Methotrexate Sub Cut Injection *(TLS amber)* (Adults)

Shared Care Guidelines: For use in dermatology and rheumatology

See BCAP Summary of Shared Care Guidelines for Monitoring of DMARDs September 2015

In most patients, subcutaneous methotrexate will replace current oral methotrexate. The same monitoring is use for subcutaneous and oral methotrexate. Patients will need to be educated and trained by 'the specialist' in safe handling, self injection and dispose of methotrexate

Licensed Indications:

Metoject® (methotrexate prefilled pen 50mg/ml) and Zlatal® (methotrexate prefilled syringe 25mg/ml) are licensed for:

- Adults with moderate to severe rheumatoid arthritis (RA) unresponsive or intolerant to conventional therapy.
- 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.
- Polyarthritic forms of severe, active juvenile idiopathic arthritis, when the response to nonsteroidal anti-inflammatory drugs (NSAIDs) has been inadequate.

Unlicensed indications:

- Unresponsive or chronically active Crohn's disease
- Connective tissue disease (SLE, myositis and vasculitis), Felty's syndrome, dermatomyositis, chronic intractable eczema

RESPONSIBILITIES and ROLES

	Hospital Clinician / Specialist responsibilities
	In addition to the responsibilities in the document BCAP Summary of shared care guidelines for DMARDs Aug 2015
1	Provide a prescription for initiating methotrexate treatment (at least 4 weeks) & train the patient on self administration
2	Ensure the patient is aware that Metoject© prefilled pens and Zlatal prefilled syringes contain an air bubble which should NOT be removed before administration.
3	Ensure the patient is given a cytotoxic waste bin and a cytotoxic spillage kit
4	If the patient requires doses in excess of 25mg per week prescribing responsibility must revert to the specialist.

	General Practitioner responsibilities
1	Prescribe cytotoxic sharps containers – IL Sharpsafe© or 1LSharpsguard© - see additional info at end of S/C
2	Advise patient to contact local authority for collection of sharps waste.

	Patient's role
1	Put used syringes, pens and needles in purple lidded cytotoxic sharps box provided by the GP on prescription.
2	Contact council for disposal of sharps waste.
3	Put any unopened syringes in cytotoxic sharps bins for disposal safely.

SUPPORTING INFORMATION

Treatment Schedule (including dosage and administration)

Dermatology

Rheumatology

- Usual starting oral dose 10-15mg ONCE a week, rapidly titrating to 20mg ONCE a week if tolerated. Subcutaneous dose usually given at the same as the oral dose.

All indications

- Maximum licensed injectable dose of Metoject for Rheumatoid Arthritis is 30mg ONCE a week.
- The lowest possible effective dose should be used.
- Elderly patients should be given a smaller test dose and titrated at a slower rate.
- Folic acid ONCE WEEKLY (not on day of methotrexate) may help reduce side effects

Contra-indications and precautions for use

- Patients receiving anti-folate drugs e.g trimethoprim, sulphonamides (glibenclamide, tolbutamide etc)
- Severe or significant renal impairment
- Significant hepatic impairment, or liver disease including fibrosis, cirrhosis, recent active hepatitis
- Active localised or systemic infectious disease e.g tuberculosis, hepatitis A, B C
- Overt or laboratory evidence of immunodeficiency syndrome(s)

- Serious cases of anaemia, leucopenia, or thrombocytopenia a
- Pregnancy (following administration to a man or woman) should be avoided for at least 3 months before conception (see section entitled 'pregnancy')
- Breast-feeding
- Patients with a known allergic hypersensitivity to methotrexate or excipients of the formulation

Adverse effects
Patients must urgently report mouth ulcers, sore throat, fever, epistaxis, jaundice, unexpected bruising or bleeding, any unexplained illness/infection and should be seen urgently for clinical assessment, FBC and LFT.
New onset of shortness of breath should also be reported.

The incidence and severity of adverse effects are considered to be dose related
Commonly these include: nausea, stomach pains, mucositis / stomatitis mouth ulcers, hair loss
Rarely these include: vomiting, diarrhoea, loss of appetite, headache, tiredness, dizziness, blurred vision, eye irritation, fever, chills, joint / muscle pain, allergic reaction, rash, acne, mood changes.

Serious adverse effects include:

Blood	Bone marrow depression – leucopoenia, thrombocytopenia and anaemia
Skin	Stevens-Johnson Syndrome, epidermal necrolysis, erythematous rashes, pruritus, urticaria, photosensitivity, pigmentary, changes, alopecia, ecchymosis, telangiectasia,, furunculosis
Lungs	Acute or chronic interstitial pneumonitis, acute pulmonary oedema, pulmonary fibrosis
Liver	Hepatic toxicity / significant elevations in LFTs (> 2-3 times ULN), fibrosis or cirrhosis
Kidney	Severe Renal failure and uraemia
Neurological	Aphasia, paresis, hemiparesis, and convulsions
Other	Malignant lymphomas

Immunization
Influenza vaccination is recommended PRIOR to the first dose of methotrexate and then annually (due to immunosuppression). A pneumovax II vaccination may also be recommended. Passive immunisation should be carried out using Varicella Zoster Immunoglobulin (VZIG) in non-immune patients if exposed to chickenpox or shingles. A list of safe vaccinations prior to travel is also available via the following link: (BAD PIL Methotrexate vaccination and immunisation) http://www.bad.org.uk/site/881/default.aspx

Pregnancy and Lactation
Because methotrexate is both abortifacient and teratogenic it is strictly contraindicated in pregnancy and during breastfeeding. Adequate contraceptive measures must be taken by women of childbearing potential during methotrexate therapy, and for at least **3 months** after treatment discontinued. Although methotrexate is not mutagenic, the drug may affect spermatogenesis. It is customary to advise men to avoid fathering children during therapy and for at least **3 months** after stopping

Interactions
Methotrexate is extensively protein-bound and may be displaced by other protein-bound drugs (e.g. diuretics, salicylates, hypoglycaemics), with a potential for increased toxicity. Concomitant use of other drugs with nephrotoxic or hepatotoxic potential (including alcohol) should be avoided.

