NICE National Institute for Health and Care Excellence

Putting NICE guidance into practice

Resource impact report:
Adalimumab, etanercept, infliximab and abatacept for treating moderate rheumatoid arthritis after conventional DMARDs have failed (partial review of TA375) (TA715)

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Summary

NICE has recommended adalimumab, etanercept and infliximab, all with methotrexate, as options for treating moderate rheumatoid arthritis in accordance with the specific criteria in the recommendations (see section 1).

The guidance is an update of the NICE technology appraisal guidance TA375 and it increases the population eligible for treatment to include people with moderate disease. Because there is no change in the guidance for people with severe disease, the resource impact assessment only considers costs associated with people with moderate disease.

Until publication of this guidance, filgotinib was the only advanced treatment available for moderate rheumatoid arthritis. Filgotinib is a targeted disease-modifying antirheumatic drug (tsDMARD). The technologies recommended for use in this guidance offer new advanced treatment options for moderate rheumatoid arthritis and are biologic DMARDs (bDMARDs).

We estimate that:

- 26,900 people with moderate rheumatoid arthritis who respond inadequately to, or are intolerant of, (two or more) conventional DMARDs are eligible for treatment. Of these, around 8,100 people are expected to receive bDMARDs or tsDMARDs once uptake has reached 30%.
- 6,780 people will receive adalimumab, etanercept or infliximab from year 2023/24 onwards once uptake has reached 84% as shown in table 1.
- this guidance will lead to the overall proportion of the eligible population receiving bDMARDs or tsDMARDs to increase from 15% to 30%.

Table 1 Estimated number of people in England receiving adalimumab, etanercept or infliximab

	2021/22	2022/23	2023/24	2024/25	2025/26
Uptake rate for bDMARDs or tsDMARDs (%)	10	20	30	30	30
Uptake rate for adalimumab, etanercept or infliximab (%)	84%	84%	84%	84%	84%
Population receiving adalimumab, etanercept or infliximab each year	2,260	4,520	6,780	6,780	6,780
In each year, some people are expected to become eligible (incident population), and some are expected to progress to severe rheumatoid arthritis. No change is anticipated in the overall eligible population as a result of this.					

This report is supported by a local resource impact template because the companies have each agreed a regional or nationally available price reduction for adalimumab, etanercept and infliximab with the Commercial Medicines Unit. The

prices are commercial in confidence. The discounted prices can be put into the template and other variables may be amended.

These technologies are commissioned by integrated care systems/clinical commissioning groups. Providers are NHS hospital trusts.

1 Adalimumab, etanercept, infliximab

1.1 Adalimumab, etanercept and infliximab, all with methotrexate, are recommended as options for treating active rheumatoid arthritis in adults, only if:

- intensive therapy with 2 or more conventional disease-modifying antirheumatic drugs (DMARDs) has not controlled the disease well enough and
- disease is moderate (a disease activity score [DAS28] of 3.2 to 5.1) and
- the companies provide adalimumab, etanercept and infliximab at the same or lower prices than those agreed with the Commercial Medicines Unit.

1.2 If more than one treatment is suitable, start treatment with the least expensive drug (taking into account administration costs, dose needed and product price per dose). This may vary because of differences in how the drugs are used and treatment schedules.

1.3 The technology appraisal includes 4 different biological medicines as either the originator medicine (the medicine first authorised for use) or a biosimilar product. A biosimilar medicine is a medicine that is developed to be similar to an existing biological medicine.

1.4 Until publication of this guidance, filgotinib was the only advanced treatment available for moderate rheumatoid arthritis. Filgotinib is a targeted disease-modifying antirheumatic drug (tsDMARD). The technologies recommended for use in this guidance offer new advanced treatment options for moderate rheumatoid arthritis and are biologic DMARDs (bDMARDs).

1.5 Abatacept with methotrexate is not recommended, within its marketing authorisation, for treating moderate active rheumatoid arthritis.

1.6 Evidence suggests that adalimumab, etanercept and infliximab after 2 or more conventional DMARDs are a cost-effective use of NHS resources.

