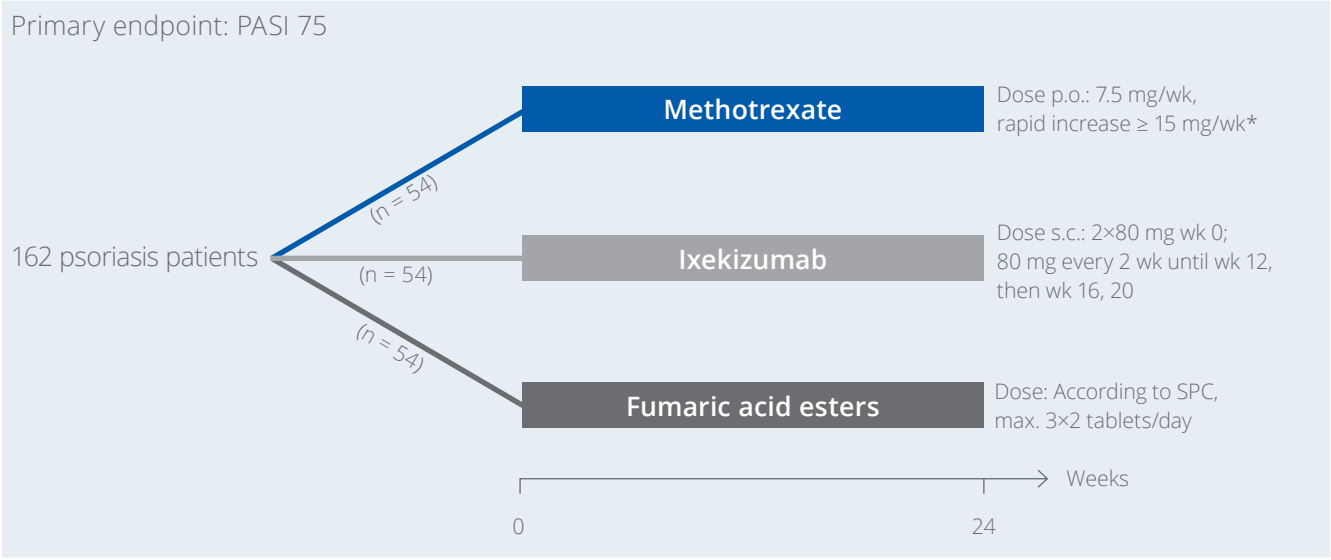
*Comparison between the three groups

Regarding side effects and convenience, SC MTX reached numerically higher patient satisfaction scores. SC MTX showed the lowest therapy interruption rate (16%) compared to apremilast (22%) or fumaric acid (84%) (data not shown).

Drug survival — MTX versus other therapies

DIRECT COMPARISON OF MTX, IXEKIZUMAB (IXE) AND FUMARIC ACID ESTER (FAE)

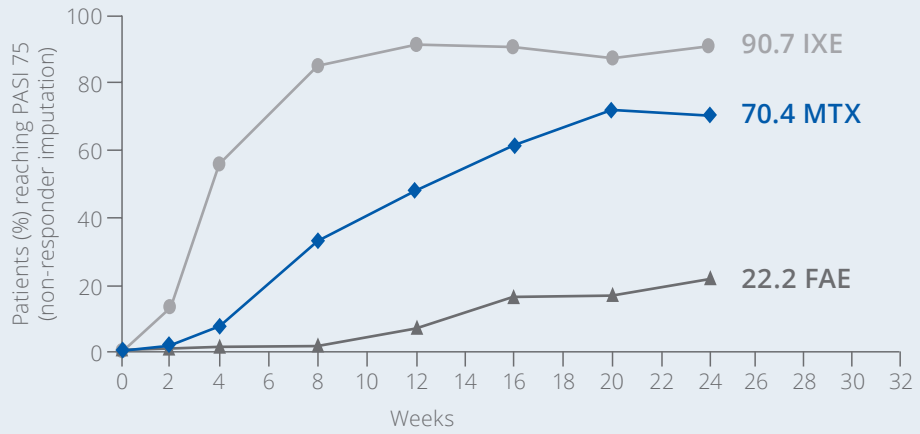
A 24-week, randomized open-label study in psoriasis therapy[3]



*75% of MTX-treated patients received ≥ 15 mg/week from week 2 until end of trial.

