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 active non-radiographic axial spondyloarthritis (TA861)		
Available at	https://www.nice.org.uk/guidance/ta861		
Date of issue	01 Feb 2023	**Implementation deadline**	03 March 2023

Medicine details[1]	
Name and brand name	Upadacitinib (Rinvoq)
Manufacturer	AbbVie
Mode of action	Upadacitinib is a selective and reversible Janus kinase (JAK) inhibitor. JAKs are intracellular enzymes that transmit cytokine or growth factor signals involved in a broad range of cellular processes including inflammatory responses, hematopoiesis, and immune surveillance. The JAK family of enzymes contains four members, JAK1, JAK2, JAK3 and TYK2 which work in pairs to phosphorylate and activate signal transducers and activators of transcription (STATs). This phosphorylation, in turn, modulates gene expression and cellular function. JAK1 is important in inflammatory cytokine signals while JAK2 is important for red blood cell maturation and JAK3 signals play a role in immune surveillance and lymphocyte function. In human cellular assays, upadacitinib preferentially inhibits signalling by JAK1 or JAK1/3 with functional selectivity over cytokine receptors that signal via pairs of JAK2
Licensed indication	RINVOQ is indicated for the treatment of active non-radiographic axial spondyloarthritis in adult patients with objective signs of inflammation as indicated by elevated C-reactive protein (CRP) and/or magnetic resonance imaging (MRI), who have responded inadequately to nonsteroidal anti-inflammatory drugs (NSAIDs).
Formulation	Each **prolonged-release tablet** contains upadacitinib hemihydrate, equivalent to 15mg, 30mg or 45mg of upadacitinib. Note; only the 15mg and 30mg are licenced for use in non-radiographic axial spondyloarthritis (nr-axSpA), although dosage is 15mg daily.
Dosage	The recommended dose of upadacitinib is 15 mg once daily (at time of NICE publication). Consideration should be given to discontinuing treatment in patients with axial spondyloarthritis who have shown no clinical response

	after 16 weeks of treatment. Some patients with initial partial response may subsequently improve with continued treatment beyond 16 weeks.
Comparison of NICE TA with Summary of Product Characteristics (SmPC)[2]	The above information is from the SmPC at time of NICE publication. Dose escalation from 15mg daily was not included within the product licence at time of publication, nor was it used in cost calculations. *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 as an option for treating active non-radiographic axial spondyloarthritis with objective signs of inflammation (shown by elevated C-reactive protein or MRI) that is not controlled well enough with non-steroidal anti-inflammatory drugs (NSAIDs) in adults. It is recommended only if:

- tumour necrosis factor (TNF)-alpha inhibitors are not suitable or do not control the condition well enough and
- the company provides upadacitinib according to the commercial arrangement.

1.2 Assess response to upadacitinib after 16 weeks of treatment. Continue treatment only if there is clear evidence of response, defined as a reduction in:

- the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score to 50% of the pre-treatment value or by 2 or more units and
- the spinal pain visual analogue scale (VAS) by 2 cm or more.

1.3 Take into account any physical, sensory or learning disabilities, or communication difficulties that could affect the responses to the BASDAI and spinal pain VAS and make any adjustments needed.

1.4 If patients and their clinicians consider upadacitinib to be 1 of a range of suitable treatments (including secukinumab and ixekizumab), discuss the advantages and disadvantages of the available treatments. After that discussion, if more than 1 treatment is suitable, choose the least expensive. Take account of administration costs, dosage, price per dose and commercial arrangements.

1.5 These recommendations are not intended to affect treatment with upadacitinib 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

Usual treatment for active non-radiographic axial spondyloarthritis in adults that is not controlled well enough with NSAIDs, and when TNF-alpha inhibitors are not suitable or do not control the condition well enough, is secukinumab or ixekizumab. These are biological treatments. Upadacitinib is another biological treatment.

(MRU note: upadacitinib is NOT a medicine of biological origin, it is completely synthetic).

Evidence from clinical trials shows that upadacitinib reduces symptoms and improves quality of life better than placebo. Indirect comparisons suggest that upadacitinib works as well as

secukinumab and ixekizumab.

