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 moderately to severely active ulcerative colitis (TA547)		
Available at	https://www.nice.org.uk/guidance/ta547		
Date of issue	28 Nov 2018	**Implementation deadline**	3 months from publication - *(28th February 2019)*

Medicine details	
Name, brand name	Tofacitinib (Xeljanz)
Manufacturer	Pfizer
Licensed indication	The treatment of adult patients with moderately to severely active ulcerative colitis who have had an inadequate response, lost response, or were intolerant to either conventional therapy or a biologic agent
Formulation	Film-coated tablet
Usual dosage	The recommended dosage of tofacitinib for induction is 10 mg taken orally twice daily for 8 weeks, then 5 mg taken twice daily for maintenance. If adequate therapeutic benefit is not achieved by week 8 the induction dose can be taken for an additional 8 weeks (16 weeks in total). Induction therapy should be stopped if there is no evidence of therapeutic benefit by week 16. For patients whose disease has responded inadequately to tumour necrosis factor antagonist therapy, consider continuing the 10-mg twice-daily dose for maintenance in order to maintain therapeutic benefit. If response decreases to tofacitinib 5 mg taken twice daily as maintenance therapy, consider increasing the dose to 10 mg taken twice daily.
NICE recommended dosage/schedule	From Section 2 of NICE TA - same as in SPC, as above

Disease and potential patient group	
Brief description of disease	Ulcerative colitis (UC) is a disease of the colon and the rectum. UC produces inflammation and ulcers in the large intestine causing symptoms of diarrhoea with blood and mucus, colicky abdominal pain and a continual or recurrent inclination to evacuate the bowels. Onset of symptoms usually between ages of 15 and 25, with a second peak at 55 to 65.
Potential patient numbers per	Approximately 146,000 people in England have UC of whom 52% have moderate to severe active disease. (Mayo score of 6 to 12)

100,000	

SUMMARY

NICE recommendation

Tofacitinib is recommended, within its marketing authorisation, as an option for treating moderately to severely active ulcerative colitis in adults when conventional therapy or a biological agent cannot be tolerated or the disease has responded inadequately or lost response to treatment. It is recommended only if the company provides tofacitinib with the discount agreed in the commercial arrangement.

Cost implications*

Cost of product:
NB: NICE TA therefore funding mandatory.

Annual cost per patient:
The list price of a 56-tablet pack of 5-mg tofacitinib is £690.03;
The list price of a 56-tablet pack of 10-mg tofacitinib is £1,380.06 (excluding VAT; British national formulary [BNF] online 2018).
The average cost per patient for the first year is estimated at £10,350.45 and for the subsequent year is estimated at £8,970.39.

Cost-effectiveness estimates (extract from NICE)
TNF-alpha inhibitor 'naive': the cost-effectiveness results showed that adalimumab, golimumab and infliximab are dominated by tofacitinib (that is, they cost more and produce fewer quality-adjusted life years [QALYs]). The incremental cost-effectiveness ratio (ICER) for tofacitinib compared with conventional therapy is £8,564 per QALY gained. Tofacitinib produced fewer QALYs than vedolizumab, but at a lower cost. This resulted in an incremental saving of £615,077 per QALY lost for tofacitinib compared with vedolizumab at list price.

TNF-alpha inhibitor 'exposed': the ICER for tofacitinib compared with conventional therapy is £10,311 per QALY gained. Tofacitinib produced fewer QALYs than vedolizumab, but at a lower cost. This resulted in an incremental saving of £7,838,381 per QALY lost for tofacitinib compared with vedolizumab at list price.

Has dose escalation been considered as part of the NICE costing template?
NICE noted that some patients may take a 10-mg dose long-term. This is likely to be people who have previously had TNF-alpha inhibitors. It concluded that the resulting small increase in the ICER would not stop tofacitinib being cost effective.

Costing information/100,000 population and per CCG:
Potential additional £0 to £9k per 100,000 per annum using costing template and local data.

Availability of PAS and details (if appropriate):
The company has a commercial arrangement. This makes tofacitinib available to the NHS with a discount. The size of the discount is commercial-in-confidence

