Administering subcutaneous methotrexate for inflammatory arthritis

RCN guidance (Third edition)
Acknowledgements

This document has been reviewed by members of the RCN Rheumatology Nursing Forum. We would like to thank the following individuals for their assistance in revising and updating the third edition of this guidance.

**Lead authors (third edition)**

Lisa K Howie, RGN, ONC, BN, MSc, NIP Rheumatology Clinical Nurse Specialist, Chair of Working Party and Lead Adult Author, Morriston Hospital Swansea

Polly Livermore, RN Child BSc, NIP, MSc, ANP Paediatric Clinical Nurse Manager and Lead Paediatric Author, Great Ormond Street Hospital for Children NHS Foundation Trust

**RCN working party (third edition)**

Patricia Cornell, Rheumatology Nurse Consultant AbbVie, Honorary Senior Rheumatology Practitioner, Poole Hospital NHS Foundation Trust

Diana Finney, RGN, MSc, NIP, Consultant Rheumatology Nurse, Interim Clinical Lead, Sussex MSK Partnership

Louise Parker, RN, BSc (Hons), MSc, NIP, Lead Nurse, Rheumatology and Connective Tissue Disease, Royal Free London NHS Foundation Trust

Helen Smith, RN, BA, Dip ANP, Rheumatology Nurse Specialist, Princess Royal Hospital, Haywards Heath, West Sussex

The RCN working party would also like to thank the expert contribution of Nicola Price MB Chir (Cantab), MA, DPHIL (Oxon), FRCPath Consultant Virologist, Public Health Wales Microbiology Cardiff, University Hospital of Wales, Cardiff.

Supported by an unrestricted educational grant from medac

**RCN Legal Disclaimer**

This publication contains information, advice and guidance to help members of the RCN. It is intended for use within the UK but readers are advised that practices may vary in each country and outside the UK.

The information in this booklet has been compiled from professional sources, but it’s accuracy is not guaranteed. While every effort has been made to ensure that the RCN provides accurate and expert information and guidance, it is impossible to predict all the circumstances in which it may be used. Accordingly, the RCN shall not be liable to any person or entity with respect to any loss or damage caused or alleged to be caused directly or indirectly by what is contained in or left out of this information and guidance.

Published by the Royal College of Nursing, 20 Cavendish Square, London, W1G 0RN

© 2016 Royal College of Nursing. All rights reserved. Other than as permitted by law no part of this publication may be reproduced, stored in a retrieval system, or transmitted in any form or by any means electronic, mechanical, photocopying, recording or otherwise, without prior permission of the Publishers or a licence permitting restricted copying issued by the Copyright Licensing Agency, Saffron House, 6-10 Kirby Street, London EC1N 8TS. This publication may not be lent, resold, hired out or otherwise disposed of by ways of trade in any form of binding or cover other than that in which it is published, without the prior consent of the Publishers.
2. Paediatric guidance

**Introduction**

Methotrexate use in paediatric rheumatology

- History
- Rationale for the use of subcutaneous methotrexate
- Dosage
- Folic acid supplementation

**Risk management**

Advice on the handling and administration of subcutaneous methotrexate and pregnancy

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

- Supply, preparation and delivery
- Storage and drug stability
- Storage at home
- Personal protective equipment (PPE)
- Disposal of sharps and clinical waste
- Spillage

**Practitioner training and competence**

Checklist for practitioners

Specialist practitioner training and competence

**Home administration**

Administration by a child or young person

Screening families for home administration

Pre-treatment checklist and baseline investigations

**Administration of subcutaneous methotrexate**

Pre-filled PEN injection

Skin preparation

Administration technique

Rotating injection sites

Review and monitoring

**Patient education and training**

When not to administer

Side effects

Needle aversion

Vaccinations

Chickenpox

Transition to adult care

Travelling away from home

---

### Audit trail and data collection

### Conclusion

### Paediatric resources

1. ILAR classification of juvenile idiopathic arthritis (JIA)
2. How to calculate body surface area
3. Vaccine information for children with rheumatic diseases receiving methotrexate
4. Teaching package for parents, young people or children (example)

### Appendices

1. Glossary of terms and definitions
2. Training checklist for home administration of subcutaneous methotrexate by a patient (adult, young person or child) or carer/parent
3. Example of specialist practitioner competence checklist
4. Reflection exercise for CPD and NMC revalidation
5. Useful websites

### References and further reading

Lead authors and contributors of the first and second edition
Welcome to this third edition of the RCN’s guidance on administering subcutaneous methotrexate for inflammatory arthritis.

This 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 second edition of this publication in 2013, 2,000 copies of the document have been distributed, nearly 5,000 electronically downloaded and injectable methotrexate is now available in a pre-filled autoinjector PEN; which is a licensed pharmacological treatment in the UK for various inflammatory conditions such as rheumatoid arthritis (RA), severe psoriatic arthritis in adult patients (PsA), polyarthritic juvenile idiopathic arthritis (JIA) and severe recalcitrant disabling psoriasis.

At the time of writing, the only commercially available subcutaneous methotrexate pre-filled autoinjector PEN is manufactured by medac (Metoject®), which is widely available in a strength of 50mg/ml, in doses from 7.5mg to 30mg and the only commercially available subcutaneous methotrexate pre-filled syringe, is manufactured by Nordic Pharma (Zlatal®), available in a strength of 25mg/ml, in doses from 7.5mg to 25mg in 2.5mg increments.

It is envisaged in the near future, that other EU directive (2013) compliant subcutaneous methotrexate injection devices will be developed and become commercially available for use in the treatment of inflammatory arthritis.

However, as the medac (Metoject®) autoinjector PEN is currently the only commercially available preparation to fully comply with the EU directive (2013), this guidance strongly supports and recommends its use and administration over that of any pre-filled syringe and, as such, is the main focus of this guidance.

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-filled PEN delivery system has made the subcutaneous administration process even more straightforward, easier and much safer to administer. This is in line with the Health and Safety Executive and European Union’s Health and Safety (Sharps Instruments in Healthcare) Regulations 2013 and the Royal College of Nursing’s Sharps safety guidance (2013). Today’s pre-filled PENs have a long shelf life (eliminating the need for patients having to regularly collect pharmacist-prepared treatments) and do not need to be (but can 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 licensed pre-filled PEN delivery system has helped reduce the risk of exposure for health care practitioners, carers and patients significantly. Therefore, this guidance strongly recommends the use of licensed methotrexate when prescribing methotrexate for subcutaneous use. 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 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.

At the time of writing, the only commercially available pre-filled methotrexate autoinjector PEN which fully complies with EU directive (2013) is manufactured by medac (Metoject®). The risk of needlestick injury and cytotoxic exposure using the PEN is minimal throughout the injection process as the needle is not exposed at any time.

A pre-filled methotrexate syringe has recently been manufactured by Nordic Pharma (Zlatal®) and is commercially available for use, which although EU compliant, there is a risk of needlestick injury prior to injection due to needle exposure. Because of this, and our awareness that unlicensed pharmacy prepared pre-filled syringes of methotrexate are also still being used in some areas of the UK, the risk of needlestick injury and cytotoxic exposure with such pre-filled syringe preparations is increased compared to the use of the pre-filled PEN.

In acknowledgement of the above, this guidance therefore strongly recommends the use of subcutaneous methotrexate autoinjector PEN over pre-filled syringe preparations and in particular any unlicensed pre-filled syringe preparations.

For those still using unlicensed preparations of subcutaneous methotrexate, please be aware of the increased potential risk of, for example, cytotoxic spillage/exposure and needlestick injury, and refer and adhere to local protocols and cytotoxic policies and procedures, to ensure the safe handling, administration and disposal of subcutaneous methotrexate.

