Briefing Paper for Area Prescribing Committee on NICE Technology Appraisals: Local implementation

NICE TA Guidance	Upadacitinib for treating moderate rheumatoid arthritis. TA744		
Available at	www.nice.org.uk/guidance/ta744		
Date of issue	10 November 2021	**Implementation deadline**	10 February 2022

Medicine details[1]	
Name, brand name and manufacturer	Upadacitinib (Rinvoq®) AbbVie
Mode of action	Janus kinase (JAK) inhibitor
Licensed indication	Rinvoq® is indicated for the treatment of moderate to severe active rheumatoid arthritis in adult patients who have responded inadequately to, or who are intolerant to one or more disease-modifying anti-rheumatic drugs (DMARDs). Rinvoq® may be used as monotherapy or in combination with methotrexate.
Formulation	15 mg and 30mg prolonged-release tablets
Usual dosage	The recommended dose of upadacitinib is 15 mg once daily.
Comparison with NICE TA use[2]	The NICE TA does not state the dosage but the only recommended dose in the SmPC for RA is 15 mg once daily. This NICE TA therefore refers to the 15mg dose *Please note:* – *The NICE TA for upadacitinib for treating severe rheumatoid arthritis was published (NICE TA665) in December 2020.* – *It is licensed for use in appropriate patients 'who have responded inadequately to, or who are intolerant to 1 or more disease-modifying antirheumatic drugs (DMARDs)'. The NICE TA recommends use after 2 or more conventional DMARDs.* – *This is the second JAK inhibitor supported for use in moderate RA (as defined by a disease activity score [DAS28] of 3.2 to 5.1). The first was filgotinib (NICE TA676) published in February 2021.* – *The tumour necrosis factor (TNF)-alpha inhibitors adalimumab, etanercept and infliximab are also available for use in moderate RA after conventional DMARDs have failed as per NICE TA715 published in July 2021.* – *The recommendations state:* *If more than 1 treatment is suitable, start treatment with the least expensive drug (taking into account administration costs, dose needed and product price per dose). This may vary because of differences in how the drugs are used and treatment schedules.* – *The definition of moderate RA is better defined within this TA than in others.* – *The committee concluded that healthcare professionals should consider any physical, psychological, sensory or learning disabilities, or communication difficulties that could affect the responses to the DAS28 and make any appropriate adjustments.* *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 Area Prescribing Committee and **will not be routinely funded** by local commissioners.*

Disease and potential patient group

Brief description of disease[3]

Rheumatoid arthritis is a long-term condition that causes pain, swelling and stiffness in the joints. The condition usually affects the hands, feet and wrists.

There may be periods where symptoms become worse, known as flare-ups or flares.

A flare can be difficult to predict, but with treatment, it is possible to decrease the number of flares and minimise or prevent long-term damage to the joints.

Some people with rheumatoid arthritis also experience problems in other parts of the body, or more general symptoms such as tiredness and weight loss.

DAS28 score
Disease severity is assessed using the disease activity score (DAS28). A DAS28 of more than 5.1 indicates severe disease, >3.2 and ≤5.1 indicates moderate disease, ≤3.2 indicates mild disease, and ≤2.6 indicates disease remission.

European League Against Rheumatism (EULAR) response criteria

Current DAS28	DAS28 improvement compared to baseline		
	>1.2	>0.6 to ≤1.2	≤0.6
≤3.2	Good response	Moderate response	No response
>3.2 to ≤5.1	Moderate response	Moderate response	No response
>5.1	Moderate response	No response	No response

Potential patient numbers per 100,000[4]

Severe RA 85/100,000
Moderate RA 48/100,000

SUMMARY

Guidance[2]

1.1 Upadacitinib, with methotrexate, is recommended as an option for treating active rheumatoid arthritis in adults whose disease has responded inadequately to intensive therapy with 2 or more conventional disease-modifying antirheumatic drugs (DMARDs), only if:

- disease is moderate (a disease activity score [DAS28] of 3.2 to 5.1) and
- the company provides upadacitinib according to the commercial arrangement.

1.2 Upadacitinib can be used as monotherapy when methotrexate is contraindicated or if people cannot tolerate it, when the criteria in section 1.1 are met.

1.3 If more than 1 treatment is suitable, start treatment with the least expensive drug (taking into account administration costs, dose needed and product price per dose). This may vary because of differences in how the drugs are used and treatment schedules.