Availability of homecare service (if appropriate): Not required

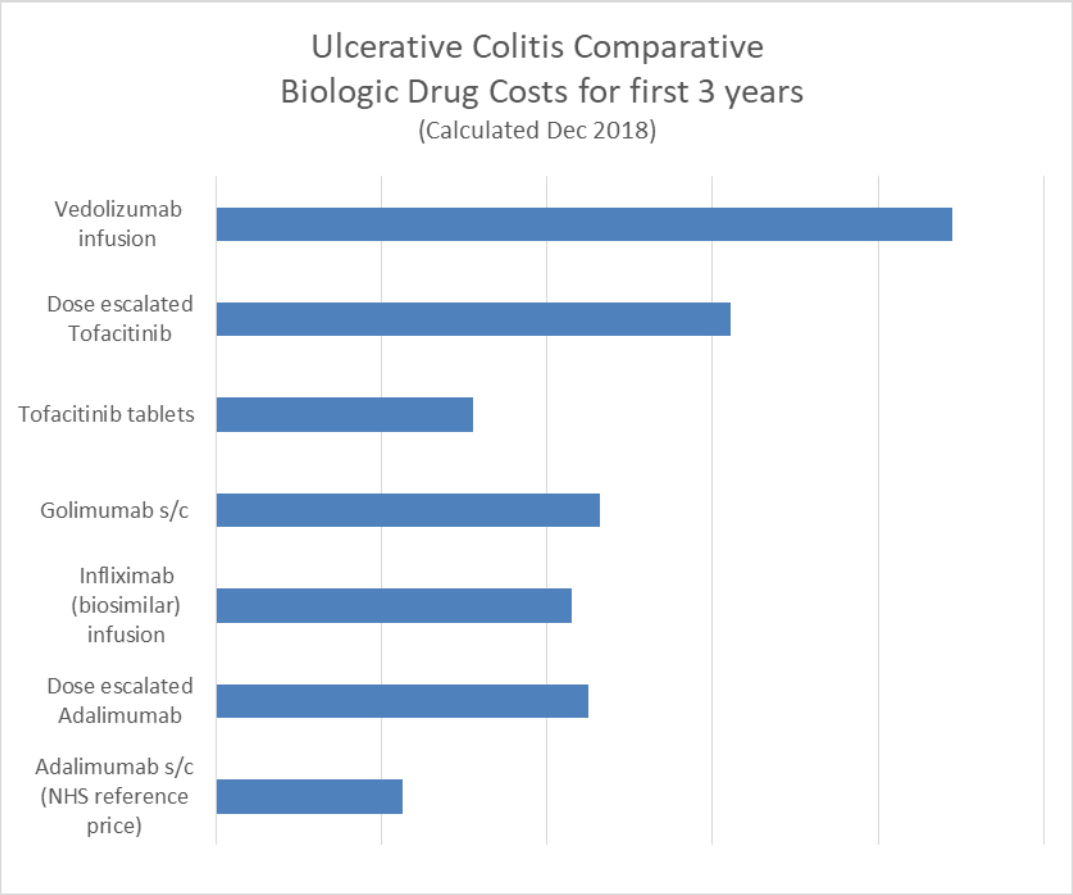
**NICE funding requirements are based on Quality Adjusted Life Years (QALY) threshold. If there is evidence that the incremental cost rises above this threshold in the future, the PCN may reconsider the commissioning status.*

Alternative treatments and cost per patient (per year / per month as appropriate)

Other NICE recommended products:
Current clinical management of moderate to severely active ulcerative colitis is conventional therapies (aminosalicylates, corticosteroids or thiopurines). If there is inadequate response or loss of response, patients may be offered a biological therapy (a tumour necrosis factor [TNF] alpha inhibitor such as infliximab, adalimumab and golimumab or the anti-integrin

agent vedolizumab).
Tofacitinib is a novel treatment with a different mode of action compared with biological therapies

NICE approved therapies and comparative costs (at PAS prices) are shown in figure 1
Figure 1



Options not reviewed by NICE but used in standard practice:
N/A

Impact to patients

- Tofacitinib is the first oral therapy available for this group of patients.
- Different mode of action to other therapies currently available to patients for ulcerative colitis
- Available under a homecare service so will be delivered directly to the patient.

Impact to primary care prescribers

- There will not be any requirement to prescribe/monitor in primary care
- Specialist prescribing in secondary/tertiary care only
- 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

- Prescribing/monitoring will be in secondary care where the responsibility for the alterative injectable therapies is currently.

Impact to CCGs

- No change in non-drug related activity
- Commissioning of another drug for first, second or third line of biologic therapy for UC treatment

Implementation

Place in therapy – current pathway for biologic use in UC requires updating to include Tofacitinib. Proposed updated pathway attached.
Dose escalation criteria require agreement.
Proposed to mirror the criteria for existing therapy – adalimumab.

- Recommend that tofacitinib is dose optimised to 10mg when a patient starts to lose response to 5mg treatment, for short periods (12 weeks) to recapture response.
- Recommend ongoing dose of 10mg is commissioned to maintain response if effect lost on return to 5mg dose.
- Recommend that when a patient is in stable clinical remission after 12 months they are encouraged to have a trial withdrawal: NB: A Patient who relapses after trial withdrawal will be able to immediately restart treatment

Recommendation to PCN

PbRe: Y
Commission for use instead of biologic therapy in patients with inadequate response to conventional therapy (aminosalicylates, corticosteroids, thiopurines) as part of pathway 4 for Ulcerative Colitis (attached).
The pathways 1, 2 and 3, as previously agreed in the gastroenterology network and PCN will be used before pathway 4.

Recommended traffic light status (see attached guidelines):
RED

Additional comments:
Blueteq forms will be available for initiation, continuation and dose escalation.

References:

1. Tofacitinib for moderately to severely active ulcerative colitis. Technology appraisal guidance [TA547] Published date: 28 November 2018 https://www.nice.org.uk/guidance/ta547

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Declaration of Interest:

NONE

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Declaration of Interest:

NONE

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VERSION CONTROL SHEET

Version	Date	Author	Status	Comment
v.1	*17/12/2018*	*E. Clark*	*Draft*	*For Peer Review*
v.2	*20/12/2018*	*G.Randall*	*Draft*	*Added requirement to think about dose escalation*
v.3	*07/01/19*	*E. Clark*	*Final*	*Circulation to Gastroenterology Network and PCN members*
V.4	*07/01/19*	*C.Johns*	*Final*	*Peer Review. Ready for consultation*