East Surrey CCG, Guildford & Waverley CCG, North West Surrey CCG, Surrey Downs CCG, Surrey Heath CCG, Crawley CCG, Horsham & Mid-Sussex CCG

Briefing Paper for Prescribing Clinical Network on NICE Technology Appraisals: Local implementation

NICE TA Guidance	Tofacitinib for moderate to severe rheumatoid arthritis Technology appraisal guidance 480		
Available at	https://www.nice.org.uk/guidance/ta480		
Date of issue	11 October 2017	**Implementation deadline**	11 January 2017

Medicine details[1]	
Name, brand name and manufacturer	Tofacitinib (Xeljanz®) 5 mg film-coated tablets Pfizer Limited
Licensed indication	Xeljanz® in combination with methotrexate (MTX) is indicated for the treatment of moderate to severe active rheumatoid arthritis (RA) in adult patients who have responded inadequately to, or who are intolerant to one or more disease-modifying antirheumatic drugs. Xeljanz® can be given as monotherapy in case of intolerance to MTX or when treatment with MTX is inappropriate.
Formulation	Xeljanz® 5 mg film-coated tablets
Usual dosage	Treatment should be initiated and supervised by specialist physicians experienced in the diagnosis and treatment of RA. Posology The recommended dose is 5 mg administered twice daily. A dose of 5 mg once daily is appropriate for patients with severe renal impairment (creatinine clearance less than 30 ml/min). A dose of 5 mg once daily is appropriate for patients with moderate hepatic impairment (Child–Pugh B). Tofacitinib should not be used in patients with severe hepatic impairment (Child–Pugh C). Tofacitinib should be interrupted if a patient develops a serious infection, until the infection is controlled. This is the same recommended dose and schedule as the NICE TA. *This is the current dose considered by NICE as part of the NICE evaluation. Subsequent changes in the license following NICE publication will need to be considered by the Prescribing Clinical Network and will not be routinely funded by local commissioners.*

Disease and potential patient group	
Brief description of disease[2]	The symptoms of rheumatoid arthritis often develop gradually over several weeks, but some cases can progress quickly over a number of days. The symptoms vary from person to person. They can come and go, and may change over time. The patient may occasionally

	experience flares when the condition deteriorates and the symptoms become more severe. Rheumatoid arthritis mainly affects the joints. It can cause problems in any joint in the body, although the small joints in the hands and feet are often the first to be affected. Rheumatoid arthritis typically affects the joints symmetrically (both sides of the body at the same time and to the same extent), but this isn't always the case. The main symptoms affecting the joints are: **Pain:** Usually throbbing and aching. It is often worse in the mornings and after a period of inactivity. **Stiffness:** Often more severe in the morning and lasting longer than 30 minutes or after a period of inactivity. **Swelling, warmth and redness:** The lining of joints affected by rheumatoid arthritis become inflamed, which can cause the joints to swell, and become hot and tender to touch. In some people, firm swellings called rheumatoid nodules can also develop under the skin around affected joints. **Additional symptoms:** As well as problems affecting the joints, some people with rheumatoid arthritis experience a range of more general symptoms, such as: • tiredness and a lack of energy • a high temperature (fever) • sweating • a poor appetite • weight loss The inflammation associated with rheumatoid arthritis can also sometimes cause problems affecting other areas of the body, such as: • dry eyes – if the eyes are affected • chest pain – if the heart or lungs are affected
Potential patient numbers per 100,000	One study in the UK found the population minimum prevalence of RA to be 1.16% in women and 0.44% in men. The incidence of the condition is low, with around 1.5 men and 3.6 women developing RA per 10,000 people per year.

SUMMARY

Guidance[3]
1.1 Tofacitinib, with methotrexate, is recommended as an option for treating active rheumatoid arthritis in adults whose disease has responded inadequately to intensive therapy with a combination of conventional disease-modifying antirheumatic drugs (DMARDs), only if: • disease is severe (a disease activity score [DAS28] of more than 5.1) and • the company provides tofacitinib with the discount agreed in the patient access scheme. 1.2 Tofacitinib, with methotrexate, is recommended as an option for treating active

rheumatoid arthritis in adults whose disease has responded inadequately to, or who cannot have, other DMARDs, including at least 1 biological DMARD, only if:

- disease is severe (a DAS28 of more than 5.1) and
- they cannot have rituximab and
- the company provides tofacitinib with the discount agreed in the patient access scheme.

