

Medical and Allied Branch

HSS(MD)22/2005

Chief Executives of HSS Boards & Trusts for cascade to:

- Risk Managers
- Clinical & Social Care Governance Leads

All General Practitioners (for cascade to Practice Staff including Sessional General Practitioners, and Clinical Governance Leads)

All Community Pharmacists

Directors of Pharmaceutical Services in HSS Boards & Trusts for cascade to:

- HSS Trusts Drugs & Therapeutic Committees

Directors of Public Health in HSS Boards

Medical Directors of HSS Trusts for cascade to:

- Consultant Rheumatologists
- Consultant Dermatologists
- Consultant Paediatricians

Chairs/Area Drug & Therapeutics Committees/Prescribing Fora

Directors of Nursing HSS Boards

Directors of Nursing HSS Trusts for cascade to:

- Community Nurses, Health Visitors and School Nurses

Northern Ireland Medicines Governance Team

Chair – Regional Group on Specialist Medicines

Interface Pharmacists for Specialist Medicines Network

Regional Governance Advisor

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Your Ref:

Our Ref:

Date: 25 July 2005

Dear Colleague

SAFETY ALERT – PRESCRIBING, SUPPLY AND ADMINISTRATION OF CERTAIN MEDICINES

The purpose of this letter is to provide further information to promote the safe use of:

Repevax and Revaxis vaccines; and
Oral methotrexate.

By way of this communication, the Department will be seeking feedback on the main recommendations by the end of December 2005.

Background

This alert is based on information produced by the National Patient Safety Agency and work undertaken locally via the Medicines Governance Team and the Regional Group on Specialist Medicines. The full text of the National Patient Safety Agency alerts relating to the above topics are available on www.npsa.nhs.uk/advice.

Repevax and Revaxis Vaccines

On 4 August 2004, circular HSS(MD)24-2004 outlined changes for the routine childhood immunisation programme. This included recommendations regarding the use of Repevax for pre-school boosting and Revaxis for teenage boosting. In addition the Northern Ireland Medicines Governance Team issued an alert on 12 October 2004 drawing attention to possible confusion between the two vaccines because of labelling similarities.

At national level there have been a number of reported patient safety incidents and near misses involving Repevax and Revaxis vaccines where staff have mistakenly given the wrong vaccine as these products have similar names, labelling and packaging. In the most recent report to the NPSA, 93 school children were vaccinated with Repevax instead of Revaxis. Repevax packaging is currently being redesigned to help distinguish it more clearly from Revaxis. However, in the interim there is a need:

- a. To ensure that local procedures are in place to check that the correct vaccine has been selected for the individual patient concerned on each and every administration;
- b. Raise awareness of the proposed changes to packaging with all staff involved in childhood immunisation;
- c. Review local procedures for risk assessment and management of new vaccine products introduced locally and strengthen procedures where necessary; and
- d. Continue to report any patient safety incidents to the Medicines and Healthcare Products Regulatory Agency, via the Yellow Card Scheme, and through local incident reporting schemes.

Further guidance is available on the NPSA web-site and is contained in a Safer Practice Notice, dated 29 April 2005.

Reducing the harm caused by oral methotrexate

Much work has been done, both locally and nationally, to reduce the harm caused by oral methotrexate. NPSA guidance on methotrexate is available on the above web-site. Attached to this letter is:

Recommendations to Improve the Safe Use of Oral Methotrexate in Northern Ireland – Northern Ireland Medicines Governance Team.

The Department supports the content of this document and acknowledges the work of the Medicines Governance Team for production of this Report.

Action

HSS Boards, Trusts and staff in Primary Care should ensure that work is undertaken locally to review procedures on oral methotrexate, repevax and revaxis vaccines, and continue work to implement change. Action to support implementation should be reviewed by each area Drug and Therapeutics Committee and, where appropriate, the Regional Group on Specialist Medicines.

Chief Executives of HSS Boards are asked to report on progress in relation to the four main elements relating to reprevax and revaxis vaccines and on progress towards implementation of all relevant recommendations contained in the Northern Ireland Medicines Governance Team report on oral methotrexate. Responses should be sent to the Department to:

Dr Norman Morrow
Chief Pharmaceutical Officer
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Castle Buildings
Stormont
BELFAST BT4 3SG

E-mail: norman.morrow@dhsspsni.gov.uk

No later than 30 December 2005.