2 Resource impact of the guidance

2.1 We estimate that:

- 26,900 people with moderate rheumatoid arthritis who respond inadequately to, or are intolerant of, (two or more) conventional DMARDs are eligible for treatment. Of these, around 8,100 people are expected to receive bDMARDs or tsDMARDs once uptake has reached 30%.
- 6,780 people will receive adalimumab, etanercept or infliximab from year 2023/24 onwards once uptake has reached 84% as shown in table 2.
- this guidance will lead to the overall proportion of the eligible population receiving bDMARDs or tsDMARDs to increase from 15% to 30%.

2.2 The current treatment and future uptake figure assumptions are based on clinical expert opinion and company submission and are shown in the resource impact template. Table 2 shows the number of people in England who are estimated to receive adalimumab, etanercept or infliximab by financial year.

Table 2 Estimated number of people receiving adalimumab, etanercept or infliximab using NICE assumptions

	2021/22	2022/23	2023/24	2024/25	2025/26
Uptake rate for bDMARDs or tsDMARDs (%)	10	20	30	30	30
Uptake rate for adalimumab, etanercept or infliximab (%)	84	84	84	84	84
Population receiving adalimumab, etanercept or infliximab each year	2,260	4,520	6,780	6,780	6,780
In each year, some people are expected to become eligible (incident population), and some are expected to progress to severe rheumatoid arthritis. No change is anticipated in the overall eligible population as a result of this.					

2.3 This report is supported by a local resource impact template because the companies have each agreed a regional or nationally available price reduction for adalimumab, etanercept and infliximab with the Commercial Medicines Unit. The prices are commercial in confidence. The discounted prices of adalimumab, etanercept and infliximab can be put into the template and other variables may be amended.

Savings and benefits

2.4 The clinical experts explained that earlier access to advanced treatments in moderate disease would reduce disease progression and increase the likelihood of remission. Therefore, use of adalimumab, etanercept or infliximab would be expected to lead to a reduced need for non-drug healthcare interventions in people with moderate rheumatoid arthritis.

3 Implications for commissioners

3.1 These technologies are commissioned by integrated care systems/clinical commissioning groups. Providers are NHS hospital trusts.

3.2 Adalimumab, etanercept and infliximab fall within the programme budgeting category 15 ‘Problems of the Musculo Skeletal System’.

4 How we estimated the resource impact

The population

4.1 The overall prevalence of rheumatoid arthritis (RA) in adults is 0.82% (NRAS - National Rheumatoid Arthritis Society). The estimated number of adults with RA in England is 365,100.

Table 3 Number of people eligible for treatment in England

Population	Proportion of previous row (%)	Number of people
Total population		56,286,961
Total adult population		44,263,393
Prevalence of rheumatoid arthritis of [1]	0.82	365,100
People with moderate rheumatoid athritis[2]	45	164,300
People who receive conventional disease-modifying anti-rheumatic drugs (cDMARDs)[3]	91	149,500
Proportion of people who receive 2 or more cDMARDs[4]	24	35,900
People in whom therapy with 2 or more cDMARDs has not controlled the disease well enough and are therefore eligible for treatment[5]	75	26,900
People in whom intensive therapy with 2 or more cDMARDs has not controlled the disease well enough who will receive bDMARDs or tsDMARD[6]	30	8,070
Total number of people estimated to receive adalimumab, etanercept or infliximab each year from year 2023/24[7]	84	6,780

[1] National Rheumatoid Arthritis Society

[2] Company submission (data from various sources) estimates ranging from 31% to 59%, mid-point taken.

[3] Nikiphorou E, Morris S et al. The Effect of Disease Severity and Comorbidity on Length of Stay for Orthopedic Surgery in RA: Results from 2 UK Inception Cohorts, 1986-2012. J Rheumatol. 2015;42(5):778-85

[4] Cole. Healthcare resource utilisation associated with management of patients with moderate RA in the United Kingdom: Initial data from a multi-centre, retrospective, non-interventional study. British Society for Rheumatology Annual Conference; May 2019; Birmingham, UK2019.