HIGH CLINICAL RESPONSE AT WEEK 24

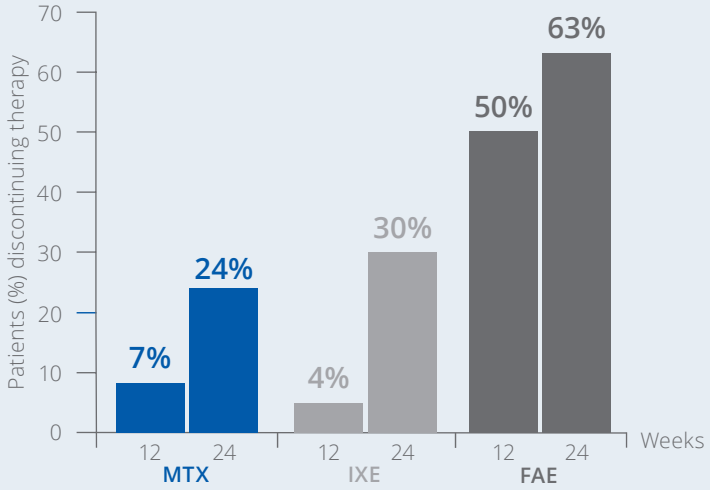
7 out of 10 MTX-treated patients achieved PASI 75. Clinical response was more than 3-fold higher with MTX than with FAE therapy.



Faster and better clinical response of MTX and IXE compared to FAE

HIGHER DRUG ADHERENCE WITH MTX AT WEEK 24

76% of MTX-treated patients were still on therapy at week 24 compared to 37% of FAE-treated patients.

