Surrey Heartlands Integrated Care System
Area Prescribing Committee (APC)

Integrated Care Partnership - Surrey Downs, Guildford & Waverley, North West Surrey, and East Surrey Places & associated partner organisations.

NICE Technology Appraisals (TA) for local implementation

NICE TA Guidance name and number	Upadacitinib for treating moderately to severely active ulcerative colitis Technology appraisal guidance [TA856]		
Available at	https://www.nice.org.uk/guidance/ta856		
Date of issue	04 January 2023	**Implementation deadline**	04 April 2023

Medicine details[1]	
Name and brand name	Upadacitinib (RINVOQ®)
Manufacturer	AbbVie Ltd
Mode of action	Upadacitinib is an oral, once-daily, reversible Janus kinase inhibitor (JAKi) that selectively inhibits JAK1 and JAK1/3.
Licensed indication	RINVOQ is indicated for 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	Each prolonged-release tablet contains upadacitinib hemihydrate, equivalent to 15, 30 or 45 mg of upadacitinib.
Dosage	Induction: The recommended induction dose of upadacitinib is 45 mg once daily for 8 weeks. For patients who do not achieve adequate therapeutic benefit by week 8, upadacitinib 45 mg once daily may be continued for an additional 8 weeks. Upadacitinib should be discontinued in any patient who shows no evidence of therapeutic benefit by week 16. Maintenance: The recommended maintenance dose of upadacitinib is 15 mg or 30 mg once daily based on individual patient presentation: • A dose of 30 mg once daily may be appropriate for some patients, such as those with high disease burden or requiring 16-week induction treatment. • A dose of 30 mg once daily may be appropriate for patients who do not show adequate therapeutic benefit to 15 mg once daily. • The lowest effective dose for maintenance should be considered. For patients ≥ 65 years of age, the recommended dose is 15 mg once daily.

	In patients who have responded to treatment with upadacitinib, corticosteroids may be reduced and/or discontinued in accordance with standard of care.
Comparison of NICE TA with Summary of Product Characteristics (SmPC)[2]	The dosage and time intervals are the same as NICE evaluation. *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, as the incremental cost per QALY would not have been considered.*

NICE TA recommendations[2]

Recommendations

1.1 Upadacitinib 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 condition has not responded well enough or has stopped responding to these treatments, and
• if the company provides upadacitinib according to the commercial arrangement.

1.2 Choose the most appropriate treatment after discussing the advantages and disadvantages of the treatments available with the person having treatment. If patients and clinicians consider upadacitinib to be one of a range of suitable options, choose the least expensive treatment (taking into account drug administration costs, dose needed and frequency, and product price per dose).

Decision making framework (DMF)

National guidance and priorities

The ICS has a legal obligation to commission this medicine in line with the NICE TA.

- This NICE TA has been assigned an implementation deadline of *3 months.*
- The implementation deadline is 4 April 2023.

Clinical effectiveness

Standard treatments for moderately to severely active ulcerative colitis after conventional treatments are biological treatments (adalimumab, golimumab, infliximab, ustekinumab or vedolizumab) or tofacitinib.

Clinical trial evidence shows that upadacitinib is more effective than placebo for treating moderately to severely active ulcerative colitis. There is no direct evidence comparing upadacitinib with treatments that are offered after conventional treatment. Indirect comparison suggests that upadacitinib is likely to be at least as effective as the treatments it was compared with.

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

Patient safety

- The product should be used within its product license.

Please note:
The committee was aware of the European Medicines Agency safety committee review of JAK inhibitors for inflammatory disorders (EMA starts safety review of Janus kinase inhibitors for inflammatory disorders | European Medicines Agency (europa.eu) (including upadacitinib for ulcerative colitis).

This is because a clinical trial of tofacitinib in rheumatoid arthritis showed people with risk of heart disease were more likely to experience a major cardiovascular problem and had a higher risk of developing cancer with tofacitinib than TNF-alpha inhibitors.

The company submitted a summary of the most recent data from a long-term extension study of upadacitinib (U-ACTIVATE). No new safety risks were identified in people who completed maintenance treatment in U-ACHIEVE and continued upadacitinib in the extension study. The committee concluded that based on the evidence presented, upadacitinib has an acceptable safety profile.