[5] Company submission for NICE technology appraisal guidance 676

[6] BSR (referenced in the Fresenius Kalbi BI submission) which estimated that 32% of those people with moderate to severe RA have an increasing HAQ score and would benefit from treatment with biologic DMARDS. We have rounded this to 30%.

[7] Expert clinical opinion

Assumptions

4.2 The resource impact template assumes that:

- When the partial update of NICE technology appraisal guidance TA375 started, the appraisal of filgotinib had not concluded. Therefore, filgotinib was not included in the scope as a comparator. However, filgotinib has since been recommended by NICE technology appraisal 676 for treating moderate to severe rheumatoid arthritis. It has therefore been included in the resource impact template for this patient group.
- The guidance recommends continuing treatment only if there is a moderate response at 6 months. If this initial response is not maintained at 6 months, treatment should be stopped.
- Adalimumab, etanercept and infliximab are available as biosimilars. Therefore, the treatment cost of each is the weighted average of the originator medicine and its biosimilars. Users can amend the template to reflect local pricing.
- Infliximab is administered intravenously while all other treatment options are self-administered orally or subcutaneously.
- Infliximab treatment cost includes an administration cost of £273 per each intravenous administration (Outpatient treatment function code 410: Rheumatology). Taken from NHS national tariff 2020/21.
- The oral or subcutaneous treatments are delivered by a homecare service. An administration cost of £50 per month is incurred. No VAT is applied.
- Based on clinical expert opinion, the uptake of adalimumab, etanercept and infliximab in a world without filgotinib, was 75%, 25% and 0% respectively. Based on NICE technology appraisal guidance 676, the uptake of filgotinib by year 5 was 15%. These market shares were reproportioned to estimate the market share of adalimumab, etanercept, infliximab and filgotinib.

- Uptake of adalimumab, etanercept or infliximab is the sum of the individual uptake of the originator medicine and the available biosimilars.
- No additional resources are required to widen use of adalimumab, etanercept and infliximab to include people with moderate rheumatoid arthritis.

Table 4 Assumptions made on current and future practice

People treated with bDMARDs or tsDMARDs		
Current practice (at year 5)	**Estimated future practice (at year 5)**	**Rationale**
4,050 people receiving bDMARDs or tsDMARDs	8,100 people receiving bDMARDs or tsDMARDs	Overall population receiving bDMARDs or tsDMARDs doubles from 15% to 30% following publication of this guidance. Assumptions can be amended in the resource impact template.
0**%** of people receive adalimumab	63% of people receive adalimumab	Clinical expert opinion. See resource impact template for further detail of uptake over time. Assumptions can be amended in the resource impact template.
0**%** of people receive etanercept	21**%** of people receive etanercept	Clinical expert opinion. See resource impact template for further detail of uptake over time. Assumptions can be amended in the resource impact template.
0% of people receive infliximab	0% of people receive infliximab	Clinical expert opinion. See resource impact template for further detail of uptake over time. Assumptions can be amended in the resource impact template.
100% of people receive filgotinib	16% of people receive filgotinib	Clinical expert opinion. Uptake of filgotinib expected to decrease from being the only one available at this stage to one of several new treatments. Assumptions can be amended in the resource impact template.
Total 100%	**Total 100%**	

Other factors

4.3 The guidance states that adalimumab and etanercept can be used as monotherapy when methotrexate is contraindicated or not tolerated. The cost of methotrexate is very small so any reduced use will not result in significant savings.

4.4 The guidance also recommends continuing treatment only if there is a moderate response measured using European League Against Rheumatism criteria at 6 months after starting therapy. If this initial response is not maintained at 6 months, stop treatment. There are no data to model people discontinuing treatment as a result of poor response to treatment. Therefore, the model may overestimate the resource impact.

4.5 Clinical experts suggests that uptake of the technologies could be slower through 2021/22 or 2022/23 because of the sizeable backlog in rheumatology work following the pandemic and because it will take time for these new recommendations to be adopted into practice.

About this resource impact report

This resource impact report accompanies the NICE guidance on adalimumab, etanercept, infliximab and abatacept for treating moderate rheumatoid arthritis after conventional DMARDs have failed (partial review of TA375) and should be read with it.