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Administering subcutaneous methotrexate for inflammatory arthritis

RCN guidance (Second edition)

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Foreword

Welcome to this second edition of the RCN’s guidance on administering subcutaneous methotrexate for inflammatory arthritis.

This updated publication contains evidence-based guidance to support practitioners in the safe and confident administration of subcutaneous methotrexate in a variety of primary and secondary care settings, including community and managed care environments.

Since the first edition of this publication in 2004, injectable methotrexate has become a licensed pharmacological treatment in the UK for various inflammatory conditions such as rheumatoid arthritis (RA), severe psoriatic arthritis in adult patients (PsA), polyarthritis juvenile idiopathic arthritis (JIA), and severe recalcitrant disabling psoriasis, and is available in pre-dosed, pre-filled syringes.

At the time of writing, two preparations have a licence for pre-dosed, pre-filled syringes of methotrexate. These include: medac (Metoject®) syringes, which are widely available in a strength of 50mg/ml, in doses from 7.5mg to 30mg, and Sandoz syringes (Ebetrex®) in a strength of 10mg/ml and 20mg/ml, which are currently unavailable for use.

In clinical practice, smaller doses than the available 7.5mg doses may be required; for example, in young children. These would need to be made up on a named patient basis (off licence), from a local pharmacy.

The availability of a pre-dosed, pre-filled syringe delivery system has made the subcutaneous administration process far more straightforward and far easier for patients, who previously had to rely on a hospital pharmacist to make up an injectable version of methotrexate. Today’s pre-filled syringes have a long shelf life (eliminating the need for patients having to regularly collect pharmacist-prepared treatments) and do not need to be stored in the fridge.

Because methotrexate has historically been used in the treatment of cancer, there is a long held perception that it is a high-risk drug. However, the doses involved in the treatment of inflammatory arthritis are small compared to the typical doses used in oncology, and the introduction of a pre-dosed, pre-filled syringe delivery system has helped minimise the risk of exposure for health care practitioners, carers and patients. However, the safe handling of the methotrexate treatment remains paramount.

It is hoped that this new publication will clarify the issues, provide guidance, and help facilitate best practice for a variety of care practitioners working in a number of settings.

Editorial Team, RCN Rheumatology Forum
Executive summary

This is a brief summary of the RCN’s updated guidance on administering subcutaneous methotrexate for inflammatory arthritis, highlighting the key issues for practitioners. The guidance covers aspects of both adult and children/young people’s care, including:

- methotrexate use
- risk management
- supply, storage, protective clothing and disposal
- home administration
- practitioner training and competence
- patient education and training
- audit trail and data collection.

Practitioners will find that key issues relating to the specific needs of children and young people can be found in the Paediatric guidance located in Section 2 of this document.

Note: the term practitioner is used throughout this document and relates to nurses or allied health care professionals who have been trained and demonstrate competence in administering subcutaneous therapies.

Risk management

The use of pre-filled syringes

- This guidance supports the use of licensed methotrexate via the subcutaneous route prepared, pre-filled syringe.


- The training and administration of methotrexate in pre-dosed, pre-filled syringes should be undertaken in accordance with manufacturer and/or local policies.

Protective clothing/spillage

- It is standard clinical practice for health care professionals and carers to wear gloves when administering methotrexate.

- When working in health care settings practitioners should be aware of local policies and access to spillage kits; this should include knowledge of how to deal with all types of accidental spillage of methotrexate.

- Advice should be given to patients on how to manage accidental spillage in the home.

Patient education and training

Patients and carers should receive adequate information (verbal and written) to enable them to make an informed decision about methotrexate therapy. Patients may elect to self-administer methotrexate injections (or elect a carer), provided they undertake the necessary training. Patients (and carers where appropriate) should be aware of their responsibilities when giving methotrexate injections.

For example, they must:

- participate in a training programme and be prepared to demonstrate that they are competent in the safe administration of subcutaneous methotrexate

- be aware of the need to use effective means of contraception (where appropriate) and be fully informed of all aspects relating to sexual health and overseas travel (BSR/BHPR, 2008; BSPAR, 2010; Butler, 2011; Dougherty and Lister, 2011; McInnes et al., 2012)

- know how to store and dispose of methotrexate and equipment safely

- attend for blood tests as per agreed monitoring schedule

- understand how and when to seek advice or guidance on treatment and related issues that may require prompt medical opinion.
Introduction

This guidance has been developed to aid practitioners in the safe and effective administration and use of licensed subcutaneous methotrexate injections for a number of rheumatological conditions, in a variety of health care settings, community environments and at home. The document also provides a framework to enable patients and/or their carers to administer treatment at home.

Some aspects of this guidance (such as the sections on the subcutaneous administration technique and patient education) may also be of value to health care colleagues working in other specialties including dermatology, gastroenterology and ophthalmology.

Research evidence has highlighted the value of using the subcutaneous route in clinical practice (Braun et al., 2008; Ortiz et al., 2009; Bijlsma et al., 2009; Visser et al., 2009; Bakker et al., 2010; Braun, 2010). The studies highlight two specific benefits arising from the subcutaneous route of drug administration:

- improved tolerability compared to oral methotrexate
- improved bioavailability.

The guidance

This document should not be considered definitive on all issues related to treatment with methotrexate, but should be read alongside the following key texts:

- the British Society for Rheumatology (BSR) and the British Health Professionals in Rheumatology (BHPR) guidelines and standards issued for the safe prescribing and monitoring of methotrexate for inflammatory arthritis (BSR/BHPR, 2008)
- guidelines issued by the British Society of Paediatric and Adolescent Rheumatology (BSPAR, 2010)
- guidelines issued by the National Patient Safety Agency (NPSA, 2006) which in 2012 became part of the NHS Commissioning Board Special Health Authority
- the statutory Health and Safety at Work Regulations for England, Scotland, Northern Ireland and Wales, including the Control of Substances Hazardous to Health (COSHH, 2002; COSHH (NI), 2003) and the Scottish Environmental Protection Agency’s (SEPA) regulations
- local policies on the handling and disposal of clinical waste and infection control
- local policies and clinical governance frameworks for risk management
- Nursing and Midwifery Council (NMC) professional regulations or similar regulatory body for those practitioners where nursing is not their primary professional qualification
- the summary of products characteristic (SPC) for methotrexate (a description of the medicinal product’s properties and conditions attached to its use) and patient information issued by the manufacturer of pre-filled methotrexate syringes
- the most current edition of the British National Formulary (BNF) and the British National Formulary for Children (BNFC).

The References section of this document contains a full listing of these and additional advisory documents.
Methotrexate use in adult rheumatology

History
Methotrexate was developed in the 1940s as a specific antagonist of folic acid. It is classed as a cytotoxic drug because, in high doses, it inhibits the proliferation of malignant cells and has teratogenic properties and irritant effects to the skin (Butler, 2011; Dougherty and Lister, 2011, McInnes et al., 2012).

In recent years research has highlighted the need for more robust management of inflammatory joint diseases such as rheumatoid arthritis (RA). As evidence has continued to build, it is clear that early treatment with methotrexate should be increased rapidly until clinical indicators of disease control demonstrate an optimum therapeutic dose (NICE, 2009; Braun, 2010; BSPAR, 2010; Smolen et al., 2010a, 2010b; Bakker et al., 2011; Jacobs, 2012a, 2012b; Gullick and Scott, 2012; McInnes et al., 2012).

There has been debate about the extent of the drug’s cytotoxic nature when it is used in low weekly doses for rheumatic diseases. For example, Cutolo (2001) states that the cytotoxic mechanism of action might be more anti-inflammatory, while more recently Wong et al., (2009) assert that the risk relating to the low dosages used in the management of inflammatory arthritis is minimal.

The exact immunosuppressive action in inflammatory joint disease remains unclear, although it is thought to be as a result of the inhibition of lymphocyte proliferation, with increased adenosine production being identified as another mechanism.

Subcutaneous administration is regularly used today in the treatment of rheumatoid arthritis (RA) and other inflammatory joint diseases such as psoriatic arthritis (PsA), and juvenile idiopathic arthritis (JIA).

Rationale for the use of subcutaneous methotrexate
Methotrexate is recognised as the most effective of the traditional (non-biologic) disease-modifying anti-rheumatic drugs (DMARDs) in current use for inflammatory arthritis (Bijlsma and Jacobs, 2009; Smolen et al., 2010a, 2010b; Bijlsma, 2012; Jacobs, 2012a, 2012b). It is recognised as the gold standard for treating people with rheumatoid conditions (BSR/BHPR, 2008; NICE, 2009; BSPAR, 2010).

The rationale for considering the administration of methotrexate using subcutaneous routes has been driven by the need to increase the therapeutic dose, ensure the maximum bioavailability and reduce symptomatic side effects for some patients (Braun et al., 2008; Ortiz et al., 2009; Bijlsma et al., 2009; Visser et al., 2009, Bakker et al., 2010; Braun, 2010; BSPAR, 2010; McInnes et al., 2012).

In recent years the development of biologic therapies has added another dimension. The effectiveness of some biologic therapies is enhanced by the co-administration of a DMARD (usually methotrexate) while also reducing the potential for antibodies to develop against the biologic agent.

Practitioners using this guidance should refer to additional key documents (see the References and further reading section of this document).

Risk management
Risk assessment and management is an integral aspect of providing safe and effective health care, and this guidance recommends that practitioners should consult and be aware of their local risk management policy and guidelines and be able to demonstrate that all potential areas of risk have been addressed.

There is emerging evidence that the cytotoxic risk relating to the low dosages used in the treatment of inflammatory arthritis is small (Wong et al., 2009). In addition, the availability of methotrexate in sealed pre-dosed, pre-filled syringes with an attached needle means the risk of spillage and accidental exposure is significantly minimised.
**Practitioner responsibilities**

Practitioners should undertake a risk assessment.

In addition, practitioners should:

- Ensure a robust blood monitoring system is in place as per BSR/BHPR (2008) and BSPAR (2010) guidelines, and NPSA (2006) advice is followed.
- Ensure any risk assessment produced is reviewed and tailored in accordance with individual needs or risks relating to individual patients/carers undertaking subcutaneous administration in the home.
- Report any errors, new risks, near misses or adverse events promptly according to local policy.

**Drug interactions**

A number of drugs have the potential to interact with methotrexate. Drug interactions can enhance the action of methotrexate resulting in an increased risk of methotrexate toxicity. Some of these drugs include salicylates, hypoglycaemics, sulphonamides, phenytoin, and trimethoprim. For a comprehensive list, please refer to the most up-to-date copy of the British National Formulary (BNF) and/or the summary of product characteristics (SPC) for subcutaneous methotrexate (medac Metoject®, 2012a).

**Advice on the handling and administration of subcutaneous methotrexate and pregnancy**

Methotrexate has the ability to impair the fertility of those using it and is embryotoxic, which means it can cause abortion or foetal defects particularly during the first trimester of pregnancy (Ostensen and Förger, 2009).

Best practice advocates that those who are pregnant (and particularly those who are in the first trimester of pregnancy) do not handle or administer methotrexate (HSE, 2003; Dougherty and Lister, 2011). Practitioners are advised to adhere to their local policy regarding this.

It is the responsibility of the physician and nurse to inform women who are pregnant, breast feeding or men/women trying to conceive about the potential risks relating to the handling and administration of methotrexate because of its teratogenic properties (BSR/BHPR, 2008).

It is therefore essential that contraceptive measures should be used by men, women and young people during treatment and for at least three to six months following cessation of treatment (BSR/BHPR, 2008; Dougherty and Lister, 2011; McInnes et al., 2012).

Having been informed of the potential risks, ultimately the final decision of individuals in relation to the handling and/or administration of methotrexate is a personal one, but one that should be well documented.

**Supply, storage, protective clothing and disposal**

**Supply, preparation and delivery**

Methotrexate is now available in licensed manufactured pre-filled syringes. Packaging and transport systems should ensure that adequate protection and storage instructions are adhered to during delivery. Practitioners should be guided by local policies.

Pre-dosed, pre-filled syringes can be issued in one of three ways: hospital pharmacy, community pharmacy or home delivery.