A cost comparison suggests upadacitinib has similar costs and overall health benefits as secukinumab and ixekizumab. So upadacitinib is recommended.

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 *fast tracked to 30 days.*
- The implementation deadline is 03 March 2023.

Clinical effectiveness

- Evidence from clinical trials shows that upadacitinib reduces symptoms and improves quality of life better than placebo. Indirect comparisons suggest that upadacitinib works as well as secukinumab and ixekizumab, which are already commissioned as per NICE guidance.

Patient safety

- Upadacitinib is licensed for this indication in the UK. It is to be taken by mouth only.
- As with all systemic immunosuppressants, prescribers should be aware of patient risk of reduced immune response to infection, and this should be considered when triaging patient exhibiting symptoms. GP practice records should be maintained accordingly (this should be reiterated in the PAD narrative).
- JAK inhibitors, such as upadacitinib, are associated with raised incidence of VTE and PE episodes (tofacitinib, not offered in non-radiographic axial spondyloarthritis, but a JAK inhibitor, is subject to MHRA alert October 2021), and also of raising blood-lipid levels. Prescribing clinicians are already aware of and monitor/counsel patients accordingly.

Patient factors

- Upadacitinib constitutes an alternative option for those patients who have yet to try a JAK inhibitor
- Upadacitinib (as a new class of drug) adds a further therapeutic line to the current treatment pathway. Patients will now have 3 lines of treatment available within the high-cost axial spondyloarthritis pathway (for nr-SpA).
- Patient education materials are provided.
- Alternative options / products are now available to those patients who will not/cannot use injectable products.
- An additional treatment option would be valued by patients.
- This medicine is available under a homecare service so will be delivered directly to the patient. When the patient is confident in self-administering, this may reduce the number of hospital appointments to those required for review and/or monitoring.

Environmental impact

- **Packaging waste** from upadacitinib would be additional to usual municipal waste recycling or landfill.
- Discharge into the **wastewater** system (post-metabolism) from an individual patient is unlikely to have a significant impact short term, however the long-term impact to the water ecosystem is unknown.

Equality & diversity

No specific statement is made within the NICE TA.

- **Age** – Upadacitinib is only licensed for adult patients – younger patients will not be able to access this treatment under this TA.
- **Other** - NICE did not anticipated that equality issues will arise with upadacitinib treatment. However, in previous technology appraisal guidance for TNFα inhibitors for AS and nr-axSpA treatment, an equality concern considering patient assessments was identified. The appropriateness of using BASDAI and spinal pain VAS scores should be taken into consideration in the presence of physical, sensory, learning or communication difficulties that could affect a patient's response to the questionnaires, and adjustments should be made appropriately.

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 spondyloarthritis immunomodulator treatment pathway for adults has been revised to include upadacitinib for this indication.
- It is currently the only JAKi commissioned for use as per NICE guidance.

Stakeholder views

The paper was sent out for consultation and *x* comments were received.
Comments to be included in the front sheet.

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 list price is £805.56 per 28-tablet pack, (15mg), and £1,281.54 per 28-tablet pack (30mg) (excluding VAT; BNF online, accessed February 2023).

The annual cost of maintenance treatment with one 15-mg tablet per day is £10,501.05 (excluding VAT; BNF online, accessed February 2023)

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.

Dose escalation from 15mg daily was not included within the product licence at time of publication, nor was it used in cost calculations.

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:

Currently there are NICE Technology Appraisals for the following drugs (ranked by cost, with the most cost-effective being first):

1. Adalimumab
2. Etanercept
3. Upadacitinib
4. Secukinumab
5. Ixekizumab
6. Golimumab
7. Certolizumab

Non-steroidal anti-inflammatory drugs (NSAIDs) are the standard first line treatment.

Section 2: NICE resource impact statement and template

Number of patients Year 1 and Year 5: NICE assumes 146 out of 485 people will be eligible for treatment. To date, the system is only aware of 13 patients accessing treatment with these comparable medicines.

