NHS
Wakefield
Clinical Commissioning Group

Commissioning Statement

Treatment	**Rituximab originator or rituximab biosimilar without methotrexate for patients with a contra-indication to methotrexate or who are unable to tolerate it**
For the treatment of	Off-label treatment of severe, active sero-positive rheumatoid arthritis in line with NICE, but without methotrexate
Commissioning position	**Wakefield CCG routinely commissions the use of rituximab originator or rituximab biosimilar without methotrexate for the treatment of rheumatoid arthritis (RA) in patients for whom methotrexate is contraindicated or not tolerated and who have undertaken and failed a 6 month trial of two conventional non-biologic disease-modifying anti-rheumatic drugs (DMARDs) as per NICE recommendations.** NICE TA195 states that rituximab plus methotrexate are recommended as an option for adults with severe active RA who have had an inadequate response to, or are intolerant of, other DMARDs, including at least one tumour necrosis factor (TNF) inhibitor [1]. Some patients have a contra-indication to methotrexate or are unable to tolerate it. British Society of Rheumatology guidance recommends that if methotrexate is contra-indicated, rituximab should be used in RA either alone or with leflunomide [2]. Rituximab without methotrexate is a first-line biological treatment option for patients who have had an inadequate response to conventional DMARDs, who cannot receive methotrexate, and for whom TNF inhibitors are not clinically appropriate due to comorbidities which give rise to medical concerns. The decision to offer rituximab without methotrexate is at the discretion of the treating clinician. The patient must be made fully aware of the unlicensed nature of the treatment and the rationale for treatment. Each patient should sign an informed consent form. Treatment with rituximab should be continued only if there is an adequate response to treatment defined as improvement in disease activity score (DAS28) of 1.2 points or more [1]. New patients should always be initiated on the least expensive brand of rituximab or biosimilar as agreed by the CCG/provider.

Date effective from	6.7.2017
Policy to be reviewed by	5.7.2020 (to be reviewed earlier if NICE issues guidance)
Background information	Rituximab is a monoclonal anti-CD20 antibody which is licensed for the treatment of RA in association with methotrexate [3].
Summary of evidence/ rationale	The efficacy and safety of rituximab without methotrexate have been evaluated using the Italian biologic register (GISEA) [4]: **Safety**: Fewer patients given rituximab alone experienced adverse events (58/142, 41%) compared to those treated with methotrexate plus rituximab (84/142, 59%). Adverse events in the rituximab alone patients were recognised side effects, including infections and infusion reactions. **Clinical effectiveness:** 176 patients had been treated with rituximab plus methotrexate and 162 on rituximab without a DMARD. The mean change in DAS28 between baseline and week 52 was 1.61±0.64 in the group on methotrexate versus 1.48±0.59 in the group without methotrexate (non-significant difference). The Health Assessment Questionnaire (HAQ) scores were also not different between the groups (0.43±0.18 vs 0.39±0.21). **Resource impact:** Rituximab is a high cost drug which is excluded from the payment by results tariff. CCGs have separate budgets for this type of drug and usage is monitored. References 1. NICE. Technology Appraisal 195. Adalimumab, etanercept, infliximab, rituximab and abatacept for the treatment of rheumatoid arthritis after the failure of a TNF inhibitor. August 2010. Accessed from https://www.nice.org.uk/guidance/ta195/resources/adalimumab-etanercept-infliximab-rituximab-and-abatacept-for-the-treatment-of-rheumatoid-arthritis-after-the-failure-of-a-tnf-inhibitor-82598558287813 on 13.4.17 2. British Society of Rheumatology. BSR and BHPR guidelines on the use of rituximab in rheumatoid arthritis. Rheumatology 2011;50(12):2311-13 3. DataPharm. Electronic Medicines Compendium. Mabthera 100mg and 500mg Concentrate for Solution for Infusion. Roche Products Ltd. Last updated on eMC on 8.6.2016. Accessed from http://www.medicines.org.uk/emc/medicine/2570 on 28.3.17 4. Sebastiani M, Anelli MG, Atzeni F et al. Efficacy and safety of rituximab with and without methotrexate in the treatment of rheumatoid arthritis patients: Results from the GISEA register. Joint Bone Spine 2014;81(6):508-12
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