DMARDs in Adult Rheumatology - Shared Care Information

Sulfasalazine

Please also refer to the Shared Care Guidelines - Principles of Shared Care and Responsibilities of Speciality Team, GP, Pharmacist & Patient

Indications:
- Licensed - Rheumatoid arthritis, ulcerative colitis and crohn's disease
- Unlicensed - Seronegative spondyloarthropathy including psoriatic arthritis and psoriasis

Time to response:
- Minimum12 weeks

Presentation and Availability:
- 500mg tablets (enteric-coated tablets recommended for Rheumatology patients)

Contraindications:
- Hypersensitivity to sulfasalazine, its metabolites or any of the excipients as well as sulphonamides/ co-trimoxaxole or salicylates
- Patients with acute porphyria

Cautions:
- Glucose- 6- phosphate dehydrogenase (G6PD) deficiency – may cause haemolysis
- Slow acetylators of the drug – may cause drug- induced lupus- like syndrome
- Renal impairment (moderate). Avoid in severe renal failure.
- May impair folate absorption

Side effects:
- *Common non-life threatening:* Nausea, diarrhoea, abdominal pain, headache
- *Serious side- effects:* Blood dyscrasias (see monitoring)
- *Miscellaneous*: Yellow/ orange discolouration of urine, photosensitivity, taste disturbances

See SPC for full list of side effects: http://www.medicines.org.uk/emc/default.aspx

Pregnancy and Breastfeeding:
- Sulfasalazine can be prescribed during pregnancy but it should only after careful consideration of risk and benefit
- Doses should not exceed 2g/day
- Adequate folic acid supplements should be provided as there is a theoretical risk of neonatal haemolysis in the third trimester due to inhibition of folate absorption
- Sulfasalazine can be prescribed to men of childbearing potential but it may cause reversible oligospermia
- Sulfasalazine can be continued while breastfeeding – small amounts are present in breast milk but are not thought to pose risk to a healthy infant. Care should be taken in G6PD deficient infants however

Drug Interactions:
- Antacids –Take at least 2- 4 hours apart
- Azathioprine – increased risk of leucopoenia when used concomitantly
- Digoxin – reduced absorption of digoxin leading to sub-therapeutic levels
- Folic acid – reduced absorption causing folate deficiency

For further information refer to BNF and SPC: http://www.medicines.org.uk/emc/default.aspx

Vaccination:
- See Appendix i

Sulfasalazine – Dosage and Monitoring

Dosage and Administration:
- Initiate at 500mg daily
- Increase by 500mg every week in divided doses to a maximum of 2-3g daily
- Occasionally doses above 3g daily are used

Pre-treatment Assessment:
- FBC
- U&Es and Creatinine
- LFTs

During Treatment:
See 'Responsibilities of Speciality Team, GP, Patient and Pharmacist in Shared Care Arrangement'

Investigation	Frequency	Specialist	GP
FBC and LFTs	Monthly for 3 months	✓	
	Reduce to 3 monthly intervals for 1 year thereafter		✓
	Reduce to 6 monthly if blood tests remain stable		
FBC and LFTs	Monthly after dose change If stable, revert to usual monitoring regime	✓	
Ask about skin rash or oral ulceration	At each visit	✓	✓

- Please monitor CRP/ ESR (usually every 3 – 6 months) to assess disease activity as requested by specialist team

Action to be taken if:

WBC <3.5 x 10^^{9}/l	Withhold until discussed with specialist team
Neutrophil <2.0 x 10^9/l	Withhold until discussed with specialist team
Platelets <150 x 10^9/l	Withhold until discussed with specialist team
AST, ALT > twice upper limit of reference range	Withhold until discussed with specialist team
MCV>105fl	Check B12, folate & TFTs and start supplementation if appropriate. If normal discuss with specialist team
Nausea, dizziness or headache	If possible continue, may have to reduce dose or stop if symptoms severe. Discuss with specialist team.
New or increasing dyspnoea or dry cough	Withhold and discuss urgently with specialist team
Abnormal bruising or severe sore throat	Withhold until urgent FBC result available. Discuss with speciality team if necessary
Unexplained acute widespread rash	Withhold seek urgent specialist (preferably dermatological) advice
Oral ulceration	Withhold until discussed with specialist team

- In addition to absolute values for haematological indices a rapid fall or a consistent downward trend in any value should prompt caution and extra vigilance

Appendix i

Guidelines for vaccinations in patients taking immunosuppressants, steroids and biological therapies

This is the BSR's most recent guidance and is subject to revision and formal review

