Briefing Paper for Surrey Heartlands Integrated Care System (ICS) Area Prescribing Committee (APC)

Surrey Downs, Guildford & Waverley, North West Surrey, East Surrey Place & associated partner organisations

NICE Technology Appraisals: Local implementation

NICE TA Guidance name and number	Filgotinib for treating moderately to severely active ulcerative colitis Technology appraisal guidance 792		
Available at	www.nice.org.uk/guidance/ta792		
Date of issue	1 June 2022	**Implementation deadline**	1 September 2022

Medicine details[1]	
Name, brand name and manufacturer	Filgotinib (Jyseleca®) Galapagos
Mode of action	Janus kinase (JAK) inhibitor – JAK 1
Licensed indication	Ulcerative colitis (UC) Jyseleca® is indicated for the treatment of adult patients with moderately to severely active ulcerative colitis who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a biologic agent.
Formulation	Each film-coated tablet contains filgotinib maleate equivalent to 200 mg of filgotinib.
Usual dosage	The recommended dose for induction and maintenance treatment is 200 mg once daily. For patients with ulcerative colitis who do not show an adequate therapeutic benefit during the initial 10 weeks of treatment, 12 additional weeks of induction treatment with filgotinib 200 mg once daily may provide additional relief of symptoms. Patients who have not shown any therapeutic benefit after 22 weeks of treatment should discontinue filgotinib. *Please note:* *There is no difference in dosing between the induction and maintenance phase.*
Comparison with NICE TA use[2]	– The NICE TA does not give length of induction or definitions of either moderate to severe disease or adequate therapeutic benefit. – As there is only one dose, 200mg, licensed for use in UC therefore dose escalation is not commissioned. *This is the current dose considered by NICE as part of this NICE evaluation. Subsequent changes in the license following NICE publication will need to be considered by the Area Prescribing Committee and **will not be routinely funded** by local commissioners.*

Disease and potential patient group	
Brief description of disease[3]	Ulcerative colitis is a chronic, relapsing-remitting, non-infectious inflammatory disease of the gastrointestinal tract. • It is characterised by diffuse, continuous, superficial inflammation of the large bowel limited to the intestinal mucosa, and usually affects the rectum with a variable length of the colon involved proximally. • People have abdominal pain and fatigue, frequent diarrhoea and extra-intestinal manifestations such as joint, skin and eye problems. • The symptoms and unpredictable nature of the disease have a profound and devastating impact on all aspects of a person's life. Ulcerative colitis and Crohn's disease are collectively known as 'inflammatory bowel disease'. • In about 5–10% of people, it is not possible to differentiate histologically between the two, and the term 'inflammatory bowel disease type-unclassified' may be used. The exact pathophysiology is unknown, but it is thought to be an immune-mediated condition resulting in impaired epithelial barrier function and chronic inflammation caused by environmental triggers (such as changes in the gut microbiome) in genetically susceptible people. Possible complications include negative psychosocial impact, toxic megacolon and bowel obstruction, anaemia, malnutrition, growth failure, and colorectal cancer. If medical treatment fails, then surgery may be needed. Surgery outcomes vary: there can be a psychological impact both from the surgery and having a stoma, even if it is temporary. Pelvic surgery can also significantly affect sexual and reproductive function.
Potential patient numbers per 100,000[4]	19/100,000

SUMMARY

Guidance[2]
Filgotinib is recommended, within its marketing authorisation, as an option for treating moderately to severely active ulcerative colitis in adults: • when conventional or biological treatment cannot be tolerated, or • if the disease has not responded well enough or has stopped responding to these treatments, and • if the company provides filgotinib according to the commercial arrangement.
Why the committee made these recommendations
Standard treatments for moderately to severely active ulcerative colitis after conventional treatment are tumour necrosis factor (TNF)-alpha inhibitors (adalimumab, golimumab or infliximab), tofacitinib, ustekinumab or vedolizumab. Clinical trial evidence shows that filgotinib is more effective than placebo for treating

moderately to severely active ulcerative colitis. There is no direct evidence comparing filgotinib with treatments that are offered after conventional treatment. Indirect comparison suggests that filgotinib is likely to be as effective as most of them.

The most likely cost-effectiveness estimates for filgotinib compared with other treatments are within the range NICE normally considers an acceptable use of NHS resources. So filgotinib is recommended.

Cost implications* [2,3,4]

Cost:
The price for filgotinib is £863.10 per bottle for thirty 200-mg tablets (BNF online, accessed March 2022).

The company has a commercial arrangement. This makes filgotinib available to the NHS with a discount. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount**.**

Annual or monthly cost per patient:
The average cost for each patient per year is estimated at £10,508 based on the list price.

Has dose escalation been considered as part of the NICE costing template?
No.

