Biological Agents – Treatment of Rheumatoid Arthritis

Eligibility criteria:¹
1. Active rheumatoid arthritis (RA) Disease activity score (DAS28) score >5.1 based on 2 measurements made 1 month apart
2. Fulfil the 1987 criteria of the ACR classification criteria for a diagnosis of RA
3. Failed standard therapy.*

Consider eligibility and exclusion criteria for biological agent AND lack of alternative treatment options.

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Exclusion criteria for biological agents:
- Pregnancy or breastfeeding
- Active infection
- Septic arthritis of native joint within last 12 months
- Septic arthritis of prosthetic joint within last 12 months or indefinitely if remains in situ
- NYHA class 3 or 4 heart failure
- Clear history of demyelinating disease
- See also individual drug SPCs and British Society of Rheumatology (BSR) Guidelines for additional cautions.

Register patient with BSR Biologics Register (or make provision for local data collection if so advised by the BSR)

Is the patient suitable for subcutaneous (s/c) administration?

In no order of preference:
- **Adalimumab** 40mg s/c once a fortnight.
- **Etanercept** 50mg s/c once a week or 25mg s/c twice a week.

**Infliximab** 3mg/kg intravenous infusion weeks 0, 2 and 6, then every 8 weeks (ensure DMARD co-prescribed – weekly methotrexate preferred)

Review at 3 months to assess response and further treatment (NB NICE Guidance states allow upto 6 months to assess effectiveness but earlier assessment considered more appropriate at WUTH)

**Full Response**
DAS28 score <3.2 or reduced by >1.2

Continue treatment & review every 3 months for 1st year then minimum of every 6 months thereafter. Consider dose or frequency reduction after 12 months if adequate response maintained.

**Partial Response**
Consider if other changes in therapy have occurred, e.g. reduction in steroid dose, continue biological agent at same dose and frequency for a further 3 months then re-assess.

If still partial response, change to alternative TNF inhibitor² and review again at 3 months.

**Non-response or drug related toxicity**
Stop drug. Consider alternative biological agent

Yes

No

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¹ Biological agents in the treatment of rheumatoid arthritis – Clinical Guideline, V2
Approved by: Wirral Drug and Therapeutics Committee June 2010
Principal author: Dr George
Review date: June 2013
Depending on clinical grounds switch to an alternative biological agent:

Second line:
- Switch from etanercept to adalimumab or adalimumab to etanercept
- If partial/no response to infliximab, will patient re-consider s/c administration and switch to etanercept. No rationale for switching infliximab to adalimumab and vice versa.

Third line:
- Rituximab 1g iv infusion - 2 doses given two weeks apart (co-prescribing of weekly methotrexate recommended)
  Review patient 6 months after infusion - further doses of rituximab should not normally be given at an interval less than every 6 months and only in those patients who showed adequate initial response (DAS28 score reduced by >1.2)

Review at 3 months after changing to assess response and determine ongoing treatment.

4th line treatment options:
PCT Health Treatment Panel request needed prior to initiation for:
- Infliximab at increased mg/kg dose or frequency.
- All other biological agents

References:
1. Update of BSR Guidelines for Prescribing TNF Blockers in Adults with RA. BSR July 2004
2. BSR Biologics Register Newsletter July 2006

* Standard therapy defined as:
Failure to respond to or tolerate adequate therapeutic trials of at least 2 standard DMARDs (IM gold, hydroxychloroquine, sulfazalazine, pencillamine, azathioprine, methotrexate or leflunomide).
One of the failed or not tolerated therapies must be methotrexate.

Adequate therapeutic trial is defined as:
Treatment for at least 6 months, with at least 2 months at a standard target dose unless significant toxicity limits the dose tolerated.
Treatment for less than 6 months where treatment was withdrawn because of drug intolerance or toxicity, but normally after at least 2 months at therapeutic doses.