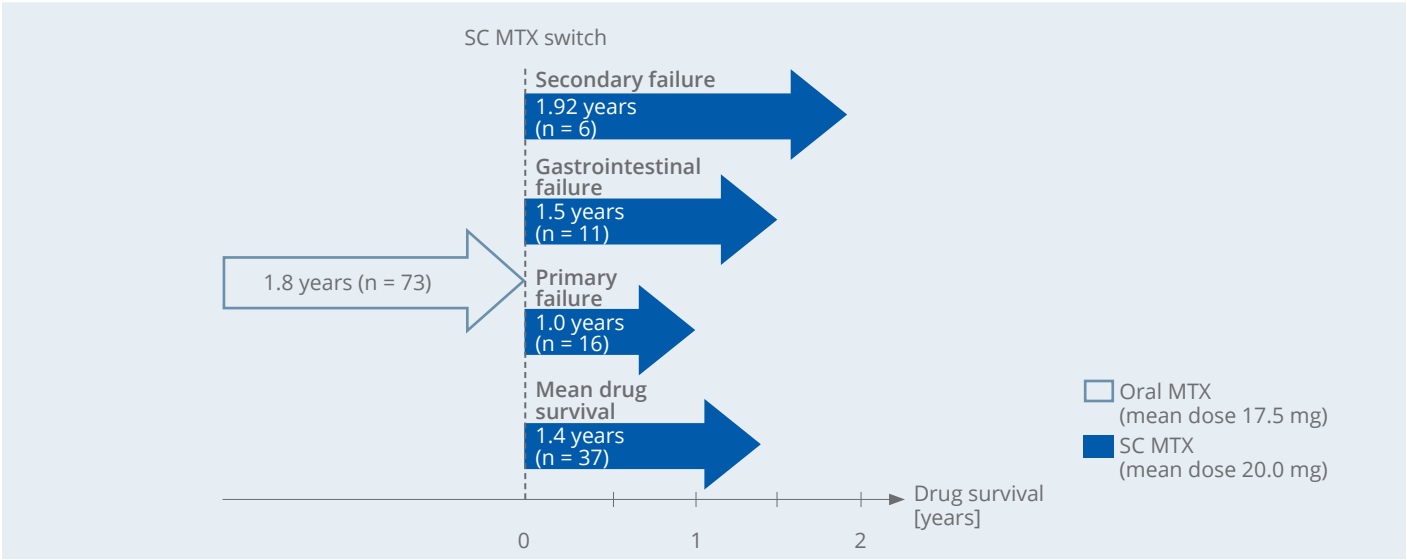


Less discontinuation with MTX and IXE therapy

Drug survival — oral versus SC MTX

EXTEND THERAPY WITH SC MTX

In this retrospective study, 37 from 73 patients with chronic plaque psoriasis who failed to tolerate or respond adequately to oral treatment were switched to SC MTX[4]. The reasons for switching to SC MTX are indicated by the blue arrows.



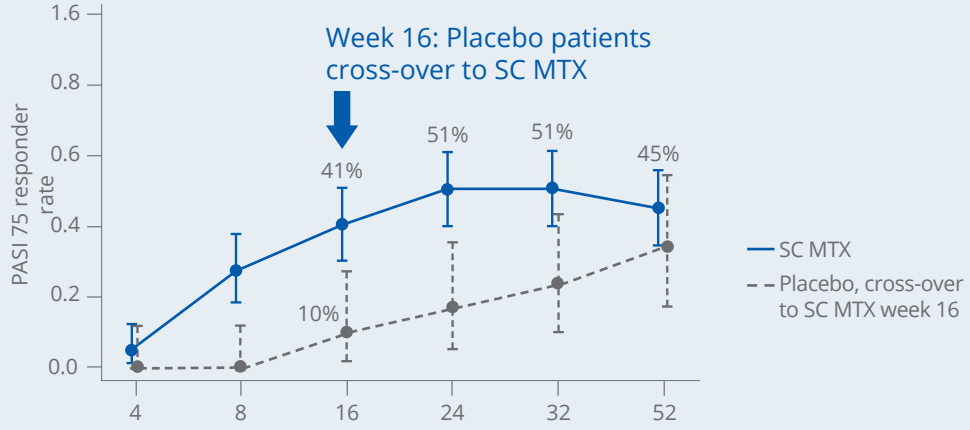
With SC MTX, patients stay longer on therapy – up to nearly 2 extra years.

Therapeutic benefits of SC MTX in psoriasis therapy — METOP study

The METOP trial was the first randomized, multicentric, double-blinded, long-term phase III trial to investigate SC MTX versus placebo in psoriasis therapy.[5] 120 patients with moderate-to-severe plaque psoriasis were randomized 3:1 to receive either SC MTX or placebo until week 16. Subsequently, all patients received SC MTX until week 52.

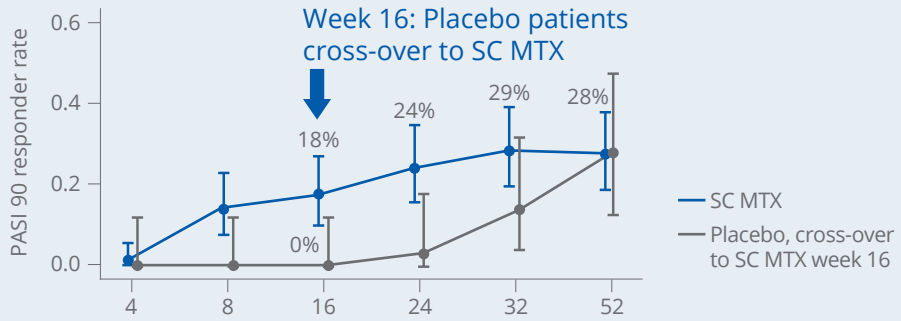
PRIMARY ENDPOINT: 75% IMPROVEMENT IN PASi

Full efficacy at week 24: Every second patient reaches PASI 75.



LONG-TERM EFFICACY OF SC MTX THERAPY

Approximately 3 of 10 psoriasis patients treated with SC MTX reach PASI 90.

