Briefing Paper for Surrey Heartlands Integrated Care System

Area Prescribing Committee on NICE Technology Appraisals:

Local implementation

NICE TA Guidance	Upadacatinib for treating severe rheumatoid arthritis Technology appraisal guidance 665		
Available at	https://www.nice.org.uk/guidance/ta665		
Date of issue	09th December 2020	**Implementation deadline**	09th March 2021

Medicine details[1]	
Name, brand name and manufacturer	Upadacatinib (Rinvoq®) 15mg Prolonged Release tablets AbbVie
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. **Medicines Management comments:** **NICE recommends upadacatinib in severe disease but the license is for use in moderate to severe disease – point to note**
Formulation	Rinvoq®15mg Prolonged Release tablets
Usual dosage	Treatment should be initiated and supervised by specialist physicians experienced in the diagnosis and treatment of RA. Posology www.medicines.org.uk 'The recommended dose of upadacitinib is 15 mg once daily. *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[2]	The symptoms of rheumatoid arthritis often develop gradually over several weeks, but some cases can progress quickly over a number of days. The symptoms vary from person to person. They can come and go, and may change over time. The patient may occasionally experience flares when the condition deteriorates and the symptoms become more severe.

	Rheumatoid arthritis mainly affects the joints. It can cause problems in any joint in the body, although the small joints in the hands and feet are often the first to be affected. Rheumatoid arthritis typically affects the joints symmetrically (both sides of the body at the same time and to the same extent), but this isn't always the case. The main symptoms affecting the joints are: **Pain:** Usually throbbing and aching. It is often worse in the mornings and after a period of inactivity. **Stiffness:** Often more severe in the morning and lasting longer than 30 minutes or after a period of inactivity. **Swelling, warmth and redness:** The lining of joints affected by rheumatoid arthritis become inflamed, which can cause the joints to swell, and become hot and tender to touch. In some people, firm swellings called rheumatoid nodules can also develop under the skin around affected joints. **Additional symptoms:** As well as problems affecting the joints, some people with rheumatoid arthritis experience a range of more general symptoms, such as: • tiredness and a lack of energy • a high temperature (fever) • sweating • a poor appetite • weight loss The inflammation associated with rheumatoid arthritis can also sometimes cause problems affecting other areas of the body, such as: • dry eyes – if the eyes are affected • chest pain – if the heart or lungs are affected
Potential patient numbers per 100,000	One study in the UK found the population minimum prevalence of RA to be 1.16% in women and 0.44% in men. The incidence of the condition is low, with around 1.5 men and 3.6 women developing RA per 10,000 people per year.

SUMMARY

Guidance[3]

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 a combination of conventional disease-modifying antirheumatic drugs (DMARDs), only if:

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

1.2 Upadacitinib, with methotrexate, is recommended as an option for treating active

rheumatoid arthritis in adults whose disease has responded inadequately to or who cannot have other DMARDs, including at least 1 biological DMARD, only if:

- disease is severe (a DAS28 of more than 5.1) and
- they cannot have rituximab and
- the company provides upadacitinib according to the commercial arrangement.

1.3 Upadacitinib, with methotrexate, is recommended as an option for treating active rheumatoid arthritis in adults whose disease has responded inadequately to rituximab and at least 1 biological DMARD, only if:

- disease is severe (a DAS28 of more than 5.1) and
- the company provides upadacitinib according to the commercial arrangement.

1.4 Upadacitinib can be used as monotherapy for people who cannot take methotrexate because it is contraindicated or because of intolerance, when the criteria in sections 1.1, 1.2 or 1.3 are met.

1.5 Continue treatment only if there is a moderate response measured using European League Against Rheumatism (EULAR) criteria at 6 months after starting therapy. After an initial response within 6 months, stop treatment if at least a moderate EULAR response is not maintained.

1.6 When using the DAS28, healthcare professionals should take into account any physical, psychological, sensory or learning disabilities, or communication difficulties that could affect the responses to the DAS28 and make any adjustments they consider appropriate.

