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) briefing paper for local implementation

NICE TA Guidance name and number	Risankizumab for treating moderately to severely active ulcerative colitis Technology appraisal guidance 998		
Available at	https://www.nice.org.uk/guidance/ta998		
Date of issue	22 August 2024	**Implementation deadline**	30 days 27 September 2024

Medicine details[1]	
Name and brand name	Risankizumab (Skyrizi®)
Manufacturer	AbbVie
Mode of action	Risankizumab is a humanised immunoglobulin G1 (IgG1) monoclonal antibody that selectively binds with high affinity to the p19 subunit of human interleukin 23 (IL-23) cytokine without binding to IL-12 and inhibits its interaction with the IL-23 receptor complex.
Licenced indication	Skyrizi is indicated for the treatment of adult patients with moderately to severely active ulcerative colitis who have had an inadequate response to, lost response to, or were intolerant to conventional therapy or a biologic therapy.
Formulation	Skyrizi 180 mg solution for injection in cartridge Skyrizi 360 mg solution for injection in cartridge Skyrizi 600 mg concentrate for solution for infusion. Please note: the 150mg dosage relates to use in plaque psoriasis and psoriatic arthritis.
Dosage	The recommended induction dose is 1 200 mg administered by intravenous (IV) infusion at Week 0, Week 4, and Week 8. Starting at Week 12 and every 8 weeks thereafter, the recommended maintenance dose is based on individual patient presentation: • A dose of 180 mg administered by subcutaneous injection is recommended for patients with adequate improvement in disease activity after induction • A dose of 360 mg administered by subcutaneous injection is recommended for patients with inadequate improvement in disease activity after induction Consideration should be given to discontinuing treatment in patients who have shown no evidence of therapeutic benefit by Week 24.

Comparison of NICE TA with Summary of Product Characteristics (SmPC)	• The NICE TA names TNF-alpha inhibitors as the biologic therapy which should be used before risankizumab. In the UK, the majority of patients with moderately to severely active UC receive TNF-α inhibitors as first-line advanced therapy, due to the wealth of experience and familiarity with their use in UK clinical practice, as well as the availability and affordability of biosimilar products for both infliximab and adalimumab. • No dose escalations but a higher maintenance dose is available for inadequate improvement in disease activity after induction. • Response is measured by the Adapted Mayo score. This is the current dose considered by NICE as part of this NICE evaluation. Subsequent changes in the licence 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 Risankizumab is recommended as an option for treating moderately to severely active ulcerative colitis in adults when conventional or biological treatment cannot be tolerated, or the condition has not responded well enough or has lost response to treatment, only if:

- a tumour necrosis factor (TNF)-alpha inhibitor:
  - has not worked (that is the condition has not responded well enough or has lost response to treatment), or
  - cannot be tolerated or is not suitable, and
- the company provides it according to the commercial arrangement.

1.2 If people with the condition and their clinicians consider risankizumab to be 1 of a range of suitable treatments (including ustekinumab), after discussing the advantages and disadvantages of all the options, use the least expensive. Take into account the administration costs, dosage, price per dose and commercial arrangements.

1.3 These recommendations are not intended to affect treatment with risankizumab that was started in the NHS before this guidance was published. People having treatment outside this recommendation 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.

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 fast tracked to 30 days.
- The implementation deadline is 27th September 2024.

Clinical effectiveness

TNF-alpha inhibitors are the most used biological treatments for moderately to severely active ulcerative colitis. When TNF-alpha inhibitors have not worked, or are not tolerated, one of the treatment options is ustekinumab. Risankizumab works in a similar way to ustekinumab and would be offered to the same population.

Clinical trial evidence shows that risankizumab is more effective than placebo for treating moderately to severely active ulcerative colitis. Risankizumab has not been directly compared with ustekinumab in a clinical trial in this population. But an indirect comparison suggests that it is similarly effective.

A cost comparison suggests risankizumab has similar costs to ustekinumab. Using NICE's cost-comparison methods, risankizumab only needs to cost less or have similar costs to 1 relevant comparator to be recommended as a treatment option. So risankizumab is recommended.

Please note:

- Whilst mirikizumab has a similar mechanism of action to risankizumab, it is not established UK clinical practice and therefore is not considered a relevant comparator.

- Risankizumab may have had similar costs to ustekinumab but ustekinumab is now available as a biosimilar.

Patient safety

- The product should be used within its product licence.
- ▼ This is a Black Triangle drug – this medicinal product is subject to reporting of all suspected adverse drug reactions to the MHRA. This will allow timely identification of new safety information.

Patient factors

- An additional treatment option would be valued by patients. However, two IL inhibitor are already available – ustekinumab and mirikizumab, so it does not constitute a novel mode of action or a new line of treatment.
- The treatment is self-administered by the patient, which avoids the need for repeated visits to the hospital/GP practice.
- 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.
- Patients must adhere to the storage requirements
- Patients would need to be reviewed on a regular basis by the prescribing clinician to ensure concordance, monitor for adverse effects and efficacy.

Environmental impact

- Additional packaging will be generated and will be an environmental impact with regards to waste management.
- Homecare deliveries – patients' home (additional carbon – increase air pollution)
- Discharge into wastewater (post metabolism unknown effect)
- Sharps waste requires safe collection and disposal

Equality & diversity

No specific comments in the NICE TA.

Note 1: 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 current pathway consists of the following options for patients with ulcerative colitis.