Patients who self-administer must be told about any change of manufacturer, as this may result in changes to the volume provided in the syringe, storage conditions, expiry date or appearance of the syringes. In addition, they must also be informed of the potential change in administration technique according to the manufacturer’s guidelines and be appropriately retrained.

**Storage and drug stability**

Methotrexate is a clear yellowish solution and is stable if stored out of direct sunlight.

Pre-filled syringes will need to be checked to clarify the particular storage recommendations for that product; for example, commercially available solutions of methotrexate often do not need refrigeration.

The shelf life and storage conditions may vary depending on the syringe provider, and these should be carefully checked and reviewed on a regular basis and prior to each administration of the drug.
Storage at home

The storage of methotrexate syringes and clinical waste bins should be out of the reach and sight of vulnerable adults, children and pets.

Practitioners and patients/carers who undertake self-administration should be trained and competent in all aspects of safe storage. This will include awareness that storage will vary according to the product used (see Supply, preparation and delivery above).

Personal protective equipment (PPE)

Previous evidence suggests that the levels of contamination appear to correlate with the amount of drugs prepared and number of vials used (Sessink et al., 1997). However, in light of emerging evidence that the cytotoxic risk relating to the low dosages of subcutaneous methotrexate used in the treatment of inflammatory arthritis is small (Wong et al., 2009), this guidance suggests that aprons, goggles, masks or armlets no longer need to be worn by practitioners when administering pre-filled subcutaneous methotrexate injections.

In promoting good clinical practice, this guidance recommends that practitioners and carers should always use gloves (latex free, ideally) and observe good hand washing protocols when administering subcutaneous methotrexate (Crauste-Manciet et al., 2005; Dougherty and Lister, 2011). It is not necessary for patients administering their own therapy to wear gloves. The key element for practitioners is documenting that the individual is aware of the risks and has made an informed choice.

Disposal of sharps and clinical waste

Local policy should dictate the storage, collection, handling and disposal of methotrexate clinical waste/sharps. Practitioners should receive regular training and updating on policies in relation to dealing with hazardous waste and sharps safety.

When methotrexate is administered in any community setting (GP surgeries, community clinics and/or directly in patients’ homes) issues relating to the management of clinical waste need to be considered (please refer to local policy). In some circumstances, companies that deliver the methotrexate to patients’ homes will also be responsible for the collection and disposal of sharps and clinical waste.

Purple topped clinical waste bins should be used for the disposal of pre-dosed, pre-filled methotrexate syringes.

Patients should be aware of the need to ensure the safe disposal of equipment using a clinical waste bin, and that the bin itself also constitutes a risk and should be safely stored when not in use. The bin should never be filled more than two-thirds of its total capacity, or transported if not securely sealed.

Spillage

Based on the assumption that methotrexate will be administered using a pre-dosed, pre-filled syringe containing a small volume of methotrexate, the risk of exposure is small and a spillage kit is unlikely to be necessary. However, some local policies may recommend this and you should refer to your local policy.

When working in health care settings, practitioners should be aware of local policies, be able to locate and access a spillage kit if required, and know how to deal with any accidental methotrexate spillage.

Patients and carers should also be aware of what to do in case of spillage.

A small spillage kit may be provided to the patient and used in the clinical area for training purposes. If provided, the spillage kit should include:

- instructions on how to manage and deal with spillages
- clinical waste bin/bag and tape/label according to local policy
- absorbent paper towels or plastic backed absorbent towels (large).

Liquid spillage on clothing

Wear protective gloves and blot dry with a paper towel or kitchen roll. As a precaution, clothing should be removed immediately (Dougherty and Lister, 2011) and washed separately from other items. Wash hands thoroughly.

Liquid spillage directly onto the skin

Wong et al., (2009), found poor dermal methotrexate penetration from deliberate contamination. However, if methotrexate is accidentally spilt onto the skin, the area should be washed “liberally with soap and cold water” (Weinstein and Plumer, 2007; Dougherty and Lister, 2011). Methotrexate is not a vesicant (blister agent).
Liquid spillage directly into the eye
The eye should be washed out using plenty of water (Weinstein and Plumer, 2007; Dougherty and Lister, 2011) for a few minutes. A doctor should be contacted if any side effects are experienced. Some care settings may have eye wash kits available, if needed.

Liquid spillage on floors or work surfaces
Wearing gloves cover the spillage with absorbent paper and clean with soap and water. Paper tissue should be bagged and disposed of in the bin.

Practitioner training and competence
No specialist training is required for the administration of subcutaneous methotrexate by practitioners, however all practitioners should be competent in the administration of the subcutaneous injection technique.

Ideally, specialist practitioners should undertake appropriate training in the administration and management of methotrexate.

Checklist for practitioners
All practitioners should adhere to the following checklist prior to administering a pre-dosed, subcutaneous methotrexate injection to a patient:

- check the methotrexate dose, dosage form and frequency prescribed and expiry date of the syringe
- ensure blood monitoring (including the monitoring of trends) is in place as per BSR/BHPR (2008) and NPSA (2006) guidelines and local protocols, that blood results are satisfactory, and patients know when they need to attend for their next blood test
- check there are no contraindications to administration (as per the SPC)
- ensure the patient has consented to have the injection
- ensure the patient knows the advice line telephone number for support or concerns
- document the injection and the site used
- be aware of protocols relating to the safe disposal of sharps
- note the date and time of next injection.

Specialist practitioner training and competence (see Appendix 3)

- Practitioners should be knowledgeable and competent in all aspects of methotrexate administration and risk management, and stay up-to-date with the latest evidence in relation to the drug’s indications and side-effects.
- Practitioners should have undertaken appropriate training to educate, support and teach patients in the self-administration of subcutaneous methotrexate, and ensure their own training is regularly updated.
- Practitioners should ensure appropriate communication and support are available for primary health care teams and patients self-administering in their own homes.
- Practitioners should be aware of clinical governance and local policies in relation to the management of patients receiving methotrexate.
- Documentation and audit should be an integral aspect of developing a service for patients receiving subcutaneous methotrexate.

Home administration
The ability of a patient to inject in their own home can provide a significant degree of independence for the patient and is also a cost effective treatment pathway, avoiding unnecessary hospital attendances and/or the need for direct health care practitioner support.

For home administration to work efficiently, good communication is vital, not only between primary, secondary, tertiary care and pharmacy services, but also with the carers. The patient and carer should be aware that the home administration of methotrexate is subject to undertaking a training programme and a review of their ability to manage home administration.

A back-up plan must be in place to ensure that in the event of a patient being unable to self-administer (for example, due to limited dexterity) or their trained carer being unavailable, they can call on specialist support or a non-specialist rheumatology practitioner’s support (for example, ward staff, practice nurse or district nurse), or a carer trained in the administration procedure.
Patients should be advised that they can elect not to self-administer methotrexate and can opt out of treatment. However, should they choose this course of action they MUST inform their health care team promptly, so their records can be appropriately updated.

Following training and risk assessment a decision will be made about whether the patient or carer:

- is competent and wishes to proceed with home administration
- has a clear understanding of their responsibilities in the safe management of methotrexate, including NPSA (2006), (ie correct dose and frequency), additional equipment and waste disposal
- will undertake regular blood monitoring and attend clinic appointments
- recognise that a risk assessment must support home administration and that this will be subject to review
- understands the back-up plan in the event of being unable to self-administer.

Patient information leaflets on subcutaneous methotrexate injections are available from a number of organisations. Manufacturers also produce illustrated patient guides.

Pre-treatment checklist for adults

The following pre-treatment checks should be undertaken for adults (please see Section 2 Paediatric guidance).

- Blood screening:
  - full blood count and differential white blood count
  - inflammatory markers ESR (Erythrocyte sedimentation rate) and/or C-reactive protein (CRP)
  - liver and renal function tests.

- Varicella immune status.

Checking varicella immune status has been identified as an important aspect of patient care, especially in those who have autoimmune inflammatory disease and require immunosuppressant medication, as it has been reported that this group of patients are at greater risk of infection and/or reactivation of latent disease/shingles (Butler, 2008; McCarthy et al., 2011; DH, 2006 (Chapter 34, updated 2012)).

This can be checked via history taking and/or varicella zoster (VZIG) blood test screening if clinically indicated (in other words, the patient has no history of chicken pox or shingles).

If varicella vaccination is required, it should ideally be administered at least two weeks prior to the commencement of methotrexate (BSR, 2002; Butler, 2008).

For those patients who cannot receive live varicella zoster vaccines but come into contact with shingles or chickenpox, varicella zoster immunoglobulin (VZIG) and/or antiviral drugs could be given, depending on local policy (BSR/BHPR, 2008; Butler, 2008; DH, 2006 (Chapter 34, updated 2012)).

If chickenpox/shingles develop, methotrexate should be discontinued until the last spot has crusted over and the patient is clinically well.

- Influenza and pneumococcal vaccination status.

The BSR/BHPR (2008) DMARD monitoring guidelines and BSR (2011) statement on vaccination in adult patients with rheumatic disease specify that individuals with immunosuppression should be given inactivated vaccines in accordance with national recommendations. It is recommended that patients with autoimmune inflammatory rheumatic diseases should be offered pneumococcal and influenza vaccination.

Vaccination should be administered at least two weeks prior to immunosuppression. In individual cases it may be necessary to discuss vaccination with an appropriate local specialist in infectious diseases and the patient's GP.

Full advice on varicella, influenza and pneumococcal vaccination can be found in the Department of Health's 'Green Book' on immunisation against infectious disease. Please see www.immunisation.dh.gov.uk and www.dh.gov.uk

- Male and female patients who wish to consider conception should be given appropriate advice and good sexual health practice should be explained.

- Chest X-ray prior to treatment or within the last six months, according to the British Society for Rheumatology Guidelines BSR/BHPR (2008) or local policy. Respiratory history should be noted.
**Note:** pulmonary toxicity can occur in patients receiving methotrexate in the form of a drug induced pneumonitis/methotrexate lung (BSR/BHPR, 2008).

- The drinking history of patients should be checked and they should be advised on the importance of restricting alcohol intake when receiving methotrexate treatment.

### Concomitant medications

All concomitant medications (including proton pump inhibitors, statins and analgesics) need to be considered and reviewed prior to and during methotrexate treatment, as several agents have the potential to cause independent hepatotoxicity (BNF).

A careful and detailed review of concomitant medications must be undertaken to exclude any potential drug interactions or absolute contraindications such as trimethoprim and co-trimoxazole. Please refer to the BNF, BNFC and the manufacturers’ specific summary of product characteristics (SPC). For further advice, contact the local prescriber.

Practitioners should also be aware of, and exercise caution, in relation to patient use of over-the-counter (OTC) medications and complementary/herbal remedies, as such agents, when taken with methotrexate, might confuse and potentially compromise a patient’s clinical management.

To promote pharmacovigilance (Human Medicines Regulations, 2012) patient safety (NPSA, 2006), therapeutic outcomes for patients, and best practice, practitioners need to ask patients specifically about their use of complementary and alternative medicines and be aware of the potential these may have for hepatotoxicity and interactions (Fogden et al., 2003; Leung, 2006; Yang et al., 2006; Joshi et al., 2008; Ulbricht et al., 2008; Toselli et al., 2009; Gonzalez-Stuart, 2011; Liu et al., 2011). Contraindications to treatment with methotrexate include:

- renal or liver impairment/failure (or recent hepatitis)
- blood dyscrasias/abnormalities
- alcoholism
- planned conception, pregnancy or breast feeding
- immunodeficiency syndromes
- active chickenpox/shingles
- recent live vaccines (within two weeks).

Over-the-counter (OTC), complementary and alternative medications (including herbal remedies) should be treated with caution.

### Folic acid supplementation

It is broadly recognised that folate supplementation should be prescribed with methotrexate, to help reduce side-effects.

The BSR/BHPR (2008) monitoring guidelines suggest that folic acid in doses of 5mg per week (taken the day after the methotrexate) is adequate.

However, there is other evidence to suggest that higher doses have no apparent negative effect on methotrexate efficacy (Ortiz et al., 1998, 2009). Indeed, a number of rheumatology units use doses of 5mg every day (except on the day that methotrexate is taken) for concordance reasons and to help further reduce methotrexate side-effects.