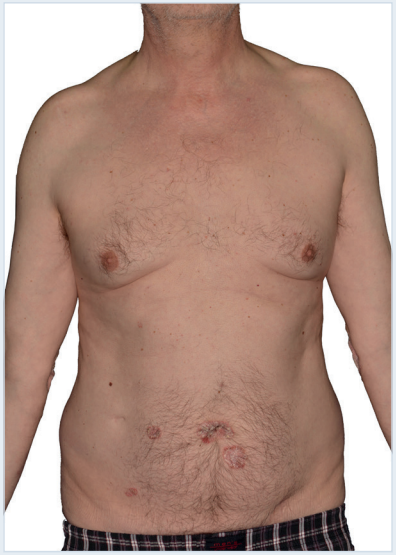


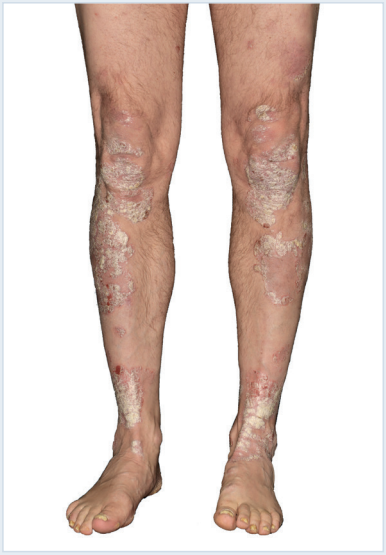
- Rapid onset of action and sustained response with SC MTX
- Advantage in long-term therapy with SC MTX

METOP CASE REPORT:
SUBCUTANEOUS metoject®/metex® — BEFORE ...

Patient data: 57-year old man with moderate-to-severe plaque psoriasis and psoriatic arthritis.

Baseline: PASI 16.2





**Images: courtesy of Dr. Wilsmann-Theis, Clinic and Polyclinic for Dermatology and Allergology, University of Bonn, Germany. Unpublished data.*

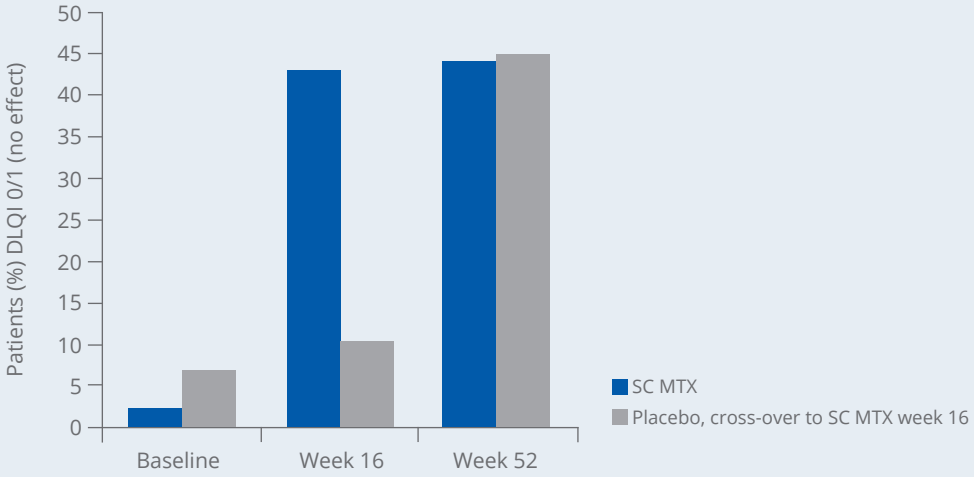
... AND AFTER THERAPY

After 33 months treatment: PASI 2.2

Remarkable clinical long-term response of skin symptoms

QUALITY OF LIFE IMPROVED IN METOP STUDY[5]

Almost half of the patients treated with SC MTX had a Dermatology Life Quality Index (DLQI) response of 0 or 1 at week 52, indicating „no effect“ of disease on their lives.

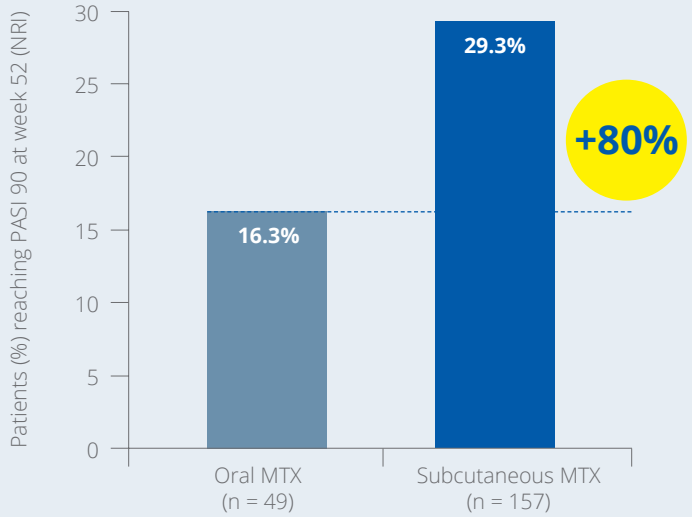


Early use of SC MTX therapy shows a clear improvement in quality of life.

SC versus oral MTX

IMPROVED EFFICACY OF SC MTX DEMONSTRATED BY REAL-WORLD DATA — PSOBEST[6]

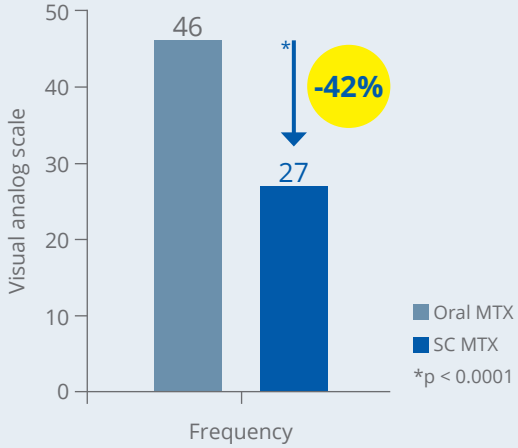
When starting psoriasis therapy with SC MTX, more patients achieved a faster onset of response, indicated by PASI 50 at week 12 (65.3% vs. 80.9%). Compared to the oral MTX group, more patients reached PASI 90 with SC MTX by week 52.



Besides a faster onset of response, SC MTX nearly doubles the patient number reaching PASI 90. SC MTX enables a more stable long-term therapy response.

SIGNIFICANT REDUCTION IN FATIGUE ...

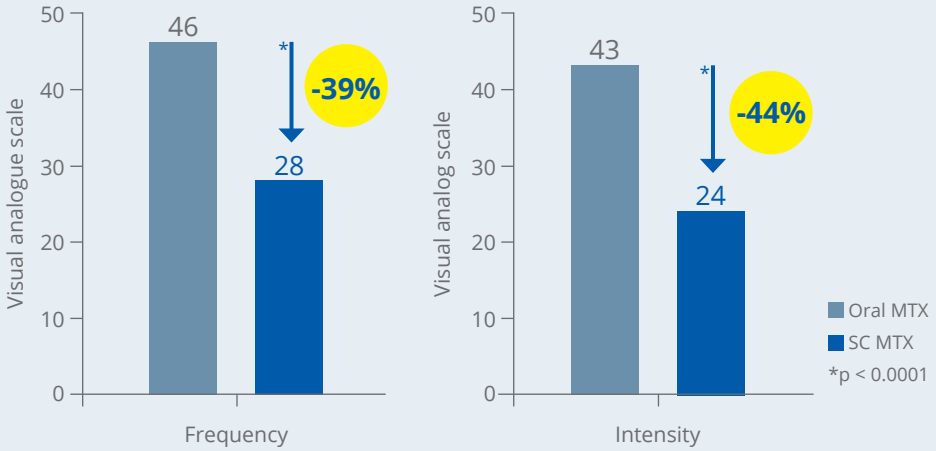
A prospective, multicenter cohort study investigated patient reported outcome measures before and after switching from oral to SC MTX (n=75).[7] MTX dosing after the switch remained almost the same with a median value of 15 mg/week. Frequency of fatigue was significantly reduced by switching from oral to SC MTX. For fatigue, a VAS between 10–20 is assumed to be clinically meaningful.



By using SC MTX fatigue can be reduced.

... AND NAUSEA WITH SC MTX

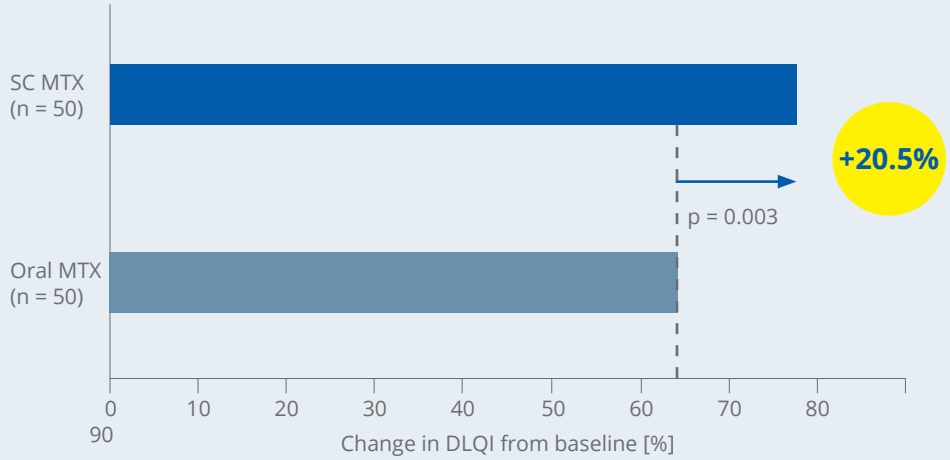
For nausea, the improvement is clinically relevant as the visual analogue scale (VAS) score surpasses the Minimal Clinical Important Difference of 15. In a subgroup (n = 35), who cited nausea as the main reason for switching, the frequency and intensity even significantly improved by ≥ 50 % (data not shown).



Switching from oral to SC MTX reduced the frequency and intensity of nausea.

IMPROVED QUALITY OF LIFE

In a prospective, single-blinded, randomized controlled trial adult patients (n = 100) with severe psoriasis were administered oral or SC MTX at the same dose (0.3 mg/kg/week (maximum 25 mg/week)) for 12 weeks.[8] SC MTX results in a greater reduction in Dermatology Life Quality Index (DLQI) at the end of 12 weeks compared to oral MTX.



Significant improvement in DLQI through use of SC MTX!

THE METHOTREXATE AUTOINJECTOR

- Enhanced bioavailability compared to oral application[1,9, 10]
- Faster onset of response, increased effectiveness with parenteral methotrexate[5, 6, 8]
- Less GI side effects and improved quality of life with SC MTX administration[2, 5, 7, 8]
- Less therapy discontinuation and more stable long-term treatment[3, 4, 5, 6]
- Can delay a therapy switch to biologic agents[4]

Up to 10 dose options available for individualized therapy*

7.5 mg	10 mg	12.5 mg	15 mg	17.5 mg
20 mg	22.5 mg	25 mg	27.5 mg	30 mg

* Availability depending on country

[1]Nast A et al. J Eur Acad Dermatol Venereol. 2020; 34(11): 2461-2498 [2]Fink C et al. J Dermatolog Treat. 2022; 33(7): 2997–3004 [3]Reich K et al. Br J Dermatol. 2020; 182(4): 869–79 [4]Hollywood A et al. Br J Dermatol. 2020; 182(5): 1290–1 [5]Warren RB et al. Lancet. 2017; 389(10068): 528–37 [6]Reich K et al. Br J Dermatol. 2021; 184(4): 765–7 [7]Fraes Diernæs JE et al. J Am Acad Dermatol. 2022;87(4): 920-922 [8]Dogra S et al. Dermatol Ther. 2022; 35(8): e15656 [9]Vena GA et al. Ther Clin Risk Manag. 2018; 14:105–16 [10]Pichlmeier U et al. Clin Exp Rheumatol. 2014; 32(4): 563–71

Metoject® PEN / metex® Pen 7.5 mg / 10 mg / 12.5 mg / 15 mg / 17.5 mg / 20 mg / 22.5 mg/ 25 mg/ 27.5 mg / 30 mg solution for injection in pre-filled pen
Qualitative and quantitative composition: 1 pre-filled pen with 0.15 ml (0.20 ml; 0.25 ml; 0.30 ml; 0.35 ml; 0.40 ml; 0.45 ml; 0.50 ml; 0.55 ml; 0.60 ml) contains 7.5 mg (10 mg; 12.5 mg; 15 mg; 17.5 mg; 20 mg; 22.5 mg; 25 mg; 27.5 mg; 30 mg) methotrexate. *Excipients:* NaCl, NaOH, HCl, water for injections.
Metoject® / metex® 50 mg/ml solution for injection, pre-filled syringe
Qualitative and quantitative composition: 1 ml of solution contains 50 mg methotrexate (as methotrexate disodium). 1 pre-filled syringe of 0.15 ml (0.20 ml; 0.25 ml; 0.30 ml; 0.35 ml; 0.40 ml; 0.45 ml; 0.50 ml; 0.55 ml; 0.60 ml) contains 7.5 mg (10 mg; 12.5 mg; 15 mg; 17.5 mg; 20 mg; 22.5 mg; 25 mg; 27.5 mg; 30 mg) methotrexate. *Excipients:* NaCl, NaOH, water for injections.
Therapeutic indications: Active rheumatoid arthritis in adult patients; polyarthritic forms of severe, active juvenile idiopathic arthritis, when the response to nonsteroidal anti-inflammatory drugs (NSAIDs) has been inadequate; severe psoriatic arthritis in adult patients; mild to moderate Crohn's disease either alone or in combination with corticosteroids in adult patients refractory or intolerant to thiopurines. *PEN additionally:* moderate to severe psoriasis in adult patients who are candidates for systemic therapy. *Syringe additionally:* severe recalcitrant disabling psoriasis, which is not adequately responsive to other forms of therapy such as phototherapy, PUVA and retinoids. **Posology and method of administration:** 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. *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. *Polyarthritic forms of juvenile idiopathic arthritis:* The recommended dose is 10-15 mg/m^2 body surface area (BSA)/once weekly, administered subcutaneously. In therapy-refractory cases the weekly dosage may be increased up to 20 mg/m^2 BSA/once weekly. Use in children < 3 years of age is not recommended as insufficient data on efficacy and safety is available for this population. *Psoriasis vulgaris, psoriatic arthritis:* 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. *Crohn's disease:* Induction treatment: 25 mg/week administered subcutaneously. Response to treatment can be expected after approximately 8 -12 weeks. Maintenance treatment: 15 mg/week. *Elderly:* Dose reduction should be considered due to reduced liver and kidney function as well as lower folate reserves. If changing the oral to parenteral administration a reduction of dose may be required due to the variable bioavailability. **Contraindications:** Hypersensitivity to methotrexate or any of the excipients; severe liver impairment; alcohol abuse; severe renal impairment (creatinine clearance < 30 ml/min); 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, breastfeeding; concurrent vaccination with live vaccines. **Special warnings and precautions for use:** In the treatment of rheumatoid arthritis, juvenile idiopathic arthritis, psoriasis and psoriatic arthritis, and Crohn's disease, Metoject PEN (methotrexate) must only be used once a week. Dosage errors in the use can result in serious adverse reactions, including death. **Undesirable effects:** Most serious adverse reactions of methotrexate include bone marrow suppression, pulmonary toxicity, hepatotoxicity, renal toxicity, neurotoxicity, thromboembolic events, anaphylactic shock and Stevens-Johnson syndrome. Most frequently (very common) observed adverse reactions of methotrexate include gastrointestinal disorders e.g. stomatitis, dyspepsia, abdominal pain, nausea, loss of appetite and abnormal liver function tests e.g. increased ALAT, ASAT, bilirubin, alkaline