DORSET MEDICINES ADVISORY GROUP

COMMISSIONING STATEMENT ON THE USE OF ADALIMUMAB, ETANERCEPT, INFLIXIMAB, CERTOLIZUMAB PEGOL, GOLIMUMAB, TOCILIZUMAB AND ABATACEPT FOR RHEUMATOID ARTHRITIS NOT PREVIOUSLY TREATED WITH DMARDs OR AFTER CONVENTIONAL DMARDs ONLY HAVE FAILED (TA375)

SUMMARY

NHS Dorset Clinical Commissioning Group commissions the use of adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab and abatacept for rheumatoid arthritis not previously treated with DMARDs or after conventional DMARDs only have failed in accordance with NICE TA375.

BACKGROUND	This guidance replaces NICE technology appraisal guidance on: • adalimumab, etanercept and infliximab for the treatment of rheumatoid arthritis (TA130) • certolizumab pegol for the treatment of rheumatoid arthritis (TA186) • golimumab for the treatment of methotrexate-naive rheumatoid arthritis (TA224) and • abatacept for treating rheumatoid arthritis after the failure of conventional disease-modifying anti-rheumatic drugs (TA280). This technology partially updates golimumab for the treatment of rheumatoid arthritis after the failure of previous disease-modifying anti-rheumatic drugs (TA225) and tocilizumab for the treatment of rheumatoid arthritis (TA247). Adalimumab, etanercept, infliximab, certolizumab pegol and golimumab inhibit the activity of tumour necrosis factor (TNF)-alpha, a pro-inflammatory mediator that is partly responsible for damage to the joints in rheumatoid arthritis. Tocilizumab inhibits the activity of interleukin-6 (IL-6), a pro-inflammatory cytokine that is also partly responsible for damage to the joints in rheumatoid arthritis. Abatacept is a selective modulator of the T-lymphocyte activation pathway. It binds to molecules on the surface of antigen-presenting cells, preventing full activation of the T-lymphocytes and interrupting the inflammatory process. Treatment for rheumatoid arthritis usually involves initially (NSAIDs) or COX-2 inhibitors, which reduce pain, fever, and joint swelling and inflammation, and disease-modifying antirheumatic drugs (DMARDs). DMARDs slow the disease process and reduce joint damage. Conventional DMARDs includes e.g. methotrexate, leflunomide and sulfasalazine. Also available are a group of drugs including monoclonal antibodies and soluble receptors that modify the disease process by blocking key protein messenger molecules (such as cytokines) or cells (such as B-lymphocytes). Such drugs are referred to as biological DMARDs. For some people their disease may not respond to DMARDs and for others the response to DMARDs often reduces over time. Therefore people need a sequence of treatments. Glucocorticoids are also used to control inflammation. Measures of response to treatment include the American College of Rheumatology (ACR) response criteria (ACR20, 50 and 70). These require a specified improvement in tender joint count, swollen joint count, global assessments, pain, disability and an acute-phase reactant (e.g. ESR or CRP). The disease activity score (DAS28) is an alternative scoring system that has been

	developed in Europe. It is calculated using a formula that includes counts for tender and swollen joints, an evaluation of general health by the person (on a scale of 0–100), and ESR or CDP. A DAS28 greater than 5.1 indicates high disease activity, between 3.2 and 5.1 moderate disease activity, and less than 3.2 low disease activity. A score of less than 2.6 indicates disease remission. The European League Against Rheumatism (EULAR) response criteria use the degree of change in DAS28 and the DAS28 reached to determine good, moderate or non-response.
RELEVANT NICE GUIDANCE	NICE TA375 states: Adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab and abatacept, all in combination with methotrexate, are recommended as options for treating rheumatoid arthritis, only if: • disease is severe, that is, a disease activity score (DAS28) greater than 5.1 and • disease has not responded to intensive therapy with a combination of conventional disease-modifying antirheumatic drugs (DMARDs) and • the companies provide certolizumab pegol, golimumab, abatacept and tocilizumab as agreed in their patient access schemes. Adalimumab, etanercept, certolizumab pegol or tocilizumab can be used as monotherapy for people who cannot take methotrexate because it is contraindicated or because of intolerance, when the criteria above are met. Continue treatment only if there is a moderate response measured using European League Against Rheumatism (EULAR) criteria at 6 months after starting therapy. After initial response within 6 months, withdraw treatment if a moderate EULAR response is not maintained. Start treatment with the least expensive drug (taking into account administration costs, dose needed and product price per dose). This may need to be varied for some people because of differences in the mode of administration and treatment schedules.
FORMULARY STATUS	Red, specialist use only
PBR STATUS	Excluded from tariff
COMMISSIONING IMPLICATIONS	Local commissioned pathway already in existence, to be reviewed in the light of this TA
RELEVANT CLINICAL WORKING GROUP	Planned and Specialist clinical working group
PATIENT PATHWAY IMPLICATIONS	Local commissioned pathway already in existence, to be reviewed in the light of this TA. Likely minimal change to current pathway.
SUMMARY OF EVIDENCE TO SUPPORT FORMULARY STATUS	Summarised in 'consideration of the evidence' section of TA375 The BNF lists adverse effects of adalimumab, certolizumab pegol, etanercept, golimumab, infliximab as; nausea, abdominal pain, worsening heart failure, hypersensitivity reactions, fever,

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<tr><td></td><td>headache, depression, antibody formation (including lupus erythematosus-like syndrome), pruritus, injection-site reactions, and blood disorders (including anaemia, leucopenia, thrombocytopenia, pancytopenia, and aplastic anaemia).

Of abatacept as;
abdominal pain, diarrhoea, dyspepsia, nausea, vomiting, stomatitis, flushing, hypertension, cough, dizziness, fatigue, headache, paraesthesia, infection, leucopenia, pain in extremities, conjunctivitis; less commonly gastritis, tachycardia, bradycardia, palpitation, hypotension, bronchospasm, dyspnoea, hyperhidrosis, weight gain, depression, anxiety, sleep disorder, menstrual disturbances, basal and squamous cell carcinoma, skin papilloma, thrombocytopenia, arthralgia, visual disturbance, dry eye, bruising, alopecia, dry skin, psoriasis; also reported lymphoma, lung cancer.

And of tocilizumab as;
abdominal pain, mouth ulceration, gastritis, raised hepatic transaminases; dizziness, peripheral oedema, hypertension, hypercholesterolaemia; headache; infection (including upper respiratory-tract infection); antibody formation, hypersensitivity, leucopenia, neutropenia; rash, pruritus; less commonly gastric ulcer, gastro-intestinal perforation, hypertriglyceridaemia, hypothyroidism, nephrolithiasis, infusion related reactions, anaphylaxis, and thrombocytopenia .

See individual SPCs for further information</td></tr>
<tr><td>ASSESSMENT OF COST IMPLICATIONS</td><td>
<table>
<tr><th>Product</th><th>Form, cost, annual cost, PAS</th><th>Dose</th></tr>
<tr><td>Abatacept (Orencia®)
125mg pre-filled syringe/ pen
250 mg powder for concentrate for solution for infusion</td><td>4 pre-filled disposable injection (pen/syringe) = £1209.60
£15,724.80 per year.

250mg vial abatacept IV infusion = £302.40. Adults 60-100 kg, treatment for the 1st year £12,700.80 and then £11,793.60 per year Confidential PAS</td><td>S/C injection
125mg wkly

IV infusion
Adult< 60kg; 500mg 60-100kg; 750 mg >100Kg; 1000mg at 0, 2 and 4 wks, then every 4 wks.</td></tr>
<tr><td>Adalimumab (Humira®)
40mg/0.8ml solution for injection</td><td>2 pre-filled disposable device, pre-filled syringes, £704.28
£9155.64 per year
Negotiated local procurement discounts.</td><td>S/C injection
40 mg every 2 wks. the</td></tr>
<tr><td>Certolizumab pegol (Cimzia®) Injection 200mg/1ml solution for injection</td><td>2 pre-filled syringes = £715.00.
£9295 per year
PAS – 1st 12 wks of therapy (currently 10 pre-loaded syringes) FOC</td><td>S/C injection
400 mg at weeks 0, 2 and 4 then 200 mg every 2 weeks or 400 mg every 4 wks. £9295</td></tr>
<tr><td>Golimumab (Simponi®)
50mg/0.5ml solution for injection</td><td>50-mg prefilled pen or prefilled syringe = £762.97
£9155.64 per year.
PAS – if a 100mg dose is required this should be supplied at the same cost as a 50mg dose</td><td>S/C injection
50 mg once a month</td></tr>
<tr><td>Etanercept (Enbrel®)
Injection</td><td>25-mg prefilled syringe = £89.38;</td><td>S/C injection
25 mg twice weekly.</td></tr>
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	25-mg prefilled syringe; 50-mg prefilled pen/prefilled syringe	50-mg prefilled pen or prefilled syringe = £178.75. *£9295 per year. Local negotiated discounts.*	Alternatively 50 mg once wkly. £9295.
	Infliximab (Remicade®/ Inflectra®/Remsima®) 100mg powder for concentrate for solution for infusion vials	Remicade® 100mg vial = £419.62 *£9063.84 for 1st year then £7930.86 per year* Inflectra®/Remsima® 100mg vial = £377.66	IV infusion Adult: 5 mg/kg, at weeks 0, 2 and 4 then every 6–8 wks.
	Tociluzimab (RoActemra®) 20 mg/ml concentrate for solution for infusion	concentrate for solution for infusion: 200mg/10ml vial = £256.00, 400mg/20ml = £512.00; 80mg/4ml = £102.40 *£9318.40 per year Confidential PAS*	IV infusion 8 mg/kg every 4 wks weeks; max. per dose 800 mg

REFERENCES	NICE TA 375 Adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab and abatacept for rheumatoid arthritis not previously treated with DMARDs or after conventional DMARDs only have failed. Joint Formulary Committee. British National Formulary. London: BMJ Group and Pharmaceutical Press; Electronic edition. Accessed via http://www.medicinescomplete.com/
Date	February 2016
Review date	February 2018 or before in the light of new information
Contact	Katie Taylor, Pharmacist, NHS Dorset CCG