Patient factors

- An oral treatment would be valued over an infusion or self-injecting.
- An additional treatment option would be valued by patients. This is now the third JAK inhibitor, all of which are oral medicines.
- This medicines is available through homecare and may reduce the burden on some services and minimise the need for patients to visit hospital pharmacy

Environmental impact

No statement is made within the NICE TA.

However use of oral medicines would reduce the impact of waste and the disposal of pre-filled pens and syringes.

Equality & diversity

No statement is made within the NICE TA.

Upadacitinib is only licensed for adult patients – younger patients will not be able to access this treatment under this TA.

Note: Drugs approved by NICE for adult conditions will be commissioned in children at specialised paediatric centres if the patient meets the NICE criteria and there is evidence to suggest that the drug is safe and clinically appropriate to use in children as per the NHS England Medicines for Children Policy (see https://www.england.nhs.uk/publication/commissioning-medicines-for-children-specialised-services/ and a Blueteq form is available.

Place in therapy relative to available treatments

The IBD Immunomodulator treatment pathway has been revised to include upadacitinib.

It is one of three JAKi available in ulcerative colitis (there are no NICE TAs for JAKi in Crohn's disease).

Upadacitinib is another option within the JAKi class of drugs of which two others have previously been approved. It is not another line of therapy so has no significant impact on costs within the UC treatment pathway.

The most cost-effective JAKi is filgotinib (NICE TA792, published June 2022).

Stakeholder views

The paper was sent out for consultation and 1 comment was received.

Cost-effectiveness

The drug cost per Place according to NICE resources is not anticipated to exceed £100,000 for this medicine.

Section 1: cost of the technology

a. Annual cost per patient (or complete course if shorter) for both primary and secondary care:

The price per 28-tablet pack is £805.56 for upadacitinib 15 mg and £1,281.54 for upadacitinib 30 mg (all prices excluding VAT; BNF online accessed October 2022).

The estimated cost for 6 weeks of induction treatment (45 mg) is £3,131 based on list price (excluding VAT).

The estimated cost of maintenance treatment is £10,472 at standard dose (15 mg) or £16,660 at high dose (30 mg) per person per year based on list price (excluding VAT).

b. Availability of CAP/PAS price:

Yes. The company has a commercial arrangement. This makes upadacitinib 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.

c. Price relative to comparable medicines:

Table 1. Annual costs of reimbursed therapies used for the treatment of moderately to severely active UC.

Drug	Year 1	Year 2
TNF inhibitors (TNFi)		
Infliximab (Remicade®)	£13,428**	£11,749
Infliximab (biosimilars)	£12,085	£39,819 - £10,574
Adalimumab (Humira®)	£10,916	££9,156
Adalimumab (biosimilars)	£9,821 - £10,016	£8,240 -£8,400
Golimumab	£10,682	£9,919
Anti-integrin		
Vedolizumab	£16,400 - £17,938	£13,325 - £14,350
Interleukin-12/23 (IL 12/23)		
Ustekinumab	£15,029	£10,735
JAK inhibitor (JAKi)		
Tofacitinib	£10,375	£8,995
Filgotinib	£10,472	£10,472
Sphingosine 1-phosphate (S1P) receptor modulator		
Ozanimod	£17,910	£17,910

*Costs are NHS list price (and exclude VAT) and do not take into account any commercial discounts, patient access scheme or service delivery costs. All costs assume no packs are split and therefore contain the cost of wastage. **Annual costs for infliximab and ustekinumab assume an estimated body weight of 70 kg. †Cost varies based on whether maintenance treatment is administered via IV infusion or SC injection.

Upadacitinib is another option within the JAKi class of drugs of which two others, tofacitinib and filgotinib have previously been approved. It is not another line of therapy so has no significant impact on costs within the UC treatment pathway.

The order of cost-effectiveness, using the weighted average drug costs calculated within the NICE resource impact template is:

1. Filgotinib
2. Upadacitinib
3. Tofacitinib

The most cost-effective JAKi (using the current CAP/PAS price) is filgotinib.

This is reflected in the revised IBD pathway.

Section 2: NICE resource impact statement and template

Number of patients Year 1 and Year 5:

Year	Number of patients
Year 1	446
Year 5	446

Potential patient numbers per 100,000: 42

a. NICE resource impact statement

No significant resource impact is anticipated

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 approximately £9,000 per 100,000 population, based on a population for England of 56.3 million people).