- Always avoid trimethoprim, co-trimoxazole and sulphonamides (increases anti-folate effect) risk of pancytopenia
- Avoid concomitant use of cytotoxics with clozapine (increased risk of agranulocytosis)
- Live vaccines should not be administered (may cause strong antigenic reaction)
- Avoid aspirin (but low-dose regular aspirin is acceptable)
- NSAIDs can be prescribed, but patients will need to be carefully monitored for any side effects, particularly at higher methotrexate doses.
- Phenytoin can increase the antifolate effect of methotrexate.
- Excretion of methotrexate possibly reduced by ciprofloxacin, penicillins
- Increased risk of toxicity when given with doxycycline, ciclosporin, probenecid, and lefluomide
- Avoid concomitant use of acitretin

Monitoring – See BCAP Summary of Shared Care Guidelines for Monitoring of DMARDs September 2015

Administration of subcutaneous or intramuscular syringe

Patients and Carers: The specialist will decide which patients are suitable to receive SC methotrexate. Patients will be assessed by the clinic nurses taking into account:

- The patient is compliant
- The patient has hand function adequate for self administration
- The patient has a good understanding of:
  - Information on injection technique – self administration
  - Awareness of contact numbers
  - Awareness of the storage requirements
  - Understanding of disposal requirements

With the final decision taken by the hospital staff in conjunction with the patient. Patients will be trained by the clinic nurses who will document that training has occurred. The training will start by the nurse demonstrating how to give the injection, and then the patient self administering while supervised by the nurse. Details of who to contact in case of difficulties to be provided by the clinic.

Where the patient cannot self-administer consideration should be given to training a carer or by using the IM route.

Nurse administration: Should a nurse administer subcutaneous methotrexate, then it is advised they follow accepted good practice as described by the RCN guidance (see ref below), then it is advised they follow accepted good practice as described in the guidance. Gloves and apron should be worn and methotrexate should NOT be administered by anyone who is, or suspects they may be pregnant.

Cost - Metoject© (50mg/ml)

Strength	Cost per Pen	Annual drug cost
7.5mg/0.15ml	£14.85	£772.20
10mg/0.2ml	£15.29	£795.08
12.5mg/0.25ml	£16.50	£858.00
15mg/0.3ml	£16.57	£861.64
17.5mg/0.35ml	£16.64	£865.28
20mg/0.4ml	£17.84	£927.68
22.5mg/0.45ml	£18.45	£959.40
25mg/0.5ml	£18.48	£960.96
27.5mg/0.55ml	£18.89	£982.28
30mg/0.6ml	£18.95	£985.40

Cost - Zlatal© (25mg/ml)

Strength	Cost per Syringe	Annual drug cost
7.5mg/0.3ml	£13.37	£695.24
10mg/0.4ml	£13.77	£716.04
12.5mg/0.5ml	£14.85	£772.20
15mg/0.6ml	£14.92	£775.84
17.5mg/0.7ml	£15.75	£819
20mg/0.8ml	£16.06	£835.12
22.5mg/0.9ml	£16.61	£863.72
25mg/1ml	£16.64	£865.28

Cytotoxic Bins – Prescribe a 1L bin (allowable on an FP10) Sharpsafe© sharpsguard© - cytotoxic bin purple lid

Sharps http://www.daniels.co.uk/catalog/browse.php?id=5 http://www.sharpsafe.co.uk/p/23/1_Litre.html

Area	Disposal of cytotoxic waste details	Telephone No.
BANES	Contact Council for waste disposal http://www.bathnes.gov.uk/services/bins-rubbish-and-recycling/recycling-and-rubbish/clinical-waste-collection	01225 394041
Somerset	Follow local procedures contact Council for waste disposal	
Wilts	Contact Council for waste disposal http://www.wiltshire.gov.uk/rubbishrecycling/householdwaste/sharpsboxesclinicalwaste.htm	0300 456 0102

References

National Guidelines for the Monitoring of Second Line Drugs. British Society for Rheumatology. July 2008 MTRAC guidance VS97/15. National Patient Safety Agency. www.npsa.nhs.uk Patient Safety Alert Number 13 June 2006 and June 2004

RCN guidance on the administration of subcutaneous methotrexate for inflammatory arthritis http://www.rcn.org.uk/__data/assets/pdf_file/0011/78608/002269.pdf

Wyeth Pharmaceuticals. Methotrexate sodium tablets 2.5 mg. Summary of Product Characteristics 2003.

Patient held booklet NPSA http://www.nrls.npsa.nhs.uk/resources/?entryid45=59800

Methotrexate treatment books available from www.nhsforms .co.uk SEE BNF for details

British National Formulary June 2012 Metoject - http://www.medicines.org.uk/EMC/medicine/19455/SPC/Metoject+10+mg+ml+solution+for+injection%2c+pre-filled+syringe/

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