Costing information per CCG:

1. NICE resource impact statement*
No significant resource impact is anticipated.

NICE has recommended filgotinib, within its marketing authorisation, as an option for treating moderately to severely active ulcerative colitis in adults:

- when conventional or biological treatment cannot be tolerated, or
- if the disease has not responded well enough or has stopped responding to these treatments, and
- if the company provides filgotinib according to the commercial arrangement.

We do not expect this guidance to have a significant impact on resources; that is, the resource impact of implementing the recommendations in England will be less than £5 million per year (or £9,000 per 100,000 population).

This is because the technology is a further treatment option and the overall cost of treatment will be comparable to the current treatment options available.

2. NICE resource impact template

The previously published template for this patient group has been updated and replaced to include filgotinib and all other treatment options for moderately to severely active ulcerative colitis.

The cost over 5 years from resource planner shows a potential decrease in costs – see appendix 1. This may be attributed to:

1. Filgotinib is the most cost-effective JAK inhibitor. This would be the preferred JAK inhibitor within the pathway.
2. Tofacitinib is subject to an MHRA alert, Tofacitinib (Xeljanz▼): new measures to minimise risk of major adverse cardiovascular events and malignancies - GOV.UK (www.gov.uk) , which may reduce the number of patients for whom tofacitinib would be appropriate and some existing patients may be switched to filgotinib or other

alternatives.
3. Potentially a reduction in the use of iv infliximab, which although available as a biosimilar, attracts administration costs from the trust.

**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 APC may reconsider the commissioning status.*

Availability of PAS and details (if appropriate):
Yes - the PAS price will be given to trusts which would reduce the cost price stated above.

The PAS price only applies to trusts and primary care services would not be able to prescribe and supply at this reduced price, in line with the NICE TA.

Availability of homecare service (if appropriate): Yes

Alternative treatments and cost per patient per year

Other NICE recommended products:

Table 1: The most appropriate comparators to filgotinib:

NICE TA	Mode of action	TA	Date issued
Infliximab, adalimumab and golimumab for treating moderately to severely active ulcerative colitis after the failure of conventional therapy	TNF-alpha inhibitors	TA329	Feb 2015
Vedolizumab for treating moderately to severely active ulcerative colitis	Integrin α4β7 receptor antagonist	TA342	June 2015
Tofacitinib for moderately to severely active ulcerative colitis	JAK inhibitor	TA547	Nov 2018
Ustekinumab for treating moderately to severely active ulcerative colitis	Interleukin (IL) 12/23	TA633	June 2020

Filgotinib is the most cost-effective JAK inhibitor.

Options not reviewed by NICE but used in standard practice:
Conventional treatments (aminosalicylates, corticosteroids or thiopurines) are used first line before treatment with biologics.

Impact to patients

- An additional option that induce and maintain remission would be valued by patients. For many people, their disease does not respond well to current treatments, or they stop working. The only option for them, other than surgery, is long-term corticosteroids.
- This is an oral treatment - it may be more convenient than other treatment options.
- This medicine is available under a homecare service so will be delivered directly to the patient.

Impact to primary care prescribers

- This is a National Tariff excluded high-cost drug and is commissioned by integrated care systems (ICS) / clinical commissioning groups (CCG) for use in secondary care. There should be no prescribing in primary care.
- Primary care prescribers should be aware that their patient is receiving this medicine 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.

• An additional treatment option would be valued by clinicians.
Impact to commissioners
• The technology is commissioned by ICS/CCGs and they are required to comply with the recommendations in a NICE TA within 3 months of its date of publication. • Providers are NHS hospital trusts. • Potential savings for out-patient appointments as this medicine is available on homecare.
Implementation
• NICE TA implementation must be within 90 days of publication • Blueteq forms to be developed • Trusts to follow internal governance procedures to add to their formulary and initiate homecare • Pathway to be discussed at Gastroenterology Network – see appendix 2 for possible positioning in the treatment pathway and appendix 3 for definitions of moderately to severe ulcerative colitis as per the SELECTION trial used as clinical evidence within the NICE submission by the company.
Recommendation to APC
National Tariff excluded high-cost drug: Yes **Recommended traffic light status:** RED

References:

1. Specification of Product Characteristics. emc. Jyseleca 200 mg film-coated tablets. Available at: https://www.medicines.org.uk/emc/product/11810/smpc Accessed <6.6.22>

2. NICE Technology Appraisal Guidance: Filgotinib for treating moderately to severely active ulcerative colitis. Available at: https://www.nice.org.uk/guidance/ta792 Accessed <6.6.22>

3. Ulcerative colitis. NICE CKS. Available at: https://cks.nice.org.uk/topics/ulcerative-colitis/ Accessed <6.6.22>

4. NICE Resource impact statement: Filgotinib for treating moderately to severely active ulcerative colitis. Available at: https://www.nice.org.uk/guidance/ta792/resources Accessed <6.6.22>

5. NICE Resource impact template: Filgotinib for treating moderately to severely active ulcerative colitis. Available at: https://www.nice.org.uk/guidance/ta792/resources Accessed <6.6.22>

Declaration of interest:

	Name	Role	Date	Declaration of interests (please give details below)
Prepared by	Tejinder Bahra	Lead Commissioning Pharmacist	6.6.22	None
Reviewed by				

Explanation of declaration of interest:

Version control sheet:

Version	Date	Author	Status	Comment
1	28.6.22	Tejinder Bahra	Draft	Out for consultation

Appendix 1: Possible impact of NICE TA792 in the change in costs for Surrey Heartlands CCG over 5 years.