These 13 patients and any new patients would be eligible to receive treatment with upadacitinib.

Potential patient numbers per 100,000:
NICE assumes 146 out of 485 people will be eligible for treatment out of the Surrey Heartlands population.

However, there are only 13 patients known to the system currently using high-cost drugs for non-radiographic axial spondyloarthritis, only one of which has moved onto a 2nd line drug so far.

	Patient count	No. of patients using as 2nd line agent
Adalimumab	**6**	0
Etanercept biosimilar	**6**	1
Secukinumab	**1**	0
Grand Total	**13**	1

a. NICE resource impact statement
No significant resource impact is anticipated

NICE does 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.

Upadacitinib can be taken orally. Both clinical and patient experts highlighted the convenience of upadacitinib over comparators because of its oral administration.

The company has a commercial arrangement (simple discount patient access scheme). 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.

A resource impact template is provided for completion at a local level. This is because there are numerous treatment options that are recommended by NICE for treating non-radiographic axial spondyloarthritis.

This technology is commissioned by integrated care systems. Providers are NHS hospital trusts.

b. NICE resource impact template

This template assumes that the system has 146 people eligible for high cost immunomodulator treatment, whereas we only know of 13 people in total currently.

Drug costs for Surrey Heartlands:
For those 13 patients, as per the cost calculator, proportionally this would cost £54,671 (or £4,205 per patient). NICE does not expect there to be any growth in patient numbers at Yr 5.

It is to be noted that there appears to be very little appetite to use the newer drugs available

on the pathway with only one patient to date requiring a second line agent, uptake of upadacitinib is expected to be low and slow.
Although NICE states that a significant impact on resources is not expected, there is still a new cost pressure even though this may be below the £9,000 per 100,000 population threshold for NICE, as this TA represents a new line of treatment.

At £9,000 per 100,000 population, this represents:

	East Surrey	Guildford and Waverley	Surrey Downs	North West Surrey	Surrey Heartlands ICB
Population*	193,532	232,784	316,690	388,466	1,131,472
Cost	£17,418	£20,951	£28,502	£34,962	£101,832

* August 2022 population figures from NHS Prescription Services through ePACT.

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 clinician – due to above status.

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

Implementation

- NICE TA implementation must be within 30 days of publication.
- Blueteq forms to be developed
- Trusts to follow internal governance procedures to add these drugs to their formulary, so that prescribers can initiate use as per NICE TA.
- Trusts to ensure that these drugs are available to prescribe to patients via the homecare route as appropriate.
- Axial spondyloarthritis high-cost drugs pathway to be discussed at Rheumatology Network (attached pathway as example)

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 will be 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.
- Homecare arrangements will be managed by the trust.
- Patients eligible for these treatments will already be known to the rheumatology clinics, so there will be very low impact to clinic capacity from current levels.

c. ICS
- The technology is commissioned by integrated care systems, and they are required to comply with the recommendations of this NICE TA within 30 days of its date of publication.
- Providers are NHS hospital trusts.
- This guidance introduces another line of treatment into the current treatment pathway i.e. there will now be 3 lines of treatment available to patients.
- Pathway to be discussed at the next Surrey Heartlands Rheumatology Network.

d. PAD and Joint Formulary
- Once agreed the pathway will need to be uploaded onto PAD/Joint Formulary for all drugs listed on the pathway, as per agreed process.

Proposed tick box forms
Blueteq® forms have been developed and included below.

Additional information required for Joint Formulary:
- *A tick box will be included here.*

References:

1 Summary of Product Characteristics. Accessed 03 February 2023, Available at: https://www.medicines.org.uk/emc/product/10972/smpc#
2 NICE Technology Appraisal Guidance: Accessed 03 February 2023, Available at: https://www.nice.org.uk/guidance/ta861
3 NICE Resource Impact Report: Accessed 03 February 2023, Available at: https://www.nice.org.uk/guidance/ta861/resources/resource-impact-statement-11371377421
4 NICE Resource Impact Template: Accessed 03 February 2023, Available at: https://www.nice.org.uk/guidance/ta861/resources