### Skin preparation and administration of subcutaneous methotrexate

**Skin preparation**

There are inconsistencies in the available literature regarding skin cleaning prior to subcutaneous injections – in other words, ‘to swab or not to swab’.

Some reports suggest that as long as the skin is socially clean at the injection site, and thorough hand washing techniques are used, there is no reason to clean the skin with alcohol impregnated swabs (Workman, 1999; Vaccine Administration Task Force, 2001; DH, 2006; Gittens and Bunnell, 2009).

Practitioners are advised to adhere to local guidelines on skin disinfection before injection.
Methotrexate subcutaneous injection technique

- Best practice recommends that practitioners and carers should use gloves, but this is not required for patients who self-administer.
- Check the skin is socially clean.
- Remove the needle cap carefully using the twist and pull technique. You are advised to check the angle of the needle in relation to the syringe, as sometimes the needle can accidentally be slightly bent. If this is the case, inject at the required angle to the needle and not the syringe. However, if in any doubt, another syringe can be tried and/or the supplier/manufacturer contacted for further advice.
- If the syringe contains a small air bubble, DO NOT EXPEL; it is required to ensure that all the drug is administered. This is completely harmless.
- There is NO need to aspirate when the needle is in situ.
- The injection should be administered into subcutaneous tissue in the thigh or stomach.
- Commercially available syringes (e.g. medac Metoject®), have a 27G (0.4 by 13mm) needle attached; however, if the injections are made up in a local pharmacy 26G (brown) or 30G (yellow) needles may be more suitable.
- Gently grip the skin at the injection site between the thumb and forefinger. Holding the bore of the syringe as a dart, with the needle at an angle of 45° to 90° to the skin, insert the needle completely, using a quick, short motion.
- Release the skin and slowly inject all the medication. Remove the syringe.

Note: some users have expressed concern that some syringes can appear to have a “blunt” needle. If this is an area of concern, a review of the pre-filled syringe and needle and/or injection technique may be required. If this fails to resolve the problem, further advice can be sought from the respective supplier/manufacturer.

For full information on the subcutaneous injection technique, please refer to Adult resources: patient/carer training guide.

Rotating injection sites

Patients or carers who self-administer treatment need to ensure that they rotate the injection sites. If giving two injections (such as methotrexate and a biologic therapy) these should be given in different sites. For example, one should be given in the right thigh and the second in the left thigh. The injections should be at least 3cm apart, if given in the same limb. If injecting in the abdomen, injections should be in a 5cm radius away from the navel. See Figure 2 in Adult resources: patient/carer training guide.

It is suggested that the patient should keep a record of injection sites used. For additional information refer to the SPC or BNF/BNFC.

Review and monitoring

The blood monitoring regime for subcutaneous methotrexate is the same as for oral methotrexate (NPSA, 2006; BSR/BHPR, 2008). However, local monitoring guidelines might also apply and should be adhered to. Primary health care teams should be sure to comply with any locally agreed shared care arrangements.

The arrangements for the prescribing, distribution of prescriptions and collection of clinical waste will vary according to local policies and arrangements between primary care organisations. It is essential that the patient and carer are provided with information about their prescriptions and clear guidance on the support they can access in the case of problems. This should include information on a telephone advice line service.

The patient or carer should be able to access additional training sessions if necessary and as required. Although it is best practice to undertake an annual review of patient or carer skills/practice in injecting and managing their prescriptions, this may not always be feasible.

To minimise reactions and promote and maintain good injection technique, practitioners should routinely ask patients/carers if they are experiencing any problems and arrange an appropriate assessment if this is required. This approach will help maintain a thorough audit trail and ensure the maintenance of safe practice by patients/carers.
**Patient education and training**

Patients and carers should be provided with adequate information (verbal and written) about the treatment and understand the contraindications, the potential risks and side-effects to enable them to make an informed decision about methotrexate therapy. They should also be given the opportunity to discuss any concerns they may have.

Patients may elect to self-administer methotrexate injections (or elect a carer), provided they undertake the necessary training.

The patient or carer should have a training plan that provides them with a clear understanding of the process and responsibilities required for home administration.

For example, they must:

- participate in a training programme and be prepared to demonstrate that they are competent in the safe administration of subcutaneous methotrexate
- be aware of the need to use effective means of contraception (where appropriate) and be fully informed of all aspects relating to sexual health (BSR/BHPR, 2008; BSPAR, 2010; Butler, 2011; McInnes et al., 2012; medac Metoject®, 2012a) and overseas travel (medac Metoject® Starter Pack Adult Guidelines, 2012b)
- know how to store and dispose of methotrexate and equipment safely
- attend for blood tests and monitoring regularly
- understand how and when to seek advice or guidance on treatment and related issues that may require prompt medical opinion
- be aware of their responsibilities when giving methotrexate injections.

In addition, patients and carers should be made aware and have a clear understanding of the aim, purpose and importance of the NPSA (2006) methotrexate monitoring booklet.

A patient education package has been developed to support patients and practitioners (see Adult resources, page 15).

The role of practitioners is to recognise the individual needs of patients and provide support in administering the most appropriate treatment for that patient. Patient preferences will vary depending on:

- the patient’s medical history and general health status
- social and psychological factors that affect their treatment options.

Please also refer to Review and monitoring on page 12.

**Vaccinations**

Please see the pre-treatment checklist on page 10.

**Chickenpox/shingles (herpes zoster)**

Please see the pre-treatment checklist on page 10.

Antiviral drugs and/or zoster immunisation may be given depending on local policy.

**Advice on handling and administration of methotrexate and pregnancy**

Please see section on Risk management on page 6.

**Training the patient or carer**

The time taken to train each patient or carer, together with the number of practice sessions that require supervision, will vary. Following an initial assessment and discussion with the patient and carer, a mutually agreed training package should be provided and tailored to meet the patient and/or carer’s individual learning needs. The practitioner, patient and/or carer, where appropriate, will determine the number of training sessions necessary to achieve competency.

**Travel**

For information on travelling with methotrexate, please refer to Adult resources on page 15.

**Audit trail and data collection**

It is essential that all patients who are self-administering methotrexate can be identified and traced promptly should the need arise.

If a unit or department wishes to collect additional data that contains personal or clinical details of an individual or a group of individuals, staff must seek the advice and gain permission from the respective local ethics and audit departments to ensure that national data protection legislation and information governance guidance and local policies are adhered to. (Data Protection Act, 1998; the Department of Health’s Code of

In addition, nurses have a professional responsibility to adhere to the NMC guidance for good record keeping (NMC, 2009).

It is important that practitioners audit the service and include the value of the educational programme. Your local audit department will provide guidance and support.

**Conclusion**

This document has been developed to inform practitioners on the key issues related to the administration of subcutaneous methotrexate in adults. There are a number of non-malignant indications for prescribing methotrexate, and this guidance has focused on the administration of subcutaneous methotrexate for certain rheumatic diseases.
Adult resources

Patient/carer training guide example

This section provides information for patients and carers about using subcutaneous methotrexate, and an example of a training guide.

Procedure

- Consultant rheumatologist and rheumatology non-medical independent prescriber formally requests and prescribes the initial treatment, stating the dose and route of administration.
- Patient satisfies the above criteria and has been fully informed of the treatment and their responsibilities including adherence to routine blood monitoring and outpatient follow-up appointments.
- Specialist practitioner is satisfied that the patient understands the process and responsibilities of administering the injection.
- Patient (and/or carer) is aware of the health and safety regulations on the storage and disposal of drugs and equipment.
- Patient (and/or carer) attends the educational sessions and satisfies the nursing service of their competence in:
  - administering the drug by the subcutaneous route
  - ability to comply with the correct storage and disposal of equipment
  - concordance with the training, follow up and blood monitoring.
- If the patient fails any of the above criteria or does not wish to proceed with subcutaneous administration, the nursing service will liaise with the prescribing doctor/non-medical independent prescriber and patient to plan future treatment options.
- Once the patient has successfully completed the training programme, a letter will be sent informing the patient's general practitioner.

Continuing patient management

Once the training programme has been completed and the patient and/or carer have demonstrated competence in all areas of administration, the patient should be provided with information to support home administration and their follow-up care. If the patient has a pharmaceutical company home care package, they should be provided with the relevant contact details.

Example patient training guide

Introduction

This is a step-by-step guide to help you give yourself a once weekly injection of methotrexate by subcutaneous (under the skin) injection. This training programme has been developed to help you have greater independence to manage your treatment for arthritis. If you feel that you do not want to inject yourself or receive this treatment, please tell your nurse or practitioner.

Some information on methotrexate:

Methotrexate is one of only a very few drugs that is only ever given once a week. It is important that you make a note of the date you give yourself the injection and choose a day when you have a good routine and can plan your once-a-week injection.

Methotrexate is used to treat patients with specific types of inflammatory arthritis. The drug slows down the body's ability to make certain cells and this helps reduce the cells that cause inflammation. This means that the damage, pain and swelling that you have when your joints are affected by arthritis is much less.

Methotrexate tablets have been used for many years to treat some types of inflammatory arthritis. It is a well recognised treatment for these types of arthritis that research studies show works well and, when appropriately managed and monitored, is safe.

In the last decade, subcutaneous methotrexate injection for inflammatory arthritis has also been shown to be effective and safe and is now a licensed drug for rheumatology conditions such as rheumatoid arthritis (RA), psoriatic arthritis (PsA) and juvenile idiopathic arthritis (JIA).

Subcutaneous injections have been shown to control inflammatory arthritis well, and often patients who have the treatment by injection get fewer side-effects such as feeling sick and having stomach discomfort.

You and/or your carer will need to understand how to give your injections. Information and help will be available to support you while you learn.
What happens when you decide to inject methotrexate

1. You and/or your carer will be given information to read about the drug and have time to ask questions.
2. You and/or your carer will be shown how to prepare the things you need to inject yourself and give the injection.
3. You and/or your carer will be able to practise giving the injection, with a nurse supervising.

A final assessment will take place when you, your carer and the nurse are sure that you are competent to self-inject at home.

Make sure that these instructions are always close to hand in case you have any queries or problems, and that you are fully aware of the information contained within the National Patient Safety Agency’s methotrexate monitoring booklet.

Remember

If you are uncertain about when you should not receive treatment or if you need advice, please remember to look at the information sheets you received or phone the nurse advice line service. It is important you follow this advice:

- you (or your carer) must not handle or give methotrexate if you are trying for a baby, or you think you may be pregnant or are breast feeding
- always make sure that you keep the methotrexate syringe in a place where it is safe and out of sight and reach of vulnerable adults, children and family pets
- always check your syringe carefully to be sure that all the details are correct, including the name of the drug, dose and that the drug is in date and the methotrexate looks normal (yellow and clear); contact the pharmacy or nurse advice line if you need to
- remember to use the injection sites you have been shown and change the sites each time you give an injection
- attend regularly for blood tests and follow-up appointments.

You should be given the date and time of your next blood test, information on repeat prescriptions and next outpatient appointment, as well as advice on telephone contact details (telephone advice line and/or general practitioner services).

If you are not able to have regular blood monitoring or attend follow-up appointments, please inform your GP/rheumatology clinic/nurse about this as without these, subcutaneous methotrexate should not be administered.

How to give a methotrexate subcutaneous injection

Equipment

Getting the equipment ready

- Methotrexate syringe for injection (you may need a needle if the treatment has been made up in a local hospital pharmacy).
- Clean table surface.
- 1 appropriate clinical waste/sharps bin.
- Pair of disposable gloves (if required/being used – though not necessary if patient self-administering).
- Cotton wool ball/clean tissue.
- Spillage kit and alcohol wipes (if issued).

