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Coventry & Warwickshire Area Prescribing Committee

Shared Care Agreement

Azathioprine: *for the treatment of inflammatory and autoimmune conditions e.g. rheumatoid arthritis, inflammatory bowel disease, autoimmune cytopenias, dermatomyositis*

AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of **Azathioprine c**an be shared between the specialist and general practitioner (GP). GPs are **invited** to participate. If the GP is not confident to undertake these roles, 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. **If a specialist asks the GP to prescribe this drug, the GP should reply to this request as soon as practicable.**

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

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

Specialist Responsibilities

1. Discuss with the patient options for treatment and the suitability of azathioprine.
2. Discuss the potential benefits and side effects of treatment with the patient.
3. Following agreement with the patient, initiate Azathioprine titrate to an effective dose and stabilise the patient on an appropriate maintenance dose before seeking to initiate shared care (Usually by 3 months).
4. Ask the GP whether he or she is willing to participate in shared care by emailing the shared care request letter, (continue to prescribe until GP has agreed to take over prescribing).
5. Explain the intention to share care with the patient/ carer.
6. Perform monitoring of Height, weight, blood pressure, FBC, U&E, LFTs, albumin, CRP, eGFR, VZV, TPMT specifying frequency of blood monitoring and communicate the results with the GP.
7. Communicate to the GP the established regimen and when to refer back to specialist care.
8. Initiate and stabilise treatment. Supply 3 months (in instalments as appropriate).
9. Inform GP and patient of dosing adjustments.
10. Have a mechanism in place to receive rapid referral of a patient from the GP in event of abnormal blood results or deteriorating clinical condition.
11. Ensure clear backup arrangements exist for GPs to obtain advice and support and be available for review if requested.

Report adverse events to the MHRA on a Yellow Card www.mhra.gov.uk/yellowcard, and to the GP and appropriate Medicines Optimisation team.

General Practitioner Responsibilities

1. Reply to the request for shared care as soon as practicable by emailing back the shared care letter. If declining the request please indicate the reason for declining.
2. Prescribe azathioprine at the recommended dose.
3. Adjust the dose as advised by the specialist.
4. Check for possible drug interactions when prescribing new medication and avoid prescribing interacting drugs.
5. To ensure blood forms issued by secondary care are used for routine blood test monitoring and if necessary patient to attend surgery for blood tests as specified on pre-printed blood form.
6. Report to and seek advice from the specialist on any aspect of patient care that is of concern and may affect treatment.
7. Refer the patient to the specialist if his/ her condition deteriorates.
8. Stop treatment on the advice of the specialist.

Report adverse events to the MHRA on a Yellow Card (www.mhra.gov.uk/yellowcard), the specialist, and the appropriate Medicines Optimisation team.

Patient/carer's Role

1. Attend follow up and other appointments.
2. Report to the specialist or GP if he or she does not have a clear understanding of the treatment.
3. Agree to routine blood monitoring for the duration of treatment.
4. Inform specialist of problems when taking medication or have stopped taking it.
5. Inform specialist or GP of any other medication being taken, including over-the-counter products.
6. Report any adverse effects or warning symptoms to the specialist or GP.

The patient may also choose to report any adverse drug reaction direct to the MHRA on a Yellow Card , available at pharmacies, GP surgeries or from the Yellow Card hotline (freephone 0808 100 3352 during business hours).
The form can also be downloaded from www.mhra.gov.uk/yellowcard

This SCA should be read in conjunction with the Summary of Product Characteristics (SPC) and the current edition of the British National Formulary

Back-up Advice and Support: See patient letter and/or other supporting information for contact details of clinician(s) initiating and stabilising patient prior to request for shared care.

SUPPORTING INFORMATION

Licensed indications: Severe rheumatoid arthritis; systemic lupus erythematosus; dermatomyositis and polymyositis; auto-immune chronic active hepatitis; pemphigus vulgaris; polyarteritis nodosa; auto-immune haemolytic anaemia; chronic refractory idiopathic thrombocytopenic purpura; prophylaxis of organ rejection following transplant.

Dosage and administration: Adults: All patients receive Azathioprine in a constant dose of 1 - 2 mg/kg/day rounded to the nearest 25 mg. Maintenance dose is then adjusted within these limits to clinical response and tolerance.