This is particularly important if the preparation comes in a prepared syringe but with no needle attached ready for use, as the potential risk for cytotoxic spillage and needlestick injury is increased further.

When updating this guidance Stop-think-best practice reflection opportunity notes have been added to help promote reflective best practice, clinical excellence and provision of quality care (in accordance with the 2013, EU and RCN sharps directive and guidance, NMC (2015) Code and NMC (2016) Revalidation recommendation).

In addition, at the end of this publication, a reflection exercise (Appendix 4) has been included to help facilitate additional practice reflection and learning. Once completed (using the standardised NMC Revalidation Reflective Accounts Form), it can be used as evidence of ongoing CPD for NMC revalidation purposes.

Further guidance for practitioners and users of medac’s (Metoject®) PEN can be found at: http://metoject.co.uk/wp-content/uploads/2015/04/adult-guidelines-WEB.pdf

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. Also, although the word device is used infrequently in this document, when used it refers to both pre-filled methotrexate PENs and syringes.

Risk management

The use of pre-filled PENs

This guidance strongly supports and recommends the use of licensed methotrexate via the subcutaneous route, for instance, pre-filled PEN.

The administration and handling of injectable methotrexate should be undertaken safely and in line with the EU and Health and Safety Executive’s Health and Safety (Sharp Instruments in Healthcare Regulations) 2013 and the RCN’s Sharps safety guidance (2013).

The training and administration of methotrexate in pre-filled PENs 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 (ideally latex free) and observe good hand washing protocols when administering methotrexate. They should also be aware of local policies and, where locally agreed, have access to spillage kits; this should include knowledge of how to deal with all types of accidental spillage of methotrexate.

Although the risk of spillage with the subcutaneous methotrexate autoinjector PEN is negligible, advice should be given to patients on how to deal with an accidental spillage at home.

**Example of practice innovation and cytotoxic policy change**

As a result of evidence found during the last edition of this document, the British Society of Adolescent and Paediatric Rheumatology (BSPAR) adjusted its methotrexate protocol for rheumatology patients by promoting the use of the then, licensed pre-filled (medac Metoject®) syringes, and highlighting the increased patient benefits and reduced level of risk. Some hospitals have now changed their clinical practice in line with this.

Patients may elect to self-administer methotrexate injections (or elect a carer), provided they undertake the necessary training – though the administration of these have been made much easier and safer since the development of the pre-filled methotrexate PEN. 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)
- be fully informed of all aspects relating to sexual health
- be aware of overseas travel
- know how to store and dispose of methotrexate and equipment safely
- attend 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.

( BSR/BHPR, 2008; BSPAR, 2010; Butler, 2011; Dougherty and Lister, 2011; McInnes et al., 2012)

**Resources**

Shared decision-making resources can be found at:

http://personcentredcare.health.org.uk/personcentred-care/shared-decision-making

Measuring shared decision making (sure score):

www.rightcare.nhs.uk

Improving patient experience – ‘ask three questions’ available at the e-learning resource for shared decision making: Advancing Quality Alliance:

www.aquanw.nhs.uk

---

**Stop-think-best practice reflection opportunity**

The above practice and policy change innovation might be something you would like to consider in your local area?

---

**Patient education and training**

Patients and carers should receive adequate information (verbal and written) to enable them to make an informed, shared decision about methotrexate therapy. For further guidance refer to NICE guidance (NICE, CG138) and the Department of Health’s Equity and excellence: Liberating the NHS (2010).
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.

- 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.
- The 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). Available at: www.medicines.org.uk
- Patient information issued by the manufacturer of the pre-filled methotrexate autoinjector PEN. Available at: http://metoject.co.uk/wp-content/uploads/2015/04/adult-guidelines-WEB.pdf

The references section of this document contains a full listing of these and additional advisory documents.
Adult guidance

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, 2012b; Bakker et al., 2011; Jacobs, 2012a, 2012b; Gullick and Scott, 2012; McInnes et al., 2012; Smolen et al., 2013).

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 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; Smolen, et al 2013). It is recognised as the gold standard for treating people with rheumatoid conditions (BSR/BHPR, 2008; NICE, 2009; BSPAR, 2010; EULAR, 2013).

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).

As previously mentioned, with the development and availability of the licensed pre-filled methotrexate PEN, the ease and safety of the administration of subcutaneous methotrexate has been further enhanced, in line with the various national safety regulations/guidance.

In view of the evidence, and in promoting best practice, this guidance strongly recommends the use of licensed pre-filled methotrexate PENs, over pre-filled methotrexate syringes and, in particular, unlicensed pharmacy prepared pre-filled syringes.

In addition, there is anecdotal evidence to suggest that many patients using/switching to subcutaneous methotrexate PEN injections, have expressed how ‘very pleased and satisfied’ they have been/are with the PEN preparation, in particular in relation to its ‘ease’ of administration and ‘tolerability’. For instance, fewer/no side-effects seem to be experienced/reported; and also the ‘positive impact the medication has had on their disease control and quality of life.’

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 disease-modifying anti-rheumatic drug (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. 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.

The evidence shows that the cytotoxic risk relating to the low dosages used in the treatment of inflammatory arthritis is small (Wong et al., 2009) and since the development and availability of a pre-filled autoinjector PEN for the administration of subcutaneous methotrexate, the cytotoxic risks have been reduced even further, making the administration of subcutaneous methotrexate even safer.

It is vitally important to ensure that the handling, administration and disposal of subcutaneous methotrexate injections is safe and that the appropriate risk assessments have been completed in line with local policy and procedures, including accidental needlestick injury.

**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® PEN, 2013). Available at: www.medac-uk.co.uk

**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 women of childbearing potential must not be treated with methotrexate until pregnancy has been excluded and that, since in men spermatogenesis can be affected by methotrexate, pregnancy should be avoided if either partner is receiving methotrexate. (Please see summary of product characteristics (SCP) for further details: www.medicines.org.uk)

In addition, those who are pregnant (and particularly those who are in the first trimester of pregnancy) **must 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 or breast feeding and 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; SPC, 2016 www.medicines.org.uk).

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.

**Stop-think-best practice reflection opportunity**

What advice should be given to patients and why?

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

**Supply, preparation and delivery**

Methotrexate is now available in a licensed, pre-filled autoinjector PEN preparation.

Packaging and transport systems should ensure that adequate protection and storage instructions are adhered to during delivery. Practitioners should be guided by local policies and the manufacturer’s guidance.
Patients who self-administer must be told about any change of manufacturer, volume or dose change, storage conditions, expiry date or appearance of the medication. 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 yellow-ish solution and is stable if stored out of direct sunlight.

The shelf life and storage conditions of methotrexate PEN injections 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 PENs 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 Suppy, preparation and delivery above).

**Personal protective equipment (PPE)**

This guidance suggests that aprons, goggles, masks or armlets no longer need to be worn by practitioners when administering licensed pre-filled subcutaneous methotrexate PEN injections.

If pre-filled syringe injections are used, practitioners are strongly advised to refer and adhere to local policy and procedures, as the risk of cytotoxic spillage/exposure is/will be increased with such preparations and the procedures and policy on use of PPE may be very different.

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 be up-to-date on policies in relation to dealing with hazardous waste and sharps safety. Purple topped clinical waste bins should be used for the disposal of methotrexate PENs.

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 recommendation and assumption that methotrexate will be administered using a licensed pre-filled autoinjector PEN containing a small volume of methotrexate, the risk of exposure is very small and a spillage kit is unlikely to be necessary. Please refer to your local policy for guidance.

Although spillage is unlikely when using pre-filled PENs, 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.

**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.
Stop-think-best practice reflection opportunity
Pre-filled methotrexate PEN versus pre-filled methotrexate syringe? Which preparation is safer to use and why?

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-filled, subcutaneous methotrexate PEN injection to a patient:

- check the methotrexate dose and frequency prescribed and expiry date of the PEN
- ensure blood monitoring (including the monitoring of trends) is in place as per BSR/BHPR (2008), DMARD monitoring 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 (or any other relevant contact numbers) 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
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.

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

Chickenpox infection is a concern in any non-immune immunosuppressed patient with a significant contact to either chickenpox or exposed shingles.

Checking varicella immune status (VZV IgG) prior to starting methotrexate 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 chickenpox or shingles).

If varicella immune status (VZV IgG) is not performed at this stage, then it should certainly be urgently performed within seven days of a significant exposure to either chickenpox or exposed shingles.

Passive protection against chickenpox (or exposed shingles) with VZIG and/or aciclovir should occur in the event of a significant contact in non-immune patients, dependent on local policy. Refer to the Department of Health’s Green Book, Chapter 34 for further information, available at: www.gov.uk/government/publications/varicella-the-green-book-chapter-34

If chickenpox develops then the patient should be urgently assessed for aciclovir treatment; methotrexate should be discontinued until the last spot has crusted over and the patient is clinically well.

In addition, consideration can be given to providing varicella vaccine to immunocompetent, healthy susceptible close household contacts of immunocompromised patients to prevent exposure situations. Again, refer to the Department of Health’s Green Book, Chapter 34 for further information.

The risk and severity of shingles is higher amongst immunosuppressed individuals, and individuals should be assessed for shingles vaccine eligibility (based on age) prior to starting treatment. At least 14 days, preferably one month, is required prior to starting methotrexate. For further information see the Green Book, Chapter 28a, available at: www.gov.uk/government/publications/shingles-herpes-zoster-the-green-book-chapter-28a

If the patient is eligible for the shingles vaccine while on methotrexate therapy, the vaccine can ONLY be given in the following circumstances: patients on long-term stable low-dose corticosteroid therapy (defined as ≤ 20mg prednisolone per day for more than 14 days) either alone or in combination with low dose non-biological oral immune modulating drugs (e.g. methotrexate ≤ 25mg per week, azathioprine ≤ 3.0 mg/kg/day or 6-mercaptopurine ≤ 1.5 mg/kg/day) are not considered to be sufficiently immunosuppressive and these patients can receive the vaccine. Specialist advice should be sought for other treatment regimens.

Immunosuppressed patients who develop a shingles vaccine rash should be urgently assessed and offered aciclovir.

It is suggested that most rheumatology teams will be aware that the use of biologic drugs and other powerful immunosuppressants is not always documented appropriately in primary care medical records, since these drugs are invariably prescribed in secondary care. The rheumatology community therefore needs to be aware that the shingles vaccine (Zostavax) may be offered by GPs to patients on biologic drugs and other potent immunosuppressants, and that it may be appropriate to contact patients aged 70 and over (and/or their GPs) on biologic drugs and other potent immunosuppressants to advise them that they should not receive the shingles vaccine (Zostavax) (BSR, 2013).

If there is doubt about the balance between the risk of shingles and the risk of immunisation then advice should be sought from an appropriate specialist (such as an immunologist or infectious diseases physician) (BSR, 2013).

For more detailed information please refer to the Green Book Immunisation against infectious diseases, which has an updated chapter on shingles (Chapter 28a, February 2016).

Measles/Mumps/Rubella (MMR) immune status

In the pre-methotrexate assessment process, the history of a completed MMR vaccination schedule or screening for measles immune status would be helpful.

A patient who is currently immunocompetent can receive two doses of MMR if they have no history of MMR
vaccination or are measles IgG negative or equivocal, and eligible to receive the vaccine. However, a period of four weeks should occur prior to initiating immunosuppression following the second dose of MMR vaccine (BSR, 2002).

In a measles exposure situation, please refer to the Health Protection Agency’s Post exposure prophylaxis for measles: revised guidance (2009). Available at: www.gov.uk/government/publications/measles-post-exposure-prophylaxis

Patients receiving methotrexate would normally be in Group A of the guidance. Please see Table 1 below for reference. If they have been previously tested and found to be measles IgG positive then they would be treated as immune. However, if they had not been tested or had previously been given MMR or measles vaccine then their further management and the issue of human normal immunoglobulin would be according to Table 1, below, where previous measles infection, vaccination and patient age are considered.

If measles develops, the patient should be urgently assessed by their GP and rheumatology team as it is a serious reportable infection, and the patient should be advised to discontinue methotrexate. Methotrexate should not be restarted until the patient has recovered fully, is clinically well and has been re-assessed by their medical team.

**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. For some 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

**Pregnancy testing**

Pregnancy testing is recommended for all women of childbearing potential prior to the commencement of methotrexate. Please see local policy for further guidance and the summary of product characteristics (SPC) at www.medicines.org.uk

**Conception**

Male and female patients who wish to consider conception should be given appropriate advice and good sexual health practice should be explained. The optimum time interval between discontinuation of methotrexate therapy in either partner and pregnancy has not been established. The recommended interval in published literature varies between three months and one year. Both men and women receiving methotrexate should be informed of the

<table>
<thead>
<tr>
<th>Age group</th>
<th>History</th>
<th>Pregnant</th>
<th>Immunosuppressed Group A</th>
<th>Immunosuppressed Group B*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Born before 1970</td>
<td>Of measles infection</td>
<td>Assume immune</td>
<td>Assume immune</td>
<td>Regardless of history, and even if known to be measles antibody positive previously, test again at time of exposure.</td>
</tr>
<tr>
<td></td>
<td>No measles infection</td>
<td>Assume immune</td>
<td>Test and issue only if measles antibody negative or equivocal</td>
<td>Issue immunoglobulin if measles antibody negative or equivocal.</td>
</tr>
<tr>
<td>Born between 1970 and 1990</td>
<td>Of measles infection</td>
<td>Assume immune</td>
<td>Test and issue only if measles antibody negative or equivocal</td>
<td>Test and issue if measles antibody negative or equivocal. If not possible to test within six days of exposure, offer immunoglobulin</td>
</tr>
<tr>
<td></td>
<td>No measles infection</td>
<td>Test and issue within six days only if measles antibody negative</td>
<td>Test and issue if measles antibody negative or equivocal. If not possible to test within three days of exposure, offer immunoglobulin</td>
<td>If not possible to test within three days of exposure, offer immunoglobulin.</td>
</tr>
<tr>
<td>Born after 1990</td>
<td>One measles vaccine</td>
<td>Test and issue within six days only if measles antibody negative</td>
<td>Test and issue if measles antibody negative or equivocal. If not possible to test within three days of exposure, offer immunoglobulin</td>
<td>Test and issue if measles antibody negative or equivocal. If not possible to test within three days of exposure, offer immunoglobulin.</td>
</tr>
<tr>
<td></td>
<td>Two measles vaccine</td>
<td>Assume immune</td>
<td>Test and issue if measles antibody negative or equivocal. If not possible to test within three days of exposure, offer immunoglobulin</td>
<td>Test and issue if measles antibody negative or equivocal. If not possible to test within three days of exposure, offer immunoglobulin.</td>
</tr>
<tr>
<td></td>
<td>Unvaccinated</td>
<td>Test and issue if measles antibody negative. If not possible to test within six days of exposure, offer immunoglobulin</td>
<td>Test and issue if measles antibody negative or equivocal. If not possible to test within three days of exposure, offer immunoglobulin</td>
<td>Test and issue if measles antibody negative or equivocal. If not possible to test within three days of exposure, offer immunoglobulin.</td>
</tr>
</tbody>
</table>

*excluding patients who are already on IVIG replacement therapy for either primary immunodeficiency or severe defects of cell mediated immunity

potential risk of adverse effects on reproduction. Women of childbearing potential should be fully informed of the potential hazard to the foetus should they become pregnant during methotrexate therapy. Please see the summary of product characteristics (SPC) at www.medicines.org.uk

Chest X-ray

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).

Drinking history

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

<table>
<thead>
<tr>
<th>Concomitant medications</th>
</tr>
</thead>
</table>
| 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 manufacturer’s 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. In promoting and improving patient safety and self-management, patients should be advised to check with pharmacists when buying OTC or herbal medicines.

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.

Stop-think-best practice reflection opportunity:

Safe home administration of subcutaneous methotrexate injections: What information do you need to know, ask and advise your patients?
Administration of subcutaneous methotrexate

As subcutaneous methotrexate PEN is, at the time of writing, the only commercially available and fully EU directive (2013) compliant subcutaneous methotrexate injection preparation, we have used this to reference the following guidance. Please refer to other manufacturers’ medicines compendium and administration guidance, if other devices are used.

Pre-filled PEN injection

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.

Administration technique

1. Best practice recommends that practitioners and carers should use gloves, but this is not required for patients who self-administer.
2. Check the skin is socially clean.
3. An air bubble MAY be visible in the PEN. This is to ensure all the medication is administered during the injection and is completely harmless. **DO NOT REMOVE THE YELLOW PROTECTION CAP UNTIL YOU ARE READY TO ADMINISTER THE INJECTION.**
4. The injection should be administered into subcutaneous tissue in the thigh or stomach.
5. Before injecting, pull off the yellow protection cap in a downwards motion, revealing the needle shield.
   **Do not twist or bend the protection cap whilst you are removing it.**
   **Do not press the yellow release button until you are ready to inject.**
   Once you remove the protection cap, administer your injection without delay.
6. Gently grip the skin at the injection site using your thumb and index finger and maintain throughout injection process. Ensure that the surface of the skin is firm.
7. Place the transparent end of the PEN at a 90° angle on your skin.
   **Without pressing the yellow release button,** push the PEN firmly against your skin until the needle shield slides fully into the viewing window. This will unlock the yellow release button.
8. Start the injection by pressing the yellow release button with your thumb.
   A clicking noise indicates the start of the injection. **Maintain the pressure** of the PEN against the skin and count slowly to five seconds until the medicine is injected. **Do not move the PEN during injection.**
9. After five seconds, release the skin and remove the PEN. There should be no remaining fluid in the PEN. The needle protection shield will automatically slide over the needle and lock into place.
10. Dab the injection site with clean cotton wool or a swab.
    Do not rub the injection site as this may irritate the skin.
11. For your safety, dispose of the PEN into a special sharps bin. All other packaging can be disposed of in your normal household waste.


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 in a 5cm radius away from the navel.

See 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,
However, local monitoring guidelines might also apply and should be adhered to. Primary health care teams should 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 have 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 and also know when not to administer the methotrexate, for example, when only part of a dose has been administered for some reason (a device failure or technique) the patient should know not to administer another dose of methotrexate until their next weekly dose is due.

- 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® SPC, 2013) and overseas travel (medac Metoject® Starter Pack Adult Guidelines, 2015)

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

- attend for blood tests and monitoring regularly, as agreed with the local team and protocol

- 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 or equivalent local methotrexate monitoring book.

For further information visit the NHS National Patient Safety Agency (NPSA) at: www.npsa.nhs.uk

A patient education package has been developed to support patients and practitioners (see Adult resources section). 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 16.

Vaccinations


Chickenpox/shingles (herpes zoster)

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

**Measles/Mumps/Rubella (MMR)**

Please see pre-treatment checklist on page 12.

MMR immunisation may be given depending on local policy. Also refer to:


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

Please see section on Risk management on page 10.

**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 19.

**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 on governance guidance and local policies are adhered to. (Data Protection Act, 1998; the Department of Health’s Code of Confidentiality, 2003; Confidentiality and Disclosure of Information, WAG, 2006; the Caldicott Guardian Manual, 2010; NHS Scotland Information Governance Competency Framework, 2011; Confidentiality, Northern Ireland, 2012 and Information Governance guidance from the Department of Health.)

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.

The introduction of the autoinjector PEN to the market is welcomed by adults with rheumatic disease and also practitioners. Home administration of methotrexate is easy and safe and, without doubt, improves quality of life.

There are a number of non-malignant indications for prescribing methotrexate, and this guidance has focused on the administration of subcutaneous methotrexate for rheumatic diseases only.
Adult resources

Patient/carer training guide example
This section provides information for patients and carers about using subcutaneous methotrexate and contains training guide examples.

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:
  - 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 from either the patient’s rheumatology team or external homecare provider who provides the training service.

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
This is a step-by-step guide to help you give yourself a once weekly injection of methotrexate by subcutaneous (under the skin) injection. The 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 verbal and written information to read about the drug, including information about the methotrexate PEN injection that has been prescribed for you, and given 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 (NPSA, 2006) 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 and where relevant, how long to stop methotrexate for prior to trying for a baby
- always make sure that you keep the methotrexate PEN injection in a place where it is safe and out of sight and reach of vulnerable adults, children and family pets
- always check and make sure that you have had the right training for the methotrexate PEN injection that has been prescribed and dispensed for you. If in doubt, please contact your rheumatology specialist nurse or person who has prescribed the medication
- always check your injection 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 PEN injection

Equipment

Getting the equipment ready:
- Methotrexate PEN for injection.
- Clean table surface.
- One appropriate clinical waste/sharps bin.
- Pair of disposable gloves – ideally latex free (if required/being used – though not necessary if patient self-administering).
- Cotton wool ball/clean tissue.
- If locally issued – spillage kit.

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 1, page 23).

9 Make sure the injection site is clean; if not, clean with soap and water. Check your skin over the proposed injection site is intact, not tender, bruised, red or hard.

10 Open the methotrexate PEN injection packet.
**Giving the methotrexate PEN injection**

1. Ensure that you have been trained on how to use the PEN and everyone is comfortable.

2. Check the medication 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 injection 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. An air bubble MAY be visible in the PEN. This is to ensure all the medication is administered during the injection and is completely harmless.

   **DO NOT REMOVE THE YELLOW PROTECTION CAP UNTIL YOU ARE READY TO ADMINISTER THE INJECTION.**

5. Before injecting, pull off the yellow protection cap in a downwards motion, revealing the needle shield. Do not twist or bend the protection cap whilst you are removing it. Do not press the yellow release button until you are ready to inject. Once you remove the protection cap, administer your injection without delay.

6. Choose your injection site, the process is the same whether for your thigh or abdomen (avoid the 5cm diameter around the tummy button).

7. Once you have selected your injection site: gently grip the skin at the injection site using your thumb and index finger and maintain throughout injection process. Ensure the surface of the skin is firm.

8. Place the transparent end of the PEN at a 90° angle on your skin. Without pressing the yellow release button, push the PEN firmly against your skin until the needle shield slides fully into the viewing window. This will unlock the yellow release button.

9. Start the injection by pressing the yellow release button with your thumb. A clicking noise indicates the start of the injection. Maintain the pressure of the PEN against the skin and count slowly for five seconds until the medicine is injected. Do not move the PEN during injection.
10. After five seconds release the skin and remove the PEN. There should be no remaining fluid in the PEN. The needle protection shield will automatically slide over the needle and lock into place.

11. Dab the injection site with clean cotton wool or a swab. Do not rub the injection site as this may irritate the skin.

12. For your safety, dispose of the PEN into a special sharps bin. All other packaging can be disposed of in your normal household waste.

13. 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.

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

Alternative technique to step 9.
If you are unable to use the ‘pinch technique’, the PEN can be placed directly onto a firm area of skin using one hand. The injection process can be started by pressing the yellow release button with the palm of your other hand.

Images reproduced by kind permission ©medac, 2016
What to do after administering the methotrexate PEN

1. Do not put any of the used items in with your normal household waste.
2. Instead you should put the used PEN 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 PENs should always be returned to your local hospital pharmacy or delivery service.
5. If used, change gloves if these are punctured or torn.
6. Wash hands thoroughly with soap and water and dry thoroughly after the procedure.
7. Record the site and date of the injection in your diary sheet (if using).
8. On very rare occasions methotrexate might 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

Due to the preparation design of the subcutaneous methotrexate PEN, spillage is much less of a risk, thus making it a much safer preparation option than the unlicensed pre-filled syringe preparations.

- Although the amount of methotrexate you are injecting is very small, and the likelihood of spillage/exposure with the PEN injection preparation is highly unlikely, accidental spills could occur when administering subcutaneous methotrexate, though by comparison, the risk of spillage/exposure is much greater when using the unlicensed syringe and needle preparations.
- Although an autinjector PEN preparation carries the least/minimal risk of spillage/exposure, for full safety reasons, the following advice has been included.
- If there is a spillage, please follow the advice you have been given and that your carer or family members are aware of: what actions to take; instructions in the spill kit (if issued); and 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

Subcutaneous methotrexate PEN

The development, introduction and use of the subcutaneous methotrexate PEN, should virtually eliminate the possibility of needlestick injuries. Whilst
nothing is 100 per cent guaranteed, it has been suggested that, to date, there have been no reports of any accidental needlestick injuries with the PEN injection. It is worth remembering that the PEN was introduced to comply with EU directive in sharps injuries and so, if used correctly, one should not be able to obtain a needlestick injury.

However, in the very unlikely event that you or your carer accidentally come into contact with the needle while preparing, administering or disposing of the PEN 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 PEN should be put into the sharps bin and a new PEN should be used.

For further information on sharps safety refer to EU and Health and Safety Executive’s Health and Safety (Sharp Instruments in Healthcare Regulations) 2013 and the RCN’s Sharps safety guidance (2013).

**Travelling and injecting methotrexate away from home**

Your PEN injections (including those for travel) should be stored as per the manufacturer’s recommendations. Make sure that you check the injection box for instructions on how to store.

You should seek specific advice on storage at high temperatures and note that extra caution needs to be exercised in hot climates/environments over 25°C, when it is recommended to place the methotrexate PEN injection in the fridge and warm to room temperature (30 minutes) prior to injection. If you have any questions or concerns about this please discuss the details of storage with your GP, nurse, practitioner or pharmacist.

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 methotrexate PEN injections 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. Live vaccines are contraindicated in patients receiving methotrexate and so it is 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 who 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 a pre-filled autoinjector PEN is now licensed for polyarthritic forms of JIA in children over three years of age who 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 autoinjector PENs have a reduced volume of drug and, in contrast to hospital manufactured methotrexate syringes, the needle is attached and non-visible, so not only safer, but preferred by the paediatric population. The PEN injections are easier to administer, especially by young people, easier to store and transport and with a decreased 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 methotrexate.

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

- not missing school/work, spending less 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 PEN injections (for example, 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.

Evidence shows that the cytotoxic risk relating to the low dosages used in the treatment of inflammatory arthritis is small (Wong et al., 2009) and since the development and availability of a PEN injection for the administration of subcutaneous methothrexate, the cytotoxic risks have been reduced even further, making the administration of subcutaneous methotrexate even safer.
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 a licensed, pre-filled PEN preparation. Packaging and transport systems should ensure that adequate protection and storage instructions are adhered to during delivery. Practitioners should be guided by local policies and the manufacturer’s guidance.

Patients or carers who self-administer must be told about any changes of manufacturer, volume or dose change, storage conditions, expiry date or appearance of their medication. 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.

The shelf life and storage conditions of methotrexate PEN injections 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 PEN 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 PENs and clinical waste bins.

Storage at home

The storage of methotrexate autoinjector PENs 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).

Personal protective equipment (PPE)

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 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 updates 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 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-filled methotrexate PENs.

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 recommendation and assumption that methotrexate will be administered using a licensed, pre-filled autoinjector PEN containing a small volume of methotrexate, the risk of exposure is minimal and a spillage kit is unlikely to be necessary. (Please refer to your local policy for guidance.)

**Stop-think-best practice reflection opportunity**

Pre-filled methotrexate PEN versus pre-filled methotrexate syringe? Which preparation is safer to use and why?

**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, frequency prescribed and expiry date of the PEN
- 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 button – 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.

Administering methotrexate with an autoinjector PEN is also often seen as easier than injecting with a syringe and needle. 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 what to do/who to contact in the event of being unable to administer or self-administer.

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.

Stop-think-best practice reflection opportunity:

Safe home administration of subcutaneous methotrexate injections: what information do you need to know, ask and advise your patients?

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 home administration is appropriate (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.

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.

Stop-think-best practice reflection opportunity

What advice should be given to patients and why?
**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 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 manufacturer’s specific summary of product characteristics (SPC). For further advice, contact the local prescribing doctor.

**Administration of subcutaneous methotrexate**

As subcutaneous methotrexate PEN is, at the time of writing, the only commercially available and fully EU directive (2013) compliant subcutaneous methotrexate injection preparation, we have used this to reference the following guidance. Please refer to other manufacturers’ medicines compendium and administration guidance, if other licensed devices used.

**Pre-filled PEN injection**

**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.

**Administration technique**

1. Best practice recommends that practitioners and carers should use gloves, but this is not required for patients who self-administer.
2. Check the skin is socially clean.
3. An air bubble **MAY** be visible in the PEN. This is to ensure all the medication is administered during the injection and is completely harmless.
   
   **DO NOT REMOVE THE YELLOW PROTECTION CAP UNTIL YOU ARE READY TO ADMINISTER THE INJECTION.**

4. The injection should be administered into subcutaneous tissue in the thigh or stomach.
5. Before injecting, pull off the yellow protection cap in a downwards motion, revealing the needle shield.
   
   **Do not twist or bend the protection cap whilst you are removing it.**

6. Gently grip the skin at the injection site using your thumb and index finger and maintain throughout injection process. Ensure that the surface of the skin is firm.
7. Place the transparent end of the PEN at a 90° angle on the skin.
   
   **Without pressing the yellow release button, push the PEN firmly against the skin until the needle shield slides fully into the viewing window. This will unlock the yellow release button.**
8. Start the injection by pressing the yellow release button with your thumb.
   
   A clicking noise indicates the start of the injection.

   **Maintain the pressure** of the PEN against the skin and count slowly to five seconds until the medicine is injected. **Do not move the PEN during injection.**
9. After five seconds, release the skin and remove the PEN. There should be no remaining fluid in the PEN. The needle protection shield will automatically slide over the needle and lock into place.
10. Dab the injection site with clean cotton wool or a swab. Do not rub the injection site as this may irritate the skin.
11. For your safety, dispose of the PEN and gloves into a special sharps bin. All other packaging can be disposed of in your normal household waste.

**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.

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 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 pediatrics 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. Whilst the PEN is preferred by many children and young people as they cannot see the needle, health professionals still need to be alert to any concerns. However, using the advantages of the PEN often is enough to allay fears. 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 and what they want to do (look at a book, watch TV, play a computer game), 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.

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 3). 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 (RCPCH, 2002) but this may be dependent on your local policy. See: www.gov.uk/government/collections/immunisation. For an up-to-date definition of ‘significant contact’ visit: www.dh.gov.uk/greenbook.

**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 daily living activities (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
- transfer 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 autoinjector PENs 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

Children and young people have been asking for years to have methotrexate available in an autoinjector PEN. The introduction of such a device to the market is very welcomed and is one step further to normalise treatment for children and young people with rheumatic disease. Home administration of methotrexate is safe and without doubt improves the quality of life of the child or young person.
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:

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</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>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</td>
</tr>
<tr>
<td></td>
<td>Rheumatoid Factor Positive</td>
<td>Five or more joints during the first six months of disease</td>
</tr>
<tr>
<td></td>
<td>Systemic onset</td>
<td>Arthritis of any number of joints with a documented typical</td>
</tr>
<tr>
<td></td>
<td></td>
<td>high quotidian spiking fever of at least two weeks duration</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• transient episodic erythematous rash</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• enlargement of liver or spleen</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• serositis</td>
</tr>
<tr>
<td>5</td>
<td>Psoriatic arthritis</td>
<td>Arthritis and psoriasis or arthritis and at least two of the</td>
</tr>
<tr>
<td></td>
<td></td>
<td>following:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• dactylitis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• nail abnormalities (pitting)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• family history of psoriasis confirmed by a dermatologist in</td>
</tr>
<tr>
<td></td>
<td></td>
<td>at least one first-degree relative</td>
</tr>
<tr>
<td>6</td>
<td>Enthesitis-related arthritis</td>
<td>Previously known as juvenile spondyloarthritis. Arthritis and</td>
</tr>
<tr>
<td></td>
<td></td>
<td>enthesitis, or Arthritis or enthesitis plus two of the following:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• sacroiliac joint tenderness, inflammatory spinal pain, or</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• HLA-B27</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• family history in first-, or second-degree relative of</td>
</tr>
<tr>
<td></td>
<td></td>
<td>medically confirmed HLA B27+ve associated disease</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• acute anterior uveitis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• onset of arthritis in a boy after the age of eight years</td>
</tr>
<tr>
<td>7</td>
<td>Other arthritis</td>
<td>any form of idiopathic chronic arthritis, which does not fit</td>
</tr>
<tr>
<td></td>
<td></td>
<td>into the above categories</td>
</tr>
</tbody>
</table>

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

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

\[
\sqrt{\frac{\text{Height (cm) x weight (kg)}}{3,600}} = m^2
\]

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

\[
\sqrt{\frac{100 \text{ cm} \times 30 \text{ kg}}{3,600}} = 0.91 m^2
\]

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

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

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

To calculate the methotrexate dose m²/week:

\[
\text{dose (mg) per week} = \text{dose m²/week BSA}
\]

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

\[
\frac{1}{\text{BSA}} \times \text{dose 10mg per week} = 10.99 mg/m²/week \times 0.91
\]

3: 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.
4: Example teaching package for parents, young people or children – how to handle methotrexate when using the pre-filled PENs

Introduction

This is a step-by-step guide to the self-injection administration of methotrexate once a week by subcutaneous (under the skin) injection. The information does not replace discussion with your doctor and nurse, and it should only be used as a guide because your local health centre or hospital will tailor it to local needs. But it is important because it gives you something to take away, read and keep for reference.

Some information on methotrexate

Methotrexate has been used to treat paediatric rheumatic diseases such as juvenile idiopathic arthritis for over 26 years, and it is now the number one choice to treat active arthritis that is not responding to simple therapies. The aim is to control the inflammation, put the disease into remission and thereby limit the damage to the joints.

If your child is unable to tolerate the tablets/syrup or if the arthritis fails to respond to the methotrexate by mouth, your child may be converted from tablet to injectable methotrexate. Methotrexate does NOT work immediately. It may be three to 12 weeks before any benefit is noticed.

Since 2014, methotrexate has become available in a pre-filled PEN, the only available licensed manufacturer currently is medac with Metoject®. These autoinjector PENs have superseded the syringe and needle, and greatly improve patient satisfaction and safety.

Side-effects

Most children have very few side-effects. However, these are the main ones:

- nausea, vomiting or stomach upset – quite common. Usually this is managed by taking the dose at night time so the upset stomach is not noticed during sleep. Taking the medicine on Friday or Saturday nights means that school is not missed if there are side effects the next day. Taking folic acid can help prevent side effects. Sometimes missing a dose of an anti-inflammatory drug, using regular anti-sickness drugs and/or changing to the injectable form of methotrexate is also helpful
- mouth ulcers – these usually respond well to treatment with folic acid
- effects on blood cells and liver function, particularly rises in liver enzymes such as AST or ALT. This is 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 PEN carefully
- the PENs will be specifically for your child only and should always contain the exact amount to be given – you must check this each time
- the PENs should usually be kept at room temperature, please store out of the reach and sight of children and pets. During very hot summers the PENs may need to be refrigerated – if unsure, ask your nurse
- If the PENs 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.
- you will be given a sharps bin to dispose of the PENs. 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:

- 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
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.

your child has come into contact with chickenpox 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 PEN injection

Equipment

Getting the equipment ready

- Methotrexate PEN for injection.
- Clean table surface.
- One appropriate clinical waste/sharps bin.
- Pair of disposable gloves (ideally latex free) (if required/being used – though not necessary if the child/young person is self-administering).
- Cotton wool ball/clean tissue.
- Spot plaster (if desired).

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.

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, page 41.).

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

10 Open the PEN packet.
Giving the methotrexate PEN injection

1. Ensure that you have been trained on how to use the PEN and everyone is comfortable.

2. Check the medication 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 injection 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. An air bubble MAY be visible in the PEN. This is to ensure all the medication is administered during the injection and is completely harmless.

   **DO NOT REMOVE THE YELLOW PROTECTION CAP UNTIL YOU ARE READY TO ADMINISTER THE INJECTION.**

5. Before injecting, pull off the yellow protection cap in a downwards motion, revealing the needle shield.

6. Choose your injection site, the process is the same whether for the thigh or abdomen (avoid the 5cm diameter around the tummy button).

7. Once you have selected your injection site: gently grip the skin at the injection site using your thumb and index finger and maintain throughout injection process. Ensure the surface of the skin is firm.

8. Place the transparent end of the PEN at a 90° angle on the skin. Without pressing the yellow release button, push the PEN firmly against the skin until the needle shield slides fully into the viewing window. This will unlock the yellow release button.

9. Start the injection by pressing the yellow release button with your thumb. A clicking noise indicates the start of the injection. Maintain the pressure of the PEN against the skin and count slowly for five seconds until the medicine is injected. **Do not move the PEN during injection.**

5. (continued)

   **Do not twist or bend the protection cap whilst you are removing it.**

   **Do not press the yellow release button until you are ready to inject.**

   **Once you remove the protection cap, administer the injection without delay.**
10. After five seconds, release the skin and remove the PEN. There should be no remaining fluid in the PEN. The needle protection shield will automatically slide over the needle and lock into place.

11. Dab the injection site with clean cotton wool or a swab. Do not rub the injection site as this may irritate the skin.

12. For your safety, dispose of the PEN into a special sharps bin. All other packaging can be disposed of in your normal household waste.

13. 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.

14. Alternate the injection site from week-to-week so it doesn’t get sore.
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 PENs and gloves 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 PEN injections 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.

Needlestick injuries

With the development, introduction and use of the subcutaneous methotrexate PEN, this should virtually eliminate the possibility of needlestick injuries.

Whilst nothing is 100 per cent guaranteed, it has been suggested that, to date, there have been no reports of any accidental needlestick injuries with the PEN injection. It is worth remembering that the PEN was introduced to comply with EU directive in sharps injuries and so, if used correctly, one should not be able to obtain a needlestick injury. However, if in the unlikely event that you or your carer accidentally come into contact with the needle while preparing, administering or disposing of the PEN 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 PEN should be put into the sharps bin and a new PEN should be used.

For further information on sharps safety refer to EU and Health and Safety Executive’s Health and Safety (Sharp Instruments in Healthcare Regulations) 2013 and the RCN’s Sharps safety guidance (2013).

Stop-think-best practice reflection opportunity

PEN versus syringe use?

Travelling and injecting methotrexate away from home

Your PEN injections (including those for travel) should be stored as per the manufacturer’s recommendations. Make sure that you check the injection box for instructions on how to store.

You should seek specific advice on storage at high temperatures and note that extra caution needs to be exercised in hot climates/environments over 25°C, when it is recommended to place the methotrexate PEN injection in the fridge and warm to room temperature (30 minutes) prior to injection. If you have any questions or concerns about this please discuss the details of storage with your GP, nurse, practitioner or pharmacist.

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 methotrexate PEN injections 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. Live vaccines are contraindicated in patients receiving methotrexate and so it is 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.
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.
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></td>
<td>N/A</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Knows how to acquire the methotrexate injections.</td>
<td></td>
<td>N/A</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Understands storage requirements.</td>
<td></td>
<td>N/A</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Knows how to check the equipment and drug.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Knows the correct hand washing techniques.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Knows the correct use and disposal of gloves (if using).</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Knows how to deal with a needlestick injury.</td>
<td></td>
<td>N/A</td>
<td></td>
<td></td>
<td></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></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Knows how to deal with spillage on surfaces, skin and eyes.</td>
<td></td>
<td>N/A</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Knows how to dispose of used sharps, and any unused methotrexate.</td>
<td></td>
<td>N/A</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Can discuss instances when not to give the injections.</td>
<td></td>
<td>N/A</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Knows who to contact in case of any problems.</td>
<td></td>
<td>N/A</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Can discuss the rationale and arrangements for blood monitoring while on methotrexate therapy.</td>
<td></td>
<td>N/A</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Knows that co-trimoxazole (septrin) and trimethoprim must not be taken with methotrexate.</td>
<td></td>
<td>N/A</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Knows what to do when travelling with methotrexate.</td>
<td></td>
<td>N/A</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Signed certificate of instruction</strong></td>
<td></td>
<td>N/A</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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**

<table>
<thead>
<tr>
<th>Patient name:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Address:</td>
<td></td>
</tr>
<tr>
<td>Telephone number:</td>
<td></td>
</tr>
</tbody>
</table>

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/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**

- **Date methotrexate therapy commenced:**

- **Dates and doses of any increases:**

- **Name and address of prescribing doctor:**

- **Telephone number (if appropriate):**

- **Name of nurse involved in your or your child’s care:**

- **Telephone number (if appropriate):**

- **Any other telephone numbers/help lines:**

- **Name and address of supplier, such as local hospital, or pharmaceutical company:**

- **Telephone number (if appropriate):**

- **Any other important information:**
Discuss the rationale for the use of subcutaneous methotrexate in rheumatic conditions.

Discuss potential issues related to treatment including:
- screening of patients
- possible side-effects or adverse events
- drug interactions
- contraindications to methotrexate therapy.

Discuss the circumstances when subcutaneous methotrexate should not be administered.

Describe interventions required to alleviate methotrexate induced side-effects.

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.

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.

Demonstrate the ability to teach a patient/carer how to administer subcutaneous methotrexate.

Demonstrate the ability to assess a patient's/carer's suitability for home administration of subcutaneous methotrexate.

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 disposal and rare situation of spillage
- ensuring a quiet and safe environment
- preventing unnecessary exposure to other people
- travelling and transporting methotrexate.

Demonstrate the ability to discuss the information/educational needs of the patient/carer in relation to home administration of subcutaneous methotrexate therapy.

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).

Describe sites on the body that would be appropriate for subcutaneous methotrexate injection.

Demonstrate the ability to maintain concise and accurate patient documentation and audit.

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.

Describe the rationale for the use of folic acid supplementation in patients receiving subcutaneous methotrexate.

Identify the ways of maintaining current competency.
4: Reflection exercise for CPD and NMC revalidation

Self-reflection exercise: To illustrate understanding behind the changes presented in this third edition

In line with the Nursing and Midwifery Council (NMC, 2016) revalidation, each practitioner is required to record a minimum of five written reflections relevant to their experience over the three years prior to the renewal of their registration. This reflection can be on a continuing professional development (CPD) activity, or a reflection of an event or experience.

Based on the NMC Reflective Accounts Form (at time of publication), the example on the next page can be used to record your thoughts on reading this document, which can then serve as one of the compulsory five written reflections. Any reflective account needs to explain what you have learnt for the CPD activity, how you have changed or improved your work as a result and how this is relevant to the code. Please ensure you visit the NMC revalidation website for the latest and most up-to-date version of the NMC Reflective Accounts Form.

Once you have read this publication, spend some time considering what you have learnt and how this will inform and change your future practice. Once you have written in the template below you can show this to your confirmer and discuss with them what you have written.

The questions that follow will assist you when writing the reflective account, but if they do not meet your individual learning needs, please feel free to develop your questions to assist your reflective learning.

Consider the following questions

<table>
<thead>
<tr>
<th>Question</th>
</tr>
</thead>
<tbody>
<tr>
<td>Which preparations of subcutaneous methotrexate are licensed?</td>
</tr>
<tr>
<td>What would your rationale be for using subcutaneous pre-filled methotrexate PEN injections over pre-filled syringe injection preparations?</td>
</tr>
<tr>
<td>What handling precautions do I need for the PEN?</td>
</tr>
<tr>
<td>Why would you give subcutaneous methotrexate compared to oral?</td>
</tr>
<tr>
<td>How often do you give methotrexate?</td>
</tr>
<tr>
<td>What information do I need to know, ask and advise patients to ensure the safe, home administration of subcutaneous methotrexate injections?</td>
</tr>
<tr>
<td>What information do I need to know and provide to patients, administering subcutaneous methotrexate injections, when travelling abroad?</td>
</tr>
<tr>
<td>What advice do I need to know and provide to patients on the handling and administration of subcutaneous methotrexate injections in relation to pregnancy?</td>
</tr>
<tr>
<td>What have I learnt from reading this third edition?</td>
</tr>
<tr>
<td>How does this relate to my practice?</td>
</tr>
<tr>
<td>What knowledge or skills have I acquired as a result of reading the article?</td>
</tr>
<tr>
<td>Is there anything that I did not understand, need to explore or read about further to clarify my understanding?</td>
</tr>
</tbody>
</table>
Example of NMC (2016) Revalidation Reflective Accounts Form

PLEASE NOTE: This is an example form only. For revalidation, please ensure you visit the NMC revalidation website for the latest and most up-to-date version of the NMC Reflective Accounts Form:
http://revalidation.nmc.org.uk/download-resources/forms-and-templates

What was the nature of this CPD activity?
Reading the Administering subcutaneous methotrexate for inflammatory arthritis. RCN guidance, (Third edition).

What did you learn from reading this best practice document?

How did you change your practice from reading this best practice document?

How is this relevant to the Code? (select either: Prioritise people, practice effectively, preserve safety, promote professionalism and trust)

Royal College of Nursing (2016) Revalidation. Available at: www.rcn.org.uk/professional-development/revalidation
5: Useful websites

Advancing Quality Alliance: www.aquanw.nhs.uk
Arthritis Care: www.arthritiscare.org.uk
Arthritis Research UK: www.arthritisresearchuk.org
British Society for Rheumatology guidelines and clinical statements: www.rheumatology.org.uk
British Society for Paediatric and Adolescent Rheumatology (BSPAR): www.bspar.org.uk
Department for Environment, Food and Rural Affairs (DEFA): www.defra.gov.uk
Department of Health legislation, reports and guidance: www.dh.gov.uk
eMC (for summary of product characteristics (SPC)): www.medicines.org.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® PEN: www.metoject.co.uk
National Patient Safety Agency: www.npsa.nhs.uk
National Rheumatoid Arthritis Society: www.nras.org.uk
NHS Right Care (for information on shared decision making): www.rightcare.nhs.uk
NHS Quality Improvement for Scotland: www.healthcareimprovementscotland.org
Nursing & Midwifery Council (NMC) Revalidation: www.revalidation.nmc.org.uk
Paediatric Rheumatology European Society (PRES): http://www.pres.eu
Royal College of Nursing (online guidance and RCN member access to rheumatology forum): www.rcn.org.uk
Scottish Environment Protection Agency (SEPA): www.sepa.org.uk
Subcutaneous injections information: www.bd.com/uk/diabetes

You can find full texts of all UK government legislation at: www.legislation.gov.uk
References and further reading


Becker ML (2013) Role of methotrexate in juvenile idiopathic arthritis: where we have been and where we are going. Int Journal of Clinical Rheumatology 8 (1): 123-135.


British Society for Paediatric and Adolescent Rheumatology (2009) Standards of care for children and young people with juvenile idiopathic arthritis, St. Albans: BSPAR.

British Society for Paediatric and Adolescent Rheumatology (2010) Methotrexate use in paediatric rheumatology, St Albans: BSPAR.

British Society for Paediatric and Adolescent Rheumatology (2011), Methotrexate patient information leaflet, St. Albans: BSPAR.


British Society for Rheumatology (2006) BSR/BHPR Management of rheumatoid arthritis (first 2 years), London: BSR. Available at online at: www.rheumatology.org.uk

British Society for Rheumatology (2011) BSR statement on vaccination in adult patients with rheumatic diseases, London: BSR. Available online at: www.rheumatology.org.uk


Health and Safety Executive for Northern Ireland (2003) COSHH(NI): a brief guide to the regulations, Belfast: HSENI. Available online at: www.healthandsafetyworksn.i.gov.uk


Royal College of Nursing (RCN) (2016) *Revalidation*. Available online at: www.rcn.org.uk/professional-development/revalidation


Royal College of Paediatrics and Child Health, Royal College of Nursing, Royal College of General Practitioners and Community Practitioners and Health Visitors Association (2002a) *Position statement on injection technique*, London: RCPCH. Available online at: www.rcpch.ac.uk


Royal College of Paediatrics and Child Health (2012) *Medicines information for parents and carers*, London: RCPCH. Available online at: www.rcpch.ac.uk


Contributors to the second edition
The second edition of this guidance was developed by the Royal College of Nursing (RCN) 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 second edition.

Lead authors (second edition)
Lisa K Howie, RGN, ONC, BN, MSc, NIP Rheumatology Clinical Nurse Specialist Nurse, Chair of Working Party and Lead Adult Author, Morriston Hospital Swansea
Polly Livermore, RN Child BSc, NIP, MSc, ANP Rheumatology Advanced Nurse Practitioner, Lead Paediatric Author, Great Ormond Street Hospital for Children NHS Foundation Trust

RCN working party (second edition)
Vicky Chamberlain, Chair of RCN Rheumatology Forum, Rheumatology Specialist Nurse, Trafford Hospital Central Manchester University Hospitals Foundation NHS Trust, and Co-chair of Working Party
Deborah Lloyd, Clinical Nurse Specialist, Community Rheumatology Team, Staffordshire and Stoke on Trent Partnership Trust and Mid Staffordshire NHS Foundation Trust
Ruth Slack, Rheumatology Specialist Nurse, West Suffolk NHS Foundation Trust
Helen Strike, Clinical Nurse Specialist, Bristol Children’s Hospital
Pamela Whitworth, Clinical Nurse Specialist, Birmingham Children’s Hospital NHS Trust

External review team (second edition)
Ailsa Bosworth, Chief Executive, National Rheumatoid Arthritis Society
Rebecca Cheatle, RCN Adviser for Primary and Community Care
Dr Stewart Glaspole, Health Economy Prescribing Pharmacist – Special Interest Rheumatology, Brighton and Sussex University Hospitals NHS Trust
Sue Oliver, Nurse Consultant Rheumatology, Sue Oliver Associates, and Chair Elect for the European League Against Rheumatism (EULAR) HCP Standing Committee
Dr Clarissa Pilkington, Consultant in Paediatric and Adolescent Rheumatology, Great Ormond Street Hospital for Children NHS Trust, Convenor of the British Society for Paediatric and Adolescent Rheumatology (BSPAR)

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.

Lead authors
Susan Oliver, Rheumatology Specialist Nurse, Chair of Working Party and lead author of the adult guidance in the document
Polly Livermore, Paediatric Rheumatology Clinical Research Nurse and lead author of the paediatric guidance in the document, Great Ormond Street Hospital for Children NHS Trust

Working party members
Gail Burbage, Rheumatology Specialist Nurse, Sherwood Forest NHS Trust
Jo Lennon, Rheumatology Nurse, South Warwickshire General Hospital NHS Trust
Janice Mooney, Lecturer/practitioner, Norfolk & Norwich University Hospital
Amanda Mooney, Rheumatology Nurse Practitioner, Northern Lincolnshire and Goole NHS Trust
Elaine Wylie, Rheumatology Liaison Nurse, Green Park HCT, Musgrave Park Hospital
Dawn Homer, Rheumatology Specialist Nurse, Selly Oak Hospital, Birmingham
Contributors
Ian Costello, Teacher/Practitioner at the Centre for Paediatric Pharmacy Research London, and member of the Royal Pharmaceutical Society of Great Britain
Meena Hunjan, Lead Pharmacist, Cancer Network, London. Member of the Royal Pharmaceutical Society of Great Britain

Contributors
Joan Roberts (Scotland), Rheumatology Specialist Nurse, Scotland, Gartnavel General Hospital
Glenys Morgan (Wales), Rheumatology Clinical Nurse Specialist, Wales, Cardiff and Vale NHS Trust University Hospital of Wales
Elaine Wylie (Northern Ireland), also a member of the working party (see above)
Jane Proctor (Community)

Patient groups and other professional contributors
Arthritis Care: Rahana Mohammed, London
National Rheumatoid Arthritis Society: Ailsa Bosworth and Lorraine Tanner
Candy McCabe, ARC Lecturer in Rheumatology Nursing, Royal United Hospital for Rheumatic Diseases, Bath
Tricia Cornell, Senior Rheumatology Practitioner and member of the RCN Rheumatology Forum, Poole Hospital NHS Trust
Jackie Green, Lead Cancer Nurse and Nurse Consultant for Haematology and RCN Cancer Nurse Forum committee member, May Day University Hospital

Paediatric contributors
Dr Clarissa Pilkington, Paediatric Rheumatology Consultant, Paediatric Consultant Reviewer, Great Ormond Street Hospital for Children NHS Trust
Liz Hutchinson, Paediatric Rheumatology Clinical Nurse Specialist, Queens Medical Centre, Nottingham
Pam Whitworth, Paediatric Rheumatology Clinical Nurse Specialist, Birmingham Children’s Hospital
Helen Strike, Paediatric Rheumatology Clinical Nurse Specialist, Bristol Royal Hospital for Children
Gill Jackson, Paediatric Rheumatology Clinical Nurse Specialist, Leeds Teaching Hospital NHS Trust
Nicky Kennedy, Paediatric Rheumatology Clinical Nurse Specialist, Oxford Region Tertiary Centre
Ruth McGowan, Paediatric Rheumatology Clinical Nurse Specialist, Great Ormond Street Hospital for Children

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.
Notes
The RCN represents nurses and nursing, promotes excellence in practice and shapes health policies

June 2016, Review date: June 2019

RCN Online
www.rcn.org.uk

RCN Direct
www.rcn.org.uk/direct
0345 772 6100

Published by the Royal College of Nursing
20 Cavendish Square
London
W1G 0RN

Publication code: 005 564

Supported by an unrestricted educational grant from

medac