Preparing your working area

1. Collect all the above equipment and take it to where the injection will be given – such as a clean table or work surface – before you start assembling. You may wish to use a piece of kitchen roll on top of your clean work surface. If possible, try to give the injection in a non-carpeted room in case there is a spillage.
2. Wash and dry your hands thoroughly and clean your preparation area (for example, a work surface, a clean tray or lid).
3. Only people who are helping you should be present in the room (avoid distractions such as children and pets).
4. Wash working surface with liquid detergent and allow it to dry.
5. Arrange the equipment on the clean surface.
6. Wash and dry your hands once more then make sure you have all the equipment close at hand before you make yourself comfortable to give the injection.
7. Carers need to put gloves on if administering the injection.
8. Decide on where you will give the injection. You will need to change the injection site each week to reduce the risk of soreness (see Figure 2).

9. Make sure the injection site is clean; if not, clean with soap and water.

10. Open the syringe packet.

**Giving the methotrexate injection**

1. Sit or stand comfortably.

2. Check the syringe is in date, has your name on it, and it is the correct dose. If it is incorrect in any way, you must not give the injection but check with your rheumatology department or pharmacy.

3. Check the syringe contents to make sure that it is a clear yellow solution. If it does not look like this, or has particles in it, you should not give the injection but contact the rheumatology department or pharmacy.

4. If the needle needs to be attached, peel-open the end of the needle packet carefully. While holding it in one hand, and the syringe in the other, remove the syringe cap and attach them together. Put the syringe cap straight into your sharps bin. DO NOT touch the syringe end or the needle tip.

5. If the syringe already has a needle attached, pick up the syringe and hold the barrel of the syringe (low down as if you are going to write your name with a pen). Hold the needle shield firmly and twist and pull until the needle shield is loose and gently remove. DO NOT touch the sterile needle.

6. Make sure the needle does not come into contact with anything on the way to the skin so to avoid contamination and the risk of introducing infection.

7. If the syringe contains a small air bubble, DO NOT EXPEL THE AIR BUBBLE; it is required to ensure all the drug is administered and there for safety reasons. It is completely harmless.

8. Inject into the thigh or stomach – but a minimum of 5cm away from the tummy button. If giving two injections (such as methotrexate and a biologic therapy), these should be given in totally different sites. For example, one should be given in the right thigh and one in the left. If given in the same limb, the injections should be at least 3cm apart.

9. Alternate the injection site from week-to-week so it doesn’t get sore.

10. With your free hand, gently grip the skin together (see Figure 1) where you are going to inject and insert the needle at a 45° to 90° angle. The needle will deliver the injection just below the skin (subcutaneously). See Figures 1 and 3 overleaf.

11. Once the needle is in place, release the pressure on the skin and support the syringe with both hands. With your preferred hand, push the syringe plunger slowly down to inject the methotrexate.

12. When you have injected all of the methotrexate remove the needle and syringe from your skin, place a cotton wool ball or tissue over the injection site. Then immediately put the used syringe, needle and tissue directly into the clinical waste/sharps bin. DO NOT re-sheath the needle.
What to do after administering the methotrexate injection

1. Do not put any of the used items in with your normal household waste.
2. Instead you should put the used syringe and needle into the clinical waste/sharps bin provided.
3. The bin must always be stored out of children’s sight and reach and always closed, but not locked. Lock it when it is two-thirds full and dispose of it according to local policy or via the home delivery service. Ask your nurse for help with this.
4. Unused syringes should always be returned to your local hospital pharmacy or delivery service.
5. If only part of the dose is given, the remainder should be discarded in the sharps bin.
6. If used, change gloves if these are punctured or torn.
7. Wash hands thoroughly with soap and water and dry thoroughly after the procedure.
8. Record the site and date of the injection in your diary sheet (if using).
9. If there is bleeding or bruising at the injection site or a small amount of blood in the very tip of the syringe do not worry as this sometimes happens if the needle has punctured a small blood vessel. It will soon stop and the bruising will fade.
10. On rare occasions methotrexate can leak into the surrounding skin causing irritation when patients give an injection. If this happens, and it causes irritation or redness, contact your GP and/or the rheumatology advice line.

What to do when dealing with spillages

- Keep the spillage kit (if issued, as per local policy) and instructions at hand whenever you inject and make sure that your carer or family members are aware of how to use it.
- The amount of methotrexate you are injecting is very small, but it is possible to accidentally spill it.
- If there is a spillage, please follow the advice you have been given; instructions in the spill kit (if issued); or advice listed below.
Spillage on clothing:
Wearing protective gloves blot the spillage dry with absorbent paper towel or kitchen roll. As a precaution, clothing should be removed and washed separately to other items.

Spillage onto skin:
Wash the affected area with plenty of soap and water for a couple of minutes. Do not scrub because unbroken skin provides protection. Contact your GP and/or rheumatology team, nurse or doctor if you are concerned or have any adverse reactions.

Spillage into the eyes:
Wash the eye(s) using plenty of water. It is recommended that you should contact your own doctor, local hospital emergency department or eye hospital if your eyes become sore, you experience any side-effects, or notice any changes in your vision.

Spillage onto work surfaces and floors:
Put on a pair of protective gloves. Cover and wipe up the spillage using absorbent paper. Wash the area with plenty of soap and water. Used paper towels should be bagged and placed into the clinical waste bin.

Accidental needlestick injuries
If you follow the instructions carefully the chances of getting an accidental needlestick injury are very small.

If you or your carer accidentally come into contact with the needle while preparing or disposing of the syringe it is important to make the puncture site bleed. Then wash the areas with plenty of running water and cover with a plaster. If a needlestick injury occurs before the injection, then the syringe should be put into the sharps bin and a new syringe should be used.

At the time of writing, it is likely that a pen will be introduced to the market within the next 12 months that should eliminate the possibility of needlestick injuries. For further information on sharps safety refer to the RCN’s guidance (2011).

Travelling and injecting methotrexate away from home
The storage of your injections will vary according to local health policy and the manufacturer’s recommendations. However, caution is needed in hot climates over 25°C. You should seek specific advice on storage at high temperatures. Discuss the details of storage with your GP, nurse, practitioner or pharmacist.

The injections you receive for travel will depend on the hospital or company that provides your methotrexate. Make sure that you check the box for instructions on how to store it if it is different from your usual treatment.

Some of the options available to you when you are going away and unable to take your injections with you are:

- tablets instead of an injection
- an injection just before you travel and then one as soon as you return. Discuss this with your GP or rheumatology department.

If you are flying there may be an issue with the transportation of pre-filled syringes and you may need to discuss this with your methotrexate supplier and get a supporting letter from your rheumatology department before you go away.

It is recommended that you always keep your medication in your hand/cabin luggage, in case the bags get mislaid, but also rough handling of luggage could damage the medication and it may freeze in the hold.

See your practice nurse or doctor to arrange any vaccinations you need well in advance of your travel. You must not be given any live vaccines, so it is also important that they are aware that you are receiving regular methotrexate treatment.

Rheumatology advice line
You should be made aware of an advice line you can call and how and when you should use this.
Paediatric guidance

Introduction

This paediatric guidance should be used when caring for children, young people and their families receiving subcutaneous methotrexate treatment.

Paediatric rheumatic diseases are different from their adult counterparts. The umbrella term Juvenile Idiopathic Arthritis (JIA) covers a heterogeneous group of conditions that combines arthritis with onset before the age of 16 years with unknown aetiology. Early onset oligoarticular JIA (50 per cent of all JIA) is not observed in adults, and systemic onset JIA (10 per cent of all JIA) is seldom found in adults. While rheumatoid factor positive polyarthritis is only seen in three per cent of all JIA cases, it accounts for 70 per cent of all cases of adult rheumatoid arthritis (Cassidy and Petty, 2011; Ruperto and Martini, 2011; Foster and Brogan, 2012). For a classification of JIA, please see Paediatric resources 1.

In addition:

- pharmacokinetic and toxicity profile of medications are different in adults and paediatrics
- indications for medications differ; chronic anterior uveitis can be a devastating complication of JIA (not seen with adult RA), which may warrant methotrexate treatment to prevent blindness, despite quiescent arthritis (Weiss et al., 1998; Cassidy and Petty, 2001)
- dexterity problems are more common in adults with RA who might want to self-inject
- children and young people have fewer complicating risk factors (for example, alcohol consumption and pre-existing lung and liver disease) compared to adult practice.

Methotrexate use in paediatric rheumatology

History

Over the last 26 years of clinical use, methotrexate has transformed the outlook for children with JIA and is considered the gold standard for patients that require a second line therapy (NICE, 2002; Ramanan et al., 2003; Foster and Brogan, 2012). Methotrexate is also widely used in other paediatric rheumatological conditions such as juvenile dermatomyositis (JDM), scleroderma (particularly localised), juvenile systemic lupus erythematosus (JSLE), idiopathic chronic anterior uveitis, and some vasculitides (Cordeiro and Isenberg, 2006; Hedrich et al., 2011).

It has been shown that subcutaneous administration in children has a 10 per cent to 12 per cent increased absorption rate compared with oral preparation (Tukova et al., 2009).

Alsufyani et al. (2004) retrospectively studied children that failed oral methotrexate, and found that changing to subcutaneous methotrexate had a high likelihood of success, with more than 70 per cent of patients with JIA achieving significant improvement. In clinical practice, subcutaneous administration is often used as first line compared to oral, due to the higher bioavailability and less gastrointestinal upset (BSPAR, 2010).

Subcutaneous methotrexate treatment can be self-administered at home, giving the patient and family a greater degree of independence and comfort.

Rationale for the use of subcutaneous methotrexate

Subcutaneous methotrexate in pre-dosed, pre-filled syringes is now licensed for polyarthritic forms of JIA in children over three years of age that have failed to respond adequately to non-steroidal anti-inflammatory drugs (NSAIDs). These are easy to obtain and safer to administer to paediatric patients and ideally should be administered within the home (BSPAR Standards of Care, 2009).
These commercially available syringes have a reduced volume of drug and, in contrast to hospital manufactured methotrexate syringes, also have a pre-attached needle and therefore are safer, as this decreases the risk of spillage.

Best practice, as advised by the ARMA Standards of care for JIA (2010), involves developing shared care between a paediatric rheumatologist who regularly sees children with rheumatic conditions and the local health care team, supported by a paediatric rheumatology nurse specialist. Ideally the family should be taught how to administer the injections.

The advantages of using subcutaneous methotrexate therapy at home for children, young people and their families include:

- not missing school/work, spending time travelling to and waiting at GP surgeries or the local hospital
- a more consistent approach to care (normalises treatment)
- the child or young person can self-administer, thereby increasing independence and concordance
- children may get car sick on journeys to hospital or GP for injection, coupled with methotrexate anticipatory nausea that may increase the chance of vomiting (Van der Meer et al., 2007; Bultovic et al., 2011)
- it may prevent the build up of negative anticipation in the child because the methotrexate can be administered when desired and is not dependent on other health professionals.

In recent years the development of biologic therapies has added another dimension. The effectiveness of some biologic therapies is enhanced by the co-administration of a DMARD (usually methotrexate) to enhance the action of the biologic agent, but also reduce the potential for antibodies to develop against the biologic agent.

**Dosage**

Unlike adult care, methotrexate use in paediatrics is usually calculated by body surface area (BSA) rather than weight alone as this gives a more accurate calculation in growing children (see Paediatric resources 2: how to calculate body surface area).

The recommended licensed dose is 10 to 15mg/m² body surface area (BSA) once weekly. In therapy-refractory cases, the weekly dose may be increased by up to 25mg/m² BSA/once weekly (BSPAR, 2010; BNFC).

Commercially available syringes (e.g. medac Metoject®), currently come in gradients of 2.5mgs, in a dose range of 7.5mg to 30mg per week. If a patient is prescribed a dose smaller than 7.5mg (i.e. off licence dose), this dose would need to be specially made up in a local hospital setting. This also has implications for weaning doses in patients in remission; due to the available syringe doses it would be good practice to reduce in 2.5mg steps.

There is no reason why non-medical prescribers cannot prescribe methotrexate locally if this is within their field of practice and:

- they are allowed (locally) to do so
- they are prescribing within their respective professional prescribing guidelines such as the NMC guidelines (2006, 2010)
- they are competent to do so.

As with any therapy, the nurse prescriber must be aware of drug dosages, preparations and contraindications.

**Folic acid supplementation**

Folic acid supplementation is used as standard practice by most paediatric rheumatologists to reduce methotrexate side effects.

The BSPAR methotrexate guidance (2010) states that if folic acid is prescribed, the usual dose is 5mg orally, weekly on a different day to the methotrexate, or 1mg orally daily. Folic acid supplementation can be initiated at the start of methotrexate therapy or added in if needed due to adverse effects.

**Risk management**

Risk assessment and management is an integral aspect of providing safe and effective health care and this guidance recommends that practitioners should consult and be aware of their local authority risk management policy and guidelines, and be able to demonstrate that all potential areas of risk have been addressed.

There is emerging evidence that the cytotoxic risk relating to the low dosages used in the treatment of inflammatory arthritis is small (Wong et al., 2009). In addition, the availability of methotrexate in sealed pre-dosed, pre-filled syringes with an attached needle means the risk of spillage and accidental exposure is significantly minimised.
Advice on the handling and administration of subcutaneous methotrexate and pregnancy

Methotrexate has the ability to impair the fertility of those using it and is embryotoxic, which means it can cause abortion or foetal defects particularly during the first trimester of pregnancy (Ostensen and Förger, 2009).

Best practice advocates that those who are pregnant (and particularly those who are in the first trimester of pregnancy) do not handle or administer methotrexate (HSE, 2003; BSPAR 2010; Dougherty and Lister 2011). Practitioners are advised to adhere to their local policy regarding this.

It is the responsibility of the physician and nurse to inform women who are pregnant, breast feeding or men/women trying to conceive about the potential risks relating to the handling and administration of methotrexate because of its teratogenic properties (BSPAR, 2010).

It is therefore essential that contraceptive measures should be used by men, women and young people during treatment and for at least three to six months following cessation of treatment (BSR/BHPR, 2008; Dougherty and Lister, 2011; McInnes et al., 2012).

Having been informed of the potential risks, ultimately the final decision of individuals in relation to the handling and/or administration of methotrexate is a personal one, but one that should be well documented.

Supply, storage, protective clothing and disposal

Supply, preparation and delivery

Methotrexate is available in licensed, pre-filled syringes. Packaging and transport systems should ensure that adequate protection and storage instructions are adhered to during delivery. Practitioners should be guided by local policies.

Pre-dosed, pre-filled syringes are issued in one of three ways: hospital pharmacy, community pharmacy or home delivery.

Patients or carers who self-administer must be told about any changes of manufacturer. This is because it may result in changes to the volume provided in the syringe, storage conditions, expiry date or appearance of the syringes. In addition, they must also be informed of the potential change in administration technique according to manufacturer’s guidelines, and be appropriately retrained.

Storage and drug stability

Methotrexate is a clear yellowish solution and is stable if stored out of direct sunlight.

Pre-filled syringes will need to be checked to clarify the particular storage recommendations for the product; for example, commercially available solutions of methotrexate often do not need refrigeration. Also, the quantity of syringes to be collected by a parent or delivered to home may also vary.

The shelf life and storage conditions may vary depending on the syringe provider, and these should be carefully checked and reviewed on a regular basis and prior to each administration of the drug.

During the teaching programme families are taught what information to check on the syringe label (such as the child’s name and drug dose). When considering families for home administration, thoroughly discuss with the family the facilities needed for safe home storage of the syringes, and clinical waste bins.

Storage at home

The storage of methotrexate syringes and clinical waste bins should be out of the reach and sight of vulnerable adults, children and pets.

Practitioners and patients/carers who undertake self-administration should be trained and competent in all aspects of safe storage. This will include awareness that storage will vary according to the product used (see Supply, preparation and delivery above).

Personal protective equipment (PPE)

Previous evidence suggests that the levels of contamination appear to correlate with the amount of drugs prepared and number of vials used (Sessink et al., 1997).

However, in light of emerging evidence that the cytotoxic risk relating to the low dosages of subcutaneous methotrexate used in the treatment of inflammatory arthritis is small (Wong et al., 2009), this guidance suggests that aprons, goggles, masks or armlets, no longer need to be worn by practitioners when administering pre-filled subcutaneous methotrexate injections.
In promoting good clinical practice this guidance recommends that practitioners and carers should always use gloves (latex free, ideally) and observe good hand washing protocols when administering subcutaneous methotrexate (Crast-Manciet et al., 2005; Dougherty and Lister, 2011). It is not necessary for a child or young person administering their own therapy to wear gloves.

Ideally, best practice for handling excreta always involves the use of gloves where there is contact with urine, faeces or vomit. However, this is not always practical or realistic. Parents should be taught safe hand washing techniques and be helped to reach an informed decision about wearing gloves.

**Disposal of sharps and clinical waste**

Local policy should dictate the storage, collection, handling and disposal of methotrexate clinical waste/sharps. Practitioners should receive regular training and updating on policies in relation to dealing with hazardous waste and sharps safety.

When methotrexate is administered in any community setting (GP surgeries, community clinics, schools and/or directly to patients’ homes) issues relating to the management of clinical waste need to be considered (please refer to your local policy). In some circumstances, companies that deliver the methotrexate to the patients’ homes are also responsible for the collection and disposal of sharps and clinical waste.

Purple topped clinical waste bins should be used for the disposal of pre-dosed, pre-filled methotrexate syringes.

Patients should be aware of the need to ensure safe disposal of equipment using a clinical waste bin, and that the bin itself also constitutes a risk and should be safely stored when not in use. The bin should never be filled more than two-thirds of its total capacity or transported if not securely sealed.

**Spillage**

Based on the assumption that methotrexate will be administered using a pre-dosed, pre-filled syringe containing a small volume of methotrexate, the risk of exposure is minimal and a spillage kit is unlikely to be necessary (although some local cytotoxic policies may recommend this and you should refer to your local policy).

When working in health care settings, practitioners should be aware of local policies, be able to locate and access a spillage kit if required, and know how to deal with any accidental spillage.

Young people and their parents should also be aware of what to do in case of spillage.

A small spillage kit may be provided to the patient and used in the clinical area for training purpose. If provided, the spillage kit should include:

- instructions on how to manage and deal with spillages
- clinical waste bin/bag and tape/label according to local policy
- absorbent paper towels or plastic backed absorbent towels (large).

**Liquid spillage on clothing**

Wear protective gloves and blot dry with a paper towel or kitchen roll. As a precaution clothing should be removed immediately (Dougherty and Lister, 2011) and washed separately from other items. Wash hands thoroughly.

**Liquid spillage directly onto the skin**

Wong et al., (2009), found poor dermal methotrexate penetration from deliberate contamination. However, if methotrexate is accidentally spilt onto the skin surface, the area should be washed “liberally with soap and cold water” (Weinstein and Plumer, 2007; Dougherty and Lister, 2011). Methotrexate is not a vesicant (blister agent).

**Liquid spillage directly into the eye**

The eye should be washed out using plenty of water (Weinstein and Plumer, 2007; Dougherty and Lister, 2011) for a couple of minutes. A doctor should be contacted if any side effects are experienced. Some care settings may have eye wash kits available, if needed.
Liquid spillage on floors or work surfaces
Wearing gloves, cover the spillage with absorbent paper and clean with soap and water. Paper tissue should be bagged and disposed of in the bin.
Young people and their parents should also be aware of what to do in case of spillage.

Practitioner training and competence
No specialist training is required for the administration of subcutaneous methotrexate by practitioners, however all practitioners should be competent in the administration of the subcutaneous injection technique.
Ideally, specialist practitioners should undertake appropriate training in the administration and management of methotrexate.

Checklist for practitioners
All practitioners should adhere to the following checklist prior to administering a pre-dosed, subcutaneous methotrexate injection to a patient:
- check the methotrexate dose, dosage form and frequency prescribed and expiry date of the syringe
- ensure blood monitoring (including the monitoring of trends) is in place as per BSPAR (2010) and NPSA (2006) guidelines and local protocols, that blood results are satisfactory, and patients know when they need to attend for their next blood test
- check there are no contraindications to administration (as per the SPC)
- ensure the patient has consented to have the injection
- ensure the patient knows the advice line telephone number for support or concerns
- document the injection and the site used
- be aware of protocols relating to the safe disposal of sharps
- note the date and time of next injection.

Specialist practitioner training and competence (see Appendix 3)
- Practitioners should be knowledgeable and competent in all aspects of methotrexate administration and risk management, and stay up-to-date with the latest evidence in relation to the drug’s indications and side-effects.
- Practitioners should have undertaken appropriate training to educate, support and teach patients in the self-administration of subcutaneous methotrexate, and ensure their own training is regularly updated.
- Practitioners should ensure appropriate communication and support are available for primary health care teams and patients self-administering in their own homes.
- Practitioners should be aware of clinical governance and local policies in relation to management of patients receiving methotrexate.
- Documentation and audit should be an integral aspect of developing a service for patients receiving subcutaneous methotrexate.

Home administration
The ability of a patient to inject in their own home can provide a significant degree of independence for the patient and is also a cost effective treatment pathway, avoiding unnecessary hospital attendances and/or the need for direct health care practitioner support.
For home administration to work efficiently, good communication is vital, not only between primary, secondary, tertiary care and pharmacy services, but also with the family. Parental or child administration is ultimately a family’s choice.
The injections may be administered at home by the trained parent, child, young person or responsible adult. But if this is not possible, the injections should be administered by an appropriately trained health professional. If the family changes their mind during the course of treatment, this will require further discussion about how to manage the situation.

Administration by a child or young person
Any child or young person that voices a desire to self-medicate must be individually assessed for his or her level of understanding and compliance. In general it has been found that encouraging children to self-inject fosters independence and compliance with the treatment programme. If a full injection is a step too far,
assisting them to participate in the process – for example, pushing the plunger – is a step towards self-administration.

There is little published evidence on the ideal age for a child or young person to self-administer subcutaneous injections. Livermore (2003) suggests an arbitrary age of ten years, however there is anecdotal evidence of children younger than this self-administering. It is important to stress that there must be ongoing supervision by an appropriately trained adult.

**Screening families for home administration**

When screening families for home administration the two important requirements (once a training programme is in place) are:

1. a desire from the parent, child or young person to give the injections
2. an assessed level of competence.

In addition, following training and risk assessment, a decision will be made whether the patient/carer:

- has a clear understanding of their responsibilities in the safe management of methotrexate, including NPSA (2006) (i.e. correct dose and frequency), additional equipment, and waste disposal
- will undertake regular blood monitoring and attend clinic appointments
- recognises that a risk assessment must support home administration and that this will be subject to review
- understands the back-up plan in the event of being unable to administer or self-administer.

A back-up plan must be in place to ensure that, in the event of a patient or carer being unable to self-administer (for example, due to limited dexterity), they can call on specialist support or a non-specialist rheumatology practitioner’s support (for example, ward staff, practice nurse or community nurse), or a carer trained in the administration procedure.

Patient information leaflets on subcutaneous methotrexate injections are readily available from a number of organisations such as Arthritis Research UK and BSPAR (*Patient information leaflet*, 2011). Manufacturers also produce illustrated patient guides.

**Suitability of family circumstances**

There has to be a willingness to do the injections, an area for safe storage and child compliance. More importantly, each family needs to be individually assessed to see whether they would cope with the administration, safe storage and disposal of the injections (Livermore, 2003). Practitioners usually know the family, and often have an insight into their understanding of treatments, their ability to manage side-effects, and the safe administration/compliance of medications.

Families need to understand that the option of home administration is subject to undertaking the training programme and a review of their ability to manage all aspects related to administration in their own home. They also need to know that they too have a responsibility in the partnership, and should always agree to check with a health care professional before they take any decision to omit an injection.

Practitioners will also need to consider if the child or young person has a needle aversion, and if this needs addressing. There may be other issues that affect self-administration, such as the dexterity of the child or young person, or whether there is a back-up person to administer the drug.

**Consideration of risk-taking behaviours**

Practitioners should identify sexually active young people and counsel them about the use of contraception and the prevention of sexually transmitted diseases, as well as the importance of minimising alcohol intake while taking methotrexate.

Further discussion may be needed about planning pregnancy in the future. For example, it is necessary for both male and female patients to stop methotrexate for six months prior to considering starting a family. This should be done with the support and advice from the rheumatology team.

**Pre-treatment checklist and baseline investigations**

The following pre-treatment/baseline investigations must be undertaken for a child or young person.

- Blood screening:
  - full blood count and differential white blood count
  - ESR (erythrocyte sedimentation rate) and/or C-reactive protein (CRP)
liver function tests
urea and electrolytes
varicella and MMR titres – if the titres are negative, have the chickenpox and MMR vaccines been offered prior to starting treatment if time allows?

Note: Chest X-rays are not routinely performed prior to starting methotrexate in paediatric rheumatology.

A careful and detailed review of concomitant medication must be undertaken to exclude any potential drug interactions or absolute contraindications. Please refer to the BNFC, and the manufacturers’ specific summary of product characteristics (SPC). For further advice, contact the local prescribing doctor.

Skin preparation and administration of subcutaneous methotrexate

Skin preparation
There are inconsistencies in the available literature regarding skin cleaning prior to subcutaneous injections – in other words, ‘to swab or not to swab’. Some reports suggest that as long as the skin is socially clean at the injection site and thorough hand washing techniques are used there is no reason to clean the skin with alcohol impregnated swabs (Workman, 1999; Vaccine Administration Task Force, 2001; DH, 2006; Gittens and Bunnell, 2009).

Practitioners are advised to adhere to local guidelines on skin disinfection before injection.

Methotrexate subcutaneous injection technique

Best practice recommends that practitioners and carers should use gloves, but this is not required for patients who self-administer.

Check the skin is socially clean.

Remove the needle cap carefully using the twist and pull technique. You are advised to check the angle of the needle in relation to the syringe, as sometimes the needle can accidentally be slightly bent. If this is the case, inject at the required angle to the needle and not the syringe. However, if in any doubt, another syringe can be tried and/or the supplier/manufacturer contacted for further advice.

If the syringe contains a small air bubble, DO NOT EXPEL; it is required to ensure that all the drug is administered. This is completely harmless.

There is NO need to aspirate when the needle is in situ.

The injection should be administered into subcutaneous tissue in the thigh, arm or stomach.

Commercially available syringes (e.g. medac Metoject®) have a 27G (0.4 by 13mm) needle attached; however, if the injections are made up in a local pharmacy; 26G (brown) or 30G (yellow) needles may be more suitable.

Gently grip the skin at the injection site between thumb and forefinger. Holding the bore of the syringe as a dart, with the needle at an angle between 45° to 90° to the skin (depending on the size of the child and the amount of subcutaneous tissue). Insert the needle completely, using a quick short motion.

Release the skin and slowly inject all the medication. Remove the syringe.

The drug can be expelled at any speed requested by the patient, but some particularly anxious young people prefer the medication is given quickly.

Note: some users have expressed concern that some syringes can appear to have a “blunt” needle. If this is an area of concern, a review of the pre-filled needle and/or injection technique may be required.

For full information on the subcutaneous injection technique, please see Paediatric resource 3.

Rotating injection sites

Patients or carers who self-administer treatment need to ensure that they rotate the injections sites. If giving two injections (such as methotrexate and a biologic therapy), these should be given in different sites. For example, one should be given in the right thigh and the second in the left thigh. The injections should be at least 3cm apart, if given in the same limb. If injecting in the abdomen, injections should be outside a 5cm radius from the navel.

It is suggested that the patient should keep a record of injection sites used.

For additional information refer to the SPC or BNFC.
**Review and monitoring**

The patient or carer should be able to access additional training sessions if necessary and as required. Although it is best practice to undertake an annual review of patient or carer skills/practice in injecting and managing their prescriptions, this may not always be feasible.

To minimise reactions and promote and maintain good injection technique, practitioners should routinely ask patients/carers if they are experiencing any problems and arrange an appropriate assessment if this is required. This approach will help maintain a thorough audit trail and ensure the maintenance of safe practice by patients/carers.

**Patient education and training**

Children, young people and their families should be provided with information (verbal and written) about the treatment and understand the contraindications, the potential risks and side-effects to enable them to make an informed decision about methotrexate therapy.

The child/young person and parent should also be given ample opportunity to discuss any concerns they may have after they have been given written and verbal information about methotrexate. If they wish to proceed with the training, consent should be obtained and documented according to local policy (see guidance in Paediatric resources section).

In addition, the young person and/or parent should have a training plan that provides them with a clear understanding of the process and responsibilities required for home administration. The time taken to train a young person or parent together with the number of practice sessions will vary.

**When not to administer**

As with any medication, the practitioner, parent or young person needs to be aware of the circumstances when they would not administer methotrexate. The two most common reasons for temporarily discontinuing methotrexate in paediatrics include:

- significant deranged blood tests: it is the responsibility of the monitoring physician/nurse to inform families of abnormal blood results that require stopping the treatment
- the child/young person develops chickenpox/shingles; the parent/young person should inform their GP or treatment centre for appropriate advice.

Usual childhood coughs, colds, or minor infections do not warrant stopping methotrexate. However, if there is any suspicion that the child is systemically unwell – for example, a high fever (over 38.5°C) or a rash (that is different to any usual fevers or rashes such as those that accompany systemic onset JIA) – then expert opinion should be sought.

**Side effects**

The main side effects seen in children and young people include nausea and vomiting, increases in liver enzymes, abnormal blood results and post-dosing reactions of generally feeling unwell.

**Nausea and vomiting**

A considerable number of children/young people suffer from methotrexate-related nausea. Practice within services differs, but it is worth considering administering an antiemetic and folic acid prophylactically when starting methotrexate to try and prevent nausea and vomiting occurring in the first place.

Although many children are converted to subcutaneous methotrexate to lessen nausea and vomiting, many continue to experience it. Anecdotal evidence suggests that nausea, vomiting, and perhaps the more troublesome anticipatory nausea, are hugely underestimated problems for our patients (Van der Meer et al., 2007; Bultovic et al., 2011).

Often the whole family will need support as they are all involved in the preparation for the procedure, including calming and supporting the child with JIA. This is probably the main reason for lack of compliance and subsequently stopping the drug.

Although antiemetics are often used, their effects on patients are variable. The sickness felt is real, and this must be emphasised to children, and to their families.

There are a number of strategies to try and lessen nausea and vomiting and the disruption it causes:

- giving the injection just before bedtime and on a Friday or Saturday (to avoid school absenteeism)
- folic acid supplementation
withholding NSAID dosage on the injection day
- administering an antiemetic dose a few hours before and one to two doses after the injection
- eating something during the injection, such as a chewy sweet bar can help (although in some patients this makes it worse).

Non-pharmacological interventions can also be used in conjunction with the above:

- self-hypnosis
- relaxation
- music therapy
- guided imagery.

Abnormal blood results and monitoring

The blood monitoring regime for subcutaneous methotrexate is the same as for oral methotrexate (BSPAR, 2010).

As Ramanan et al. (2003) states, children usually tolerate methotrexate well and haematological abnormalities rarely occur. Baseline bloods should be obtained (see screening section above), and repeated on a regular basis (Kocharla, 2009). The BSPAR methotrexate guidelines (Methotrexate use in paediatric rheumatology, 2010) state that full blood count and liver transaminase (asparate transaminase (AST) and/or alanine transaminase (ALT)) levels should be monitored at two to four monthly intervals and serum creatinine at six monthly intervals.

Blood dyscrasias, such as neutopenia and lymphopenia will often lead to a temporary halt of the methotrexate until blood values have normalised. If the liver enzymes are raised above three times the upper limit of normal, the methotrexate is usually discontinued for one or two weeks and the results rechecked. If these have returned to normal, methotrexate can be restarted at the same dose. If the enzymes are still high, the dose can be discontinued for a further fortnight or the dose reduced by 20 per cent, and then rechecked. There is little evidence of liver damage or long-term toxicity in JIA patients taking methotrexate (Hashkes et al., 1997; Ramanan et al., 2003; Foster and Brogan, 2012).

Responsibility for blood monitoring should be agreed locally and a shared care agreement entered into if monitoring is to take place in primary care. Good practice often involves a patient-held record (such as the NPSA’s blood monitoring booklet), particularly when the parents or young person administer the injections. Encouraging families to have ownership of their blood monitoring record and be aware of any abnormal trends supports good shared care.

Please see the BSPAR methotrexate guidelines (2010) for further information.

Needle aversion

Strong dislike or ‘aversion’ of needles is a major concern in many paediatric areas. In some children referral to a child psychologist or play therapist may be necessary, although this may not be available in all local areas. Topical anaesthetic creams or sprays can be used, or a wrapped frozen bag from the freezer can be used to numb the skin. The use of distraction techniques, bravery certificates and stickers may also prove useful.

Giving the child as much control as possible, for example, in which room they want their injection done, what they want to do (look at a book, watch TV, play a computer game), or the speed of the injection; are often useful strategies. There are some commercially available products which families can buy to aid subcutaneous injections in young people, by for example vibrating on the skin surface and thus lessening the pain signals to the brain.

Note: some commercial companies are in the process of developing a pen device for the administration of methotrexate where the needle will not be visible.

Vaccinations

As with any immuno-suppressant therapy, guidelines on immunisation in the immuno-compromised child should be followed. The RCPCH guidelines (2002) state that live vaccines should not be given (see Paediatric resources 4). Inactivated vaccines can be given, but the child may not build up the appropriate immune response to vaccines while on methotrexate and must have these checked if they discontinue the methotrexate.

It is recommended that all children and young people are brought up-to-date with the pneumococcal vaccine for those who have not had it previously and annual flu vaccines should be given while on this treatment.
Chickenpox
Chickenpox is a major concern in paediatric practice, much more so than in adults.

The treatment of a child who has been in contact with chickenpox, or who develops chickenpox, differs from area to area and this document advises consultation with local centres. Further advice can be sought from BSPAR guidance on methotrexate use in paediatric rheumatology (2010).

Measuring chickenpox titres in all children prior to starting methotrexate is now standard practice and some even offer the chickenpox vaccine to those who have negative titres. The vaccine is live and thus this may delay starting methotrexate treatment, depending on local guidance. Consideration should be given to providing immunisation to close relatives that have not been previously infected with chickenpox.

It is also vital to note that if chickenpox develops, methotrexate should be discontinued until the last spot has crusted over and the child is clinically well. Antiviral drugs are usually prescribed. Passive protection against chickenpox (or herpes zoster) with VZIG and/or aciclovir should be given in the event of significant contact in non-immune patients. Ideally oral anti-viral medication should be given (Immunisation of the immunocompromised child: best practice statement, RCPCH, 2002) but this may be dependent on your local policy. See: www.imunisation.dh.gov.uk and check the Green Book www.dh.gov.uk/greenbook for an up-to-date definition of ‘significant contact’.

Transition to adult care
At least one-third of children with JIA continue to have active inflammatory disease into their adult life, and up to 60 per cent of all patients continue to have some limitation to activities of daily living (Nigrovic and White, 2006). Specific figures for many rheumatic diseases that continue into adulthood are harder to find, particularly since conditions such as ankylosing spondylitis (AS) and juvenile systemic lupus erythematosus (JSLE) primarily present in adolescence rather than childhood. Adolescence can be a challenging transitional time (McDonagh, 2009) and the following needs special attention:

- identification and counselling of risk-taking behaviours, such as alcohol, recreational drugs and unprotected sex
- transition and transfer to adult care.

Transfer to adult care often does not happen seamlessly and therefore needs special consideration – for example, the development of self-management skills in paediatric care in preparation for adult care. The importance of having similar systems in place between paediatric and adult care are vital. For example, if the young person self-administers, the nurse needs to know whether this can continue in the adult setting. Also, if a paediatric nurse administers the injections in the family home, will there be an adult equivalent willing to take over this role?

Travelling away from home
In relation to the storage of injections, caution is recommended when travelling to hot climates over 25°C, and the manufacturer’s guidelines/local prescriber should be consulted for advice on storage in high temperatures.

Advice should be given to patients if the injections they receive for travel require different storage to their usual treatment.

Options available to patients who cannot take their injections away with them are:

- tablets/liquids instead of an injection
- an injection just prior to travelling and one immediately on return.

There may be an issue with the transportation of pre-filled syringes when flying and patients may require a supporting letter before they travel.

Patients should be advised to carry the medication in their hand/cabin luggage, in case the bags get mislaid, but also as any rough handling of luggage could damage the medication and it may also freeze in the hold.

Patients should be advised to arrange any vaccinations they may require well in advance of travel and the importance of informing the vaccination provider they are receiving regular methotrexate treatment (to ensure they do not receive any live vaccines).
Audit trail and data collection

It is essential that all patients who are self-administering methotrexate can be identified and traced promptly should the need arise.

Further information relating to data collection and audit trails can be found in the adult practice section of this document.

Conclusion

When used appropriately, the home administration of methotrexate is safe and ultimately improves the quality of life experienced by a child or young adult and their family.
Paediatric resources

1: International League of Associations for Rheumatology (ILAR) 2001: classification of juvenile idiopathic arthritis (JIA), updated 2004

The following can only be diagnosed after six weeks:

<table>
<thead>
<tr>
<th></th>
<th>Description</th>
<th>Criteria</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>Oligoarticular onset:</td>
<td>Four or fewer total joints involved</td>
</tr>
<tr>
<td></td>
<td>Extended oligoarticular:</td>
<td>&gt; Four joints involved after the first six months of disease</td>
</tr>
<tr>
<td>2</td>
<td>Polyarticular onset</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rheumatoid Factor Negative:</td>
<td>Five or more joints during the first six months of disease with no detectable Rheumatoid Factor</td>
</tr>
<tr>
<td>3</td>
<td>Polyarticular onset</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rheumatoid Factor Positive</td>
<td>Five or more joints during the first six months of disease and when Rheumatoid Factor is detected on at least two occasions at least three months apart</td>
</tr>
</tbody>
</table>
| 4 | Systemic onset | Arthritis of any number of joints with a documented typical high quotidian spiking fever of at least two weeks duration and one or more of the following: 
  - transient episodic erythematous rash 
  - enlargement of liver or spleen 
  - serositis |
| 5 | Psoriatic arthritis | Arthritis and psoriasis or arthritis and at least two of the following: 
  - dactyliitis 
  - nail abnormalities (pitting) 
  - family history of psoriasis confirmed by a dermatologist in at least one first-degree relative |
| 6 | Enthesitis-related arthritis | Previously known as juvenile spondyloarthropathy. 
  1) Arthritis and enthesitis, or 
  2) Arthritis or enthesitis plus two of the following: 
  - sacroiliac joint tenderness, inflammatory spinal pain, or both 
  - HLA-B27 
  - family history in first-, or second-degree relative of medically confirmed HLA B27+ve associated disease 
  - acute anterior uveitis 
  - onset of arthritis in a boy after the age of eight years |
| 7 | Other arthritis | any form of idiopathic chronic arthritis, which does not fit into the above categories |

(Cassidy and Petty, 2011)
2: How to calculate body surface area

Body surface area (BSA) is calculated in square meters (the Mosteller formula).

\[
\text{BSA} = \sqrt{\frac{\text{Height (cm)} \times \text{Weight (kg)}}{3600}} \text{ m}^2
\]

Example calculation for a patient with a height of 100cm and weight of 30kg:

\[
\sqrt{\frac{100 \times 30}{3600}} = 0.91 \text{ m}^2
\]

If this patient receives methotrexate 15mg/m²/week, she/he will receive weekly:

\[0.91 \text{ m}^2 \times 15 \text{ mg} = 13.65 \text{ mg/week}\]

This will be rounded up or down to the nearest 2.5mg by the prescriber.

To calculate the methotrexate dose m²/week:

\[
\frac{\text{dose (mg) per week}}{\text{BSA}} = \text{dose m}^2/\text{week}
\]

To calculate the methotrexate dose m²/week if this child receives 10mg methotrexate per week:

\[
\frac{1}{0.91} \times 10 \text{ mg per week} = 10.99 \text{ mg/m}^2/\text{week}
\]
why regular blood tests are taken, and if they are abnormal the next dose will be withheld and the blood results rechecked. Blood results are affected by many things such as tummy bugs, or if you are fighting an infection. Symptoms will often improve on their own, and the drug can be restarted without any problems.

**An introduction to safe home administration**

The process of teaching you how to give the injections will vary depending on your local area. At each stage of the teaching process you may be asked to sign that you are happy with the training you have been given and that you feel confident to continue. At any point during the training, or afterwards, you can decide that you do not want to give the injections anymore. This is OK, but please inform your nurse, so that they can make other arrangements.

Below are the main points to remember when preparing equipment, handling the drug and disposing of used equipment afterwards:

- wash your hands thoroughly before and after giving the injection
- always handle the syringe and needle carefully
- the syringes will be specifically for your child only and should always contain the exact amount to be given – you must check this each time
- look carefully at your syringes to see whether you need to store them in the fridge or at room temperature – if you are unsure, ask your nurse for help
- if syringes need to be stored in the fridge, keep in a box on the bottom shelf and away from food. If there are young children in the family it may be wise to fit a fridge lock. Some drug companies provide a separate fridge to store the syringes (the syringe can be kept at room temperature for 30 minutes prior to injection)
- if the syringes are to be kept at room temperature, please store out of the reach and sight of children and pets. During very hot summers the syrings may need to be refrigerated – if unsure, ask your nurse
- you will be given a sharps bin to dispose of the syringes. This should be kept closed until two-thirds full when it should be locked and disposed of. Waste should be disposed of as per local policy. Your nurse will be able to give you guidance
if you (male or female), are trying for a baby, are pregnant or breast-feeding it is recommended that you do not handle the drug – please discuss this further with your child’s doctor.

You should not inject if:
1. your child is unwell, and you do not know why. Your child has a high fever (over 38.5°C) or an unusual rash. Usual childhood coughs and colds are nothing to worry about, but if your child is sicker than normal contact your GP or local medical team for advice
2. you are aware that your child’s blood results are abnormal. Children with rheumatic diseases often have raised blood values. If these are outside the expected normal limits contact someone for advice
3. your child has come into contact with chicken pox or develops chickenpox/shingles. Please contact your nurse or doctor straight away for advice.

Never give the injection if you are at all unsure. Please call your nurse or advice line number.

How to give a methotrexate subcutaneous injection

Equipment
Getting the equipment ready
- Methotrexate syringe for injection (you may need a needle if the treatment has been made up in a local hospital pharmacy).
- Clean table surface.
- One appropriate clinical waste/sharps bin.
- Pair of disposable gloves (if required/being used – though not necessary if the child/young person is self-administering).
- Cotton wool ball/clean tissue.
- Spot plaster (if desired).
- Spillage kit and alcohol wipes (if issued).

Preparing your working area
1. Collect all the above equipment and take it to where the injection will be given – such as a clean table or work surface – before you start assembling. You may wish to use a piece of kitchen roll on top of your clean work surface. If possible, try to give the injection in a non-carpeted room in case there is a spillage.

Giving the methotrexate injection
1. Ensure everyone is comfortable.
2. Check the syringe is in date, has the correct name on it and it is the correct dose. If it is incorrect in any way you must not give the injection but check with your rheumatology department or pharmacy.
3. Check the syringe contents to make sure that it is a clear yellow solution. If it does not look like this, or has particles in it, you should not give the injection but contact the rheumatology department or pharmacy.
4. If the needle needs to be attached peel-open the end of the needle packet carefully. While holding it in one hand and the syringe in the other, remove the syringe cap and attach them together. Put the syringe cap straight into your sharps bin. DO NOT touch the syringe end or the needle tip.
5. If the syringe already has a needle attached, pick up the syringe and hold the barrel of the syringe (low down as if you are going to write your name with a pen). Hold the needle shield firmly and twist and pull until the needle shield is loose and gently remove. DO NOT touch the sterile needle.

2. Wash and dry your hands thoroughly and clean your preparation area (for example, a work surface, a clean tray or lid).
3. Only people who are helping you should be present in the room (avoid distractions such as pets).
4. Wash working surface with liquid detergent and allow it to dry.
5. Arrange the equipment on the clean surface.
6. Wash and dry your hands once more, then make sure you have all the equipment close at hand before you make yourself comfortable to give the injection.
7. Carers need to put gloves on if administering the injection but if you are a child or young person administering your own injection, it is up to you whether you want to wear gloves or not.
8. Decide on where you will give the injection. You will need to change the injection site each week to reduce the risk of soreness (see Figure 1).
9. Make sure the injection site is clean; if not, clean with soap and water.
10. Open the syringe packet.

2. Wash and dry your hands thoroughly and clean your preparation area (for example, a work surface, a clean tray or lid).
3. Only people who are helping you should be present in the room (avoid distractions such as pets).
4. Wash working surface with liquid detergent and allow it to dry.
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8. Decide on where you will give the injection. You will need to change the injection site each week to reduce the risk of soreness (see Figure 1).
9. Make sure the injection site is clean; if not, clean with soap and water.
10. Open the syringe packet.
6. Make sure the needle does not come into contact with anything on the way to the skin so as to avoid contamination and the risk of introducing infection.

7. If the syringe contains a small air bubble, DO NOT EXPEL THE AIR BUBBLE; it is required to ensure all the drug is administered and there for safety reasons. It is completely harmless.

8. Inject into the thigh, back of arms, or stomach – but a minimum of 5cm away from tummy button. If giving two injections (such as methotrexate and a biologic therapy), these should be given in totally different sites. For example, one should be given in the right thigh and one in the left. If given in the same limb the injections should be at least 3cma part. Some children do not have much subcutaneous fat on their arms, so their thighs are often the most appropriate place (Figure 1).

9. Alternate the injection site from week to week so it doesn’t get sore.

10. With your free hand, gently grip the skin together (see Figure 2), where you are going to inject and insert the needle at a 45° to 90° angle. The needle will deliver the injection just below the skin (subcutaneously). See Figures 2 and 3.

11. Once the needle is in place release the pressure on the skin and support the syringe with both hands. With your preferred hand, push the syringe plunger slowly down to inject the methotrexate.

12. When you have injected all of the methotrexate remove the needle and syringe from your skin, place a cotton wool ball or tissue over the injection site. Then immediately put the used syringe, needle and tissue directly into the clinical waste/sharps bin. DO NOT re-sheath the needle.

Note: some users have expressed concern that some syringes can appear to have a “blunt” needle. If this is an area of concern, please discuss this with your nurse specialist, GP or community nurse, as a review of the pre-filled syringe and needle and/or your injection technique may be required.
**What to do after administering methotrexate**

1. Do not put any of the used items in with your normal household waste.
2. Instead you should put the used syringe and needle into the clinical waste/sharps bin provided.
3. The bin must always be stored out of children’s sight and reach and always closed, but not locked. Lock it when it is two-thirds full and dispose of it according to local policy, or by the home delivery service. Ask your nurse for help with this.
4. Unused syringes should always be returned to your local hospital pharmacy or delivery service.
5. If only part of the dose is given, the remainder should be discarded in the sharps bin.
6. If used, change gloves if these are punctured or torn.
7. Wash hands thoroughly with soap and water and dry thoroughly.
8. Record the site and date of the injection in your diary sheet (if using).
9. If there is bleeding or bruising at the injection site or a small amount of blood in the very tip of the syringe do not worry as this sometimes happens if the needle has punctured a small blood vessel, and will soon stop and the bruising will fade.
10. On rare occasions methotrexate can leak into the surrounding skin causing irritation when patients give an injection. If this happens, and it causes irritation or redness, contact your GP and/or the rheumatology advice line.

**What to do when dealing with a spillage**

- Keep the spillage kit (if issued, as per local policy) and instructions at hand whenever you inject and make sure that your carer or family members are aware of how to use it.
- The amount of methotrexate you are injecting is very small, but it is possible to accidentally spill it.
- If there is a spillage, please follow the advice you have been given; instructions in the spill kit (if issued); or advice listed below.

**Spillage on clothing**

Wearing protective gloves blot the spillage dry with absorbent paper towel or kitchen roll. As a precaution clothing should remove and washed separately from other items.

**Spillage on skin**

Wash the affected area with plenty of soap and water for a couple of minutes. Do not scrub because unbroken skin provides protection. Contact your GP and/or rheumatology team, nurse or doctor for advice if you are concerned or have any adverse reactions.

**Spillage into the eyes**

Wash the eye(s) using plenty of water. It is recommended that you should contact your own doctor, local hospital emergency department or eye hospital if your eyes become sore, you experience any side-effects, or you notice any changes in your vision.

**Spillage onto work surfaces or floors**

Put on a pair of protective gloves. Cover and wipe up the spillage using absorbent paper. Wash the area with plenty of soap and water. Used paper towels should be bagged and placed into the clinical waste bin.

**Accidental needlestick injuries**

If you follow the instructions carefully the chances of you getting an accidental needlestick injury are very small.

If you or your carer accidentally come into contact with the needle while preparing or disposing of the syringe it is important to make the puncture site bleed. Then wash the areas with plenty of running water and cover with a plaster. If a needlestick injury occurs before the injection, then the syringe should be put into the sharps bin and a new syringe should be used.

At the time of writing, it is likely that a pen will be introduced to the market within the next 12 months that should eliminate the possibility of needlestick injuries. For further information on sharps safety refer to the RCN’s guidance (2011).

**Travelling and injecting methotrexate away from home**

The storage of your injections will vary according to local health policy and the manufacturer’s recommendations. However, caution is needed in hot climates over 25°C. You should seek specific advice on storage at high temperatures. Discuss the details of storage with your GP, nurse, practitioner or pharmacist.

The injections you receive for travel will depend on the hospital or company that provides your methotrexate. Make sure that you check the box for instructions on how to store it if it is different from your usual treatment.
Some of the options available to you when you are going away and unable to take your injections with you are:

- tablets/liquid instead of an injection
- an injection just before you travel and then one as soon as you return. Discuss this with your GP or rheumatology department.

If you are flying there may be an issue with the transportation of pre-filled syringes and you may need to discuss this with your methotrexate supplier and get a supporting letter from your rheumatology department before you go away.

It is recommended that you always keep your medication in your hand/cabin luggage, in case the bags get mislaid, but also rough handling of luggage could damage the medication and it may freeze in the hold.

See your practice nurse or doctor to arrange any vaccinations you need well in advance of your travel. You must not be given any live vaccines, so it is also important that they are aware that you are receiving regular methotrexate treatment.

**Rheumatology advice line**

You should be made aware of an advice line you can call and how and when you should use this.
4: Vaccine information for children with rheumatic diseases receiving methotrexate

Inactivated (dead) vaccines can be given to children on immunosuppressive therapy, such as methotrexate, steroids, anti-TNF (etanercept or infliximab) and cyclophosphamide. These include:

- cholera
- diphtheria
- haemophilus influenza HIB
- hepatitis A
- hepatitis B
- HPV (cervical cancer vaccine)
- influenza (flu vaccine)
- meningitis C
- pneumococcal
- rabies
- tetanus
- typhoid (by inactivated injection only)
- only the injectable polio (SALK)

Live vaccines cannot be given, these include:

- BCG
- individual measles
- individual mumps
- individual rubella
- MMR
- oral polio
- typhoid (oral)
- yellow fever
- varilrix (chickenpox) – sometimes this can be organised prior to starting methotrexate, however, this may delay commencement of drug.
Appendices

1: Glossary of terms and definitions

Bioavailability
The amount of drug that reaches the blood system regardless of how it is given. After an intravenous injection bioavailability is 100 per cent, but the bioavailability of drugs given by mouth is often much less because the drugs are broken down by the digestive enzymes and may be poorly absorbed.

Cytotoxic
Toxic to cells. Any agent or process that kills cells.

Hazard
The Health and Safety Executive defines a ‘hazard’ as: “Anything that may cause harm, such as chemicals, electricity, working from ladders, an open drawer etc.” (HSE, 2012)

Risk
“A risk is the chance, high or low, that somebody could be harmed by these or other hazards, together with an indication of how serious the harm could be.” (HSE, 2012).

Risk management
“‘A means of reducing the risk of adverse events occurring in an organisation by systematically assessing, reviewing and then seeking ways to prevent their occurrence. Clinical risk management takes place in a clinical setting.” (National Health Service Executive, 2001, cited in Dimond, 2002a).

Teratogen
Any substance, agent, or process that induces the formation of developmental abnormalities in a foetus.

Vesicant
An agent that causes blistering of the skin.
# Administering Subcutaneous Methotrexate for Inflammatory Arthritis

## 2: Training checklist for home administration of subcutaneous methotrexate by a patient (adult, young person or child) or carer/parent

<table>
<thead>
<tr>
<th>Skill</th>
<th>Date shown/trainer discusses</th>
<th>Date supervised</th>
<th>Date completed/proved competence by trainee</th>
<th>Patient and/or carer's signature</th>
<th>Assessor's signature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Understands verbal and written information given on subcutaneous methotrexate, including potential complications/side effects. Can discuss why it's given.</td>
<td>N/A</td>
<td></td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Knows how to acquire the syringes.</td>
<td>N/A</td>
<td></td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Understands storage requirements.</td>
<td>N/A</td>
<td></td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Knows how to check the equipment and drug.</td>
<td>N/A</td>
<td></td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Knows the correct hand washing techniques.</td>
<td>N/A</td>
<td></td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Knows the correct use and disposal of gloves (if using).</td>
<td>N/A</td>
<td></td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Knows how to deal with a needlestick injury.</td>
<td>N/A</td>
<td></td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Can give the subcutaneous methotrexate injection using a safe technique and can identify where the injection can be given.</td>
<td>N/A</td>
<td></td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Knows how to deal with spillage on surfaces, skin and eyes.</td>
<td>N/A</td>
<td></td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Knows how to dispose of used sharps, and any unused methotrexate.</td>
<td>N/A</td>
<td></td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Can discuss instances when not to give the injections.</td>
<td>N/A</td>
<td></td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Knows who to contact in case of any problems.</td>
<td>N/A</td>
<td></td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Can discuss the rationale and arrangements for blood monitoring while on methotrexate therapy.</td>
<td>N/A</td>
<td></td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Knows that co-trimoxazole (septrin) and trimethoprim must not be taken with methotrexate.</td>
<td>N/A</td>
<td></td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Knows what to do when travelling with methotrexate.</td>
<td>N/A</td>
<td></td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

**Signed certificate of instruction**

One copy for patient and one to be retained in patient's notes.
Certificate of instruction for the home administration of subcutaneous methotrexate by patient or patient’s carer

This is to certify that I have received teaching about subcutaneous methotrexate and how to give the injections. I now feel confident and competent in giving the injectable treatment at home. I understand what problems may arise and what to do if they occur.

Patient name: 

Address: 

Telephone number: 

Patient/carer name: 

Signature: 

Date: 

Assessor name: 

Assessor signature: 

Date: 

One copy for patient and one copy to be retained in patient’s notes.
## Useful information

<table>
<thead>
<tr>
<th>Description</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date methotrexate therapy commenced:</td>
<td></td>
</tr>
<tr>
<td>Dates and doses of any increases:</td>
<td></td>
</tr>
<tr>
<td>Name and address of prescribing doctor:</td>
<td></td>
</tr>
<tr>
<td>Telephone number (if appropriate):</td>
<td></td>
</tr>
<tr>
<td>Name of nurse involved in your or your child's care:</td>
<td></td>
</tr>
<tr>
<td>Telephone number (if appropriate):</td>
<td></td>
</tr>
<tr>
<td>Any other telephone numbers/help lines:</td>
<td></td>
</tr>
<tr>
<td>Name and address of supplier, such as local hospital, or pharmaceutical company:</td>
<td></td>
</tr>
<tr>
<td>Telephone number (if appropriate):</td>
<td></td>
</tr>
<tr>
<td>Any other important information:</td>
<td></td>
</tr>
</tbody>
</table>
### 3: Example of specialist practitioner competence checklist

<table>
<thead>
<tr>
<th>Element of competence to be achieved</th>
<th>Date of achievement</th>
<th>Practitioner signature</th>
<th>Supervisor signature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discuss the rationale for the use of subcutaneous methotrexate in rheumatic conditions.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discuss potential issues related to treatment including: • screening of patients • possible side-effects or adverse events • drug interactions • contraindications to methotrexate therapy.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discuss the circumstances when subcutaneous methotrexate should not be administered.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Describe interventions required to alleviate methotrexate induced side-effects.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discuss the process for assessing the patient's suitability for methotrexate therapy. For example, medical history, concomitant medications, allergies, level of disease activity, dexterity and attitude to treatment.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Demonstrate the ability to check the validity of the current prescription. This includes expiry date, dose, route by which the drug is to be administered and the checking of the patient identification.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Demonstrate the ability to teach a patient/carer how to administer subcutaneous methotrexate.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Demonstrate the ability to assess a patient's/carer's suitability for home administration of subcutaneous methotrexate.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Describe local health and safety guidelines and risk assessment required for providing a subcutaneous methotrexate service in hospital and in the patient's home. With particular relevance to: • safe storage and handling • dealing with spillage and disposal • ensuring a quiet and safe environment • preventing unnecessary exposure to other people • travelling and transporting methotrexate.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Demonstrate the ability to discuss the information/educational needs of the patient/carer in relation to home administration of subcutaneous methotrexate therapy.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Demonstrate the ability to provide the patient/carer with information about the treatment in order that they are able to give informed consent (written/verbal – in line with local guidelines).</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Describe sites on the body that would be appropriate for subcutaneous methotrexate injection.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Demonstrate the ability to maintain concise and accurate patient documentation and audit.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Describe the local monitoring requirements and follow up arrangements for subcutaneous methotrexate therapy and the actions that must be taken in the event of a blood dyscrasia.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Describe the rationale for the use of folic acid supplementation in patients receiving subcutaneous methotrexate.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Identify the ways of maintaining current competency.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
4: Useful websites

Arthritis Care: www.arthritiscare.org.uk

Arthritis Research UK: www.arthritisresearchuk.org

British Society for Rheumatology guidelines: www.rheumatology.org.uk

British Society for Paediatric and Adolescent Rheumatology (BSPAR): www.bspar.org.uk

Department for Environment, Food and Rural Affairs (DEFRA): www.defra.gov.uk

Department of Health legislation, reports and guidance: www.dh.gov.uk

Environment Agency in England and Wales: www.environment-agency.gov.uk

Health and Safety Executive for all health and safety regulations, including information on the EU Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) regulations: www.hse.gov.uk

medac Metoject®: www.medac-uk.co.uk

National Electronic Library for Medicines: www.nelm.nhs.uk

National Patient Safety Agency: www.npsa.nhs.uk

National Rheumatoid Arthritis Society: www.nras.org.uk

NHS Quality Improvement for Scotland: www.healthcareimprovementscotland.org

Northern Ireland Environment Agency (NIEA): www.ni-environment.gov.uk

Paediatric Rheumatology European Society (PReS): www.pres.org.uk

RCN for members-only access to rheumatology forum website and online guidance, some available for non-members: www.rcn.org.uk

Scottish Environment Protection Agency (SEPA): www.sepa.org.uk

Subcutaneous injections information: www.bddiabetes.co.uk

You can find full texts of all UK government legislation at: www.legislation.gov.uk
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Royal College of Paediatrics and Child Health (2012) Medicines information for parents and carers, London: RCPCH. Available at www.rcpch.ac.uk


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Original contributors to the first edition
The original guidance was developed by the Royal College of Nursing Rheumatology Nursing Forum and the RCN Paediatric Rheumatology Specialist Nurses Group. We would like to thank the following for their help, and hard work in putting together this first edition.

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NHS trust subcutaneous methotrexate administration guidance reviewed by the working party included:

- Doncaster and Bassetlaw Hospitals NHS Trust
- Great Ormond Street Hospital for Children NHS Trust
- Sherwood Forest Hospital NHS Trust
- University Hospital Birmingham NHS Trust
- Selly Oak Hospital, Birmingham
- Worcestershire Acute Hospital NHS Trust
- Leeds Teaching Hospital NHS Trust.