This is because the technology is a further treatment option and the overall cost of treatment for this patient group will be similar.

b. NICE resource impact template

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

Drug costs for Surrey Heartlands:
There are currently 42 patients on JAKi out of 352 patients on immunomodulator medicines for UC in SH.

Of the 42 patients, 3 are on filgotinib and 39 are on tofacitinib. It is anticipated that over time, there will be fewer patients on tofacitinib due to the MHRA alert, Tofacitinib (Xeljanz▼): new measures to minimise risk of major adverse cardiovascular events and malignancies - GOV.UK (www.gov.uk) and new patients will be started or switched to filgotinib as it is established as the most cost-effective JAKi, which may generate a saving.

There may also be savings as fewer patients start on infliximab as an oral JAKi may be preferred.

The increased cost in this indication will be from the uptake of ozanimod.

The Surrey Heartlands Director of Pharmacy and Medicines Optimisation has delegated authority to enable the Committee to be a decision-making committee providing the impact of any single decision does not exceed £100,000 within an individual Place per annum. Decisions with a cost impact of over £100,000 within an individual Place per annum require authorisation from Surrey Heartlands Health & Care Professionals Committee at their next meeting. Exception to this will be for any decision made in relation to a NICE Technology Appraisal (which are subject to requiring mandatory funding by commissioners) and other urgent items. The exceptions will be taken to the next Executive Meeting (which meets weekly) for authorisation.

Traffic light recommendation to APC

NHS Payment Scheme (NHSPS) excluded high-cost drug:
Yes

Recommended traffic light status and rationale:
RED – Specialist ONLY drugs - treatment initiated and continued by specialist clinicians.

PAD definitions, available at: Traffic Light Status (res-systems.net)

Implementation

NICE TA implementation must be within 3 months of publication.

Actions to implement:

a. Primary care

- This is a National Tariff excluded high-cost drug and is commissioned by ICSs 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.

b. Secondary care

- Providers are NHS hospital trusts.
- Trusts to follow internal governance procedures to add to their formulary and initiate homecare.
- The initiation, administration and on-going treatment is managed by secondary care.
- Specialists will be required to notify the high-cost drugs teams of initiation and response to treatment using the Blueteq® system.
- Provides an additional option for oral therapy in both the induction and maintenance phases of treatment, and as such may help reduce burden on IV infusion clinics and minimise outpatient visits for SC administration
- Homecare arrangements will be managed by the trust.

c. ICS

- This technology is commissioned by integrated care systems.
- Pathway to be discussed at the next Gastroenterology Network meeting to
    - agree pathway and the inclusion of filgotinib, ozanimod and upadacitinib as treatment choices in line with their respective NICE TAs.
    - Agree filgotinib as the most cost-effective JAKi

d. PAD and Joint Formulary

- Revised IBD immunomodulator treatment pathway to be uploaded to the PAD.
- Blueteq® forms to be made available to the trusts.

Proposed tick box forms

Blueteq® forms have been developed and included below.

Additional information required for Joint Formulary:
None
References:

1 Summary of Product Characteristics. RINVOQ 15 mg prolonged-release tablets (Great Britain). emc. Available at: RINVOQ 15 mg prolonged-release tablets (Great Britain) - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk) Accessed <4.1.23>

2 NICE Technology Appraisal Guidance: Upadacitinib for treating moderately to severely active ulcerative colitis. Technology appraisal guidance [TA856] Published: 04 January 2023. Available at: Overview | Upadacitinib for treating moderately to severely active ulcerative colitis | Guidance | NICE Accessed <4.1.23>

3 NICE Resource Impact Report: Upadacitinib for treating moderately to severely active ulcerative colitis. Technology appraisal guidance [TA856] Published: 04 January 2023. Available at: Tools and resources | Upadacitinib for treating moderately to severely active ulcerative colitis | Guidance | NICE Accessed <4.1.23>

4 NICE Resource Impact Template: Upadacitinib for treating moderately to severely active ulcerative colitis. Technology appraisal guidance [TA856] Published: 04 January 2023. Available at: Tools and resources | Upadacitinib for treating moderately to severely active ulcerative colitis | Guidance | NICE Accessed <4.1.23>