1.3 Tofacitinib can be used as monotherapy for adults who cannot take methotrexate because it is contraindicated or because of intolerance, when the criteria in sections 1.1 and 1.2 are met.

1.4 Continue treatment only if there is a moderate response measured using European League Against Rheumatism (EULAR) criteria at 6 months after starting therapy. After an initial response within 6 months, withdraw treatment if at least a moderate EULAR response is not maintained.

1.5 These recommendations are not intended to affect treatment with tofacitinib that was started in the NHS before this guidance was published. People having treatment outside these recommendations may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

Why the committee made these recommendations

Clinical trial evidence shows tofacitinib plus conventional DMARDs is more effective than conventional DMARDs alone for treating moderate and severe active rheumatoid arthritis that has not responded adequately to conventional or biological DMARDs.

Clinical trial evidence also shows that tofacitinib plus methotrexate is not worse in effectiveness than the biological DMARD adalimumab plus conventional DMARDs in people whose disease has responded inadequately to conventional DMARDs. Because there are no trials comparing tofacitinib with other biological DMARDs, the company did an indirect comparison. This shows that tofacitinib works as well as most of the biological DMARDs which NICE has already recommended in this indication.

Based on the health-related benefits and costs compared with conventional and biological DMARDs, tofacitinib plus conventional DMARDs is recommended as a cost-effective treatment for severe active rheumatoid arthritis, in line with previous recommendations in NICE technology appraisal guidance on:

- baricitinib
- certolizumab pegol (after a TNF-alpha inhibitor)
- adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab and abatacept (after conventional DMARDs)
- tocilizumab
- golimumab (after DMARDs)
- adalimumab, etanercept, infliximab, rituximab and abatacept (after a TNF-alpha inhibitor).

Tofacitinib for *moderate* active rheumatoid arthritis that has responded inadequately to conventional DMARDs is not cost effective based on what NICE normally considers acceptable, that is, £30,000 per quality-adjusted life year gained.

Please note that tofacitinib is licensed for moderate (a disease activity score [DAS28] between 3.2 and 5.1) to severe (a disease activity score [DAS28] of more than 5.1) active rheumatoid arthritis but the NICE TA recommendations are for severe disease i.e. DAS28 of more than 5.1 only.

Cost implications*,[3,4]

Cost:
The list price of a 56-tablet pack of 5mg tofacitinib is £690.03 (excluding VAT).

Annual or monthly cost per patient:
The average cost per patient for the first 6 months is estimated at £4,050.60 based on the list price. The average cost per patient for subsequent years is estimated at £9,001.19 based on the list price.

Availability of PAS and details (if appropriate): Yes
The company has agreed a patient access scheme with the Department of Health. This scheme provides a simple discount to the list price of tofacitinib, with the discount applied at the point of purchase or invoice.

The level of the discount is commercial in confidence. The Department of Health considered that this patient access scheme does not constitute an excessive administrative burden on the NHS.

Availability of homecare service (if appropriate): Yes

NICE Resource impact statement:
'No significant resource impact is anticipated. We do not expect this guidance to have a significant impact on resources. This is because the technology is an option alongside current standard treatment options'.

**NICE funding requirements are based on Quality Adjusted Life Years (QALY) threshold. If there is evidence that the incremental cost rises above this threshold in the future, the PCN may reconsider the commissioning status.*

Alternative treatments and cost per patient per year

Other NICE recommended products:

Table 1: Cost of comparators[5]

Medicine	Dose Regimen	Cost per year
baricitinib	2 to 4mg orally once a day	£10,473
abatacept	125mg SC once a week	£15,725
tocilizumab	162 mg SC once a week	£11,871
tocilizumab	8mg/kg IV every four weeks	£9,984
certolizumab pegol	400mg SC at weeks 0, 2, 4 then 200mg SC every two weeks	£9,295 (£10,368 in year 1)
etanercept	50 mg SC once a week or 25mg twice a week	£9,295
adalimumab	40mg SC every two weeks	£9,156
golimumab	50 mg SC once a month	£9,156
infliximab	Initially 3 mg/kg by IV infusion at weeks 0, 2, 6, then every eight weeks	£6,786 £10,179 (in year 1)

Doses are for general comparison and do not imply therapeutic equivalence. Costs are from eVadis on 16 May 2017, except infliximab (MIMS). Dose assumes weight of 70kg. Costs calculated using the full cost of vials/ampoules assuming wastage. Costs do not take any patient access schemes into consideration. IV = intravenous; SC = subcutaneous

This table from the Scottish Medicines Consortium (SMC) does not include the price of biosimilar etanercept which is slightly over £5,000 per year and the additional infusion suite costs associated with the IV treatments.

Impact to patients

- An additional treatment option of tofacitinib would be valued by patients. It is an oral preparation and as a selective Janus kinase (JAK) 1 and 3 inhibitor has a new mode of action.
- An oral route of administration which may be preferred by patients over having to have a regular infusion or inject themselves. This is an important factor for people who have difficulty injecting themselves because of the disease affecting their hands.
- Carers often have to help patients with their biologic therapy and with an oral medicine like tofacitinib, the patient becomes more independent in taking their medication.
- Tofacitinib is available under a homecare service so will be delivered directly to the patient.

Impact to primary care prescribers

- This is a PbRe drug and is commissioned by CCGs for use in secondary care. There should be no prescribing in primary care.
- Primary care prescribers should be aware that their patient is receiving tofacitinib and ensure that this is recorded in the patient's notes in order to be alert to potential side-effects and interactions with other medicines prescribed in primary care. This will also ensure that GP records, which are accessed by other healthcare providers, are a true and accurate reflection of the patient's medication.

Impact to secondary care

- The initiation, administration and on-going treatment is managed by secondary care.
- Homecare arrangements will be managed by the trust.
- Tofacitinib is available on homecare and patients will only require appointments for review and/or monitoring.
- An additional treatment option of tofacitinib would be valued by clinicians.

Impact to CCGs

- The technology is commissioned by clinical commissioning groups (CCGs).
- Providers are NHS hospital trusts.
- There is a cohort of patients who are eligible to receive tofacitinib although they have been through the available lines of treatment within the rheumatoid arthritis pathway.

Implementation

- NICE TA implementation must be within 90 days of publication – 11th January 2017.
- Blueteq forms to be developed.
- Trusts to initiate homecare.
- Pathway discussed at Rheumatology Network. At present, the pathway comprises of 4 lines of treatment, of which tofacitinib is expected to be an option.

Recommendation to PCN

PbRe: Y

Recommended traffic light status (see attached guidelines):
RED

Additional comments:

References:

1 Specification of Product Characteristics. Xeljanz 5mg Film-Coated Tablets. Available at: https://www.medicines.org.uk/emc/medicine/33167 Accessed <2.11.17>

2 NHS Choices. Rheumatoid arthritis – symptoms. Accessed 3.11.16. Available at: http://www.nhs.uk/Conditions/Rheumatoid-arthritis/Pages/Symptoms.aspx Accessed <6.9.17>

3 NICE Technology appraisal 480: Tofacitinib for moderate to severe rheumatoid arthritis. Published 11 October 2017. Available at: https://www.nice.org.uk/guidance/ta480 Accessed <2.11.17>

4 NICE Resource impact report: Tofacitinib for moderate to severe rheumatoid arthritis. Published 9 August 2017. Available at: https://www.nice.org.uk/guidance/ta480/resources Accessed <2.11.17>

5 SMC. Baricitinib 2mg and 4mg film-coated tablet (Olumiant®) SMC No 1265/17. Available at: http://www.scottishmedicines.org.uk/SMC_Advice/Advice/1265_17_baricitinib_Olumiant Accessed <12.9.17>

Prepared by:

Tejinder Bahra, Lead Commissioning Pharmacist, Surrey Downs CCG

Declaration of Interest:

Indirect Pfizer shares

Date: 2.11.17

Reviewed by: Sarah Watkin, Head of Pharmaceutical Commissioning, Surrey Downs CCG

Declaration of Interest:

None.

Date: 10.11.17

Comments:

VERSION CONTROL SHEET

Version	Date	Author	Status	Comment
1	7.11.17	T. Bahra	Draft	Out for peer review
2	16.11.17	T. Bahra	Final	Out for clinician comment
3	29.11.17	T. Bahra	Final	Final version for PCN