The most appropriate comparator for risankizumab is ustekinumab.

Please note: risankizumab already has a NICE TA for previously treated moderately to severe Crohn's disease – TA888 published in May 2023.

Mode of action		Drug	Ulcerative colitis
TNF alpha inhibitor		Adalimumab biosimilar	✓
		Infliximab biosimilar #	✓
		Golimumab	✓
Integrin α4β7 receptor antagonist		Vedolizumab #	✓
Interleukin (IL) inhibitor	IL 12/23	Ustekinumab	✓
	IL 23	Risankizumab	✓
		Mirikizumab	✓
Janus Kinase (JAK) inhibitor (oral)	JAK 1 and JAK 3	Tofacitinib	✓
	JAK 1	Filgotinib	✓
	JAK 1	Upadacitinib	✓
Sphingosine 1-phosphate (S1P) receptor modulator	Subtype 1 and 5	Ozanimod	✓
	Subtype 1,4 and 5	Etrasimod	✓

SC and IV presentations available (IV should be used at clinician's discretion)

Table 1: Options available or the treatment of ulcerative colitis.

Stakeholder views

The paper was sent out for consultation and comments are listed on the front sheet.

Cost-effectiveness

A resource template is not available for this TA.

The drug cost per Place according to NICE resources does not exceed £100,000.

Section 1: cost of the technology

The list price of risankizumab is £3,326.09 per:

- 600 mg vial of concentrate for solution for intravenous infusion (excluding VAT; BNF online accessed July 2024)
- 360 mg doses of solution for injection for subcutaneous administration (excluding VAT; BNF online accessed July 2024)
- 180 mg doses of solution for injection for subcutaneous administration (excluding VAT; provisional).

a. Annual cost per patient (or complete course if shorter)
Costs in secondary care:

Time	Dose	Cost per unit	Cost
Year 1: Induction	1 200 mg administered by intravenous (IV) infusion at Week 0, Week 4, and Week 8	£3,326.09 per 600mg vial.	£6,652.18
Year 2: Maintenance	Starting at Week 12 and every 8 weeks thereafter either 180 mg or 360mg	£3,326.09 per 180mg or 360mg vial.	£19,956.54
Total year 1			**£26,608.72**
Subsequent years	Every 8 weeks thereafter either 180 mg or 360mg	£3,326.09 per 180mg or 360mg vial.	**£23,282.63**

Table 2: Annual costs – first year with induction and subsequent years (full cost, no discounts).

b. Availability of CAP/PAS price:
The company has a commercial arrangement. This makes risankizumab available to the NHS with a discount. The size of the discount is commercial in confidence.

c. Price relative to comparable medicines:
Ustekinumab represents established UK clinical practice in the proposed target population. Additionally, feedback from UK clinical experts is that risankizumab would be considered as an alternative treatment to ustekinumab in the proposed target population.

Both treatments have a related mechanism of action of targeting interleukins (IL) and both treatments inhibit IL-23. They also have a similar route of administration; intravenously (IV) in the induction phase and subcutaneously (SC) in the maintenance phase.

Whilst mirikizumab has a similar mechanism of action to risankizumab, it is not established UK clinical practice and therefore is not considered a relevant comparator.

Risankizumab may have had similar costs to ustekinumab but ustekinumab is now available as a biosimilar. There are currently 3 biosimilars available, and more may be available shortly.

Given the cost difference between the originator for ustekinumab, Stelara®, and the biosimilars, this would make ustekinumab biosimilar more cost-effective than risankizumab.

Section 2: NICE resource impact statement and template

a. NICE resource impact statement
We expect the resource impact of implementing the recommendations in England will be less than £5 million per year (or approximately £8,800 per 100,000 population, based on a population for England of 57.1 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.

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.

Implementation

Because risankizumab has been recommended through the cost-comparison process, NHS England and integrated care boards have agreed to provide funding to implement this guidance 30 days after 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 using the Blueteq® system.
- Homecare arrangements will be managed by the trust.

c. ICS
- This technology is commissioned by integrated care systems.
- Pathway to be discussed virtually at the next Gastroenterology Network to consider:
    - The new pathway
    - Use of ustekinumab biosimilar

d. PAD and Joint Formulary
- Remove pathway from all treatments for this condition from PAD and replace with revised pathway.
- New PAD profile will be required

Proposed tick box forms
Blueteq® forms have been developed.

References:

1 Summary of Product Characteristics. emc. Available at: Search Results - (emc) (medicines.org.uk) Accessed <2.9.24>

2 NICE Technology Appraisal Guidance: Risankizumab for treating moderately to severely active ulcerative colitis. Available at: https://www.nice.org.uk/guidance/ta998 Accessed <2.9.24>

3 NICE Resource Impact Report: Risankizumab for treating moderately to severely active ulcerative colitis. Available at: https://www.nice.org.uk/guidance/ta998 Accessed <2.9.24>

Declaration of interest:

	Name	Role	Date	Declaration of interests (please give details below)
Prepared by	Tejinder Bahra	Lead Pharmacist, MRU	3.9.24	None
Supported by				
Reviewed by				

Explanation of declaration of interest:
None.

Version control sheet:

Version	Date	Author	Status	Comment
1	9.9.24	Tejinder Bahra	Draft	Out for consultation
2	25.9.24	Tejinder Bahra	Final	Out for clinical comment

Blueteq® form: