Royal College of Nursing

Administering subcutaneous methotrexate for inflammatory arthritis

RCN guidance for nurses

Wyeth®

Acknowledgements

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

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

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Contents

Foreword

Supporting the development of this RCN guidance Elizabeth Fradd, formerly the Director of Nursing for the Commission for Health Improvement, stated:

"CHI does not currently inspect against national standards. However, as part of the clinical effectiveness component of clinical governance CHI expects the NHS to be aware of agreed national guidance. It would also be expected that the NHS should disseminate and audit against such standards. Additionally CHI expects staff to be able to provide evidence that they use guidelines to shape the delivery of care. CHI attaches great importance to the use of guidelines, which can ensure high standards of care with equity of access across all health care settings."

Elizabeth Fradd
Director Nursing
CHI

Executive Summary

This is a brief summary of the RCN's guidance *Administering subcutaneous methotrexate for inflammatory arthritis*, highlighting the key issues for practitioners. For information relating to care and treatment of children and young people See Section 9, *Paediatric guidance*.

Cytotoxic issues and risk management

The use of pre-filled syringes:

- the guidance supports the use of methotrexate via the subcutaneous route prepared for the named patient using a pre-dosed, pre-filled syringe prepared in a dedicated pharmacy with an aseptic preparation area
- methotrexate is a cytotoxic agent. Risk assessment and management should always be in the context of managing potential low-dose long term exposure
- the transporation, training and administration of methotrexate pre-filled syringes should be undertaken in the appropriate facilities by staff trained in the management of cytotoxic therapies in accordance with manufacturer and/or local trust policies.

Protective clothing/spillage:

- methotrexate administration using a pre-dosed pre-filled syringe requires the use of gloves and aprons (for health care professionals and carers)
- a spillage kit should be available in all training areas and the patient's home. When working in trust premises practitioners should be aware of local trust policies and access to spillage kits. This should include knowledge of how to deal with all types of accidental spillage of methotrexate.

Patient education and training:

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

- consent to participation in a training programme and be prepared to demonstrate that they are competent in the safe administration of subcutaneous methotrexate (if self-administering)
- be aware of the need to use effective means of contraception (where appropriate)
- store and dispose of methotrexate and equipment safely
- attend for blood tests and monitoring regularly
- understand how and when to seek advice or guidance on treatment and related issues that may require prompt medical advice.

Practitioner training and competency:

- practitioners should be trained in the management of patients with inflammatory arthritis receiving subcutaneous methotrexate
- practitioners should be knowledgeable and competent in all aspects of methotrexate administration and risk management strategies for cytotoxic therapies
- practitioners should have undertaken appropriate training to educate, support and teach patients in self-administration of subcutaneous methotrexate
- 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 trust policies in relation to management of patients receiving methotrexate
- business planning, documentation and audit should be an integral aspect of developing a service for patients receiving parenteral methotrexate.

Method of administration

- Subcutaneous methotrexate should be administered using a 26 Gauge (brown) needle, length 8mm or 3/8th inch.
- Do not swab the skin prior to injecting if the skin is socially clean.
- Insert the injection at a 90^{o} angle combined with the use of the skin pinch.
- Administer the injection into subcutaneous tissues.
- There is no need to aspirate prior to injection.
- Injection sites should be rotated.
- Co-administration of subcutaneous biologic therapies can be undertaken provided appropriate site rotation is adhered to.

General management issues

- Patient screening, assessment and monitoring should be in accordance with nationally agreed guidance for patients receiving oral methotrexate.

1 Introduction

The Royal College of Nursing Rheumatology Nursing Forum members together with the RCN Paediatric Rheumatology Specialist Nurses Group identified the need for clear guidance for practitioners and patients in the administration of subcutaneous methotrexate. This has provided the catalyst for the development of this guidance.

The Rheumatology Forum and the Paediatric Rheumatology nurses have worked collaboratively to develop a document that has key guidance for both adults and children. To ensure clarity there are two separate sections to the document and practitioners should refer to the appropriate section for adult or paediatric guidance. This document also provides a framework to enable patients, and/or their carers, to administer treatment at home.

The guidance is to aid practitioners in the safe and effective administration of the unlicensed use of subcutaneous methotrexate injections for a number of rheumatic diseases including inflammatory joint diseases. This complements the work already undertaken by cancer care (RCN, 1998). Practitioners should be aware that there is very little specific research on the practical aspects of subcutaneous administration of methotrexate, and therefore evidence from cancer and diabetes care has informed the working party. In particular, the review of work undertaken in the development of cancer frameworks has brought to light the wealth of literature dedicated to the use of cytotoxic agents in the treatment of cancer, and importantly specific issues that require clarity for rheumatology practitioners.

With the development of any innovative practice there can sometimes be a gap between a growing body of knowledge and recognised national guidance. However, the emergence of subcutaneous methotrexate for inflammatory joint diseases has confirmed that it is valuable for practitioners to develop care based around patient need.

The guidance

In preparing this guidance document the working party set out to:

- review the evidence and clarify issues related to methotrexate as a cytotoxic agent in this specialist area of practice
- identify risk assessment and management strategies
- review evidence in relation to the administration of subcutaneous injection techniques
- provide competency frameworks to support practitioners, patients and carers
- highlight the business planning needs required to develop a service for the administration of subcutaneous methotrexate.

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

- the British Society for Rheumatology's safe prescribing and monitoring of methotrexate for inflammatory arthritis guidance (1998)
- the statutory health and safety at work regulations for England and Wales that include COSHH (controls of substances hazardous to health), and in Scotland the Scottish Environmental Protection Agency's (SEPA) regulations
- local NHS trust policies on the handling and disposal of cytotoxic waste and infection control
- local trust policies and clinical governance frameworks for risk management
- Nursing and Midwifery Council (NMC) professional regulations or similar regulatory body for practitioners where nursing is not their primary professional qualification
- the RCN's clinical practice guidelines in the administration of cytotoxic chemotherapy (1998).

See the *References* section for the complete listings of the above text, and for additional advisory documents.

The term *practitioner* is used throughout the main document. The term practitioner relates to nurses or allied health care professionals who have been trained and demonstrated competence in administering subcutaneous therapies.

However, in section 9 *Paediatric guidance* we refer to nurse as the health care practitioner throughout. Also the term *parent* is used interchangeably with *carer* in the paediatric section.

2

Rationale for administration

The efficacy of oral methotrexate therapy in rheumatology is well established (Maini, 2003), and is recognised as the *gold standard* for treating people with rheumatoid arthritis and other inflammatory arthritidies (Weinblatt et al, 1992, Furst 1995).

In recent years research has highlighted the need for more aggressive 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 (Porter et al, 2003). This approach can be limited by drug toxicities or by the inability of the patient to tolerate higher doses of oral methotrexate. In addition some individuals may benefit from the improved bioavailability of methotrexate administered subcutaneously.

How methotrexate works

Methotrexate is an anti-metabolite cytotoxic agent that competively inhibits the enzyme dihydrofolate reductase, preventing the necessary synthesis of deoxyribonucleic acid (DNA) and cell replication. 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 (SPC, 2003).

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 refer to the British National Formulary (BNF, 2003) or the Summary of Product Characteristics (SPC) of methotrexate (2003).

Methotrexate is widely distributed into body tissues and is retained by the kidneys for several weeks and in the liver for months (SPC, 2003). Methotrexate has the ability to impair fertility and is embryotoxic, which causes abortion or fetal defects particularly during the first trimester of pregnancy. It is therefore essential that contraceptive measures should be used by men or women of childbearing potential during and for at least six months following cessation of treatment (Mayne Pharma plc, SPC, 2003).

Methotrexate is licensed for the treatment of various forms of carcinoma, and for these treatments they are sometimes administered via intrathecal, intravenous and intramuscular routes. Subcutaneous and intramuscular administration are increasingly being used in the treatment of RA, however these are currently unlicensed for RA and other inflammatory joint diseases. The administration of intramuscular or subcutaneous methotrexate appears to have comparable rates of absorption and efficacy (Bannwarth et al, 1996). The pharmacokinetic similarities of parenteral treatment have been supported in small clinical research studies comparing oral, subcutaneous and intramuscular administration (Jundt et al, 1993, Arthur 2002, Brooks et al, 2003).

Why use methotrexate?

Methotrexate is recognised as the most effective of the traditional (non-biologic) disease modifying anti-rheumatic drugs (DMARDs) in current use for RA (Hamilton & Kremer, 1997). Oral therapy of methotrexate has been the traditional route of administration, particularly when maximum doses did not exceed 10mg to 15mg weekly. However, a growing body of evidence supports clinical opinion that the optimum therapeutic dose of disease-modifying drugs should be achieved to minimise disease progression and joint erosions (Emery et al, 2002). Current guidance suggest methotrexate should be prescribed at doses from 7.5mg to 25mg once weekly (BSR, 2000).

The rationale for considering the administration of methotrexate using parenteral routes has been driven by the need to increase the therapeutic dose, ensure the maximum bioavailability and reduce symptomatic side-effects for some patients (Brooks et al, 1990). Parenteral administration of methotrexate has demonstrated effective therapeutic benefit and similar rates of absorption to the oral administration. However, an additional benefit achieved was that methotrexate at increased doses demonstrated higher plasma drug concentrations and greater bioavailability via the parenteral (Balis et al, 1988, Brooks et al, 1990, Bingham et al, 2003). Rheumatology specialists have been encouraged by small research studies that have demonstrated the value of such an approach (Jundt, et al, 1993, Conte, et al, 1987). The additional benefits have been those of improving the patient's quality of life and satisfaction with treatment (Arthur, Jubb and Homer, 2002, Livermore, 2003).

An additional driver for change has been the potential to switch patients from receiving methotrexate in a primary

or secondary care setting using an intramuscular route to subcutaneous therapy. Subcutaneous administration has the advantage over intramuscular injections because it can be self-administered, enhances independence and is cost-effective.

In recent years the development of biologic therapies (Adalimumab, Anakinra, Etanercept and Infliximab) has added another dimension to the drive for effective methods of administration for methotrexate therapies. Some biologic therapies require 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. A number of studies have added biological therapies to existing treatment with methotrexate and have reported significant improvements in disease activity. A recently published paper for the first time looked at starting methotrexate and a biologic etanercept, at the same time, and show statistically significant advantages for this combination over either drug used alone (Klareskog, et al, 2004). These biologic agents are effective but costly. The option to continue treatment with methotrexate for those unable to tolerate oral preparations, or who require higher doses to maintain disease control, has the potential to prolong the time a patient remains on DMARDs before they need the addition of a biologic. Extending effective treatment with methotrexate can result in a significant cost saving to the NHS (Bingham et al, 2003).

To summarise the rationale for administration of methotrexate using the parenteral route (intramuscular or subcutaneous) has been based on a number of sound principles:

- improving bioavailability and tolerance of methotrexate
- reducing the side-effects from oral adminstration
- sustaining treatment with methotrexate to extend the time before more costly therapies need to be introduced to control disease
- improving patient satisfaction, and enhancing patient independence
- providing a less painful route for parenteral administration (subcutaneous route).

Practitioners using this guidance should refer to additional key documents that have been used and extensively reviewed to guide and inform the working party *(see References)*.

3 Cytotoxic issues and risk management

It is widely acknowledged that cytotoxic therapies should be recognised and managed as an occupational hazard to all staff, patients and carers involved in the preparation and administration of therapies (Royal College of Nursing, 1998, Allwood, Mallett and Dougherty, 2000, Stanley and Wright, 2002). Although there remains controversy around the evidence base for the effects of low grade long-term exposure, there are technical and statistical issues about current research evidence that can be used alongside the national guidelines on safe handling of cytotoxic therapies, which must be adhered to (NHS, 2000, Allwood, Stanley and Wright, 2002).

The potential risk related to preparation and administration of methotrexate should not preclude the use of methotrexate, but it highlights the need for appropriate and informed management of the risks.

In recent years there has been some debate as to whether low dose methotrexate (below 40mg weekly) should be categorised as cytotoxic (Wallace, 1998). There is no definitive category A, B or C research work to support assumptions that methotrexate at low dose fails to act as a cytotoxic agent. Therefore, this guidance recommends that practitioners should continue to practice based on current evidence and legislation that stipulates methotrexate is a cytotoxic agent with teratogenic properties and irritant effects to the skin (Wyeth and Mayne Pharma Summary of Product Characteristics, 2003).

Note: See *Glossary of terms* for definition of category A, B or C evidence.

Risk management

Practitioners should undertake a thorough risk assessment and prepare a risk management strategy. A framework to guide practitioners can be found below:

1. identify organisational structures to support risk assessment and management
2. plan the patient's pathway and identify potential hazards using a stepwise approach
3. decide who might be harmed and how
4. evaluate the risk and potential degree of harm that might occur as a result of the hazard (see appendix 2)

5. in the case of patients or carers undertaking subcutaneous administration in the home a risk assessment may need to be reviewed and tailored according to specific individual needs or risks
6. identify strategies to prevent or reduce the level of risk where appropriate in accordance with local trust policies
7. document your findings and ensure thorough audit trails
8. report any errors, new risks, near misses or adverse events promptly according to local policy
9. review assessment and management strategies using audit and quality control checks.

The issues outlined above have been taken from key documents developed to aid practitioners in recognising and managing risk (National Patient Safety Agency (NPSA) 2003, Control of Substances Hazardous to Health documents (COSHH) 2002).

An overview of the factors that should be considered in a risk assessment for the administration of subcutaneous methotrexate can be found in *Appendix 2*, which also includes a risk assessment check list.

Risk management responsibilities

Risk assessment and management is an integral aspect of providing safe and effective health care. The NHS Clinical Governance Framework requires structures that identify and manage risk (DH, 1998, 2000a 2000b). A thorough risk assessment strategy is considered an integral responsibility for all employees in all aspects of health care provision. The Health and Safety Regulations (1999) and the Controls of Substances Hazardous to Health (or SEPA in Scotland) and Safety Regulations (2002) support the clinical governance frameworks.

The level and detail of risk assessment should be commensurate with the likelihood and degree of potential harm that the hazard may cause. An assessment and subsequent risk management plans should be undertaken in an informed and structured manner.

The safe management of patients receiving cytotoxic therapies is the responsibility of:

- the organisation by providing appropriate education, training and the infrastructure to support practitioners in safe practice
- the employee whose responsibility it is to attend training days, adhere to national and local policies and guidelines as well as professional responsibilities to ensure they are working within their competencies
- staff working in areas administering cytotoxic therapies, who should be informed of their responsibilities in risk assessment and management
- practitioners administering subcutaneous methotrexate, who must be trained and informed of the safety issues related to handling and administration of this cytotoxic agent.

A practitioner's responsibilities include ensuring that:

- a risk assessment and management strategy has been carried out and additional staff working in the area should be aware of the COSHH Regulations and have undertaken appropriate Health and Safety Executive training
- practitioners who are wishing to conceive, father a child, or who may be pregnant or breast feeding must seek advice from their occupational health departments. Practitioners should have access to all the relevant information (and guidance from occupational health if required). This should help practitioners or other members of staff to seek information about methotrexate to ensure they can make an informed decision about the risks of exposure
- the pharmacy department is included in the planning and development of the service
- reviews of risk management strategies and reporting of *near misses or errors* according to local trust policy.

Risk assessment

Risk assessment should be undertaken to evaluate the level of risk at local level taking into account the environment and treatment preparation. Appropriate measures should then be put in place to reduce the risk of any potential accidental exposure to an acceptable level (COSHH, 2002).

The assessment and management of risk should be documented and may be subject to scrutiny from local clinical governance reviews. This could possibly include organisations such as the Commission for Healthcare Audit and Inspection (CHAI), or the NHS Quality Improvements for Scotland (QIS).

Dimond (2002b) writes: "The risk of cytotoxic therapies should be assessed and managed "so far as is reasonably practicable".

While in their cancer care guidance Mallet and Dougherty (2000) say: "The risk to health associated with exposure is measured by the time, dose and routes of exposure." Such guidance documents have rightly focussed on these key issues particularly as therapies are administered in large dosages using intrathecal, intravenous and parenteral routes on an intensive and regular basis. This document clarifies the different level of risk associated with using pre-filled syringes for subcutaneous methotrexate administration.

It is essential that:

- a thorough risk assessment is undertaken (see *Appendix 2* for an example)
- practitioners should ensure that all potential risks are identified and appropriate action is taken to ensure these are reduced to a clinically acceptable level.
- practitioners caring for patients receiving subcutaneous methotrexate should be competent in the administration of subcutaneous therapies and have received appropriate training. This should include regular reviews and sessions to update their knowledge on all aspects of methotrexate management (see the competencies framework in *Appendix 3*)
- patients, and carers receiving or administering methotrexate should be informed that methotrexate is a cytotoxic agent
- patients have made an informed decision about treatment based on written and verbal information about side-effects, and be aware of the risks and benefits of receiving methotrexate subcutaneously
- patients, or carers should be assessed and trained in the safe storage, administration and disposal of equipment. This includes dealing with accidental exposure or spillage (see patient training and competencies in *Appendix 4*)
- informed consent to treatment should be documented in accordance with Department of Health or local trust policy guidelines using appropriate consent forms.

Note: There are specific issues that need to be taken into account when a patient is being considered for methotrexate therapy administered in their own home, either by self-administration or with the help of a carer. (See section *Patient education*).

Recommendations on risk management

This guidance strongly recommends that the preparation of methotrexate should be undertaken in:

- an appropriately equipped pharmacy department dedicated to the preparation of cytotoxic agents
- adherence with COSHH Regulations (2002) and Health and Safety Executive Regulations (2002)
- the use of named patient pre-dosed pre-filled syringes with a leur lock system clearly labelled for subcutaneous use. This will reduce the need for additional precautions including the use of goggles, armlets and face masks (see *Pharmacy issues* section).

The Health and Safety Executive advocates the following best practice for the administration of subcutaneous methotrexate:

- carry out a risk management analysis taking into account risks related to potential drug errors as well as accidental exposure or spillage during preparation and administration of treatment protecting the patient, practitioner and working area throughout the process of administration.

4 Pharmacy, cytotoxic storage and disposal issues

You should refer to other sections in this guidance when using the information about pharmacy issues and cytotoxic storage and disposal.

Supply, preparation and delivery

All aspects of pharmacy management should reflect the potential risk of cytotoxic exposure. Parenteral methotrexate should be prepared in a dedicated pharmacy by appropriately trained pharmacy staff. Alternatively doses can be purchased in pre-prepared pre-filled syringes from independent pharmaceutical organisations. Packaging and transport systems should ensure that adequate protection and storage instructions are adhered to during delivery. Practitioners should be guided by local trust policies (Shaw and Stanley, 2002).

Patients who collect their own treatment either from a pharmacy department or local community pharmacist are *usually advised* not to travel with the methotrexate on public transport. However, in some circumstances packaging and storage in transit may satisfy the local trust policy.

In all circumstances it is essential that the potential risks of transporting securely packaged pre-filled syringes of methotrexate have been assessed and management strategies put in place to ensure safe transportation. This may also include the use of a coolbag depending on storage instructions.

When named patient pre-dose pre-filled syringes are prepared they may be issued in one of four ways:

1. the individual patient dose will be dispensed from the hospital pharmacy either to the individual patient or to an appropriately trained practitioner for administration by the hospital outpatient service
2. the patient may collect their syringes from the hospital pharmacy or community pharmacist to take home
3. transferred by appropriate transport to primary care practitioners (community or practice nurses) to administer in primary care
4. delivered directly to the patient's home by pharmaceutical companies that have a contract with the NHS or primary care trust. These companies may also be responsible for the collection of and disposal of cytotoxic waste.

There may be other examples of collection and delivery and it is therefore essential that practitioners refer to the pharmacy department to determine the most appropriate method of preparation and delivery.

Note: Refer to the section on cytotoxic waste and spillage kits for additional information.

Storage and drug stability

Methotrexate is a clear yellowish solution and is generally stable if stored out of direct sunlight. Depending on individual suppliers' recommendations fridge storage (in temperatures between 2 to 8 degrees Centigrade) may be required. Local trust policies might recommend this to minimise the potential for microbial colonisation. This is relevant when the environment for storage is assessed, particularly for home settings. Practitioners should ask the pharmacy department for guidance on manufacturers' recommendations.

Although there is evidence to suggest that some formulations of commercially prepared pre-filled syringes of methotrexate are stable for some months, the shelf life and storage conditions may vary depending on the syringe provider. They should be carefully checked and reviewed on a regular basis.

When practitioners assess best practice for patient care and risk reduction they should take into account:

- frequency of dispensing
- practical aspects of management
- varying recommendations on storage, shelf life and size of syringes
- supply or shortage problems that may necessitate changes in suppliers.

Patients who self-administer must be told about any changes of manufacturer. This is because it may result in changes to the volume provided in the syringe, storage conditions, expiry date or appearance of the syringes.

When preparing a business case consider a cost benefit analysis that takes into account risk management and patient preference. (See *Appendix 8* for an outline business proposal.)

Storage and delivery safety issues

Practitioners and staff should be trained and competent in all aspects of safe storage and delivery of cytotoxic agents. There are different factors to consider about drug storage depending on whether the methotrexate is being administered in a clinical environment or self-administered. Storage will also vary according to the product used. (See section on *Preparation and delivery*).

Storage at home

The storage of methotrexate syringes, needles, and cytotoxic waste bins should be out of reach and sight of children and pets. The pre-filled syringes should be stored in a secure system in a fridge (where appropriate). Make an individual risk assessment if there are any additional safety factors that alter the identified storage risks such as the need for fridge locks.

Protective clothing

The level of protective clothing required should be based on the potential risks the practitioner, patient or carer may experience when handling methotrexate. The RCN (1998) review of protective clothing highlights the lack of definitive research in this area, and states that protective clothing does not guarantee total protection and must be used in conjunction with good handling.

Evidence to date shows that the risk cytotoxic agents pose relates mainly to the administration of intravenous therapies at high doses. This does not include the use of named patient pre dosed pre-filled syringes for subcutaneous injections (RCN, 1998). Practitioners will need to make a judgement based on a local risk assessment.

It is for this reason that the guidance advocates the use of methotrexate in a ready to administer form. Where protective equipment is used it should be marked with the European CE standard that ensures it complies with legal requirements (HSE, 2002).

There is potential for inhibiting the practitioner or patient in the handling of the equipment and syringes if excessive protective equipment is used. Further, the risk of accidental spillage or exposure will be need to be balanced against how easy it is to train the patient, particularly if exposure or spillage has been significantly reduced by using pre-filled syringes.

Aprons

Protective water resistance aprons should be worn when administering treatment (RCN, 1998; Allwood, Stanley and Wright, 2002). It may not be appropriate for the patient administering their own therapy to wear an apron. For example, in some circumstances the use of an apron could hinder access to the abdominal injection site and increase the risk of accidental injury or spillage.

Gloves and armlets

Methotrexate is classified as a moderate irritant to the skin (Allwood, Stanley and Wright, 2002). It is not necessary for patients administering their own therapy to wear gloves. However, patients should be informed of the irritant effects of methotrexate and have information on how to deal with accidental spillages onto the skin.

If practitioners use latex gloves a separate risk assessment should be undertaken to ensure excessive exposure to latex and potential allergies is managed appropriately. Powder free gloves should be used (Allwood, Stanley and Wright, 2002). There is no glove material that can provide total protection for an unlimited period of use for cytotoxic therapies (HSE, 2002). Gloves should be changed frequently (every one to two hours or after each patient administration) during clinical care and immediately if in contact with a cytotoxic agent or if punctured (RCN, 1998; Allwood, Stanley and Wright, 2002). The selection of gloves should ensure suitable thickness and integrity to maximise protection yet maintaining manual dexterity (Allwood, Stanley and Wright, 2002). The use of gloves for spillages can be found in Section 5 under cytotoxic waste and spillages.

Armlets have been advocated in the past but are not necessary unless reconstituting methotrexate.

Goggles and masks

The use of goggles and masks is essential if cytotoxic therapies are being prepared because there is a risk of splashing or aerosal formation (Royal Marsden Hospital, 2002). There is no need to dispel the small amount of air from a pre-filled syringe with a leur lock system, as it is not harmful to the patient and is rapidly absorbed in the subcutaneous tissues. If practitioners adhere to the procedures set out in this document the use of goggles or masks will not be required.

It is therefore unlikely that protection of eyes, nose or mouth will be necessary for appropriately trained and competent practitioners, patients or their carers administering methotrexate using a pre-filled syringe.

5 Safe management of methotrexate

Cytotoxic waste

Cytotoxic waste should be disposed of in clearly labelled waste bins indicated in local trust policies. Local policy should also dictate the separate storage, collection and handling of methotrexate waste. Staff should receive regular training and updating on policies in relation to clinical risk and dealing with hazardous waste (HSE, 2002).

When methotrexate is being administered in the community or directly to patients' homes there are specific issues about managing cytotoxic waste that should be considered. To ensure that methotrexate waste disposal is efficiently managed practitioners must establish good communication between primary care teams and their hospital unit. In some circumstances companies delivering the methotrexate to the patients' homes are also responsible for the collection and disposal of cytotoxic waste, while in other cases the primary care team arrange collection. Concerns about adequate management of cytotoxic waste disposal has the potential to block the development of home administration programmes, so a thorough assessment should be undertaken before implementing any changes.

Cytotoxic waste bins

Cytotoxic waste bins are clearly identifiable and should only be used for the disposal of methotrexate syringes, needles and other equipment used in preparation and administration. The exact style of bin, method of sealing or whether there is a need to have a specific anti-spill mat to be placed under the bin may vary slightly from trust to trust.

Patients should be aware of the need to ensure safe disposal of equipment using a cytotoxic waste bin, and that the bin 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. Patients should be told not to transport cytotoxic waste bins by public transport. Practitioners should ensure they adhere to local trust policy for the collection and disposal of cytotoxic waste bins.

Methotrexate waste and body fluids

Patients receiving methotrexate therapies will excrete some of the drug in faeces for around seven days, and in urine for three days after administration (Allwood, Stanley, Wright, 2002). It is assumed that patients receiving oral treatment excrete at a similar rate to those receiving subcutaneous preparations. The routine treatment of sewage is considered to provide adequate safety measures for reducing the risk of unintended exposure to cytotoxic waste. (Allwood, Stanley Wright, 2002)

In-patients receiving methotrexate or other cytotoxic therapies may be receiving a high level of nursing care. In these situations it is essential that practitioners ensure that nursing staff are aware of the risks and that all excretions are disposed of promptly, and routine infection control measures are carried out.

Spillage kits

All areas that handle, administer or transport methotrexate and any cytotoxic agent or substance hazardous to health should be trained in contamination or accidental spillage procedures. Practitioners, patients and carers should have access to a spillage kit and first aid equipment as set out in COSHH regulations (COSHH, 2002). It is vital that patients and carers know how to deal with accidental spillages and to dispose of any equipment used. This should be in adherence with national/local guidelines.

The contents of trust spillage kits can be large and cumbersome. It may be possible to negotiate a smaller more appropriate version for patients to have at home, and for areas providing clinical care and subcutaneous administration of methotrexate training. However, practitioners will need to review the options with the dedicated lead for clinical risk and ensure adherence to local trust policy.

The risk related to accidental spillage from a 2ml pre-filled syringe is relatively small, and this should be considered in the context of risk management and the appropriate spillage kit equipment. The level of risk will be higher during the administration of the drug (see Section 7, Patient eduction). Spillages must be recorded as an incident to enable a thorough review of risk management strategies.

Spillage kit content

For the purpose of this guidance, based on the assumption that methotrexate will be administered using a pre-filled syringe, a small spillage kit could be provided to the patient and used in the clinical area for training purposes. The spillage kit should include as a minimum:

- instructions on dealing with spillages
- cytotoxic waste bin/bag and tape/label according to local policy
- absorbent paper towels or plastic backed absorbent towels (large)
- gloves of thickness >45mm or 2 pairs of latex gloves
- plastic apron.

Recommended spillage procedures

Practitioners should also refer to their local trust policy, but these are the main points to consider when dealing with a spill:

- restrict the area immediately and notify additional staff
- if anyone has received any injury or spillage directly onto the skin or into the eyes they should be dealt with promptly (see below)
- the spillage kit should be opened and protective gloves and apron should be worn
- the fluid spillage should be circled by absorbent towel to contain the fluid. If necessary use additional towels. Once all the fluid has been adequately absorbed the towels should be disposed of into the cytotoxic waste bin/bag
- wash all the contaminated surface with copious amounts of water and wipe clean and discard of the paper towels used to do this into the cytotoxic waste bin/bag. Repeat the process five times working from just outside the spillage into the central area. All protective clothing should be discarded in the cytotoxic waste bin
- the area should be routinely cleaned with hot soapy water
- remove protective gloves and wash hands
- replace spillage kit
- complete an incident report.

Liquid spillage on clothing

If methotrexate is spilt onto protective clothing they should be removed promptly and replaced. Ordinary clothing should be rinsed using running tap water and squeezed dry before being washed separately in the hottest wash cycle twice. If the clothing is to be disposed of it should be incinerated. Practitioners should also refer to local policy.

Liquid spillage directly onto the skin

Methotrexate is a moderate irritant. The contaminated area should be washed thoroughly with copious amounts of water and then washed using a liquid soap. Methotrexate is not a vesicant.

Liquid spillage directly into the eye

The eye should be flushed thoroughly for at least five minutes with large amounts of normal saline or cold tap water if necessary. In some areas eye wash kits are available. Emergency medical attention should then be sought promptly and occupational health advised.

6 Patient care

The focus of this document is to provide a practice framework that enables patients to have effective treatment, and greater choice of treatment and delivery. As with any new therapy patients should be given full information and ample opportunity to discuss the risks and benefits of treatment. Patients should be advised that they can elect not to self-administer methotrexate and that they can opt out of treatment. When a patient elects to have home administration, and if they consent, the carer should be included in all treatment-related discussions and training sessions.

The patient and carer should be aware that home administration of methotrexate is subject to undertaking a training programme and a review of their ability to manage home administration.

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 safe management of methotrexate, 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
- recognise that an annual review of home administration and competency may be undertaken to ensure safe practice.

The ability of a patient to inject in their own home will:

- provide a greater degree of independence for the patient
- require a suitable infrastructure to allow screening, assessment, safe delivery, administration and disposal of methotrexate. In addition, adequate resources should include training and monitoring of patients
- reduce the nursing workload and enable greater flexibility in the provision of care
- free outpatient appointments and maintain greater efficiency
- require the support of the hospital pharmacy department
- require good communication between primary and secondary care, and appropriate support for primary health care teams where community teams are involved in supporting patient care.

Note: See the example patient information leaflet in *Appendix 5*.

Screening

When screening and preparing patients receiving methotrexate therapy you should refer to key texts that are relevant to oral methotrexate therapy. This should include methotrexate SPCs, guidelines on monitoring, immunisation and vaccination (BSR, 2000 and BSR website) and other nursing text (Hill, 1998).

Screening prior to consideration for methotrexate therapies should include:

1. blood screening
   - full blood count, plasma viscosity or C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), urea and electrolytes to include creatinine, and liver function tests
2. patients of child-bearing age who wish to consider conception should be referred to the prescribing physician to discuss treatment options
3. chest X-ray prior to treatment or within the last six months according to the British Society for Rheumatology Guidelines or local trust policy (BSR, 2000, SPC, 2003). Respiratory history should be noted

   Note: Pulmonary toxicity can occur in patients receiving methotrexate in the form of a drug induced pneumonitis
4. review of concomittant medications to exclude any drug *interactions* or absolute *contraindications*. Some drugs should be used with caution when co-prescribed with methotrexate. They include drugs that enhance the potency of methotrexate or reduce excretion, for example (this is not a comprehensive list):
   - folate antagonists or drugs with anti-folate properties such as trimethoprim
   - salicylates prescribed concomitantly with non-steroidal anti-inflammatory drugs (NSAIDs) (particularly in elderly people)
   - drugs with hepatotoxic properties should be avoided unless clinically indicated (azathioprine, retinoids and leflunomide)
   - plasma protein bound drugs that may displace methotrexate such as salicylates, sulphonamides (co-trimoxazole), hypoglycaemics

- oral antibiotics may decrease intestinal absorption of methotrexate such as tetracycline.

5. A careful history should include a review of medications and interactions, the use of aspirin or any other over-the-counter products (OTCs) such as NSAIDs.

   Note: Current opinion supports the use of low dose methotrexate (5mg to 25mg weekly) in adults with normal renal function who are routinely monitored (BNF, 2003). Potential interactions related to methotrexate and co-prescribing of NSAIDs have been identified. It is therefore essential to monitor blood counts and renal function (Stockley, 2002). Elderly people require more careful monitoring because they are at an additional risk from toxicities if they have reduced renal excretion.

Contra-indications to treatment with methotrexate include:

- renal or liver failure (or recent hepatitis)
- blood dyscrasias
- alcoholism
- pregnant or breastfeeding
- immunodeficiency syndromes.

(*Summary of product characteristics*, Wyeth 2003)

Folic acid supplementation

It is broadly recognised that folate supplementation should be prescribed with methotrexate. However, there remain some differing opinions about the dose and frequency of folate supplementation necessary to reduce adverse effects, and the possible impact this might have on methotrexate efficacy. Doses of 5mg per week appear to be adequate, though higher doses have been used with no apparent effect on methotrexate efficacy (Ortiz et al, 1998). Many units use doses of 5mg every day except the day that methotrexate is taken for concordance reasons. There is no reason to use folinic acid for routine folate supplementation as folic acid is efficacious and cost effective (Ortiz, et al, 1998. Category A evidence). If there are concerns about the effect on methotrexate efficacy, avoid folic acid 24 hours either side of the treatment.

Assessing and preparing patients and carers

Assessing and preparing patients (and carers) for consideration and eligibility for subcutaneous administration should include:

- ensuring the eligibility and screening criteria have been met (see section on *Screening*)
- an assessment of the patient's preference and potential ability to receive treatment using subcutaneous injection
- a carer may elect to administer treatment to the patient, if the patient is in agreement and the carer has the ability to undertake the task
- an assessment of the patient's or carer's knowledge, expertise and ability in the handling of the equipment and administration of the treatment
- specific issues relating to the safe delivery/collection of the drug and disposal /collection of cytotoxic waste
- the ability to ensure a safe environment to store and administer the treatment within their own home
- the patient or carers ability to access health care support when needed.

Self-administration

Before undertaking self-administration of methotrexate the patient should have consented to treatment and be fully informed of the risks and benefits, as well as issues related to training. Ensure that the local trust policies on managing cytotoxic therapy and safety issues are clearly and concisely conveyed to the patient.

Provide the patient with a training programme once routine screening and eligibility for treatment have been confirmed.

Skin preparation

If the skin is socially clean and thorough hand washing techniques are used there should be no reason to clean the skin with alcohol impregnated swabs (Workman, 1999; Vaccine Administration Task Force, 2001). Studies have demonstrated no increased incidence of infection when swabbing is omitted (Koivisto and Felig, 1978, Mallet & Dougherty, 2000). A study of 5,000 patients over a six-year period reported no infections following injections without skin preparation (Dann, 1969).

If local trust policies require the use of skin cleaning 30 seconds should elapse between wiping with an alcohol impregnated swab and injection to allow the skin to dry before injection (Workman, 1999; Royal College of Nursing, 2002).

Pinching skin before injection and needle size

The decision to pinch or not to pinch the skin for injections relates to the needle length, angle of injection and the need to ensure that the drug is injected subcutaneously and not intramuscularly.

The needle colour is an indicator of the gauge (external diameter of the needle) but is not the indicator for the length or internal bore size of the needle. Practitioners should be aware that needle gauges, length of needle and internal bore may vary from supplier to supplier. For example, there are at least two different internal bore sizes for the 26 gauge needle.

The shorter needle length (8mm or 3/8th of an inch) inserted at a 90^{o} angle to the skin combined with skin pinching will ensure that the drug is administered into the subcutaneous tissues (Wood, Wilbourne & Kyne-Grzebalski, 2002, Winslow, Jacobson and Peragallo-Dittko, 1997). See figure 1 in Appendix 4 *Patient information and training*.

If a 26 gauge needle is chosen with a wide internal bore this allows wider dissemination into the subcutaneous tissues and less pressure to administer the injection with no increase in leakage from the injection site (Hanas, Lytzen and Ludvigsson, 2000, Chiodini, 2001). The skin pinching and reduced force required when injecting is important to rheumatology patients who may have reduced manual dexterity or strength (Birkebaek et al, 1998). The use of finer gauge needles has demonstrated less intense pain during injections in some studies, although further work needs to be undertaken in this area (Coley et al, 1987).

A study using ultrasound demonstrated that average skin thickness varies between 1.5mm and 3mm, and that obese patients do not have thicker skin than other people (Pemberton & Holman, 1989 cited in King, 2003).

Aspirating

Research examining the practice of aspiration prior to administering a subcutaneous injection using lean and obese patients demonstrated no accidental injection into blood vessels (Winslow, 1997). Aspiration when the needle is in situ is also linked to an increase risk of haematoma formation for patients receiving heparin (Springhouse Corporation, 1993).

Rotating injection sites

Patients or carers who self-administer treatment will need to ensure that they rotate the injections sites. Injections should be given at least 3cm apart. If injecting in the abdomen injections should be a 5cm radius away from the navel. See figure 2 in Appendix 4 *Patient information and training* for suitable injection sites. It is suggested that the patient should keep a record of injection sites used. See figure 4 in *Appendix 4* for an example of an injection site chart. Manufacturers of biologic therapies support this advice. For additional information refer to the SPC or BNF.

The clinical trials into the concurrent use of subcutaneous methotrexate and biologic therapies identified no additional safety concerns for patients receiving both therapies subcutaneously, compared to patients receiving subcutaneous biologic therapy only (Weinblatt et al, 1999; Weinblatt et al, 2003).

Angle of injection

Subcutaneous injections should be given using a 90^{o} angle (Workman, 1999). Evidence supports this technique combined with the use of an 8mm needle (Burden, 1994; Workman, 1999). See figure 3 in Appendix 4 *Patient information and training*.

Subcutaneous administration recommendations

It is recommended that subcutaneous administration of methotrexate should be carried out using:

- 26 gauge needle
- length should be 3/8th inch or 8mm
- a pinch technique (see figure 1)
- an angle of 90^{o} to the skin (see figure 3 in Appendix 4 *Patient information and training*)
- aspiration is not required prior to injection.

Overdosing and severe toxic reaction

If a patient has a severe toxic reaction to methotrexate the drug should be stopped and practitioners should seek medical advice. Folinic acid (calcium folinate or calcium levoleucovorin) is an antidote for neutralising the immediate effects of methotrexate. The time interval between methotrexate and calcium folinate administration should be as short as possible to ensure the maximum effectiveness.

In cases of accidental overdose calcium folinate/levoleucovorin should be administered within one hour. It should be equal or higher than the dose of methotrexate. Intravenous doses of up to 75mg within 12 hours of overdose should be followed by 12mg by intramuscular injection every six hours for four doses. Calcium folinate can be administered by oral, intramuscular, or intravenous routes. Monitoring of serum concentration levels need to guide the optimal dose of calcium folinate (*Summary of product characteristics*,

Mayne Pharma 2003; Wyeth 2003). A severe overdose may require therapies such as blood transfusions or renal dialysis.

Review and monitoring

It is recommended that a subcutaneous patient self-administration programme should be implemented only where there are guidelines, and where there are primary and secondary responsibilities for monitoring of patients receiving DMARDs. The guidelines should include effective channels of communication and support to reduce risk. Patients will also need the support from the rheumatology service if there are problems experienced in home administration, and for prescription provision.

The blood monitoring regime for subcutaneous methotrexate will be the same as for oral methotrexate (BSR, 2000). In many units there will be local monitoring booklets but practitioners should be aware that the National Patient Safety Agency will be producing a generic patient information leaflet and monitoring booklet for methotrexate (NPSA, 2003). Primary health care teams should be advised of changes in treatment by letter. See the specimen letter in *Appendix 6*.

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

The patient or carer should be able to access additional training sessions if necessary. An annual review of practice should be maintained to ensure a thorough audit trail and maintenance of safe practice. This process should include an annual review of patient or carer skills in injecting and managing their prescriptions.

7 Patient education

Patients and carers should receive information about the treatment, and understand the contra-indications, the potential risks and side-effects. In addition 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 of subcutaneous methotrexate injections. The patient and carer should be provided with written and verbal information and have an opportunity to discuss any concerns they may have. If they wish to continue with the training, patient consent should be obtained and documented in line with the local trust policy. A patient education package has been developed to support patients and practitioners. See *Appendix 4* for the patient training package and assessment of patient competency.

The expertise 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.

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 carer's individual learning needs. The practitioner and patient, and or carer where appropriate, will determine the number of training sessions necessary to achieve competency.

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. A unit or department must get permission from the local ethics committee to clarify adherence to the Data Protection Legislation if they wish to collect additional data that contains personal or clinical details of an individual or a group of individuals (DH, 2003).

It is important that practitioners audit the service and include the value of the educational programme. The trust's audit department will provide guidance and support.

8 Preparing a business case

The development of a new service rests on building a thorough business case. To fund a new service prepare a full analysis of current resources, patient needs and the likely cost implications. After completing the analysis prepare the business case. This should set out the likely costs and long-term strategy, and also the possible savings and improvements in delivering a new patient-focussed service.

It is the responsibility of the specialist practitioner to ensure that appropriate resources are available to provide safe and effective treatment. Some units will already have an established service for the administration of subcutaneous methotrexate and may wish to use the guidance to inform and review practice. In some circumstances units will be considering developing a new service for subcutaneous methotrexate administration.

Practitioners need to take into account all aspects of service provision when identifying potential additional costs or benefits in terms of changes or reduction costs. A cost-benefit analysis is a powerful tool in the development of the service, but is not the only factor. Additional factors include:

- reducing risk
- improving the overall quality of care
- enhancing effectiveness and improving access to treatment
- including patients' views
- enabling patient choice and promoting self management strategies (DH, 1998, 2001)
- planning the service in collaboration with primary care providers.

An outline business proposal is in *Appendix 7*.

9 Paediatric guidance

Introduction

This paediatric section of the RCN's *Administering subcutaneous methotrexate for inflammatory arthritis: guidance for nurses* has been developed by the RCN Paediatric Rheumatology Specialist Nurses Group. The aim of the document is to highlight the key issues relating to the specific needs of children and young people, and to standardise the care and practice of administering subcutaneous methotrexate across the UK. There are clear differences between paediatric and adult usage of low dose methotrexate for rheumatic disease, and this section provides a comprehensive overview.

The paediatric guidance should be used as a guide to caring for children, young people and their families receiving subcutaneous methotrexate treatment, but it should be understood that they are not exhaustive. There is very little published evidence available specifically focussing on methotrexate in paediatric rheumatology care, therefore, the content is based on what is considered best practice. Nurses should use this document as guidance, and refer to existing local trust policies to inform practice.

Methotrexate use in paediatric rheumatology

Methotrexate was developed in the 1940s as a specific antagonist of folic acid. It is classed as a cytotoxic drug because it inhibits the proliferation of malignant cells and has teratogenic properties and irritant effects to the skin (Wyeth and Mayne Pharma Summary of Product Characteristics, 2003). There has been debate about the extent of the drug's cytotoxic nature when it is used in low weekly doses for rheumatic disease. For example, Cutolo (2001) states that the cytotoxic mechanism of action might be more anti-inflammatory than anti-proliferative. However, because there is no published research to say otherwise, this guidance has to recommend that nurses should continue to practice based on current evidence and legislation that stipulates methotrexate is a cytotoxic agent.

The first study of methotrexate usage in juvenile idiopathic arthritis (JIA) was published in 1986 (Truckenbrodt and Hafner 1986). Six years later the first randomised double blind, placebo-controlled trial demonstrated that methotrexate at 10mg/m^2 per week had a significant therapeutic advantage in 70% of JIA patients (Giannini et al 1992, Ruperto and Martini 2003). Over the last ten years of clinical use, methotrexate has transformed the outlook for children with JIA, and it is considered the gold standard for patients that require a second line therapy (Ravelli and Martini 2000, Ramanan et al 2003). Methotrexate is also widely used in other paediatric rheumatological conditions, such as juvenile dermatomyositis (JDM), scleroderma (particularly localised), juvenile systemic lupus erythematous (JSLE), idiopathic chronic anterior uveitis and some vasculitides (Laxer 1999).

Paediatric use of methotrexate has been considered separately to adult treatment in this guidance for the following reasons:

- paediatric rheumatic diseases are different from their adult counterparts. The umbrella term JIA covers a heterogeneous group of conditions that combines arthritis with onset before the age of 16 years with unknown aetiology. Early onset oligo articular JIA (50% of all JIA) is not observed in adults, and systemic JIA (15% of all JIA) is seldom found in adults. While rheumatoid factor positive polyarthritis is only seen in 3% of all JIA cases, it accounts for 70% of all cases of adult rheumatoid arthritis (RA) (Cassidy and Petty 2001, Ruperto and Martini 2003). For classification of JIA see *Paediatric resources 1*
- pharmacokinetic and toxicity profile of medications may be different in adults and paediatrics
- effectiveness of medications are different: controlled trials in the late 1980s found that penicillamine, and oral gold salts, which were effective in adult RA, were no more effective than placebo in JIA (Cited by Ruperto and Martini 2003)
- indications for medications differ. Idiopathic 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 commonly a problem in adults with RA who might want to self-inject
- there are fewer complicating risk factors than in adults, such as alcohol consumption and pre-existing lung and liver disease.

There are also other specific paediatric issues that will be looked at in this section, such as:

- childhood vaccinations
- use of local anaesthetic creams
- teaching parental administration
- pregnant mothers and those planning pregnancy
- transition from adolescent to adult care.

It is recommended that methotrexate should only be prescribed by consultants who regularly see children and young people with paediatric rheumatic diseases. Ideally, there should be shared care with a specialist paediatric rheumatology centre, and a paediatric rheumatology consultant. Prior to starting methotrexate treatment, there needs to be discussion and agreement about who takes responsibility for prescribing and monitoring the child or young person once on therapy. In addition, there must be a paediatric nurse specialist involved who is able to support both children receiving methotrexate therapy and their parents, and who is able to teach injection techniques if appropriate.

Differences between oncology and rheumatology

The differences can be summarised as:

- rheumatological methotrexate doses are significantly less than those used by oncologists
- dosage regimen is frequently different
- intrinsic factors in cancer patients that affect absorption, bioavailability and excretion are likely to be different
- concomitant medications differ permitting different opportunities for drug interactions. For example, in rheumatology non-steroidal anti-inflammatory drugs (NSAIDs) are often used in conjunction with low dose methotrexate. However, in oncology NSAIDs should not be used with high dose methotrexate because they can alter the clearance of methotrexate (Wallace et al 1989, Giannini and Cassidy 1993).

Rationale for parenteral methotrexate

Several studies have demonstrated that children absorb methotrexate at different rates (Alsufyani et al 2004). Absorption depends on variables such as the amount of food in the stomach (Dupuis et al 1995) and the dosage given. Therefore, parenteral administration is more effective than oral, particularly with doses greater than 15mg/m^2/week because of the decreased oral bioavailability of the drug at higher doses. It has been shown that subcutaneous administration has 10% to 12% increased absorption when compared with oral preparations (Ravelli et al 1998; Wallace et al 1998; Ramanan et al 2003).

Many children are given parenteral methotrexate on the assumption that gastrointestinal complications may improve, however this is not always the case as proven by Ravelli et al (1998). Subcutaneous methotrexate treatment can be self-administered at home, giving the patient and family a greater degree of independence and comfort as well as enhancing the cost-effectiveness of treatment. This improves the child and family's quality of life and treatment satisfaction (Arthur, Jubb and Homer, 2002; Livermore, 2003).

Alsufyani et al (2004) retrospectively studied children that failed oral methotrexate either because of inefficacy or toxicity, and found that changing to subcutaneous methotrexate in their cohort had a high likelihood of success with more than 70% of patients with JIA achieving clinically significant improvement, without clinically significant toxicity.

Why use subcutaneous (SC) rather than intra-muscular (IM)?

There have been numerous studies comparing the efficacy and tolerance of SC and IM methotrexate. They found that there is no difference in efficacy, although SC is more convenient, less painful and easier to self-administer (Brooks et al 1990; Jundt et al 1993; Ostrov et al 1998). Therefore, as Arthur (2002) recommends, all children currently receiving IM methotrexate should be switched to the SC route, and in the future only SC should be prescribed.

Licence

As Ramanan et al (2003) highlight, methotrexate therapy is not licensed in the UK for use in paediatric rheumatology diseases. However, this is a common situation for drug treatments in children (RCPCH 2000). Moreover, as Ruperto and Martini (2000) state most, if not all of the drugs for paediatric rheumatic diseases, are prescribed outside the terms of their product licence in most European countries.

Methotrexate as a disease modifying anti-rheumatic drug (DMARD)

Despite previous debate about whether methotrexate is a true disease-modifying, anti-rheumatic drug, the general consensus is that it is (Ravelli and Martini 2000). Harel et al (1993) evaluated wrist radiographs in 23 JIA patients

before, and during methotrexate treatment. They concluded that methotrexate therapy resulted in radiological improvement in the majority of children with JIA who had a clinical response to methotrexate. Ravelli et al (1998) studied 26 patients' X-rays at baseline and at two years later. They again concluded that methotrexate does have disease-modifying effects.

Dose

Unlike adult care, methotrexate use in paediatrics is usually calculated by body surface area (BSA) rather than weight alone because this gives a more accurate calculation in growing children (see *Paediatric resources 2*). After Giannini et al's (1992) eminent paper proved the efficacy of methotrexate in JIA, the unanswered question concerning most paediatric rheumatologists is what is the optimum dose – particularly for children who are resistant to the standard dose of 10mg/m^2/week? Therefore, a multinational randomised trial began looking at the safety and efficacy of methotrexate in medium (15mg/m^2/week) versus high dose (up to 30mg/m^2/week) in polyarticular JIAs, who failed to improve on the standard dose. The results from 633 patients showed that the methotrexate efficacy plateau is reached at 15mg/m^2/week, and that further dosage increases do not give any additional therapeutic benefit (work in press, as cited by Ruperto and Martini 2003). Children are therefore usually started on doses of between 10mg to15mg/m^2/week. However, it is widely acknowledged that since methotrexate is cleared from the body more rapidly in children than in adults, children can tolerate much higher doses. Some studies report children receiving 20mg to 25mg/m^2/week for refractory disease (Ramanan et al 2003).

Folic acid supplementation

Methotrexate is a folic acid antagonist that decreases folic acid uptake at cell level. As folate deficiency has been thought to play an important role in the development of methotrexate side-effects, folic acid supplementation is used as standard practice by most paediatric rheumatologists to reduce toxicity. There is little evidence to support this and little consensus on the regime in paediatric rheumatology. Ravelli et al (1999), however, conducted a retrospective study looking at the efficacy of folinic acid supplementation. Doses of 2.5mg to 7.5mg were given in a single weekly dose 24 hours after methotrexate administration to 43 JIA patients. The researchers found a significant reduction in the most common side-effects of methotrexate, such as stomatitis and GI symptoms, without affecting the clinical efficacy of the drug.

However, this guidance will not advise on dose or frequency. It is suggested that nurses investigate the preferences of their local prescribing physician. It is important to note that folate supplementation issues are considered to be less of a concern in children, who are more likely to receive vitamin supplements or artificially enriched foods such as breakfast cereals (Ravelli and Martini 2000; Ramanan et al 2003).

Risk management issues

Risk assessment and management is an integral aspect of providing safe and effective health care. As methotrexate is classified as a cytotoxic drug, it is important to identify and consider the risks, however minimal. Nurses should be aware of their trust's need to be able to demonstrate that it has addressed all potential areas of risk, and documented the decisions made to reduce risk to an acceptable level

For detailed information on all risk management issues go to sections three to five in the adult section of this publication.

Cytotoxic issues and risk management

Pre-filled syringes, personal protective equipment and spillage are important risk management issues specifically relating to the handling of subcutaneous methotrexate, and therefore will be covered in turn.

Named patient, pre-filled, pre-dosed syringes

This document only advocates the use of named patient pre-filled, pre-dosed syringes with a luer lock system. This removes the risk of accidental exposure if local areas are preparing and reconstituting from vials. It significantly reduces the risk of accidental spillage protecting the child/young person, parent, nurse, and working area throughout the process of administration. Using pre-filled, pre-dosed syringes also reduce the chance of drug dosage error. These preparations are widely available either through on-site hospital cytotoxic departments, or as pre-prepared pharmaceutical products.

Personal protective equipment (PPE)

Personal protective equipment concerns the wearing of gloves, aprons, armlets, masks and goggles. As the adult section at the start of this document stipulates, the level of protective clothing required should be linked to the level of risk that faces the nurse, parent, child or young person when handling methotrexate.

The risk of potential exposure is significantly reduced using a sealed pack containing a prepared pre-filled, pre-dosed syringe with a leur lock system. It is particularly important in paediatrics to think carefully about wearing the full PPE

made up of gloves, aprons, armlets, goggles and masks, or *the spaceman outfit*. It can be quite scary not only to the children, but also to the parents who have concerns about administering a drug to their child that warrants such protection. Therefore, if careful handling is maintained, only the wearing of gloves should be necessary (Mallett and Dougherty 2000). There is no recommended glove manufacturer. It is more important to consider if the drug administrator or patient has a latex allergy, so that non-latex gloves are used. Plastic aprons may be required depending on the stipulations of local policy. Obviously, if the child or young person is self-injecting their own methotrexate, then the need for gloves is questionable. The key element is documenting that the individual is aware of the risks and has made an informed choice.

Spillage kits

All areas that handle, administer or transport methotrexate should be trained in procedures related to accidental spillage of cytotoxic drugs and have access to a spillage kit (COSHH 2002). Young people and their parents should also be aware of what to do in case of spillage, and have the necessary equipment available in their home. From using pre-filled, pre-dosed syringes and small volumes of methotrexate, the risk of spillage is negligible. The spillage should be dealt with in accordance with local policy, which usually includes: mopping up; washing with copious amounts of soapy water; rinsing well; and disposing of all contaminated equipment in the cytotoxic bin.

Supply, storage and disposal

Supply

Named patient pre-filled, pre-dosed syringes can be acquired from a variety of different pharmaceutical companies, or made up on site by hospital cytotoxic pharmacies. Most of the pharmaceutical companies also provide a home care delivery service, which can provide additional services such as: supply of gloves; spillage kits; collection of waste; and telephone helplines. Depending on the supplier, the syringes may have different storage recommendations, differing expiry durations and possibly different syringe sizes.

Storage

Methotrexate is a clear yellow solution that should be stored out of direct sunlight. The pre-filled syringes will need to be checked to clarify the particular storage recommendations for the product, for example to refrigerate or not. Also, the quantity of syringes to be collected by a parent or delivered to home may also vary.

During the teaching programme the families are taught what information to check on the syringe label such as the child's name and drug dose. It is also vital to tell them to be alert to any changes in the syringes, particularly the storage instructions. When considering families for home administration thoroughly discuss the facilities needed for safe home storage of the syringes, cytotoxic sharps bin and needles with the family. All three items should be stored safely out of sight and reach of children and pets. The best way to do this is to use a non-transparent, rigid, lockable box (or to fit a refrigerator lock if appropriate). Some home delivery companies provide a refrigerator to store the syringes in so that they are kept separate from food. If this is not available, the syringes should be stored in their own box on the bottom shelf of the fridge (if they are to be stored refrigerated).

Disposal

Cytotoxic waste collection differs in every local area, although it should always be disposed of in clearly identified cytotoxic sharps bins and in adherence with local trust policy. Home care packages can provide a delivery and collection service for all items including cytotoxic sharps bins and spillage kits. Find out more about these issues at local level.

Home administration

The potential to switch patients previously receiving methotrexate in a primary or secondary care setting to using subcutaneous therapy at home enhances cost-effectiveness, and gives the patient a greater degree of independence. The advantages for children, young people and their families are:

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

Requirements for 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 family. 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.

Another consideration for home administration is the suitability of the family circumstances – this is discussed further in the screening section. It is also important to have an alternative person to administer in case of any difficulties. This also applies if the child or young person is the only one who can inject and they later refuse, or become too sick to self-administer.

Ethics of parents administering to children

While some believe that parents should not administer subcutaneous injections to their children in case they alienate them, most parents do not believe this is an issue. In fact it may bring them closer to their child. Teaching methotrexate administration should include discussion about the potential risks and side-effects of using a cytotoxic drug. Reassurance should also be given that it is a safe procedure if guidelines are adhered to. Parental or child administration is ultimately the families' choice.

Administration by a child or young person

There is very little work published on the ideal age for a child or young person to self-administer subcutaneous injections. Therefore, each child or young person that voices a desire to self-medicate must be individually assessed for his or her level of understanding and compliance. Livermore (2003) suggests an arbitrary age of ten years, however there is anecdotal evidence of children younger than this self-administering. It is important to stress that there must be ongoing supervision by an appropriately trained adult.

Screening families for home administration

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

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

Suitability of family circumstances

There has to be a willingness to do the injections, an area for safe storage and child compliance. More importantly, each family needs to be individually assessed to see whether they would cope with the administration, safe storage and disposal of the injections (Livermore 2003). Nurses usually know the family, and often have an insight into their understanding of treatments, their ability to manage side-effects, and the administration/compliance of medications. The 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 responsibility in the partnership, and need to be conversant with situations when they wouldn't give the injection without checking with a health care professional first.

Baseline investigations

The child or young person must have had baseline investigations.

Bloods:

- full blood count and differential white blood count
- liver function tests
- urea and electrolytes
- ESR (erythrocyte sedimentation rate) and C-reactive protein (CRP)
- varicella and MMR titres - if the titres are negative, have the *chicken pox* and *MMR vaccines* been offered prior to starting treatment (see *Paediatric resources 4*)?

  Note: Chest X-rays are not routinely performed prior to starting methotrexate in paediatric rheumatology (see side-effects section on pulmonary disease).

Consideration of risk taking behaviours

Nurses should identify sexually active young people and counsel them about the use of a reliable form of contraception, 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 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.

Reviewing concomitant medications

Review concomitant medications to exclude any potential drug interactions or contraindications (*British national formulary* BNF 2003, and *Summary of product characteristics of methotrexate* (2003). For further advice contact the local prescribing doctor.

Other screening issues

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

Subcutaneous injection technique

In the development of this guidance an audit of subcutaneous methotrexate administration technique around the UK was undertaken. Although the majority of practices are similar, there are a few minor differences, particularly in relation to needle size and angle of injection.

After reviewing the literature, this document advocates the following subcutaneous injection technique:

- socially clean skin is recommended, rather than the use of alcohol impregnated wipes
- there is no need to aspirate when the needle is in situ
- 12mm or less (preferably 8mm or 3/8th inch) length needles should be used
- current recommendations suggest that the finer 26G (brown) or 30G (yellow) are more appropriate for subcutaneous injections than the previously universally used 25G needles (orange)
- when using these 8mm or 12mm length needles pinch up the skin prior to injection at an angle of 90^{o} to ensure subcutaneous administration. If using longer needles pinching up of the skin and an angle of 45^{o} to 90^{o} might be more appropriate.

  Note: Despite colour end, there are varying needle lengths and internal bores of needle available.

It is important to note that this is guidance, and there is no general consensus in the literature about best practice. Children and young people differ considerably in size and amount of subcutaneous tissue, so it is important that the nurse assesses every patient individually to identify the size needle and technique that would be best for them. Weekly injections are often quite distressing for children because, despite age-appropriate explanations, they cannot always understand the reasons for their therapy. Therefore, there is a definite need to consider individual patient needs and preferences for needle colour, angle of insertion and speed of injection.

Training

Children, young people and their families should receive information about the treatment, understand the contra-indications, potential risks and side-effects. 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.

The child/young person and parent should have 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 trust policy. A training package has been developed to support families and nurses. This is intended as a guide and can be amended to suit individual need (see *Paediatric resources 3*).

The family should be informed that an annual review of home administration and competency will be undertaken to ensure safe practice.

When not to administer

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

- significant deranged blood tests (see side-effects section below). 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 chicken pox (see *Paediatric specific issues* and *Paediatric resources 5*). The parent/young person should inform their GP or treatment centre for appropriate advice.

Usual childhood coughs, colds and 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^{o}C) or a rash (that is different to any usual fevers or rash 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, post-dosing reaction, rises in liver enzymes and blood dyscrasias. Fertility concerns, lymphoma risk and pulmonary disease are less of an issue than in adults, but are considered here. Some children do get very distressed at even the thought of their weekly injection, and sometimes the hardest part (particularly in the younger child) can be to determine exactly what it is that is the most distressing for them - the sickness, the injection, or just the whole procedure.

Nausea and vomiting

Although many children are converted to parenteral methotrexate to lessen nausea and vomiting, many continue to experience it, and for some it may intensify as the dosage increases. Nausea, vomiting and perhaps the more troublesome anticipatory nausea, are hugely underestimated problems in children. Although anti-emetics are often used, their effects on patients are variable and rarely stop anticipatory nausea. Anticipatory nausea often affects the child for the whole day that their injection is due. It is thought to result from stimulation received by the vomiting centre from the cerebral cortex and the limbic system (Pearman 2002). The sickness felt is real, and this must be emphasised to them, 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
- folic acid supplementation
- withholding NSAID dosage on the injection day
- giving the injections on a Friday (to avoid school absenteeism)

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

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

The use of these measures has many advantages such as minimising side-effects, the practicality of use and ease of learning (Pearman 2002). Sometimes the sickness may be so disrupting to the young person and family that a clinical psychologist needs to be involved to promote coping skills. The sickness many children report must be taken seriously by health professionals. Often the whole family is involved in the preparation for the procedure, including calming and supporting the child with JIA, for as many as three-to-four days every week. This is probably the main reason for lack of compliance and subsequently stopping the drug.

Post-dosing reaction

Some children report "feeling yucky" the following day or two after their injection. They report GI upset, fatigue, malaise, and occasionally central nervous system symptoms such as headaches and mood changes (Ravelli and Martini 2000). Unfortunately, there is little help to offer except understanding, support, and reassurance that their symptoms are believed.

Liver toxicity and monitoring

Unlike adult RA, methotrexate-related liver fibrosis is not seen in paediatric rheumatology. However, rises in liver enzymes have been observed in children. Although there are no hard and fast rules concerning raised liver enzymes, Ramanan et al (2003) offers some advice. He states that current guidelines allow the transaminases to be raised up to twice the upper limit of normal. If the liver enzymes are higher than this, then the methotrexate is usually discontinued for 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%, 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).

Blood dyscrasias and monitoring

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. The ideal is fortnightly until stable, then monthly, and perhaps increasing to six-weekly. Responsibility for monitoring needs should be agreed locally. Good practice often involves a patient-held record, particularly when the parents or young person administer the injections.

Fertility concerns

According to Segal and Wilke, cited by Giannini and Cassidy (1993 p335), "because of the young age of many JIA patients, the effects of methotrexate on reproductive and sexual functioning are of less concern than in adult rheumatology, and the risks of long-term fertility problems or of delayed teratogenicity appear non existent".

However, due to its powerful teratogenic properties, best practice would be to counsel all young people of child-

bearing age to practice effective contraception (Ravelli and Martini 2000; Ramanan et al 2003).

Lymphoma risk

It is important to note that the oncogenic risk from low dose methotrexate therapy does not exceed that which would normally be expected in the normal paediatric population (Giannini and Cassidy 1993). There are only five published cases of lymphoma in children with JIA who were treated with low dose methotrexate (Cleary et al 2002).

Pulmonary Disease

Pulmonary disease is well documented in adults treated with methotrexate for RA. Over 60 cases have been reported, and therefore adults have a screening X-ray prior to starting methotrexate. There has only been one reported case in paediatric rheumatology (Cron et al 1998). Therefore, children do not routinely have pre-screening chest X-rays prior to methotrexate treatment.

Paediatric specific issues

Needle phobia

Needle phobia is a major concern in many paediatric areas. This has been addressed thoroughly in the literature, and many psychological interventions have been suggested (Smalley 1999). In some children referral to a child psychologist or play therapist may be necessary, although this may not be available in all local areas. The use of distraction techniques, bravery certificates and stickers may also prove useful. Topical anaesthetic creams can be used. However, many children, who use the creams for venepuncture, say that they do not work for methotrexate injections. Some families report that sometimes the anticipatory build up of putting the cream on for one hour prior to the injection can actually be worse than the injection. In such instances nurses may consider using a cold spray (although highly flammable).

Vaccinations

As with any immuno-suppressant therapy, guidelines on immunisation in the immuno-compromised child should be followed. The RCPCH guidelines (2002) state that live vaccines should not be given (see Paediatric resources 4). Family members should also avoid live polio vaccines because it is excreted in the faeces (Ramanan et al 2003). Inactivated vaccines can be given, but the child may not build up the appropriate immune response to vaccines while on methotrexate.

Chicken pox

Chicken pox is a major concern in paediatric practice, much more so than in adults. Paediatric resources 5 highlights the care for a child thought to be at risk of, or who develops chicken pox (the same can be applied to shingles infections). Measuring chicken pox titres in all children about to start methotrexate is now standard practice in most centres, and some even offer the chicken pox vaccine (Varilrix) to those who have negative titres. The vaccine is live and is given prior to starting methotrexate treatment. It is reported as being 70% to 90% effective. The vaccine is a single SC injection for children aged 12 months to 12 years. Adolescents over 13 years-of-age should receive two doses eight weeks apart. Unfortunately this will further delay starting methotrexate treatment. Infants under the age of one cannot receive the vaccine (Varilrix SPC information 2002).

It is also vital to note that if chicken pox develops, methotrexate should be discontinued until the last spot has crusted over and the child is clinically well. Antiviral drugs are usually prescribed. If a sibling develops chicken pox, and the child or young person on methotrexate has negative titres, varicella zoster immune globulin (VZIG) should be given.

Young people and 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% of all patients continue to have some limitation to activities of daily living (Martin and Woo 1997). Specific figures for many rheumatic diseases that continue into adulthood are harder to find, particularly since conditions such as ankylosing spondoylitis and juvenile systemic lupus erythematosus (JSLE) primarily present in adolescence rather than childhood. Adolescence is a difficult transitional time (Kroll et al 1999, Rapoff 2001) and the following needs special attention:

- identification and counselling of risk-taking behaviours, such as alcohol, drugs and unprotected sex
- lack of compliance, particularly when self-administering injections
- the practicalities of transition to adult care.

Patient empowerment is vital in promoting independence, and subcutaneous methotrexate administration is one such area where young people can begin to take control (McDonagh et al 2000). Encouraging, supporting and teaching young people about their treatments, side-effects, and how to self-administer medication usually encourages

their compliance. However, it has to be remembered that if the young person is self-administering, there need to be checks in place to ensure that they are continuing to comply.

Transition to adult care often does not happen seamlessly and therefore needs special consideration. 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?

Excreta

Best practice for handling excreta involves the use of gloves where there is contact with urine, faeces or vomit. In paediatric care, nurses, nursery teachers and schoolteachers are used to safe handling techniques for body fluids and excreta. Evidence suggests that methotrexate is excreted in urine for three days and in faeces for seven days (Allwood, Stanley and Wright 2002). This would mean that parents would have to constantly wear gloves when changing nappies or toilet training to protect themselves, which in the long term may prove impractical. Parents should be informed that there may be a potential risk of absorbing methotrexate metabolities from urine or faeces if there is significant skin contact. Research is needed to establish if there are any risks to facilitate future practice. Parents should be taught safe hand washing techniques and be helped to reach an informed decision about wearing gloves.

Pregnant mothers administering methotrexate to their children

It is the responsibility of the physician and nurse to inform women who are pregnant, breast feeding or those who are trying to conceive, about the potential risks of handling methotrexate because of its tetrogenic properties. There is very little evidence on this. Ultimately, it is personal choice, but the final decision made by the parent should be well documented. However, best practice advocates that parents do not give methotrexate injections in these circumstances.

Competencies

Ultimately each individual nurse is accountable for their own actions, and should not take on roles outside their abilities (NMC 2002). This section contains a background and guide to caring for children and young people receiving subcutaneous methotrexate. This document aims to inform, but does not assess an individual nurse's competency to administer and/or teach methotrexate administration. Therefore, rather than provide a list of competencies, it was felt that after reading this section the nurse should decide whether they feel competent to take on this role. The following are key areas the nurse should be able to discuss:

- what is methotrexate and why it is used in paediatric rheumatology, particularly SC route?
- the risks associated with handling and administering methotrexate, and ways to minimise risks
- the suggested administration technique
- what to do in case of accidental spillage
- paediatric specific issues that are relevant to caring and supporting families in our care
- risk management and clinical governance issues.

Summary of key points

This section of the document should be used as a guide for paediatric nurses caring for children, young people and their families receiving subcutaneous methotrexate. Only those qualified in caring for children and young people should care for them, and only those trained and competent in the handling of methotrexate should administer it. Due to limited published evidence, the content of this document is based on what is considered best practice at the present time. The aim is to provide guidance and to standardise care across the United Kingdom. Home administration of methotrexate is safe and ultimately improves child and family quality of life.

Paediatric resources

1. ILAR (International League of Associations for Rheumatology) 1997: classification of juvenile idiopathic arthritis (JIA)

The following can only be diagnosed after six weeks:

1. Oligoarticular onset: – 4 or fewer total joints involved.

   Extended Oligoarticular: – > 4 joints involved after the first 6mths of disease.

2. Polyarticular onset rheumatoid

   Factor Negative: – 5 or more joints during the first six months of disease with no detectable Rheumatoid Factor.

3. Polyarticular onset rheumatoid

   Factor Positive: – 5 or more joints during the first six months of disease and when Rheumatoid Factor is detected on at least two occasions at least

   3 months apart.

4. Systemic onset: – arthritis of any number of joints with a documented typical high quotidian spiking fever of at least two weeks duration and one or more of the following:
   - transient episodic erythematous rash,
   - enlargement of liver or spleen
   - serositis.

5. Psoriatic arthritis: – arthritis and psoriasis or arthritis and at least two of the following:
   - dactylitis
   - nail abnormalities (pitting)
   - family history of psoriasis confirmed by a dermatologist in at least one first-degree relative.

6. Enthesitis-related arthritis: – previously known as juvenile spondyloarthropathy.
   1) Arthritis and enthesitis, or
   2) arthritis or enthesitis plus two of the following:
   - sacroiliac joint tenderness, inflammatory spinal pain, or both
   - HLA-B27
   - family history in first, or second degree relative of medically confirmed HLA-B27-ve associated disease
   - acute anterior uveitis
   - onset of arthritis in a boy after the age of 8 years.

7. Other arthritis: – any form of idiopathic chronic arthritis, which does not fit into the above categories.

(Cassidy and Petty 2001)

2. How to calculate body surface area

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

$$\sqrt{\frac{\text{Height (cm) X weight (kg)}}{3{,}600}} = \text{m}^2$$

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

$$\sqrt{\frac{100\text{ (cm) X }30\text{ (kg)}}{3{,}600}} = 0.91\text{m}^2$$

If this patient receives MTX 15mg/m^2 / week, she/he will receive weekly:

0.91m^2 (BSA) x 15mg = 13.65mg/week

To calculate the MTX dose m2 /week:

$$\frac{1}{\text{BSA}} \text{ X dose (mg) per week} = \text{dose m}^2\text{ / week}$$

To calculate the MTX dose m^2 /week if this child receives 10mg MTX per week:

$$\frac{1}{0.91} \text{ X dose10mg/week} = 10.99\text{mg /m}^2\text{ /week}$$

3. Teaching package for parents, young person or child: how to handle methotrexate when using pre-dosed, ready-to-use syringes

This is a step-by-step guide to giving 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 15 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. Methotrexate is a cytotoxic drug that is used in high doses to treat cancer patients. In rheumatology the drug is used in much smaller doses to produce an anti-inflammatory effect.

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. Most often, children will be started on a moderate dose that is gradually increased until the disease is controlled.

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 nights means that school is not missed if there is some stomach upset the next day. The vitamin folic acid can help to prevent this. Sometimes missing a dose of anti-inflammatory drug, using regular anti-sickness drugs and/or changing to the injectable form of methotrexate is helpful
- mouth ulcers - these usually respond well to treatment with folic acid
- effects on the blood count, 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. Reassurance is often needed that the symptoms will improve on their own, and the drug restarted.

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 will 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 alright, but please inform your nurse so that they can make other arrangements.

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

- wash your hands thoroughly before and after giving the injection
- always handle the syringe and needle carefully
- the syringes will be specifically for your child only. They should always contain the exact amount to be given, but each time you must check this
- keep the syringes in a storage box with a lid such as non-transparent plastic box
- look carefully at your syringes to see whether you need to store them in the fridge or at room temperature and follow the instructions. If you are unsure, please ask your nurse for help
- if they are to be stored in the fridge, please keep the box on the bottom shelf and away from food. If there are young children in the family it may be wise to fit a fridge lock. Some drug companies provide a separate fridge to store the syringes (the syringe can be kept at room temperature for 30mins prior to injection)
- if the syringes are to be kept at room temperature, please store the box out of reach and sight of children and pets. During very hot summers the syringes may need to be refrigerated. If unsure ask your nurse
- you will be given a sharps bin to dispose of the syringes, needles and gloves. This should be kept closed until three-quarters 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, but further information can be obtained from the Environment Agency www.environment-agency.gov.uk

- if you are trying for a baby, pregnant or breast-feeding it is recommended that you do not handle the drug. Please discuss this further with your child's doctor.

What to do when dealing with spillages:

On the skin

Wash the affected area with plenty of soap and water. Do not scrub as intact skin provides protection. Contact your rheumatology team or nurse for advice if you are concerned.

In the eyes

Wash the eye(s) using plenty of water for a couple of minutes. Contact your doctor for advice if your eyes become sore or if you notice any changes in your vision.

On work surfaces or floors

While wearing protective gloves, cover the spillage using absorbent paper to mop up any excess liquid. Wash the area with plenty of water, then soap and water. All paper/cloths used should then be put in the cytotoxic sharps bin provided.

On clothing

Wear a pair of gloves blot dry with paper towel. Clothing should be changed and washed separately to other items.

Always wash hands thoroughly.

When not to give subcutaneous methotrexate

You would not give the methotrexate injections if:

- your child is unwell, and you do not know why. Your child may have a high fever (over 38.5^{o}) or an unusual rash. Usual childhood coughs and colds are nothing to worry about, but if your child is sicker than normal contact someone for advice
- your child's blood results are abnormal. Children with rheumatic diseases often have raised blood values. However, if they are outside the expected normal limits contact someone for advice
- your child has come into contact with chicken pox or develops chicken pox. **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 helpline number.

How to give methotrexate injections at home

Checking you have the right equipment:

- methotrexate syringe for injection
- clean table surface
- appropriate needle
- cytotoxic-labelled sharps bin
- pair of disposable gloves (unnecessary if the child/young person is self-administering)
- scissors
- a cotton wool ball or clean tissue
- spot plaster if desired
- spillage kit accessible just in case.

Preparing your working area:

1. collect the equipment and take it carefully to where the injection will be given before you start assembling. If possible, try to give the injection in a non-carpeted room in case there is a spillage
2. your child should be present in the room before beginning
3. only people who are helping you should be present in the room - no pets
4. wash working surface with liquid detergent and allow to dry
5. arrange the equipment on the clean surface
6. wash your hands carefully, dry with kitchen roll
7. put on gloves (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. make sure the injection site is clean by using soap and water
9. cut the top off the sealed bag containing the syringe, and gently tip out onto your working area.

Giving the methotrexate:

1. check the injection has your child's name on it, has not expired and is the right dose
2. peel open the end of the needle packet carefully. While holding it in one hand and the syringe in the other, remove the syringe cap and attach them together. Put the syringe cap straight into your sharps bin. Do not touch the syringe end or the needle tip
3. alternate the injection site from week-to-week so it doesn't get sore
4. inject into the thigh, back of the upper arms, or stomach - but a minimum of 5cms away from tummy button. If giving two injections (such as methotrexate and etanercept) they should be given in totally different sites. For example, one should be given in the right thigh and one in the left. They should be at least

3cms apart if given in the same limb. Some children do not have much subcutaneous fat on their arms, so the thighs are often the most appropriate place (see figure 1)

5. gently pinch the skin together (see figure 2) and insert the needle fully at 45º to 90º angle depending on the size of the child, the amount of subcutaneous fat, length of needle and the site. Inject the methotrexate. Generally use a fairly slow and even speed. However, many children request their injections are given fast, and this is also fine
6. let the skin go, withdraw the needle and press gently on the injection site with a clean tissue
7. straight away dispose of the used syringe, needle, tissue and gloves in the cytotoxic-labelled sharps bin
8. the date of the injection and site used can be recorded on a diary sheet.

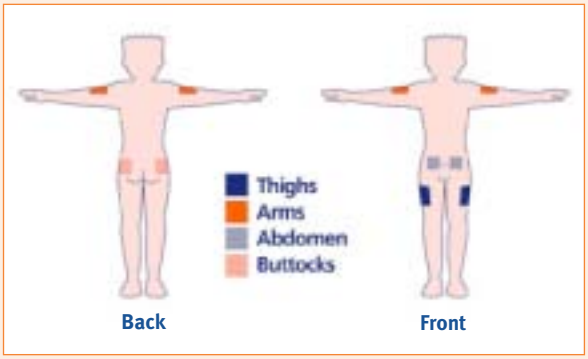


figure 1

figure 2

After administering the methotrexate:

1. used syringes, needles and gloves must be placed in your cytotoxic-labelled sharps bin. The bin must always be stored out of children's sight and reach and always closed. 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
2. unused syringes should always be returned to your local hospital pharmacy or delivery service
3. if only part of the dose is given, the remainder should be discarded in the sharps bin
4. change gloves if they are punctured or torn
5. wash hands thoroughly with soap and water after the procedure.

Training checklist for home administration of subcutaneous methotrexate by child, young person or parent

Patient name:

Person taught:

Assessor:

Skill	Date shown/ trainer discusses	Dates supervised	Date completed/ proved competence by trainee	Patient and/or carers signature	Assessors signature
1. Been given verbal and written information on methotrexate. Can discuss why it's given		N/A			
2. How to acquire the syringes		N/A			
3. Understand storage requirements		N/A			
4. Can discuss side-effects		N/A			
5. Preparation of equipment					
6. Correct hand washing techniques					
7. Use and disposal of gloves					
8. Checking and opening of all equipment					
9. Administration of subcutaneous methotrexate					
10. Tidying up the equipment					
11. Knowledge of handling of spillage and use of spillage kit		N/A			
12. How to dispose of any unused methotrexate		N/A			
13. Can discuss instances when not to give the injections		N/A			
14. Knows who to contact in case of any problems.		N/A			
Signed certificate of instruction	**N/A**	**N/A**			

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

Patient name:	
Address:	
Telephone number:	

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:	
Starting dose:	
Dates and doses of any increases:	
Name and address of prescribing doctor:	
Telephone number (if appropriate):	
Name of nurse involved in 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:	

4. Vaccine information for children with rheumatic diseases receiving methotrexate

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

- cholera
- diptheria
- haemophilus influenza HIB
- heaf (6 needles) /mantoux (PPD) test
  (can be difficult to interpret if immuno-compromised)
- hepatitis A
- hepatitis B
- influenza (flu vaccine)
- meningitis C
- Pneumovax
- rabies
- tetanus
- typhoid (by inactivated injection only)
- only the *injectable* polio **(SALK)**.

Live vaccines *cannot be given*, these include:

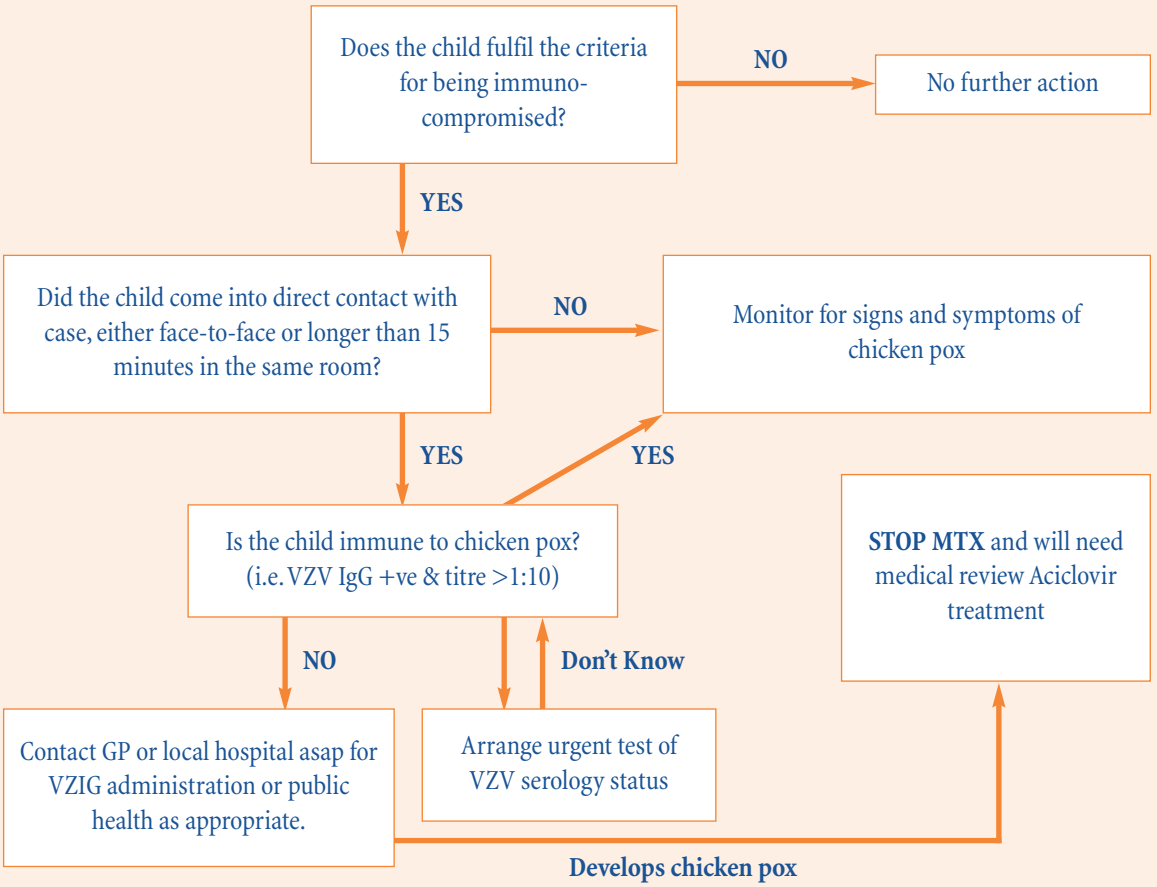
- BCG
- individual measles
- individual mumps
- individual rubella
- MMR
- oral polio
- typhoid (oral)
- yellow fever
- Varilrix (chicken pox) - sometimes this can be organised
  prior to starting methotrexate, however, this does delay commencement of drug.

5. Algorithm for chicken pox contact

Criteria for immuno-compromised child:

- receiving MTX
- receiving prednisolone at daily dose (or equivalent) of 2mg/kg for at least 1 wk or 1mg/kg for at least 1 mth. (Anyone taking >40mg total dose for 1 wk)
- anyone receiving above Rx in last 3 months.

(Children receiving anti-TNF therapy [etanercept, infliximab, humira], cyclophosphamide and long-term low dose oral steroid therapy, may also be considered to be immuno-compromised, although not cited in this 2002 RCPCH algorithm.)



Please note:

1) VZV serology may be difficult to interpret if IVIG has recently been given
2) VZIG is not indicated according to current guidelines if 10+ days have elapsed since contact, but risks remain
3) protection from VZIG lasts for 4 weeks
4) children on MTX alone are thought to be at lower risk than those also taking steroids
5) MTX should be discontinued until the last spot has crusted over.

Immunisation of the immuno-compromised child: Best practice statement 2002, RCPCH

10 Conclusion

This document has been developed to inform practitioners on the key issues related to the administration of the cytotoxic agent subcutaneous methotrexate in adults and children. There are a number of non-malignant indications for prescribing methotrexate, and this guidance has focused on the administration of subcutaneous methotrexate for rheumatoid arthritis and inflammatory arthritidies.

Clinical practice has been to initiate treatment with oral methotrexate. However, recent research evidence has highlighted the value of using the subcutaneous route, starting methotrexate promptly at diagnosis and rapidly increasing the prescribed weekly dose until clinical indicators demonstrate effective disease control (Porter et al, 2003).

The report highlighted two specific issues focused on research using parenteral routes of drug administration:

1. some individuals are unable to tolerate oral methotrexate
2. bioavailability is improved using subcutaneous treatment.

As a result of evolving needs in clinical practice the use of parenteral methotrexate is now becoming established practice in the field of rheumatology care.

Appendices

Appendix 1: Glossary of terms and definitions

Arthritidies

This is the plural of arthritis - often referrred to as inflammatory arthritidies - covering the group of inflammatory forms of arthritis.

Bioavailability

The amount of drug that reaches the blood system regardless of how it is given. After an intravenous injection bioavailability is 100%, 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

…*"drugs which are active against neoplastic disease (Perry, 1992), but they can be classified according to their mode of action as alkylating agents, anti-metabolites, anti-tumour antibiotics, plant alkaloids, hormones and a wide range of other drugs which exhibit cytotoxic effects"*
(Holmes, 1990 cited in RCN, 1998).

Hazard

The Approved Code of Practice (ACOP) published in the Health and Safety at Work Regulations (1999) states: *"A hazard is something with the potential to cause harm (this can include articles, substances, plant or machines, methods of work, the working environment and other aspects of work organisation"*

(Dimond, 2002b).

Parenteral

Administered by any way other than through the mouth.

Research categories

Taken from Agency for health care policy and research (AHCPR, 1992) and quoted in the RCN (1998).

Grade A:
requires at least one randomised controlled trial as part of the body of literature of overall good quality and consistency addressing specific recommendations.

Grade B:
requires availability of well conducted clinical studies but no randomised clinical trials on the topic of recommendation.

Grade C:
requires evidence from expert committee reports or opinions and/or clinical experience of respected authorities. It indicates absence of directly applicable studies of good quality.

Risk

A *risk* is the likelihood of potential harm as a result of a hazard.

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 fetus

Vesicant

An agent that causes blistering of the skin.

Appendix 2: Risk assessment checklist

The aim of risk assessment is to examine working practice and identify hazards or risks that have the potential to cause harm. In the process of undertaking this assessment you should ensure that you have a clear understanding of the level of risk (high, medium, low) and ensure appropriate measures are used to reduce all risks to an acceptable level. Support and advice on what constitutes an acceptable level of risk will be subject to clinical governance frameworks for the organisation and what are considered national agreed standards of practice.

Practitioners should ensure they are familiar with:

- Nursing and Midwifery Council (2002) *Code of professional practice, Guidelines for records and record keeping and Guidelines for the administration of medicines.* London: NMC
- Health and Safety Executive (2002) *Health and safety at work legislation related to risk assessment and management.* London: HSE
- local trust policies related to clinical governance and risk management
- trust ethics committee (Caldecott guardian) in relation to any data collection or issues of patient confidentiality (Department of Health, 2003).

The proforma in this guidance document has been prepared as an example of documentation that could be modified or used in its current form to aid practitioners in carrying out a risk assessment for the development of a patient self administered subcutaneous methotrexate programme.

Five steps to risk assessment (HSE, 1999):

1. identify hazards/risks
2. decide who might be harmed and how
3. evaluate the risk and decide whether existing precautions are adequate or whether more should be done
4. document your findings
5. review your assessment and revise it if necessary.

Example of risk assessment checklist

Likelihood rating = the likely outcome if objective fails to be achieved

Risks calculated in example are theoretical. Weighting of some risks will be relevant to individual patient/practitioner/trust

MR = minor risk - non-permanent harm (up to one month)

MO = moderate risk - semi-permanent harm (up to one year)

MA= major risk - major or permanent harm

C= catastrophic - death likely outcome

Process	Planned action	Tick if achieved	Risk if objective not achieved: Category
Preparation, screening and assessment of patient for treatment with methotrexate	✦ formal education pathway ✦ assessment and screening ✦ written and verbal information ✦ patient consent obtained		✦ poor concordance in treatment and monitoring **(MO)** ✦ poor understanding of side-effects and reasons to stop treatment **(MA/C)** ✦ pregnancy while on treatment **(MA/C)**
Patient training package for administration via subcutaneous route	✦ patient (and carer) competent in safe storage, preparation, administration and disposal of waste ✦ good injection technique ✦ informed, knowledgeable patient		✦ unsafe practice subjecting to patient/family and community to risk of exposure to cytotoxic agent or accidental injury **(MO)** ✦ Personal injury to patient **(MO)**
Facilities, infrastructure and financial resources	✦ safe environment ✦ appropriate equipment ✦ appropriate staffing levels ✦ pharmacy department support including appropriate productions facilities if necessary ✦ recognised area for training patients ✦ trust staff aware of work and processes/risks ✦ primary care team and supporting teams informed and able to communicate effectively ✦ telephone helpline support		✦ risk of drug errors/accidental spillage injury **(MO/MA)** ✦ increased risk of staff areas due to workload ✦ poor communication increases risk of patient errors **(MO/MA/C)** ✦ failure to adhere to protocols and monitoring **(MO/MA)** ✦ patient waiting times and support affected **(M)** ✦ patient waiting times/demands on service increase with additional strain on resources **(MO/MA)**

Process	Planned action	Tick if achieved	Risk if objective not achieved: Category
Drug management	✦ protocols to support patient/pharmacy and practitioners in clinical practice ✦ use of named patient pre dosed pre-filled syringes to reduce medication errors and reduce risk of exposure/spillage ✦ training and regular review of practitioners and staff in competencies		✦ unreliable standards of care leading to errors in prescribing and management of methotrexate **(MO/MA)** ✦ additional need for protective clothing and safety measures leading to increased risk of accidental exposure or drug errors. Procedures that are more complex for patients and therefore increased risk of errors in preparation **(M)** ✦ drugs unavailable at appropriate time for patient **(MR)**
Practitioner training and review	✦ aware of legislation governing cytotoxic therapies ✦ aware and attends statutory training days ✦ regularly updated ✦ documentation & audit trail ✦ expert practice ✦ able to develop service according to needs of patients & service		✦ risk of dangerous practice **(MO/MA)** ✦ documentation fails to reflect care and provide audit trail for review and monitoring of patients **(MO/MA/C)** ✦ service fails to develop according to risk assessment and patient need **(MO/MA)** ✦ identification of system errors fail due to poor knowledge and practice **(MO/MA)** ✦ service fails to develop in line with national guidance/evidence based practice **(MO/MA)**
Patient training and review	✦ patient understands rationale for practice ✦ confidence in administration and support ✦ informed of side-effects/risks of treatment and when to seek help/or withhold treatment ✦ self-management enhanced ✦ review of competencies maintains standards		✦ errors occur due to misunderstanding or poor concordance **(MO/MA)** ✦ anxiety and poor technique may put patient (or carer) at risk **(MO/MA/C)** ✦ safe practice in storage and disposal of waste not fully understood **(MO/MA)** ✦ treatment given when it should be withheld (eg breathlessness) **(MA/C)** ✦ continuing stress on services and unpredictable crisis intervention **(MO/MA)** ✦ standards deteriorate over time - poor practice increases overall risk **(MO)**

Appendix 3: Practitioner training and competencies

Practitioner training package

This is a suggested training package for rheumatology practitioners supporting patients, or their carers, in the administration and management of subcutaneous methotrexate.

An in-house course/in-house training/seminar/workshop/specialist training programme should contain the following elements:

Pharmacology

- the cell cycle and methotrexate mechanism of actions
- dealing with short and long term side-effects
- indications, contra-indications and interactions
- folic acid supplementation and folinic acid rescue
- fertility and contraception.

Health and safety

- COSHH
- risk assessment
- dealing with spillage
- disposal of methotrexate.

Patient care

- screening for eligibility of treatment
- counselling a patient for methotrexate therapy
- assessment of the disease process
- holistic care
- monitoring
- providing education and training of the patient/carer
- patient consent.

Principles of practice

- accountability
- code of conduct
- scope of professional practice
- competency
- clinical governance.

Assessment

- evidence of supervised practice with a competent practitioner
- reflection on independent competent practice
- annual review at professional development review scheme/appraisal.

Training in the administration of chemotherapy

There are rigorous training and competency criteria for specialist oncology staff administering a wide range of cytotoxic therapies using various parenteral routes such as intravenous and intrathecal for specialist oncology services. The training criteria reflect the level of risk related to daily practice in an oncology unit using a range of invasive procedures and routes of administration.

There are currently no equivalent training packages for rheumatology practitioners. This guidance is based on ensuring that the competent practitioner can undertake a thorough risk assessment, and provide appropriate clinical care to improve patient management of self-administration. Practitioners should maintain their knowledge base and expertise by ensuring good liaison with the oncology team, sharing good practice and maintaining access to potential training opportunities.

Clinical need may vary from unit to unit and some practitioners may provide support to other rheumatology patients receiving intravenous cyclophosphamide and other cytotoxic therapies. It is essential that practitioners assess the level of risk and identify the competency frameworks that they should attain in order to maintain safe practice. It may be appropriate for some practitioners to undertake the N59 course (or equivalent).

Competencies framework

Supervision and competency achievement should ensure that the practitioner is able to:

- administer methotrexate by the subcutaneous route
- teach patients and/or carers to perform home administration.

The following competencies framework shows how to achieve this.

Name of practitioner:

Name of supervisor:

ELEMENT OF COMPETENCE TO BE ACHIEVED	Date of achievement	Practitioner signature	Supervisor signature
Discuss the rationale for the use of subcutaneous methotrexate in rheumatic conditions			
Describe the physiological effects of methotrexate			
Discuss potential issues related to treatment including: ✦ unlicensed indication for treatment ✦ screening of patients ✦ possible side-effects or adverse events ✦ drug interactions ✦ contra-indications 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 handing ✦ contamination ✦ preparation (and where applicable reconstitution) ✦ policy for hand washing			

ELEMENT OF COMPETENCE TO BE ACHIEVED	Date of achievement	Practitioner signature	Supervisor signature
✦ dealing with spillage and disposal of cytotoxic waste ✦ the use of protective clothing ✦ ensuring a quiet and safe environment ✦ preventing unnecessary exposure to other people ✦ travelling and transporting methotrexate.			
Demonstrate the ability to provide the patient/carer with a suitable and clean environment			
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 trust 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. These should include: ✦ medical records/assessment sheets ✦ patient/carer completed documentation ✦ prescription sheet ✦ helpline follow up ✦ evidence of audit trail for patients on treatment numbers of patients commencing and discontinuing treatment and reasons for stopping treatment (according to local trust policy).			
Discuss accountability in relation to the administration of subcutaneous methotrexate			
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 and folinic acid rescue treatment in patient's receiving subcutaneous methotrexate			
Identify the ways of maintaining current competency			

Practitioner's acceptance of accountability

1. I have read and understood the Scope of professional practice (NMC,1992)
2. I have read and understood the Professional code of conduct (NMC, 2002)
3. I have attended a *course/workshop/seminar/specialist training programme.

Organised by | (Date attended)

*(*delete as appropriate)*

4. I have completed supervised practice to a level at which I feel confident and competent to:
   - practice the administration of subcutaneous methotrexate
   - teach patient's/carer's home administration of subcutaneous methotrexate.

Name of practitioner: (PRINT)

Signature of practitioner:

Title:

Date:

I declare that I have supervised this practitioner and found her/him to be competent to perform subcutaneous methotrexate and teach patients and carers to administer the therapy at home as judged by the above criteria.

Name of practitioner supervising

Signature of practitioner supervising:

Title:

Date:

Appendix 4: Patient information and training

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

Procedure

- consultant rheumatologist 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 (or carer) is aware and able to comply with health and safety regulations on the storage and disposal of drugs and equipment
- patient (and/or carer) attend the educational sessions and satisfies the nursing service of their competence in:
  - administering the drug by the subcutaneous route
  - ability to comply with the correct storage and disposal of equipment
  - concordance with the training, follow up and blood monitoring.
- if the patient fails any of the above criteria or does not wish to proceed with subcutaneous administration the nursing service will liaise with the prescribing doctor and patient to plan future treatment options
- once the patient has successfully completed the training programme a letter will be sent informing the patient's general practitioner.

Continuing patient management

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

Patient training guide

Introduction

This is a step-by-step guide to help you give yourself an injection of methotrexate by subcutaneous (under the skin) injection. This training programme helps you have more control and independence at the same time as receiving treatment for your arthritis. If you feel that you do not want to inject yourself or receive this treatment please let the nurse or practitioner know.

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 chose a day when you have a good routine and can plan your once a week injection.

Methotrexate is a cytotoxic drug. Methotrexate is used in small doses to treat patients with 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 about ten years to treat arthritis. It is a well recognised treatment for arthritis that research studies show works well and that is reasonably safe.

The tablet form *is licensed* but it is important for you to know that methotrexate injections are *not licensed*. In the last few years methotrexate injections for arthritis have been shown to be effective and safe. If you have concerns or wish to understand more about the treatment and why it is not licensed please ask your nurse or doctor for more information.

Subcutaneous injections have been shown to control arthritis well and often people 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 prepare and give your injections. Information and help will be available to support you while you learn.

What happens when you decide to inject methotrexate

You and/or your carer will be:

1. given information to read about the drug and have time to ask questions
2. shown how to prepare the things you need to inject yourself and give the injection

3. able to practice getting the injection ready and giving the injection with a nurse or a member of the team supervising.
4. when you have managed this you or your carer will prepare and give the injection at home.

At each stage of the teaching process you or your carer will be asked to sign a form. The form asks you to sign if you feel you have been given enough support and training to be able to give your own injections. It is important that the rheumatology team know that you are confident and safe to continue with the next step.

A final assessment will take place when you, your carer and the nurse are sure that you are competent to self-inject at home. You and/or your carer will be asked to sign a consent form and record to say that you are able to do the injection safely and understand how to handle any possible problems.

Make sure that these instructions are always close to hand in case you have any queries or problems.

Remember

It is safe for anyone to handle the methotrexate syringe sealed in the wrapper, but only people trained to handle methotrexate should touch the syringe or equipment once out of the wrapper. The storage of the methotrexate should be in a non-transparent secure plastic box in the bottom of your fridge.

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 helpline service. It is important you follow this advice:

- you (or your carer) *must not handle* or give methotrexate if you are trying for a baby or you think you may be *pregnant* or are *breast feeding*
- always make sure that you keep the methotrexate syringe in the plastic sleeve and in a plastic box where it is safe and out of sight and reach of children and family pets
- remember to keep the information about spillage kits close to hand in case of breaks or accidental spillage
- always check your syringe carefully to be sure that all the details are correct, including the name of the drug, dose and that the drug is in date and the methotrexate looks normal (yellow and clear). Contact the pharmacy or nurse helpline if you need advice
- 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
- do not transport methotrexate injections on public transport.

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

If you are not able to have regular blood monitoring or attend follow up appointments you will not be given methotrexate.

Equipment

You will be given the following equipment:

- a cool bag for collection of pre-filled syringes (local variations may apply)
- a cytotoxic sharps waste bin/cytotoxic tape
- needles (Brown) 26G 8mm
- cotton wool balls
- dot plasters
- gloves and apron if a carer is undertaking the administration
- spillage kit.

The pack containing the syringe will already have your dose of methotrexate in it. Store the syringes in a plastic container with a lid in the refrigerator unless directed otherwise.

If you have a young family or live with a young family you may need to buy a locking device for the fridge. It is important that you warn children of the dangers.

Supplies of methotrexate and equipment

Make sure you know how you get your methotrexate syringes. Sometimes the syringes need to be collected by you and/or your carer from the hospital or community hospital pharmacy. It may also be delivered directly to you at home or to your health centre.

How to give a methotrexate subcutaneous injection

Getting the equipment ready:

Use the lid from your plastic storage box as an injection tray

- 1 methotrexate syringe for injection (if refrigerated, you can allow the injection to come up to room temperature by taking out of the fridge for approximately 30 minutes)
- 1 brown needle
- 1 cytotoxic sharps waste bin and tape (if provided by your hospital)
- 1 cotton wool ball
- 1 dot plaster (optional)
- spillage kit
- kitchen roll
- pair of disposable gloves and plastic apron (carer only)
- 1 pair of scissors.

Preparing your working area:

1. wash and dry your hands thoroughly and clean your preparation area (for example a work surface a clean tray or lid)
2. collect all of the above equipment and place onto a clean table or worktop surface (you may want to use a piece of kitchen roll on top of your clean work surface)
3. only people who are helping you should be present in the room (avoid distractions such as children and pets)
4. 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
5. decide where you will give the injection. You will need to ensure you change the injection site each week to reduce the risk of soreness (see figures 2 and 4 overleaf)
6. use dedicated scissors to cut the top off the sealed bag containing the methotrexate syringe and tip onto your injection tray, and handle the syringe carefully. Do not tear bag open with teeth.

Giving the methotrexate injection:

1. sit or stand comfortably
2. check the syringe is in date, has your name on it and it is the correct dose. If it is incorrect in any way you must not give the injection but check with your rheumatology department or pharmacy
3. check the syringe contents to make sure that it is a clear yellow solution. If it does not look like this or has particles in it you should not give the injection but contact the rheumatology department or pharmacy
4. if everything is correct peel open the needle packet
5. remove the screw stopper at the end of the syringe and then screw the needle onto the syringe
6. loosen the needle cover. Do not allow the needle to touch the injection tray or anything else because it will contaminate it. If this happens discard the needle in the sharps box and use a new needle
7. place the ready syringe with needle cover loosely in place back onto the injection tray
8. ensure that there is a cotton wool ball ready and an open dot plaster if used
9. pick up the syringe and remove the needle cover. Hold the syringe low down the barrel as if you are going to write your name with a pen
10. make sure the needle does not come into contact with anything on the way to the skin so to avoid contamination and the risk of introducing infection
11. with your free hand pinch the skin where you are going to inject and insert the needle at right angles (90^0 degrees). The needle will deliver the injection just below the skin (subcutaneously). See figures 1 and 3
12. once the needle is in place release the pinch on the skin and support the syringe with both hands. With your preferred hand push the syringe plunger slowly down and deliver the injection
13. when you have injected all of the methotrexate remove the needle and syringe from your skin and put the syringe directly into the sharps bin and place a cotton wool ball firmly over the injection site
14. when there is no leaking of fluid or blood from the injection site apply a small dot plaster, which can be removed after half an hour.

Figure 1: Picture showing how to pinch the skin before injecting

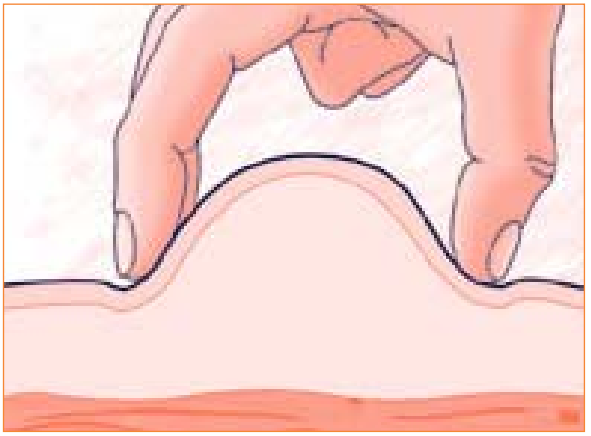


Figure 2: Picture showing injections sites

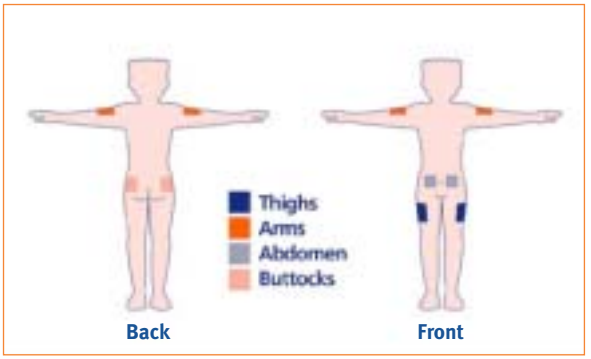


Figure 3: How to inject the needle at right angles or a 90° angle

Figures 1, 2 and 3 reproduced by kind permission. © 2003 Becton, Dickinson and Company

Figure 4: Example injection site diary sheet

If you have to give yourself two injections of different drugs, for example, methotrexate and etanercept, it is important that you don't inject both drugs close to each other. It will be helpful if you can keep a record of what you are injecting, into which site. The example below uses one biologic therapy (adalimumab) given once every fortnight.

Date	Right Leg	Left Leg	Stomach	Comments
10 June 2004	Methotrexate			Blood test yesterday
13 June 2004			Adalimumab	Results of blood tests – okay
17 June 2004			Methotrexate	
24 June 2004		Methotrexate		
27 June 2004	Adalimumab			

What to do after the injection

Do not put any of the used items in with your normal household waste just discard the used syringe, cotton wool ball, screw top, packaging, gloves and apron (if using) into the sharps bin. The bin must be stored out of sight and reach of children and closed, but not locked. Your next injection will be due in one week's time.

After the injection:

1. wash and dry your hands
2. replace the lid onto your methotrexate storage box
3. record the site and date of the injection in your diary sheet if using
4. 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. This sometimes happens if the needle has punctured a small blood vessel, and will soon stop and the bruising fade
5. on rare occasions methotrexate can leak into the surrounding skin causing irritation when patients give a injection. If this happens and it causes irritation or redness contact the rheumatology helpline.

Dealing with spillage

- keep the spillage kit and instructions at hand whenever you inject and make sure that your carer or family members are aware of how to use it
- the amount of methotrexate you are injecting is very small, but it is possible to accidentally spill it
- if there is a spillage follow the instructions in the spillage kit.

Spillage onto skin:

Wash the affected area with plenty of soap and water. Do not scrub because unbroken skin provides protection. Contact your rheumatology nurse or doctor if you have any adverse reactions.

Spillage into the eyes:

Wash the eye(s) with plenty of water for at least five minutes. It is recommended that you should contact your own doctor, local hospital emergency department or eye hospital.

Spillage onto work surfaces and floors:

Cover the spillage with absorbent paper such as paper towels or kitchen roll. Make sure they surround the outside area and absorb all the fluid to prevent the methotrexate spreading. Wear the protective rubber gloves and discard the used paper towels into the cytotoxic waste bin or bag.

Wash the spillage area well with lots of water, then clean with soap and water. Discard all waste into the cytotoxic waste bin.

Spillage onto clothing:

Wear the protective rubber gloves and blot dry with paper towel or kitchen roll. Clothing should be removed immediately and washed separately from other clothing.

All equipment used to handle spillage should be placed into the cytotoxic waste bin or bag. You will need to inform your rheumatology department or methotrexate waste collection to arrange for disposal of the waste and for supply of another spillage kit.

If you have spilt and lost a treatment then you may not have enough methotrexate before your next prescription. Contact the rheumatology department or pharmacy to arrange for collection or delivery of a further supply.

Accidental needlestick injuries

If you follow the instructions carefully the chances of you getting an accidental needlestick injury are very small. If you or your carer accidentally come in contact with the needle while preparing or disposing of the syringe it is important to make the puncture site bleed. Then wash the areas with copious amounts of running water and cover with a plaster. Contact your own doctor's hospital, and let the rheumatology department know that you have had a needlestick injury. They will record what has happened and check to see whether anything else can be done to ensure this doesn't happen again.

Travelling away from home when you inject methotrexate

The storage of your injections will vary according to local health policy and the manufacturer's recommendations. However, caution is needed in hot climates over 30 degrees centigrade. You should seek specific advice on storage at high temperatures. Discuss the details of storage with your nurse, practitioner or pharmacist. The injections you receive for travel will depend on the hospital or company that provides your methotrexate. Make sure that you check the box for instructions on how to store it if it is different from your usual treatment.

Some of the options that are available for when you are going on away are to have:

- tablets instead of an injection
- methotrexate injections in a cool bag and using ice blocks until you reach your destination

- methotrexate injections that do not require refrigeration if your rheumatology department/pharmacy can supply them
- an injection just before you travel and then one as soon as you return. Discuss this with your rheumatology department.

If you are flying it may be possible to get the airline company to refrigerate your methotrexate when you are on the plane. Check this because some companies do not do this because of security risks. Needles and equipment will only be allowed on flights if they are stored in your checked-in luggage, *and not in your hand luggage*. Again check this with the airline in good time. You may need to discuss this with your methotrexate supplier, and get a supporting letter from your rheumatology department before you go away.

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

Care when you have been on methotrexate for some time

If you have been using methotrexate for some time it may be possible for you to collect your injections and have your blood test without seeing the rheumatology nurses on a regular basis. Check with your local hospital how often you will need to be seen, what to do about your blood tests and what to do if there is a problem with the blood tests. You should receive written information on the possible problems.

Rheumatology helpline

You can always use the helpline for advice. You should be given information about how your helpline works and how long you will have to wait for advice. You should also be told what to do when the helpline service is not available.

Training checklist for home administration of subcutaneous methotrexate by patient or carer

1. The principles of subcutaneous methotrexate therapy
2. The safe and effective administration of subcutaneous methotrexate

Name of practitioner:	
Name of patient:	
Name of carer: (where appropriate)	

ELEMENT OF COMPETENCE TO BE ACHIEVED	Date shown	Dates supervised	Date completed sign	Nurse assessor sign	Patient/carer sign
Patient/carer is able to discuss the reasons for using subcutaneous methotrexate in their case					
Patient/carer is aware that subcutaneous methotrexate is an unlicensed drug					
Patient/carer can describe and recognise the potential complications/side-effects and interactions of methotrexate					
Patient/carer can describe the circumstances when they would not give the methotrexate injection					
Patient/carer can describe the circumstances when they need to contact the rheumatology department					
Patient/carer can accurately check injection details such as dose, expiry date and person it should be given to					
Patient/carer can give the subcutaneous methotrexate injection using a safe technique					
Patient/carer can describe the following health and safety requirements for methotrexate injections: ✦ how it should be stored ✦ checking the equipment and drug ✦ how to prepare the methotrexate safely ✦ the type of environment required for home administration ✦ how to protect others from methotrexate and how to avoid distractions ✦ how to avoid needle contamination ✦ how to deal with a needlestick injury ✦ the reasons for hand washing					

ELEMENT OF COMPETENCE TO BE ACHIEVED	Date shown	Dates supervised	Date completed sign	Nurse assessor sign	Patient/carer sign
✦ how to deal with spillage on surfaces, skin and eyes ✦ how to dispose of used sharps, waste and unused injections ✦ why protective clothing is required (carer only) ✦ how to transport and travel with methotrexate.					
Patient/carer can identify areas on the body where subcutaneous methotrexate injection can be given					
Patient/carer can discuss the rationale and arrangements for blood monitoring while on methotrexate therapy					

Appendix 5: Patient information leaflet for subcutaneous methotrexate injections

Information for patients and carers about subcutaneous methotrexate injections

Please remember that methotrexate is to be given only once weekly

What do I need to know?

The Arthritis Research Campaign (**arc**) has over 80 booklets, leaflets and information sheets for people with arthritis. The arc information sheet *Drugs for arthritis: methotrexate* gives helpful information about using subcutaneous methotrexate.

All arc publications are free and can be downloaded from their website at www.arc.org.uk

arc can be contacted at:

Arthritis Research Campaign

Copeman House
St Mary's Court
St Mary's Gate
Chesterfield S41 7TD

0870 850 5000
info@arc.org.uk

The **arc** leaflet *must* be read alongside this information. This leaflet has been prepared to give you information about having injections of methotrexate. The injection is placed under the skin and into the subcutaneous tissues using a very fine short needle (see figure 1). Many patients who have diabetes have to inject themselves in the same way with insulin. Some new treatments for arthritis (called biologics such as etanercept, adalimumab and anakinra) are also given by subcutaneous injection.

Why is it being suggested that I have methotrexate by injection?

There are two possible reasons why you might need methotrexate by injection.

1. Some people find they are unable to take higher doses of methotrexate by mouth because of side effects such as feeling sick or having diarrhoea. If the methotrexate is given by injection these symptoms can improve.
2. It may be that your doctor wishes to ensure that you absorb as much as possible of the methotrexate in order to improve your arthritis. There may be specific reasons why you don't absorb methotrexate properly by tablet. If you are concerned and wish to understand more about why you have been prescribed treatment by injection please contact your rheumatology department who can advise you.

Your doctor may have discussed other reasons why methotrexate by injection would be a suitable way of you receiving treatment. If you are unclear about the reason treatment is being suggested you can ask for further

information and an opportunity to discuss this with your doctor.

Are injections different to tablets?

The injection medication is absorbed directly into your body without having to be taken by mouth first. This avoids some of the problems that can be experienced when taking tablets. The methotrexate is also more rapidly absorbed and can be more effective by injection. The main difference between tablets and injections are the things you will have to do to make sure that you know how to manage the syringes, needles and the methotrexate liquid in the syringe to keep them safe and to give yourself the injections.

How will I learn to do the injections?

Your nurse or practitioner will arrange a time for you to be shown the things you need to know and then you will be taught how to do the injections. Your partner or carer will also be welcome to attend the training sessions if you wish them to do so. In some cases people ask their partner or carer to inject the methotrexate for them. The training time spent with you is usually in the hospital or health centre. When you are ready to inject yourself the nurse or practitioner will be there to help you and give you support through each step of preparing and giving the injection. When you feel confident and ready to give the injections at home you will be asked to sign a consent form and the nurse/practitioner will then ensure you understand all the information you have been given and that you are confident to start injecting yourself at home.

How do I get the injections and things I need to give the injection?

Exactly how this is done can vary from hospital to hospital. Sometimes everything is delivered to your home and collected from there. In other places you will need to collect everything from the hospital or health centre. Your rheumatology practitioner will go through this with you and give you information on collecting your prescriptions and where to hand in your waste bins. It is important you keep a careful record of how many injections you have to make sure that you don't run out of your methotrexate. In some hospitals you have to telephone the nurse or practitioner to tell them when you need another prescription.

Do I need blood tests when taking methotrexate?

You will need to have regular blood tests whether you are having methotrexate by tablet or injection. It is very important that you attend regularly for your blood tests. You must also make sure that you know when you should check with your rheumatology department or health centre about the results of your test.

What happens if I want to go on holiday abroad?

People who have to take insulin have to do this all the time so there isn't too much of a problem. It is likely you may need to take everything in a cool bag but your rheumatology department will provide you with more detailed information according to the way your syringes need to be stored. The way your syringes need to be stored may vary depending on the way the methotrexate was prepared and put into the syringe. In some hospitals the methotrexate is prepared at the hospital and in other hospitals methotrexate is bought ready prepared. You need to ensure you keep the syringes, needles and other equipment in your personal luggage. You may need to take with you a letter from your rheumatology department to explain what the medications is and why you need to travel with it.

What happens if I don't want to give the injections myself?

It is possible for a partner or carer to give the injection to you instead, as long as they are happy to do this and have carried out all the training and they are able to manage it safely. It may also be possible that you can have the injections given at your doctor's surgery or health centre if you feel that you or your partner are unable to do it. This might take a little bit of time to organise and will depend upon the support available in your community. Some units have a regular injection clinic. You will need to check with your doctor or specialist practitioner what is available in your area.

What happens if I have a problem when I am at home?

During normal working hours the telephone helpline service can be used.

The telephone number for your nurse helpline service is:

This service is available on _____ days

During the hours of _____

During the time that you are trained you will learn how to manage some problems, but you will also be given information about when to seek urgent help and how to get that help.

Appendix 6: Specimen letter for GP or primary care team

Use headed paper
with contact number
and address.

Date:

Dear Dr

Re: [Patient name, hospital number, and date of birth]

TREATMENT COMMENCED: [dose] METHOTREXATE ONCE A WEEK

BY SUBCUTANEOUS INJECTION

Treatment has been prescribed for:…….. (for example, rheumatoid arthritis)

[Patient name] has now completed their training programme and is competent in self-administering subcutaneous injections of methotrexate. Prior to starting treatment [patient name] has given full informed consent to treatment. [Patient name] started subcutaneous injection on [date]. The patient's blood monitoring results were reviewed on [date] according to the trust shared care monitoring protocol/or the rheumatology department blood monitoring/BSR guidelines.

[Patient name] will be reviewed again in outpatients and has access to the telephone helpline service. Please refer to local monitoring guidelines/shared care guidelines/protocols. [Include possible websites such as BSR or local guidelines]. For information on the patient's clinical management or advice on monitoring contact:

[Name of identified person and telephone number]

Alternatives for letter according to local practice:

1. [Name of patient] has been advised to telephone your health centre to arrange to collect their next prescription for methotrexate and to deliver their cytotoxic waste bin to the hospital or health centre according to local protocol/guidelines
2. [Name of patient] will be collecting prescriptions from the hospital pharmacy department. Monitoring will be undertaken by our nurse specialist [name] telephone [number here]
3. [Name of patient] has been supplied with a prescription for [number] weeks, and will be returning to the department for a further review and repeat prescriptions.

Yours sincerely,

Appendix 7: Example business case

The development of patient self-administered subcutaneous injection programmes rest on building a thorough business case that gives careful consideration to the best options for: risk management; patient preference; and local need. Some rheumatology units with a service may wish to review care against this guidance, others may want to set up a new service.

The aim of the business case is to document the current service provision and then identify the resource implications (financial and physical) of developing the new service. Although there may be cost implications to improving care, it is essential to highlight improvements that will enhance a patient-centred approach to care, and manage/reduce all aspects of clinical risk.

This example can be used as a template for writing your business case.

Decision-making tables for reviewing services or planning a new service

This is a simple example that can be modified according to local hospital or department needs. There are three tables aimed at aiding decision-making. The first section identifies the current standards of care, and the second looks at the potential benefits set against cost implications.

Specific costs are not included as this will vary depending on the size of the unit and pharmacy, the infrastructure already provided and the level of liaison between primary and secondary care (secondary or shared care monitoring). Practitioners may be able to discuss costs with their local business manager and define the three levels (minimal, moderate or high costs) with financial estimates.

It is essential to also include potential cost savings or quality improvements. These should be identified in table 3. The categories that should be used for cost savings/quality improvements should be based upon minimal, moderate or high as set out in table 2. Where possible the actual cost savings should be calculated and documented alongside the category. Quality improvements should be discussed alongside this table.

Standards of care

A global score has been devised to encompass three key areas that should be identified when developing a service. It may be appropriate to add extra sections according to local issues. The key areas are:

- staffing
- provision of patient-centred care
- risk management.

The three key areas should then be scored according to current or proposed provision as outlined below:

0 = poor

1 = minimal acceptable standard

2 = acceptable standard

3 = excellent standard

Staffing

This section should include:

- the provision of the appropriate number of competent staff needed to provide care and the provision of sufficient time to deliver care. For example, specialist practitioners, pharmacy personnel, clerical support
- necessary competencies and training needs.

Provision of patient-centred care

This should be an assessment of patient needs and whether the service is able to provide a reasonable level of patient-focussed care. This section should include:

- scoring should include patient access to treatment, waiting times, level of education/empowerment and available patient support. Adequate practitioner support for the patient on treatment, screening, training programme, helpline and follow-up care
- flexibility in care - patient (or nominated carer) can elect to self-administer treatment or receive treatment at the hospital or health centre
- patient informed and empowered according to their individual needs for example in blood monitoring information and follow up care
- effective method of review, assessment and delivery/collection of methotrexate.

Risk management

The process of care should be based on a risk assessment that identifies potential risk throughout the preparation, administration, management and monitoring of patients receiving subcutaneous methotrexate. It should also consider the use of appropriate guidance, training packages and infrastructure that supports patients, primary health care teams and practitioners in secondary care. This section should include:

- assessments and risk management in the care process are documented and reduced to the minimal acceptable standard
- incidents or accidental spillage/errors are reported and reviewed to inform future management
- health care staff and patients (and carers) are informed and aware of risk management strategies.

Quality improvements

Quality improvements could include:

- improved patient outcomes such as reduction in admissions for poor disease control, patient satisfaction and quality of life
- reduced waiting times from consultant prescribing to commencing treatment
- patients receiving treatment in their own home instead of attending outpatient department
- reduction of risk by empowering patient and improving overall management.
- improved patient outcomes such as reduction in admissions for poor disease control, patient satisfaction and quality of life

Business case assessment tables

Once you have reviewed relevant documents and assessed your service or planned provision, tables one, two and three may help you analyse your service needs.

Table 1: Standards of care

Standard	Score 0 poor	Score 1 acceptable	Score 2 good	Score 3 excellent
Staffing Number of staff Competency				
Patient-centred care Infrastructure Empowerment Follow-up care				
Risk management Assessment Documentation and review All staff/patients aware of risk management				

Table 2: Cost and resource implications

Standard	Score minimal costs	Score moderate costs	Score high
Staffing Number of staff Competency			
Patient-centred care Infrastructure Empowerment Follow-up care			
Risk management Assessment Documentation and review All staff/patients aware of risk management			

Table 3: Cost savings

Standard	Score minimal	Score moderate	Score high	Describe quality improvements
Staffing Number of staff Competency				
Patient-centred care Infrastructure Empowerment Follow-up care				
Risk management Assessment Documentation and review All staff/patients aware of risk management				

Analysis of resources and costings

It is important to complete a service needs assessment because many of the potential costs for a new service may be met by restructuring an existing service. Developing good links with primary care groups means that costs and the benefits of improved management may be shared.

In this section some highlighted areas (see below) will already be part of current service costs. Items asterisked (**) identify care already provided, or are equivalent to treating patients with oral methotrexate. This is likely to be the situation for most cases because standard practice has been to start oral methotrexate treatment, then change to subcutaneous administration if optimum benefit is not achieved, or if the patient is in intolerant to oral methotrexate.

You should identify and include the following in your analysis:

Drug preparation:

This will vary according to the:

- facilities available for the preparation of cytotoxic therapies and capacity of the pharmacy unit
- staff trained and available to support additional preparation of pre-filled syringes
- length of time drugs can be prepared and stored before use/dispensing. This will vary according to the level of service/facilities that pharmacy is able to provide.
- drug cost analysis may need to include recruitment of additional pharmacy staff in the preparation and co-ordination of the service.

In some cases the business proposal may need to consider the use of contracted non-NHS pharmaceutical companies, and this should be carried out in liaison with the pharmacy department. Some pharmaceutical companies dispense, deliver and dispose of waste for named patient pre-dosed, pre-filled methotrexate syringes. Delivery is often direct to the patient's home. These services vary, and some also provide a collection service for cytotoxic waste bins.

A cost analysis may show that an economy of scale may preclude additional development within the local trust. The analysis of drug preparation should consider:

- in-house facilities and staffing. This should include equipment and capacity to manage additional methotrexate prescriptions as well as staff time to prepare and dispense
- patient access to treatment such as waiting times, and frequency of journeys to collect prescriptions/ treatments
- storage length of specific pre-filled syringes. This varies from trust to trust and within non-NHS organisations.

Distribution of prescriptions:

This practice will vary from unit to unit and options should be reviewed. For example:

- the patient may pick up their prescriptions at the hospital pharmacy, or from their local community pharmacist
- prescriptions that are transported to the community for collection may incur an additional cost
- if a non-NHS health care organisation is contracted to distribute methotrexate, transportation may include delivery of the drug to the patient's home and collection of cytotoxic waste bins.

Additional Costs

Storage:

Any special equipment for methotrexate storage needed in the hospital, community, or patients' homes must be included in the cost analysis (additional fridge capacity in pharmacy). Patient home storage should not incur any additional costs, although in some circumstances a lockable box or fridge lock may be needed. A decision should be made prior to the cost analysis as to whether the NHS or the patient will fund the locks. Some units have raised support for such additional costs from a patient charity group in the hospital.

Administration costs:

This includes any protective clothing or equipment required such as gloves. Although all trusts have spillage kits available in every area, if an additional patient spillage kit or training kits are needed these should be included in the costs.

Disposal costs:

Specialised cytotoxic waste bins and appropriate their disposal are based on local trust policies. There maybe additional costs incurred in the community for the collection of cytotoxic waste bins from health centres, therefore it is important to liaise with primary care groups.

Practical issues

Current workload:

If there is a current service for subcutaneous methotrexate consider the number of clinics for assessment, possible administration, monitoring, reviewing and patient training and calculate the potential increase. In the cost

analysis it is also important to highlight potential savings and quality issues such as ease of access for patients. For example, is there a need for an evening clinic for patients in the hospital, and would the introduction of a subcutaneous administration enable many more patients to self-administer? These issues have the potential to alter the cost/quality analysis.

*Screening costs**:*

Screening should include blood investigations and chest X-rays (as for oral methotrexate) and practitioner /team time. If the patient has received oral therapy first it is likely screening has already been carried out and should be highlighted as neutral cost (that is, no additional funding required above current service provision).

*Assessment and training costs**:*

This should include practitioner time needed to review patient eligibility for treatment, patient education relating to risk and the benefits of treatment, obtaining consent and training the patient to self-inject. (** some of these aspects will be included in oral methotrexate preparation.)

*Monitoring**:*

Cost and frequency of investigations as set out according to local and national guidelines.

Facilities and equipment costs

This should include clinic space for assessment, review and training with any equipment used in the training for self administered subcutaneous injection. The cost and facilities required will vary according to the use of pharmacy prepared pre-filled syringes or practitioner prepared and administered treatment in a clinical area. Costs should include additional needs in relation to the appropriate environment with any specialised equipment. Additional hidden costs include the storage, stock and medicines management for pharmacy.

Specialist personnel needs and costs

It is essential to consider the provision of a specialist practitioner trained in the administration of cytotoxic medication, along with pharmacy personnel. Each service will have varying needs depending on the existing staff. It may be necessary to identify training or supervision time rather than additional personnel.

Administrative support

Administration personnel should be included for arranging appointments, completing/ filing appropriate documentation and maintaining a database. Also include any necessary equipment.

Potential savings

It is essential that you include the potential savings made when setting up the service. Patient self-administration will reduce the costs of:

1. nurse-led clinic time for administration of parenteral methotrexate
2. patient transport costs to clinic
3. less time required to train patients for subcutaneous biologic therapies
4. improved disease control and reduction in emergency or outpatient visits.

The costs of the proposed service should be considered in the context of other treatment options for patients failing on oral methotrexate. For example, starting a patient on a parenteral methotrexate may delay the prescribing of a more expensive biologic therapy, yet maintain treatment efficacy. Self-administration also enhances patient independence, quality of life and empowerment it therefore, demonstrates a high quality, efficient and cost effective method of managing patients with rheumatic conditions.

*Specialist rheumatology practitioner**:*

The analysis should state the grade or band (*Agenda for Change*, 2003) for the appointed practitioner. Employment costs need to include additional organisational costs, often called on-costs. Organisational costs usually include statutory employers' costs, as well holiday and sick leave cover. Calculations should be set out for all aspects of care at each step of the process, as well as the proposed total number of patients that the appointed practitioner will see over a one-year period. This analysis will need to take into account patient assessment, training and monitoring, together with follow-up support where appropriate.

Examples of other cost analyses used to develop services for biologic therapies may be useful. These can be found in RCN *Guidance* (2003,) and on the British Society of Rheumatology (BSR) website www.rheumatology.org.uk

This example uses an F grade nurse based on one patient per visit

(time and funding needs to be added to overall outline below)

Service provision	Sessions to include	Time per session or clinic (approximate)
Patient assessment and training	Pre-therapy screening: - education - obtaining consent - preparing/reviewing base line investigations - training and support for self-administration	1 hour
Monitoring and reviewing	Checking: - blood results - side-effect profile - technique - finalising competencies	10 mins – 20 mins (standard review) 1 hour (final session)
Staff training	See staff competencies	Time may vary Needs to be assessed on profile of team and training needs
Telephone helpline	Dealing with patient and staff queries	20 mins per clinic *time will vary according to number of patients/number established on treatment
Liaising with other relevant personnel and departments	- primary care to arrange ongoing safety monitoring - pharmacy staff for prescriptions - laboratories for results	30 mins per clinic *see comment above

Additional staff costs to consider

Pharmacy personnel Clerical staff	- prescription checking, preparation, dispensing, stock control, storage and training of personnel - liasing with patients and staff	Will vary according local trust facilities and services and number of patients Seek advice from pharmacy department
	- retrieving and filing notes - supporting practitioner in administrative duties	Will vary according to current service provision

Conclusion

The business case should be prepared and reviewed with your line manager and in liaison with the rheumatology team to ensure you recognise all service needs.

Appendix 8: Websites

Arthritis Research Campaign (arc): www.arc.org.uk

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

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

Guidelines on cytotoxic therapies: www.marcguidelines.com

Health and Safety Executive for all health and safety regulations: www.hse.gov.uk

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

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

NHS Quality Improvement for Scotland: www.nhshealthquality.org

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

Arthritis Care: www.arthritiscare.co.uk

Subcutaneous injections information: www.bddiabetes.co.uk

Text of government legislation: www.hmso.gov.uk

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