phosphatase. Other frequently (common) occurring adverse reactions are leukopenia, anaemia, thrombopenia, headache, tiredness, drowsiness, pneumonia, interstitial alveolitis/pneumonitis often associated with eosinophilia, oral ulcers, diarrhoea, exanthema, erythema and pruritus. *Effects:* Pharyngitis, infection (incl. reactivation of inactive chronic infection), sepsis, conjunctivitis. Lymphoma. Leukopenia, anaemia, thrombopenia, pancytopenia, agranulocytosis, severe courses of bone marrow depression, lymphoproliferative disorders, eosinophilia. Allergic reactions, anaphylactic shock, hypogammaglobulinaemia. Precipitation of diabetes mellitus. Depression, confusion, mood alterations. Headache, tiredness, drowsiness, dizziness, pain, muscular asthenia or paraesthesia/ hypoaesthesia, changes in sense of taste (metallic taste), convulsions, meningism, acute aseptic meningitis, paralysis, encephalopathy/ leukoencephalopathy. Visual disturbances, impaired vision, retinopathy. Pericarditis, pericardial effusion, pericardial tamponade. Hypotension, thromboembolic events. Pneumonia, interstitial alveolitis/pneumonitis often associated with eosinophilia. Symptoms indicating potentially severe lung injury (interstitial pneumonitis) are: dry, not productive cough, short of breath and fever, pulmonary fibrosis, Pneumocystis jirovecii pneumonia, shortness of breath and bronchial asthma, pleural effusion, epistaxis, pulmonary alveolar haemorrhage. Stomatitis, dyspepsia, nausea, loss of appetite, abdominal pain, oral ulcers, diarrhoea, gastrointestinal ulcers and bleeding, enteritis, vomiting, pancreatitis, gingivitis, haematemesis, haematorrhea, toxic megacolon. Abnormal liver function tests (increased ALAT, ASAT, alkaline phosphatase and bilirubin), cirrhosis, fibrosis and fatty degeneration of the liver, decrease in serum albumin, acute hepatitis, hepatic failure. Exanthema, erythema, pruritus, photosensitivity reactions, loss of hair, increase in rheumatic nodules, skin ulcer, herpes zoster, vasculitis, herpetiform eruptions of the skin, urticarial, increased pigmentation, acne, petechiae, ecchymosis, allergic vasculitis, Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell's syndrome), increased pigmentary changes of the nails, acute paronychia, furunculosis, telangiectasia, skin exfoliation/ dermatitis exfoliative. Arthralgia, myalgia, osteoporosis, stress fracture, osteonecrosis of jaw (secondary to lymphoproliferative disorders). Inflammation and ulceration of the urinary bladder, renal impairment, disturbed micturition, renal failure, oliguria, anuria, electrolyte disturbances, proteinuria. Inflammation and ulceration of the vagina, loss of libido, impotence, gynaecomastia, oligospermia, impaired menstruation, vaginal discharge. Fever, wound-healing impairment, asthenia, injection site necrosis, oedema. Local damage (formation of sterile abscess, lipodystrophy) of injection site following intramuscular or subcutaneous administration. Subcutaneous application of methotrexate is locally well tolerated. Only mild local skin reactions (such as burning sensations, erythema, swelling, discolouration, pruritus, severe itching, pain) were observed, decreasing during therapy. **Overdose:** Calcium folinate is the specific antidote for neutralising the toxic undesirable effects of methotrexate. **Legal classification:** POM **Marketing authorisation holder:** medac GmbH, Theaterstr. 6, 22880 Wedel, Germany.
Date of revision of text: 19.09.2024
PEN or syringe are registered in the following countries: Austria, Belgium, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Latvia, Lithuania, Netherlands, Norway, Poland, Portugal, Slovak Republic, Slovenia, Spain, Sweden, United Kingdom

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