Yours sincerely

DR IAN CARSON
Chair of Safety in Health & Social Care
Steering Group
Deputy Chief Medical Officer

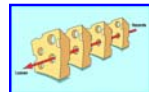
DR NORMAN MORROW
Chief Pharmaceutical Officer

cc: Members of the Safety in Health & Social Care Steering Group
Directors of Primary Care – HSS Boards
Central Services Agency
Directorate Information System – DHSSPS
The Queen's University, Belfast – Medicine/Pharmacy/Nursing
University of Ulster
Open University
NIMDTA
NIPPET
NIPEC

**Recommendations to improve the
safe use of oral methotrexate in
primary and secondary care in
Northern Ireland (revised)**

July 2005

**Northern Ireland Medicines
Governance Team**



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Background

Oral methotrexate is a safe and effective medicine if taken at the correct dose and with appropriate monitoring. Medication incident reporting in secondary care in Northern Ireland and a review by the Committee on Safety of Medicines¹ have highlighted a number of potential safety concerns with the use of oral methotrexate.

These include:

- Weekly doses prescribed to be taken on a daily basis;
- Confusion between 2.5mg and 10mg strengths;
- Higher doses for malignant conditions being confused with doses for non-malignant conditions; and
- 'Monday' being misread as 'morning'.

The National Patient Safety Agency (NPSA), a special health authority for England and Wales, has documented that 137 patient safety incidents involving oral methotrexate have occurred over the last ten years in England. Of these cases, 25 resulted in patient death and a further 26 in patient harm.^{1,2}

Consideration of a typical journey of a patient initiated on oral methotrexate (Appendix 1) illustrates the many stages involved, with a potential for error at any stage.

To address these issues the Northern Ireland Medicines Governance team issued a 'Policy for the use of oral methotrexate' on 13/9/03.³

This policy sought to strengthen the systems for the use of oral methotrexate within acute hospitals to prevent incidents involving the incorrect dose and/or frequency being used in the treatment of non-malignant conditions. This involved collaboration with colleagues in primary care to standardise tablet and liquid strengths. The HPSS Boards issued recommendations for GPs and community pharmacists based on the policy.

On 29/7/04 the NPSA issued a patient safety alert 'Reducing the harm caused by oral methotrexate'² together with 'Towards the safer use of oral methotrexate'³ – a

background report on the NPSA's work with oral methotrexate. The patient safety alert identified three potential solutions to prevent harm caused by oral methotrexate:

- Information for the patient prior to treatment and patient-held records during treatment;
- Improved warnings and flags for prescribing and dispensing systems; and
- Repackaging tablets using novel designs and in reduced quantities.

This patient safety alert was issued to primary and secondary care in England and Wales, for action by March 2005. It was not issued in Northern Ireland.

The Northern Ireland Medicines Governance team reviewed these documents, together with the report from Cambridgeshire health authority (July 2000); 'Methotrexate toxicity. An inquiry into the death of a Cambridgeshire patient in April 2000.'⁵ On completion of the review, this report was prepared. This report focuses on areas of risk with oral methotrexate that are outside the scope of the Northern Ireland Medicines Governance team 'Policy for the use of oral methotrexate.'⁴

Review of current arrangements

Recommendation 1

A review of primary care arrangements for the use of oral methotrexate should be conducted. A similar review of the implementation of the 'Policy for the use of oral methotrexate'⁴ in secondary care should also be carried out. This is to audit compliance with the measures recommended in primary care and the policy issued to secondary care in 2003.

Responsibility for implementation:

HSS Boards and the Medicines Governance Team in collaboration with Nationally Enhanced Service Providers (NES) (Methotrexate) and the Regional Multidisciplinary Audit Group.

Shared care and patient information

Recommendation 2

Regionally approved Shared Care Guidelines (SCGs) should be available for all non-malignant conditions requiring the use of oral methotrexate. Currently there is a regionally approved SCG for the use of oral methotrexate in rheumatology.

While regionally approved SCGs are being developed and approved, local interim guidelines should be developed.

Responsibility for implementation:

Interface pharmacists for specialist medicines network/Regional Group on Specialist Medicines in collaboration with clinicians.

Recommendation 3

The regionally approved SCG for oral methotrexate and accompanying patient information should be reviewed before or by current review date of February 2006 to reflect that the strength of methotrexate liquid to be used is 10mg/5ml.⁴ Confusion may arise as a number of different strengths of methotrexate liquid may be available.

Responsibility for implementation:

Interface pharmacists for specialist medicines network/Regional Group on Specialist Medicines and NES providers.

Recommendation 4

The regionally approved SCG and accompanying patient information in Northern Ireland for oral methotrexate should be reviewed in light of current recommendations.²⁻⁵

Particular consideration should be given to the provision of patient information prior to commencement of treatment and the use of patient held records. Provision of patient information is identified as a key measure by the NPSA. The NPSA patient safety alert provides a template and core content for the patient information leaflet and patient held monitoring and dosage record. The NPSA recommends that these tools are used in conjunction with existing guidance and patient information from authoritative sources.

Responsibility for implementation:

Interface pharmacists for specialist medicines network/Regional Group on Specialist Medicines and NES providers.

Induction and training

Recommendation 5

Induction programmes for medical, nursing, midwifery and pharmacy staff, including locum staff, should include information on the dose and frequency of oral methotrexate in the treatment of non-malignant disease.⁵

Undergraduate training in medicines safety should include specific teaching on oral methotrexate.

Responsibility for implementation:

HSS Boards, HSS Trusts, NES providers, Queen's University, Belfast, the University of Ulster and the Open University.

Recommendation 6

Healthcare staff should be trained to recognise the signs and symptoms of methotrexate toxicity or intolerance.³ These signs and symptoms may be misinterpreted as suggestive of, for example, infection rather than methotrexate toxicity.

Responsibility for implementation:

HSS Trusts, NES providers, HSS Boards and postgraduate education organisations.

Safe prescribing

Recommendation 7

When a hospital prescriber is initiating or altering the dose of oral methotrexate therapy, the GP should be provided with information regarding the dose, frequency, formulation and day the oral methotrexate is to be taken.

Discharge summary information from hospitals must be complete, legible and include in full the form, strength, dose and directions.

- **Responsibility for implementation:**

HSS Trusts and Interface pharmacists for specialist medicines network/Regional Group on Specialist Medicines.

Recommendation 8

Trusts should review arrangements for delivery of this written information to the GP. Hand delivery by patients as a sole method of information transfer may not reach the GP in a timely manner, particularly in the advent of 28 day dispensing at discharge.

- **Responsibility for implementation:**
HSS Trusts

Recommendation 9

Prescribing systems in primary and secondary care, both electronic and paper based, for oral methotrexate in Northern Ireland should be reviewed in light of current recommendations.²⁻⁵

Particular consideration should be given to the improvements to prescribing software detailed in these reports, both as it applies to current systems and any future electronic prescribing systems that may be introduced. The NPSA patient safety alert and background report provides valuable information as to system improvements to electronic prescribing systems that may facilitate the safer prescribing of oral methotrexate.

- **Responsibility for implementation:**
HSS Boards, HSS Trusts and GP system suppliers and clinical and social care governance leads

Recommendation 10

In primary care, all entries related to oral methotrexate treatment on practice electronic prescribing systems should be made by a GP and should not be free-typed. As a potentially toxic drug, all entries relating to oral methotrexate should be the responsibility of the GP. The option to free-type dosing directions should be removed so that software improvements that support correct selection of dose and frequency are not bypassed.

- **Responsibility for implementation**
HSS Boards in collaboration with GP practices.

Recommendation 11

'As directed' is unacceptable as a dosage instruction for oral methotrexate. A specific dose should always be stated on oral methotrexate prescriptions.³⁻⁵

- **Responsibility for implementation:**
HSS Boards and Trusts to alert all appropriate practitioners in primary and secondary care, and work with clinical and social care governance leads.

Recommendation 12

If an incorrect dose, strength, formulation or frequency has been entered in an electronic prescribing record this should be removed and the correct information input (with an annotation that an incorrect dose, strength, formulation or frequency had been erroneously entered. The date of the incorrect entry should also be annotated.)⁵ If an erroneous record is not corrected, the incorrect information could be used in future prescriptions and possibly lead to the re-issue of an incorrect prescription.

- **Responsibility for implementation:**
HSS Trusts and GP practices supported by HSS Boards.

Recommendation 13

In primary care, consideration needs to be given to the frequency of issue of repeat prescriptions. An inappropriate request for a repeat prescription of oral methotrexate could identify a patient who is taking their medicine at a greater than intended frequency, or could lead to a stockpiling of this high risk medicine.

- **Responsibility for implementation:**
GP practices supported by HSS Boards.

Recommendation 14

In primary care, repeat prescriptions for oral methotrexate should be removed from the surgery repeats pile and retained separately for prescriber review prior to authorising by signature.³

- **Responsibility for implementation:**
GP practices supported by HSS Boards.

Recommendation 15

Explicit systems need to be in place to ensure both paper medical records and computer-based records are kept up to date with respect to oral methotrexate.⁵

Where both systems are in place, it is essential that alterations to the prescribing of oral methotrexate are documented in both locations.

- **Responsibility for implementation:**
HSS Trusts and GP practices supported by HSS Boards.

Recommendation 16

If a GP practice uses paper records solely, or in addition, to an electronic prescribing system, a flag/visible prompt for oral methotrexate should be placed on paper notes as well to enable easy identification of patients taking this high risk medicine.⁵

- **Responsibility for implementation:**
GP practices supported by HSS Boards.

Recommendation 17

Information accompanying patients from primary care to hospital should provide details of dose, frequency, formulation and day oral methotrexate is to be taken.

- **Responsibility for implementation:**
GP practices supported by HSS Boards.

Recommendation 18

The NPSA recommends that patients receiving oral methotrexate in hospital should have their medication reviewed by a pharmacist on admission. Prescribing, monitoring and administration requirements should be recorded in the patient's notes.³ Similarly at discharge, a pharmacist should review the patients' medication, irrespective of a supply being made.

- **Responsibility for implementation:**
HSS Trusts.

Recommendation 19

Within hospital, when weekly oral methotrexate is prescribed, the prescriber must cross out the six days of the week when a dose must not be administered in the administration section of the Kardex.³

Not all Kardexes in Northern Ireland will allow prescribers to fulfil this requirement. Where this is the case, Trusts should consider redesigning Kardexes to allow this safety measure to be incorporated.

Current electronic prescribing systems may require modification to meet this requirement.

Specifications for future electronic prescribing systems should ensure incorporation of this safety measure.

- **Responsibility for implementation:**
HSS Trusts

Information Technology

Recommendation 20

Electronic prescribing and dispensing systems in primary and secondary care for oral methotrexate in Northern Ireland should be reviewed in light of current recommendations.²⁻⁵

The NPSA background report, 'Towards the safer use of oral methotrexate' details several requirements that GP prescribing systems must incorporate to reduce or remove harm associated with oral methotrexate.³

The Northern Ireland Medicines Governance team 'Policy for the use of oral methotrexate' and the regionally approved rheumatology SCG for oral methotrexate both recommend the use of methotrexate 2.5mg strength tablet only, to avoid the risk of confusion with methotrexate 10mg tablets. This creates a problem, as the changes recommended by the NPSA for GP prescribing systems leads the prescriber to prescribe a dose of, for example 15mg, as one 10mg tablet and two 2.5mg tablets. This function can be overridden but requires a number of extra keystrokes.

Prescribing and dispensing software in Northern Ireland should be adapted to ensure that methotrexate 2.5mg is the sole strength that can be chosen as an option. In Northern Ireland, GP electronic prescribing systems and pharmacy dispensing system must only allow methotrexate 10mg/5ml liquid and methotrexate 2.5mg tablets as strength options.

- **Responsibility for implementation:**
HSS Boards and Trust Pharmacy Managers with General Practitioners and Community Pharmacists.

Recommendation 21

In primary care repeat prescribing, changes should be made to printer driver software to shade prescription signature space on a prescription, alerting the prescriber to a prescription for a high risk medicine.³

- **Responsibility for implementation:**
HSS Boards and GP practices.

Safe dispensing

Recommendation 22

The dispensing process for oral methotrexate in Northern Ireland should be reviewed in light of current recommendations.²⁻⁵

Particular consideration should be given to the improvements to dispensing software detailed in these reports. The NPSA patient safety alert and background report provides valuable information as to system improvements to electronic pharmacy systems that may facilitate the safe dispensing of oral methotrexate.

Responsibility for implementation:

Trust Pharmacy Managers, HSS Boards, Pharmaceutical Society of Northern Ireland and Community Pharmacists.

Recommendation 23

All pharmacies should have a Standard Operating Procedure for dispensing oral methotrexate irrespective of the number of methotrexate patients seen.

- **Responsibility for implementation:**
HSS Boards, Trust Pharmacy Managers and the Pharmaceutical Society of Northern Ireland and Community Pharmacists.

Recommendation 24

Queries to prescribers concerning oral methotrexate should be made directly with the prescriber rather than non-medical staff and a note of the query made on the prescription.⁵

- **Responsibility for implementation:**
HSS Boards and Trust Pharmacy Managers, Community Pharmacists and GP practices.

Recommendation 25

If methotrexate liquid is not stocked in a hospital pharmacy and is required for a hospital patient on discharge, it should either be ordered for later collection by the patient or carer, or transported to the patient's nearest hospital for collection.

Alternative arrangements may be made for prescription and dispensing in primary care, in accordance with the SCG where applicable, and supported by written and verbal transfer of information, according to agreed procedures.

- **Responsibility for implementation:**
HSS Trusts.

Recommendation 26

Counselling should be provided for the patient regarding the handling, and disposal of oral methotrexate. This should be supplemented by written information. For liquid oral methotrexate, information should also be provided for dealing with spillage.

- **Responsibility for implementation:**
HSS Trust Pharmacy Managers, HSS Boards and the Interface pharmacists for specialist medicines network/Regional Group on Specialist Medicines.

Recommendation 27

As methotrexate liquid is a 'special' it may not be available to order by community pharmacists through their usual wholesalers. The details of where the liquid can be obtained and that only the 10mg/5ml strength is to be used should be provided to the patient's nominated community pharmacist in writing.

- **Responsibility for implementation:**
HSS Trust Pharmacy Managers.

Recommendation 28

Oral methotrexate should not be dispensed solely from an 'owing'; the original prescription must be referred to. A mistake may have been made in generating the 'owing', therefore the original prescription should be referred to when dispensing oral methotrexate.

- **Responsibility for implementation:**
HSS Boards and Trust Pharmacy Managers in collaboration with Community Pharmacists.

Recommendation 29

If an incorrect dose, strength, formulation or frequency has been entered in a community pharmacy Patient Medication Record (PMR) system, or other pharmacy electronic dispensing/record system in use in secondary care, this should be removed and the correct information input (with an annotation that an incorrect dose, strength, formulation or frequency had been erroneously entered. The date of the incorrect entry should also be annotated.) If an erroneous record is not corrected, the incorrect information may be used in future dispensing.

- **Responsibility for implementation:**
HSS Boards and Trust Pharmacy Managers in collaboration with Community Pharmacists.

Recommendation 30

Reimbursement arrangements for dispensing should be linked to compliance with the policy requirement for the safe use of methotrexate.

- **Responsibility for implementation:**
DHSSPSNI and Central Services Agency

Purchasing

Recommendation 31

Purchasing of oral methotrexate tablets and folic acid tablets should take account of the need for these medicines to be easily differentiated by healthcare staff and patients.³

- **Responsibility for implementation:**
HSS Boards and the Standing Group for Contract Evaluation

Recommendation 32

Purchasing of oral methotrexate should ensure the packaging carries the warning '*Check dose and frequency – methotrexate is usually taken once a week*'. Future

proposals as to the original pack size of oral methotrexate recommended by the NPSA should be taken into account in purchasing.^{2,3}

- **Responsibility for implementation:**
HSS Boards and the Standing Group for Contract Evaluation

Learning from medication incidents with oral methotrexate

Recommendation 33

If a medication incident involving oral methotrexate has occurred, the practitioner discovering the medication incident should ensure that the incident is reported and shared with other colleagues involved in the care of the affected patient. There should be wide dissemination of any learning points identified following a review of the incident. This needs to occur across the primary–secondary care interface and across disciplines.

- **Responsibility for implementation:**
HSS Boards and Trusts/Risk Managers/Clinical & Social Care Governance
Leads in Primary and Secondary Care.

Recommendation 34

There should be continued review of medication incidents involving oral methotrexate in Northern Ireland to identify any remaining or emerging causal or contributory factors.

- **Responsibility for implementation:**
Medicines Governance Team, HSS Boards and Trusts/Risk Managers.

Evaluation of progress with these recommendations

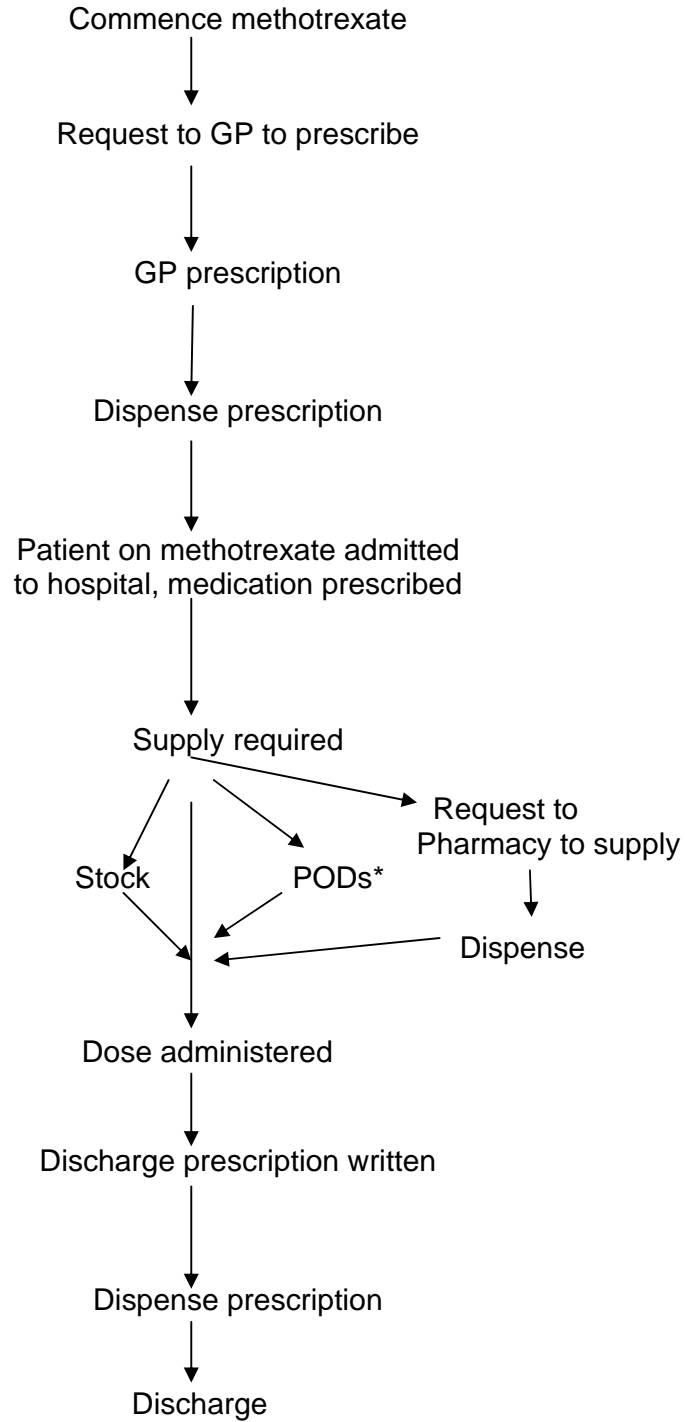
Recommendation 35

An action plan and reporting mechanisms to ensure the recommendations in this report are carried out should be developed. Progress with these recommendations should be shared with the NPSA.

- **Responsibility for implementation:**
DHSSPSNI

Appendix 1

Oral methotrexate initiated in outpatients



* Patient's own drugs

References

1. MCA/CSM Current Problems in Pharmacovigilance 2000; 26:10
2. 'Reducing the harm caused by oral methotrexate.' NPSA Patient safety alert July 2004. www.npsa.nhs.uk
3. 'Towards the safer use of oral methotrexate' A background report on the NPSA's work with oral methotrexate. July 2004. www.npsa.nhs.uk
4. Policy for the use of oral methotrexate. Northern Ireland Medicines Governance team August 2003
<http://www.dhsspsni.gov.uk/pgroups/pharmaceutical/NIMedicalGovernance/bestpractice.asp>
5. Methotrexate toxicity. An inquiry into the death of a Cambridgeshire patient in April 2000. Cambridgeshire health authority July 2000.