MSK Clinical Commissioning Programme

The use of Cytokine/ Biologics in rheumatoid arthritis in Dorset

Patient eligible for biologic due to the following characteristics:

- Active rheumatoid arthritis as measured by disease activity score (DAS28) greater than 5.1 confirmed on at least two occasions, 1 month apart.
- Have undergone trials of two disease-modifying anti-rheumatic drugs (DMARDs), including methotrexate (unless contraindicated). A trial of a DMARD is defined as being normally of 6 months, with 2 months at standard dose, unless significant toxicity has limited the dose or duration of treatment.

First line choices

If methotrexate can be taken concomitantly first line choice may be, generally, certolizumab. It is anticipated that at least 80% of patients will receive certolizumab as their first-line agent. Response will be assessed at 12 weeks, where no response is seen a switch of first line agent is indicated, generally to a different sub-cut delivered anti-TNF agent.	If methotrexate is contra-indicated or patient is intolerant first line choice may be tocilizumab as monotherapy.	For patients who are rheumatoid factor positive and have a concomitant lung disease, such as bronchiectasis, first line choice may be rituximab.

Assessment and review

- Treatment with TNF-α inhibitors should be continued only if there is an adequate response at 6 months following initiation of therapy. An adequate response is defined as an improvement in DAS28 of 1.2 points or more
- After initial response, treatment should be monitored no less frequently than 6-monthly intervals with assessment of DAS28. Treatment should be withdrawn if an adequate response is not maintained.
- An alternative TNF-α inhibitor may be considered for patients in whom treatment is withdrawn due to an adverse event before the initial 6-month assessment of efficacy, provided the risks and benefits have been fully discussed with the patient and documented

Second line choices

Patients who are rheumatoid factor positive should receive rituximab with methotrexate (unless received first-line). Where a patient is unable to take methotrexate rituximab may be used in combination with leflunomide or as monotherapy.	Patients who are rheumatoid factor negative should receive tocilizumab with methotrexate (unless received first-line) Where a patient is unable to take methotrexate tocilizumab may be used as monotherapy.

Assessment and review

- Treatment with rituximab or tocilizumab should be continued only if there is an adequate response following initiation of therapy and if an adequate response is maintained following retreatment with a dosing interval of at least 6 months. An adequate response is defined as an improvement in disease activity score (DAS28) of 1.2 points or more
- Treatment should be monitored, with assessment of DAS28, at least every 6 months and continued only if an adequate response is maintained.

Third line choices

Abatacept, adalimumab, etanercept, golimumab, infliximab and tocilizumab, each in combination with methotrexate, are recommended as treatment options only for adults with severe active rheumatoid arthritis who have had an inadequate response to, or have an intolerance of, other DMARDs, including at least one TNF inhibitor, and who cannot receive rituximab therapy because they have a contraindication to rituximab; when rituximab is withdrawn because of an adverse event or there is non-response or loss or response to rituximab.

Abatacept, adalimumab, etanercept, golimumab and infliximab, each in combination with methotrexate, are recommended as treatment options only for adults with severe active rheumatoid arthritis who have had an inadequate response to, or have an intolerance of, other DMARDs, including at least one TNF inhibitor, and who are rheumatoid factor negative and therefore unsuitable for rituximab therapy; when tocilizumab is withdrawn because of an adverse event or there is non-response or loss or response to tocilizumab

Assessment and review

- Treatment with a third line agent should be continued only if there is an adequate response following initiation of therapy and if an adequate response is maintained following retreatment with a dosing interval of at least 6 months. An adequate response is defined as an improvement in disease activity score (DAS28) of 1.2 points or more.
- Treatment should be monitored, with assessment of DAS28, at least every 6 months and continued only if an adequate response is maintained.

Fourth line choice

Abatacept with methotrexate may be considered as a fourth line agent where a patient has been contra-indicated, not tolerated or not responded or has an inadequate response to alternative biologic options.

Assessment and review

- Treatment with a fourth line agent should be continued only if there is an adequate response following initiation of therapy and if an adequate response is maintained following retreatment with a dosing interval of at least 6 months. An adequate response is defined as an improvement in disease activity score (DAS28) of 1.2 points or more.
- Treatment should be monitored, with assessment of DAS28, at least every 6 months and continued only if an adequate response is maintained.

Drug	Annual Cost (based on BNF no 65, March-Sept 13)
Certolizumab (sub-cut)	£7,150 for year 1 (first 12 weeks of therapy provided free of charge) Second and subsequent years: £9,295
Adalimumab (sub-cut)	£9,155 at 40mg on alternate weeks N.B licensing allows for weekly dosing if monotherapy but equates to £18,311 therefore not recommended locally
Etanercept (sub-cut)	£9,295 for 25mg twice weekly or 50mg once a week
Golimumab (sub-cut)	£9,155 for 50mg monthly N.B must be given with methotrexate
Tocilizumab (iv infusion, therefore VAT incl. and administration costs will also be incurred)	Weight based: For 50kg patient at 400mg every 4 weeks = £7,987 For 60kg patient at 480mg every 4 weeks = £9,585 For 70kg patient at 560mg every 4 weeks = £11,182
Tocilizumab (sub-cut)*	Each pre-filled syringe contains 162 mg of tocilizumab in 0.9 ml, cost £228.28 (£913.12 per 4 weeks) Dose = 162mg sub cutaneous injection once every week = £11,871
Abatacept (If IV infusion loading doses VAT incl. and administration costs will also be incurred). May be initiated without an IV loading dose	Weight based, loading dose (IV unless not appropriate): <60kg 500mg@ 0,2 and 4 weeks = £2,177 60-100kg 750mg@ 0,2and 4 weeks = £3,266 >100kg 1gm @ 0,2 and 4 weeks = £4,355 Subsequent sub-cut doses in first year, 125mg given within a day of the loading dose, then 125mg weekly = £14,515 If initiated without IV loading dose, administer 125mg weekly by SC inj regardless of weight = £15,725 Second and subsequent years, 125mg weekly = £15,725
Rituximab (iv infusion therefore VAT incl. and administration costs will also be incurred)	1gm dose at 0 and 2 weeks = £4,191 May be repeated at a minimum of six monthly intervals

*Personal communication from manufacturer. August 14