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DMARD MONITORING GUIDELINES –Reviewed 23.01.15

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The current BSR DMARD and Denosumab Monitoring Guidelines are now available via the following link: http://www.rnhrd.nhs.uk/our-services/for-clinicians

Ciclosporin

A. Indications: (Licensed) RA, psoriasis and atopic dermatitis

B. Dose: Grade of evidence: C

(1) RA starting dose: 2.5 mg/kg/day in two divided doses for 6 weeks and then may be increased at 2–4 weeks intervals by 25mg until clinically effective or the maximum dose of 4 mg/kg/day is reached [1–3].
Maintenance dose: Often effective between 2.5–3.2 mg/kg/ day. Adjust to patient's tolerance and benefit. Constantly evaluate response and toxicity before increasing to the
maximum dose.
Maximum dose: 4 mg/kg/day [1–3].

(2) Psoriasis and atopic dermatitis (BAD) starting dose: 2.5–5 mg/kg/day depending on disease severity and then treated according to response;
Maximum dose: 5 mg/kg/day.

C. Route of administration: Oral

D. Time to response: 3 months; If no clinical response at maximum tolerated dose for 3 months, then withdraw the treatment [3, 4].

E. Cautions: Grade of evidence: A & C

(1) Pregnancy and lactation [5, 6].
(2) Grapefruit including grapefruit juice must be avoided for 1 h before or after taking ciclosporin tablets as bioavailability is increased [2].
(3) Malignancy such as lymphomas, etc [4, 6].

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F. Contraindications: Grade of evidence: C

(1) Uncontrolled hypertension [1, 4, 6–8].
(2) Renal and liver failure (in patients with RA) [6].
(3) Severe electrolyte imbalance i.e. hyperkalemia [1, 2].
(4) Suspected systemic infection or sepsis [6].

G. Notable drug interaction (refer to BNF and SPC)

(1) Diclofenac: Reduce the dose of diclofenac by 50% [1–3]
(2) Colchicine: To be avoided [1, 2].
(3) Simvastatin: maximum dose 10 mg/day [6].
(4) Nifedipine: use with caution [6].
(5) Digoxin: May increase the serum levels of digoxin [6].
(6) St. John's Wort: decreases ciclosporin activity [6].
(7) Potassium sparing diuretics.

H. Monitoring schedule: Grade of evidence: C

	BSR and BAD
(a) Pre-treatment assessment	**FBC including differential white cell count, U&E, creatinine: (check twice, 2 weeks apart, to obtain a mean value for creatinine), LFT, fasting lipids, creatinine clearance prior to starting the drug. Blood pressure: to be ≤ 140/90 before treatment on two measurements 2 weeks apart [8]. If greater than this, treat hypertension before starting ciclosporin. In patients with psoriatic arthritis: assess whether patient has received PUVA before commencing ciclosporin. If total dose exceeds 1000J discuss with dermatologists.**
(b) Monitoring	**FBC & LFT: once a month until dose and trend stable for 3 months, and then 3-monthly. Serum electrolytes including potassium and creatinine every 2 weeks until dose and trend stable for 3 months and then monthly. Watch when NSAID is added, particularly diclofenac. Chest fasting lipids periodically [3]. Blood pressure (BP): check BP each time patient attends monitoring clinic and maintain ≤ 140/90.**

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I. Actions to be taken: Grade of evidence: C

Creatinine rises >30% from baseline	**Repeat in 1 week and if still >30% above baseline withhold until discussed with the specialist team.**
Potassium rises to above the reference range	**Withhold until discussed with the specialist team.**
Platelets <150 x 10^9/l	**Withhold until discussed with the specialist team.**
'Significant' rise in fasting lipids	**Withhold until discussed with the specialist team.**
High BP: ≥ 140/90 on two consecutive readings 2 weeks apart	**Treat blood pressure before stopping the ciclosporin (note interactions with several anti-hypertensives). If BP cannot be controlled, stop ciclosporin and obtain BP control before restarting ciclosporin. Discuss with the specialist team.**
AST, ALT or alkaline phosphatase more than 2x upper limit of reference range	**Withhold until discussed with the specialist team. Check any other reason such as alcohol, drug interaction including over the counter medication.**
Abnormal bruising	**Check FBC immediately and withhold until discussed with the specialist team.**

AST: aspartate aminotransferase; ALT: alanine aminotransferase.

J. Immunization:

(1) Patients receiving ciclosporin must not receive immunization with live vaccines. Inactivated polio is available although suboptimal response may be seen.
(2) Annual flu vaccination is recommended.
(3) In patients receiving ciclosporin exposed to chickenpox or shingles, passive immunization should be carried out using VZIG.

References

Ciclosporin

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3 Summary of Product Characteristics from Novartis as makers of Neoral, (in respect of Rheumatoid Disease). Novartis Pharmaceuticals UK Ltd, Surrey, UK. http://emc.medicines.org.uk/emc/assets/c/html/DisplayDoc.asp?DocumentID=1307 (17 October 2007, date last accessed).

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