Drug costs	**Cost of current practice**	**Cost of future practice**	**Impact of change on cost**
Proportion of people receiving treatment with ustekinumab	£56,388	£56,388	£0
Proportion of people receiving treatment with tofacitinib	£129,411	£29,864	-£99,547
Proportion of people receiving treatment with vedolizumab	£512,142	£492,444	-£19,698
Proportion of people receiving treatment with adalimumab	£162,940	£133,315	-£29,625
Proportion of people receiving treatment with infliximab (IV infusion)	£794,578	£728,363	-£66,215
Proportion of people receiving treatment with infliximab (Subcutaneous injection)	£0	£0	£0
Proportion of people receiving treatment with golimumab	£0	£0	£0
Proportion of people receiving treatment with filgotinib	£0	£101,545	£101,545
Total drug costs	**£1,655,459**	**£1,440,374**	**-£215,085**

Administration costs			
Proportion of people receiving treatment with ustekinumab	£1,173	£1,173	£0
Proportion of people receiving treatment with tofacitinib	£0	£0	£0
Proportion of people receiving treatment with vedolizumab	£0	£0	£0
Proportion of people receiving treatment with adalimumab	£0	£0	£0
Proportion of people receiving treatment with infliximab (IV infusion)	£215,321	£197,378	-£17,943
Proportion of people receiving treatment with infliximab (Subcutaneous injection)	£0	£0	£0
Proportion of people receiving treatment with golimumab	£0	£0	£0
Proportion of people receiving treatment with filgotinib	£0	£0	£0
Total administration costs	216,494	198,551	-17,943

Total impact all recommendations	**£1,871,954**	**£1,638,925**	**-£233,029**

Appendix 2: Positioning within pathway (extract from NICE TA792)

Filgotinib could be used at 3 different positions in the treatment pathway

3.4 Filgotinib has a marketing authorisation for treating moderately to severely active ulcerative colitis when conventional or biological treatment cannot be tolerated, or if the disease has not responded well enough or stopped responding to treatment. The company's submission presented filgotinib at 3 positions in the treatment pathway:

- A first-line treatment for the 'biologic-naive' – people who have never had a biological treatment (a TNF-alpha inhibitor or vedolizumab) or tofacitinib (a Janus-associated kinase [JAK] inhibitor), but have had conventional treatment and their disease has likely not responded to it or lost response to it.

- A second-line treatment for 'biologic-experienced' – people who have had 1 biological treatment or tofacitinib and either their disease did not respond to it, lost response to it, or they could not tolerate it.

- A third-line treatment for biologic-experienced – people who have had 2 or more biological treatments or tofacitinib and either their disease did not respond or lost an initial response, or they could not tolerate it.

The company clarified that in the biologic-experienced subgroup it assumed the same efficacy for filgotinib as a second or third-line treatment because of the lack of evidence. The ERG noted that efficacy reduces when moving from the first biologic to a second or third biologic when the disease does not respond adequately or loses response. It explained that in the SELECTION trial (see section 3.6) remission at 10 weeks reduced from 16.3% in people taking their second biologic to 7.4% in people taking their third biologic. The clinical experts explained that they would expect efficacy to reduce when moving from second to third-line treatment because of previous drug exposure or because people needing further treatments have disease that is more difficult to treat. The clinical and patient experts agreed with the company's positioning of filgotinib because it would offer an additional choice at each line of treatment. The committee noted it was not presented with evidence of filgotinib's effectiveness specifically as a third-line treatment. The committee considered that the company's assumption that filgotinib would have the same efficacy, regardless of how many biologics treatments people had previously, was unlikely and optimistic. But it noted that this applies to all treatments and not just filgotinib. The committee considered that having another option at each of the 3 positions in the pathway offers people more choice, and agreed with the company's positioning.

Appendix 3: Definitions of moderately to severe ulcerative colitis as per the SELECTION trial used as clinical evidence within the NICE submission by the company.

SELECTION was a phase 2b/3 randomised, double-blind, multicentre trial comparing filgotinib 200 mg, filgotinib 100 mg and placebo. It included adults with **moderately to severely active ulcerative colitis, defined by a Mayo clinic score of between 6 and 12, and component sub scores of at least 1 for stool frequency and rectal bleeding and at least 2 for endoscopic findings and physicians' global assessment.**