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. If this initial response is not maintained, stop treatment.

1.5 Take into account any physical, psychological, sensory or learning disabilities, or communication difficulties that could affect the responses to the DAS28 and make any appropriate adjustments.

1.6 These recommendations are not intended to affect treatment with upadacitinib that was started in the NHS before this guidance was published. People having upadacitinib for treating moderate rheumatoid arthritis (TA744) 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 suggests that upadacitinib plus conventional DMARDs (including methotrexate) is more effective than placebo plus conventional DMARDs for treating moderate disease that has not responded well enough to conventional DMARDs. Evidence also suggests that upadacitinib alone is more effective than methotrexate for the same population.

Using methods accepted in NICE technology appraisal guidance 375 and NICE technology appraisal guidance 715, the cost-effectiveness estimate was within what NICE normally considers an acceptable use of NHS resources, although these methods may have to be reconsidered in future appraisals. So upadacitinib, alone or with methotrexate, is recommended for people with moderate rheumatoid arthritis whose disease has responded inadequately to intensive therapy with 2 or more conventional DMARDs.

Cost implications*,[2,3,4]

Cost:
The list price for upadacitinib is £805.56 per 28-day pack (company submission).

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.

Availability of PAS and details (if appropriate):
There is a 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.

Availability of homecare service (if appropriate):
Yes.

1. NICE Resource impact statement:

No significant resource impact is anticipated

NICE has recommended upadacitinib, with methotrexate for active rheumatoid arthritis in adults whose disease has responded inadequately to intensive therapy with 2 or more conventional disease-modifying antirheumatic drugs (DMARDs), only if:
•disease is moderate (a disease activity score [DAS28] of 3.2 to 5.1)
•the company provides upadacitinib 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 in England (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 will be similar.

2. NICE resource impact template

<u>Moderate RA:</u>
Having an advanced treatment option for moderate disease, that is more effective in achieving disease control, would be valuable. This is because RA can affect other organs such as the eyes, it causes mobility problems and has cardiovascular effects.

The NICE Evidence Review Group (ERG) concluded that it was appropriate to assume that 19% of people with moderate disease have disease progression to severe disease after 2 years.

Achieving disease control at this stage could reduce the need for costly operations and frequent attendances to NHS services.

The number of people with moderate RA eligible for biologic therapy in moderate RA, in England is 27,000 and in Surrey Heartlands CCG is 496.

Table 1: Number of people with moderate RA who are eligible for treatment in Surrey Heartlands ICS and ICP.

	Local assumption current practice	Local assumption current practice number of people				
	% of people	**Surrey Heartlands**	**East Surrey**	**Guilford & Waverly**	**North West Surrey**	**Surrey Downs**
Adult population		815,884	143,478	165,668	270,500	227,163
Prevalence of rheumatoid arthritis (RA)	0.82%	6,730	1,183	1,366	2,231	1,874
People who have moderate RA	45%	3,028.38	533	615	1,004	843
People who receive conventional disease modifying anti-rheumatic drugs (cDMARDs).	91%	2,756	485	560	914	767
Proportion of people who receive 2 or more cDMARDs	24%	661.40	116	134	219	184
People in whom intensive therapy with 2 or more cDMARDs has not controlled the disease well enough	**75%**	**496**	**87**	**101**	**164**	**138**

Table 2: Change in treatment costs (£'000) of moderate rheumatoid arthritis for upadacitinib for NHS Surrey Heartlands over 5 years.

Total costs: drugs and administration	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
People receiving adalimumab	-£19	-£38	-£57	-£57	-£57
People receiving etanercept	-£7	-£14	-£20	-£20	-£20
People receiving infliximab	£0	£0	£0	£0	£0
People receiving filgotinib	£0	£0	£0	£0	£0
People receiving upadacitinib	£31	£61	£92	£92	£92
Total costs	**9**	**9**	**14**	**14**	**14**

The cost is the impact of using upadacitinib in moderate RA: this is the fact that fewer people will have adalimumab and etanercept. It may mean that fewer people then enter the severe RA pathway if they are maintained at moderate disease.

This additional patient cohort will impact on capacity for secondary care clinical teams, homecare teams in trusts, homecare providers, workload and demand in biologics clinics.

Funding of this NICE TA is mandatory.

**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.

Alternative treatments and cost per patient per year

Other NICE recommended products:

There are now three NICE TA which support the use of bDMARDs in moderate use:

Name	NICE TA	Date published
Filgotinib for treating moderate to severe rheumatoid arthritis	TA676	24 February 2021
Adalimumab, etanercept, infliximab and abatacept for treating moderate rheumatoid arthritis after conventional DMARDs have failed	TA715	14 July 2021
Upadacitinib for treating moderate rheumatoid arthritis	TA744	10 November 2021

There are biosimilar versions of adalimumab, etanercept and infliximab.

Impact to patients

- An additional treatment option would be valued by patients.
- An oral treatment would be welcomed by some patients particularly those who are needle phobic or have significant hand disability.
- Upadacitinib 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 upadacitinib 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 in managing moderate disease would be valued by clinicians.
- The additional patient cohort of those with moderate disease will impact on capacity for secondary care clinical teams, homecare teams in trusts, homecare providers, workload and demand in biologics clinics.

Impact to CCGs

- The technology is commissioned by clinical commissioning groups (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.

Implementation

- NICE TA implementation must be within 90 days of publication.
- Blueteq forms to be developed.
- Trusts to initiate homecare.
- Pathway to be discussed at Rheumatology Network. Points to consider:
    - Adapt the treatment pathway to include treatment of moderate RA and inclusion of upadacitinib as a treatment choice.
    - Identify the least expensive drug (taking into account administration costs, dose needed and product price per dose).

Recommendation to PCN

National Tariff excluded high-cost drug (NTexHCD): Yes

Recommended traffic light status (see attached guidelines): Red

References:

1. Specification of Product Characteristics. RINVOQ 15 mg prolonged-release tablets. Available at: https://www.medicines.org.uk/emc/product/10972/smpc# Accessed <10.11.21>

2. NICE Technology appraisal: Upadacitinib for treating moderate rheumatoid arthritis. Technology appraisal guidance [TA744] Published: 10 November 2021. Available at: https://www.nice.org.uk/guidance/TA744 Accessed <10.11.21>

3. Rheumatoid Arthritis NHS. Available at: https://www.nhs.uk/conditions/rheumatoid-arthritis/ Accessed <2.3.21>

4. NICE Tools and resources. Resource impact statement and resource template: Upadacitinib for treating moderate rheumatoid arthritis. Technology appraisal guidance [TA744] Published: 10 November 2021Available at: https://www.nice.org.uk/guidance/ta744/resources Accessed <10.11.21>

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Declaration of interest	None	

Explanation of declaration of interest:

UPADACITINIB – 1st line treatment of Rheumatoid Arthritis TA744 (MODERATE DISEASE ACTIVITY)

Please indicate whether patient meets the following NICE criteria:	**Please tick**
1. Patient has active Rheumatoid Arthritis with a DAS score of 3.2 and 5.1 inclusive (Moderate disease activity) DAS score: Date of score::	○ Yes ○ No
3. Patient has responded inadequately to intensive therapy with 2 or more conventional DMARDs. Please provide details below	

Start date	Stop date	Treatment	Reason for stopping

4. FOR INFORMATION ONLY Initial funding will be approved for 6 months. The high cost drugs team will request an objective response to treatment at this point so that further funding can be considered. Funding will only be re-approved if there is a moderate response at 6 months i.e. improvement in DAS28 score of more than 0.6 in the absence of severe drug related toxicity. After initial response DAS28 should be monitored at least every 6 months and treatment withdrawn if improvement is not maintained.	

Continuation - UPADACITINIB for Rheumatoid Arthritis (MODERATE DISEASE ACTIVITY -NICE TA 744

Please indicate whether patient meets the following NICE criteria:	**Please tick**
1. I herewith provide you with the requested information: Current DAS28 score (no more than 3 months old) | Date DAS28 taken |	
2. Is there an improvement in current DAS28 score by >0.6 (moderate disease at initiation - EULAR response) compared to DAS score when 1st line treatment was initiated?	○ Yes ○ No
3. Patient has not experienced malignancy, severe drug related toxicity, pregnancy, severe inter current infection? (yes= not experiences)	○ Yes ○ No
4. COMMISSIONER USE ONLY: **Funding will be approved at 6 monthly intervals if response to treatment is maintained.**	