GENERAL INFORMATION LIVE VACCINES

- Live vaccines are contraindicated while on immunosuppressive therapy
  - e.g Azathioprine, Ciclosporin, Leflunomide, Mycophenolate, Cyclophophamide
- Immunosuppressive therapy should be stopped for 3 months prior to live vaccine administration
- Live vaccines if needed should be ideally given at least 2 weeks, preferably 4 weeks, before immunosuppressive therapy is commenced
- In immunosuppressed patients, the immunological response may be suboptimal. Consider repeating 3 months after therapy has ceased if viral titres low
- Consider using immunoglobulins if contact risk is significant (e.g. Varicella, Measles)

INACTIVE VIRUS VACCINES

- In immunosuppressed patients, the immunological response may be suboptimal but can be given in accordance with national recommendations
- There is an increased risk in the immunocompromised from secondary bacterial infections following influenza
- Pneumococcal and the Annual flu vaccination is recommended in patients with autoimmune inflammatory rheumatic disease
- Immunisation against Meningococcal, Haemophilus B, Tetanus and Hepatitis B infection might be indicated. Check Hepatitis B titres 3 months after the 3rd injection
- Check Varicella zoster titres prior to immunisation if appropriate

VACCINES FOR TRAVEL ABROAD

- Yellow fever vaccine must not be given. Patients should be advised not to travel to countries requiring this e.g. mid-Africa. If travel necessary, an exemption statement may be accepted but the patient will be at risk
- Polio vaccine - the oral live polio vaccine (OPV) must not be given. Killed inactivated vaccine can be given but may need to be obtained from abroad so adequate notice must be given
- Typhoid vaccine - the live form should not be given. Killed vaccine is available but only 70% protective
- Inactive viruses can be given e.g. Rabies, Anthrax, Cholera, Plague

VACCINES FOR HOME

- Polio - OPV is contraindicated and in household contacts. Inactivated form (IPV) can be used
- Measles, Mumps, Rubella (MMR) - all three live vaccines is contraindicated but not in household contacts. Exposure to measles should be treated with immunoglobulin regardless of prior immunization
- BCG is contra-indicated. Consider giving it in juvenile arthritis 4 weeks before immunosuppressives started. Juvenile arthritis patients should be brought up to date with vaccination schedules prior to receiving methotrexate

Zostavax (Zoster Vaccination)

- A live attenuated vaccine with high antigen level of varicella zoster virus
- Eligible individuals previously not immunised should receive a single dose of vaccine at least 14 days (preferably a month) before starting immunosuppressive therapy as the risk and severity of shingles is considerably higher amongst immunosuppressed individuals
- Zostavax should not be given to a person who is receiving immunosuppressive therapy such as high-dose corticosteroids
- Zostavax can be given to patients receiving low dose corticosteroids, low dose methotrexate (<0.4/kg/week) and azathioprine (<3.0mg/kg/day) for treatment of rheumatoid arthritis, psoriasis, polymyositis and sarcoidosis
- Immunosuppressed individuals who are inadvertently vaccinated with Zostavax should be urgently assessed by a clinician to establish the degree of immunosuppression and the need for prophylactic acyclovir. If a varicella rash develops following inadvertent vaccination, patients can be treated with aciclovir

See link for full guidance:
https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/239892/2013181_Shingles_QA_for_healthcare_professionals_final.pdf

PATIENTS ON STEROIDS

- Live vaccines must not be given to patients taking moderate or high doses of steroids for longer than 2 weeks
- Long-term moderate to high dose steroids should be stopped for 3 months before live vaccines can be administered

There are no contra-indications to using live vaccines if steroid therapy is:

- for less than 2 weeks
- by topical application
- by intra-articular or soft tissue injection
- used as replacement therapy in physiological doses e.g. adrenal insufficiency
- long-term low dose steroids (10mg per day or less)

BIOLOGICS

- Live vaccines should not be given concurrently with biological therapies as no data is available on the effects of vaccination in these patients e.g. anti- TNF therapy, Tocilizumab or Anakinra

LEFLUNOMIDE

- The long half-life of Leflunomide should be considered when contemplating administration of a live vaccine after stopping the drug

References

- BSR/BHPR guideline for disease-modifying anti-rheumatic drug (DMARD) therapy in consultation with British Association of Dermatologists. Rheumatology. 2008 K Chakravarty *et al* http://rheumatology.oxfordjournals.org/content/suppl/2008/05/31/kel216a.DC1/kel216b.pdf

- SPC (Summaries of Product Specification) for each drug are available on the EMC website: http://www.medicines.org.uk/emc/default.aspx Please ensure you refer to the correct brand where appropriate (especially for ciclosporin and mycophenolate mofetil) as some information is brand specific.

- Vaccinations in the immunocompromised person guidelines for the patient taking immunosuppressants, steroids and the new biologic therapies January 2002 http://www.rheumatology.org.uk/includes/documents/cm_docs/2009/v/vaccinations_in_the_immunocompromised_person.pdf

- BSR statement on Vaccination in Adult Patients with Rheumatic Diseases November 2011