FULL SHARED CARE AGREEMENT FOR

6-Mercaptopurine, Azathioprine and Methotrexate

In the treatment of

Gastroenterological Disease

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**Full Shared Care Agreement for the prescribing of 6-mercaptopurine, azathioprine and methotrexate in the treatment of gastroenterological disease**

**Introduction and purpose**

This shared care agreement has been produced following classification of 6-mercaptopurine, azathioprine and methotrexate in the Leicestershire drug traffic light scheme. See website at [www.lmsg.nhs.uk](http://www.lmsg.nhs.uk)

Shared care has been defined as the mechanism of sharing patient care between primary and secondary care providers. This document sets out these responsibilities from initial diagnosis to ongoing support.

**Disease Background**

- Inflammatory bowel disease is a chronic lifelong condition.
  - Ulcerative colitis is a non-transmural condition involving the colon. Patients are classified as follows Proctitis, Left sided disease or Pancolitis.
  - Crohn’s disease is a patchy transmural condition and can affect the whole gastrointestinal tract.
- Autoimmune hepatitis is a chronic inflammatory liver condition causing abnormal transaminases.

Diffuse inflammatory bowel disease or disease that does not respond to local therapy requires oral treatment with an aminosalicylate with or without an adjunctive corticosteroid.

All these conditions are characterised by episodes of relapse and remission. Relapses are not predictable and patients with frequent relapses will require intervention with corticosteroids.

Patients requiring repeated courses of corticosteroids will require immunomodulating agents for maintaining remission and treatment of active disease i.e. 6-mercaptopurine, azathioprine or methotrexate.

**Drugs covered by the agreement**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
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<tbody>
<tr>
<td></td>
<td>Licensed</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>Ulcerative colitis</td>
</tr>
<tr>
<td></td>
<td>Crohn’s disease</td>
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<tr>
<td></td>
<td>Autoimmune hepatitis</td>
</tr>
<tr>
<td>6-Mercaptopurine</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Methotrexate oral</td>
<td>Only the 2.5mg methotrexate</td>
</tr>
<tr>
<td></td>
<td>tablets should be prescribed and dispensed.</td>
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</table>

Although 6-mercaptopurine and methotrexate are unlicensed to treat these indications, their use is widely established in inflammatory bowel disease (see BNF Section1.5, BSG Guidelines 2010, MIMS December 2013).

The main toxic effect is myelosuppression, although unpredictable hepatotoxicity is also recognised and drug interactions may increase the risk.

Pulmonary toxicity can occur with methotrexate.
These medications are contra-indicated in immunodeficiency syndromes.

Effective contraception is required by both men and women whilst on treatment and for three months after.

Methotrexate interactions are common and include many common antibiotics, NSAIDs and some drugs used for gastro-protection, Co-trimoxazole and trimethoprim are contra-indicated with methotrexate.

Live vaccines may not be appropriate with these medications. Always check the green book [www.gov.uk](http://www.gov.uk)

Further information regarding contraindications, cautions, side effects and interactions are available in the BNF and the relevant summary of product characteristics [https://www.medicines.org.uk/emc](https://www.medicines.org.uk/emc).

**Secondary Care Clinician Responsibilities**

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing and monitoring of these drugs in the conditions named above can be shared between the specialist and general practitioner (GP). GPs are invited to participate.

If the GP is not confident to undertake the monitoring requirements, then he or she is under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist.

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care should be explained to the patient by the doctor initiating treatment. It is important that patients are consulted about treatment and are in agreement with it.

The doctor who prescribes the medication assumes legal clinical responsibility for the medicine and the consequences of its use.

**Hospital clinician responsibilities:**

1. Perform baseline tests (see Appendix). Discuss treatment and monitoring with the patient. Patients are provided with the patient information leaflet before commencing therapy. **Methotrexate:** Ensure that the patient understands that dosing is at weekly intervals and which warning symptoms to report. Provide patient with patient information leaflet and blood monitoring booklet. Record that information has been given and is understood by the patient in the notes. Prescribe folic acid 5mg once weekly to be taken on a different day to methotrexate.
2. Discuss the benefits and side effects of treatment with the patient. Ensure that the patient is aware of what symptoms and side effects to report. Record that information has been given and is understood by the patient in the notes.
3. Prescribe initial course of treatment and arrange testing and full monitoring of blood tests as outlined in the Appendix.
4. Return to follow up where bloods and the patient are reviewed. Adjust treatment as appropriate for the individual patient.
5. Ask the GP whether, using the shared care agreement form, he or she is willing to participate in shared care using the Shared Care Request Form.
6. Provide results of baseline tests and recommend frequency of monitoring.
7. Periodically review the patient’s condition and communicate promptly with the GP when treatment is changed.
8. Communicate promptly with the GP in writing when to adjust the dose, stop or change treatment, and when to consult with specialist.

9. Report adverse events to the MHRA where appropriate and GP.

10. Ensure that clear backup arrangements exist for GPs to obtain advice and support.

**GP responsibilities:**

1. Confirm or decline the request for shared care within 10 working days, using the shared care request form.
2. Prescribe treatment at the dose recommended as directed.
3. Arrange full monitoring and follow up of regular blood tests once care is transferred (see Appendix). Check recent results are available (see Appendix for recommended maximum interval) before issuing a prescription. Seek advice from Inflammatory Bowel Disease Helpline in all cases of concern.

4. **Methotrexate:** Prescribe folic acid 5mg once weekly to be taken on a different day to methotrexate, update monitoring booklet with blood test results, stop treatment and discuss with specialist if new dyspnoea or cough (risk of pulmonary fibrosis) or significant fall in albumin (risk of liver fibrosis).

5. Ensure compatibility with other concomitant medication.

6. Adjust the dose as advised by the specialist.

7. Stop treatment on the advice of the specialist, or immediately if an urgent need to stop treatment arises.

8. Report adverse events to the specialist and MHRA where appropriate.

**Community pharmacist responsibilities**

1. Ensure that the patient is taking the medication as prescribed. Advise that regular blood tests must be undertaken (see Appendix).

2. Ensure compatibility with other concomitant medication, including over-the-counter medicines.

3. Seek advice from GP in cases of concern.

**Patient’s role/responsibilities:**

1. Attend all blood tests and appointments with GP and specialist.

2. Report to the specialist or GP if he or she does not have a clear understanding of the treatment.


4. Inform specialist, GP or pharmacist of any other medication being taken, including over-the-counter products.

5. Report any adverse effects or warning symptoms to the specialist or GP such as unexplained sore throat, bruising, mouth ulcers, nausea, vomiting, dark urine colour and shortness of breath.

6. Inform other professionals of current treatment as necessary.

7. Use appropriate contraception where applicable.

8. Where applicable carry your methotrexate booklet and show to healthcare professionals such as community pharmacists.

9. When buying over the counter medicines, herbal products or vitamins always ask for pharmacist advice.

The responsibility for arranging and taking action on blood test results where necessary remains with the prescribing clinician.
Contact for support and advice

Inflammatory Bowel Disease Helpline 0116 2584352

LGH Consultants -
Richard Robinson 0116 2584797
Adrian Gelsthorpe 0116 2584796
Sejal Shah 0116 2584787

LRI Consultants -
Barrie Rathbone 0116 2586630
Peter Wurm 0116 2585855
James Stewart 0116 2586480
Allister Grant 0116 2586480
Toby Delahooke 0116 2587296
Sanjeev Pattni 0116 2586480
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Ka-Kit Li 01162586630
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Patricia Hooper 01162584797
Rekha Ramiah 01162586480

Supporting Information


BNF provided by NICE [https://bnf.nice.org.uk](https://bnf.nice.org.uk)

AZATHIOPRINE | Drug | BNF Provided by NICE


BSR/BHPR guideline for disease-modifying anti-rheumatic drug (DMARD) therapy in consultation with the British Association of Dermatologists Rheumatology 2008. [https://www.yorkhospitals.nhs.uk/seecmsfile/?id=1445](https://www.yorkhospitals.nhs.uk/seecmsfile/?id=1445)

<table>
<thead>
<tr>
<th>Version</th>
<th>Section</th>
<th>Description of amendments</th>
<th>Date</th>
<th>Author / amended by</th>
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<tbody>
<tr>
<td>1.1</td>
<td>Appendix</td>
<td>Title added and platelets amended to less than 150</td>
<td>June 14</td>
<td>HH</td>
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<tr>
<td>1.2</td>
<td>Drugs covered</td>
<td>Mesalazine clarified as mesalazine oral and rectal mesalazine does not require a shared care agreement. Sulphasalazine EC amended to include suppositories too. Dr Mayberry’s details removed as he has left the Trust</td>
<td>Feb 16</td>
<td>HH</td>
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<td>1.3</td>
<td>Drugs covered</td>
<td>Brand names of mesalazine added to enable searching via the LMSG website Specified applies to methotrexate oral CRP removed from drug monitoring requirements as relates to disease monitoring only</td>
<td>Apr 16</td>
<td>HH</td>
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<td>1.4</td>
<td>All over review</td>
<td>Removal of aminosalicylates, update need for contraception and info around interactions. Clarity of community pharmacist role</td>
<td>October 18</td>
<td>SG/RD/AS</td>
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## Appendix Drug Monitoring

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Pre-treatment</th>
<th>Routine</th>
<th>Discuss with specialist urgently</th>
<th>Possible dose reduction (discuss with specialist)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Azathioprine</strong></td>
<td>IBD 2-2.5mg/kg/day increased as tolerated</td>
<td>FBC, U&amp;E, LFT, Creatinine</td>
<td>FBC and LFT every week for 4 weeks then monthly; if dose and results stable for 6 months, monitor 3 monthly FBC, LFTs. U&amp;E and creatinine – 6 monthly.</td>
<td>WCC falls &lt;3.5 x 10^9/l</td>
<td>If &gt;50% rise in ALT/AST (but less than 2-fold rise).</td>
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<td></td>
<td>AH 1-2mg/kg/day increased as tolerated</td>
<td>TPMT – if &lt;35nmol then continue monthly FBC and LFTs</td>
<td>After dose increase – repeat FBC and LFTs after 2 weeks, then monthly. If dose and results stable for 6 months, monitor 3 monthly FBC, LFTs. U&amp;E and creatinine – 6 monthly.</td>
<td>Neutrophils &lt;2.0 x 10^9/l</td>
<td>If side effects such as mouth ulcers, rash, nausea &amp; diarrhoea occur.</td>
</tr>
<tr>
<td><strong>6-Mercaptopurine</strong></td>
<td>IBD and AH 1-1.5mg/kg/day</td>
<td>Consider monthly FBC, U&amp;E, LFT</td>
<td>Following initiation and after any dose increase, FBC, U&amp;E and LFTs every 2 weeks for 8 weeks then monthly until dose and disease stable for a year. Thereafter reduce frequency of monitoring to 2-3 monthly FBC, U&amp;E and LFTs.</td>
<td>Eosinophils &gt;0.5 x 10^9/l</td>
<td>If there is significant deterioration in renal function.</td>
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<tr>
<td><strong>Methotrexate oral</strong></td>
<td>Crohn's 10-25 mg ONCE a week. Rarely max 30mg/week.</td>
<td>FBC, U&amp;E, LFT, Creatinine</td>
<td>Following initiation and after any dose increase, FBC, U&amp;E and LFTs every 2 weeks for 8 weeks then monthly until dose and disease stable for a year. Thereafter reduce frequency of monitoring to 2-3 monthly FBC, U&amp;E and LFTs.</td>
<td>Platelets &lt;150 x 10^9/l</td>
<td>Severe rash or bruising or ulceration of mucous membranes.</td>
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<td>MCV &gt; 105 f/l</td>
<td>Any unexplained illness occurs including nausea or diarrhoea.</td>
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<td>Creatinine &gt;30% baseline</td>
<td>Methotrexate – new dyspnoea, cough or significant fall in albumin.</td>
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