Monitoring: *Pre-treatment Assessment:* Height, weight, blood pressure, Full Blood Count, U&Es, CRP, eGFR, Liver Function Tests, TMPT. **TPMT level checked and results must be back before treatment commences.**

After commencing treatment: Check FBC, creatinine/calculated GFR, ALT and/or AST and albumin every 2 weeks until on stable dose for 6 weeks; then once on stable dose, monthly FBC, creatinine/calculated GFR, ALT and/or AST and albumin for 3 months; thereafter, FBC, creatinine/calculated GFR, ALT and/or AST and albumin at least every 12 weeks. More frequent monitoring is appropriate in patients at higher risk of toxicity

Dose increases should be monitored by FBC, creatinine/calculated GFR, ALT and/or AST and albumin every 2 weeks until on stable dose for 6 weeks then revert to previous schedule

Combination with any other DMARD will require standard monitoring schedules as above

Interruption of Treatment: Contact rheumatology team urgently and withhold treatment if any of the following develop: white cell count <3.5 x 10^9/l; mean cell volume >105 Fl and if B12 or folate low start supplementation; neutrophils <1.6 X 10^9/l; creatinine increase >30% over 12 months and/or calculated GFR <60 ml/min; unexplained eosinophilia >0.5 X10^9/l; ALT and/or AST >100 U/l; platelet count < 140 X 10^9/l; unexplained reduction in albumin <30 g/l

During a serious infection, discontinue until the patient has recovered from the infection

As well as responding to absolute values in laboratory tests, it is also relevant to observe trends in results (e.g. gradual decreases in white blood cells or albumin, or increasing liver enzymes).

Cessation of Treatment Platelets <120,000; White Blood Cells <3.5 x 10^9/l, Neutrophils < 2.0 x 10^9/l; LFTs twice the upper limit of normal (AST or ALP); dose reduction If WBC <4.0, Neutrophils <2.5 halve dose

Reduce dose if patient suffering from nausea, rash or recurrent infections

Cautions: Elderly patients or those with renal or hepatic impairment should have doses initiated at the lower end of the dosage range and haematological response should be monitored closely. Individuals with inherited deficiency of the enzyme thiopurine methyltransferase (TPMT) are more susceptible to bone marrow suppression and toxicity.
There is an increased risk of skin malignancies- patients should be advised to wear protective clothing and use sunscreen with a high protection factor.

Contra-indications: Pregnancy or breastfeeding; Known Hypersensitivity

Side effects: Common- Nausea (dose related), diarrhoea, headache, arthralgia. These symptoms often improve overtime.
Rash or mouth ulcers may respond to a dose reduction otherwise treatment should be discontinued
Less Common- Hair Loss, neutropenia, leucopenia, pancreatitis, hepatitis discontinues treatment.
For a full list of ADRs refer to the product SPC.

Azathioprine does not have black triangle (▼) status. All serious suspected adverse reactions (even well recognised or causal link uncertain) should be reported to the MHRA.

Drug interactions (see also above under cautions): See SPC for a detailed list. Relevant interactions include:

- Allopurinol- may enhance the drugs effect and therefore increase the risk of toxicity. Avoid concurrent treatment.
- May affect INR - monitor regularly if on warfarin treatment
- Antibacterials - toxicity increased with trimethoprim or co-trimoxazole
- Clozapine - avoid concurrent use
- Aminosalicylates - may enhance toxicity particularly in patients with TPMT deficiency

Cost: At current prices one year's treatment of azathioprine 100 mg daily will cost £28.16
(Prescription Pricing Division (PPD). NHS Business Services Authority. Drug Tariff March 2018. Accessed 6.3.18 via www.nhsbsa.nhs.uk)

References:

1. Summary of Product Characteristics. Azathioprine. Last updated 21.10.16. Available via www.medicines.org.uk accessed 14/8/2018
2. Ledingham J, Gullick N, Irving N et al. on behalf of the BSR and BHPR Standards, Guidelines and Audit Working Group; BSR and BHPR guideline for the prescription and monitoring of non-biologic disease-modifying anti-rheumatic drugs, Rheumatology, Volume 56, Issue 6, 1 June 2017, Pages 865–868. Available at https://academic.oup.com/rheumatology/article/56/6/865/3053478/BSR-and-BHPR-guideline-for-the-prescription-and