1.7 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

Clinical trials show that upadacitinib with methotrexate or conventional DMARDs is more effective than methotrexate or conventional DMARDs for treating moderate to severe active rheumatoid arthritis that has not responded adequately to conventional DMARDs. The trials also show that for moderate to severe active rheumatoid arthritis that has not responded adequately to conventional DMARDs, upadacitinib with methotrexate is more effective than adalimumab with methotrexate or placebo with methotrexate.

Because there are no trials comparing upadacitinib with the full range of biological DMARDs, the company did an indirect comparison. This shows that upadacitinib with conventional DMARDs (including methotrexate) or on its own works as well as the biological DMARDs that NICE has already recommended.

Based on the health-related benefits and costs compared with conventional and biological DMARDs, upadacitinib alone, or with methotrexate, is recommended only for severe active rheumatoid arthritis, in line with recommendations in NICE's technology appraisal guidance on:

- sarilumab for moderate to severe rheumatoid arthritis
- tofacitinib for moderate to severe rheumatoid arthritis
- baricitinib for moderate to severe rheumatoid arthritis

- certolizumab pegol for treating rheumatoid arthritis after inadequate response to a TNF-alpha inhibitor
- adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab and abatacept for rheumatoid arthritis not previously treated with DMARDs or after conventional DMARDs only have failed
- tocilizumab for the treatment of rheumatoid arthritis
- golimumab for the treatment of rheumatoid arthritis after the failure of previous disease-modifying anti-rheumatic drugs
- adalimumab, etanercept, infliximab, rituximab and abatacept for the treatment of rheumatoid arthritis after the failure of a TNF inhibitor.

Cost implications

Cost:
The list price of upadacatinib is £805.56 per 28 day tablet pack.

Annual or monthly cost per patient: £10,105/year

Availability of PAS and details (if appropriate): Yes – Commercial in confidence

Availability of homecare service (if appropriate): Yes

NICE Resource impact statement:
"NICE has recommended upadacitinib alone or in combination with methotrexate, as an option for treating active rheumatoid arthritis in adults in accordance with the criteria specified in the guidance. Please see the guidance for further details.

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 £9,000 per 100,000 population).

This is because the technology is a further treatment option and is available at a similar price to the current treatment options.

Upadacitinib has a discount that is commercial in confidence."

ICP	Cost impact/ICP
Surrey Downs	£8,636
East Surrey	£5,454
Guildford & Waverley	£6,298
North West Surrey	£10,283

**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

Upadacatinib is a similarly priced alternative to other currently commissioned treatments options.

Other NICE recommended products:
- Adalimumab

- Biosimilar infliximab (Flixabi),
- Biosimilar etanercept (Benepali), Biosimilar etanercept (Enbrel)
- Certolizumab
- Golimumab
- Abatacept
- Rituximab
- Tocilizumab
- Sarilumab
- Baricitinib
- Tofacitinib

Impact to patients

- This would be an alternative oral option for patients within the current pathway

Impact to primary care prescribers

- None, other than to accept prescribing of this drug is occurring outside of practice (should be recorded as a hospital prescribed drug in patient's GP record) and recognise possible side effects. This is, in effect, no different to any other drug on the current pathway.

Impact to secondary care

- To set up appropriate supply routes to patients
- Appropriate clinical review processes
- Use of Blueteq system to register funding application
- Homecare is available and will be managed by the trust
    - Alcura
    - Lloyds Pharmacy Clinical Homecare
    - Healthcare@Home
    - Healthnet
- As upadacatinib is available via homecare patients will only require appointments for review and/or monitoring

Impact to CCGs

- Additional option to current treatment pathway
- NICE state that this drug does not add further cost impact on resources
- Blueteq form to be published

Implementation

- To amend current treatment pathway
- Develop a Blueteq form
- Communicate decision to Rheumatology teams and provider formulary teams
- Publish decision on PAD

Recommendation to PCN

PbRe: Y

Recommended traffic light status (see attached guidelines):
RED

Additional comments:

References:

1. Overview | Upadacitinib for treating severe rheumatoid arthritis | Guidance | NICE

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Declaration of Interest: None

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Reviewed by:

Declaration of Interest:

Date: