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	Risankizumab for previously treated moderately to severely active Crohn's disease (TA888)		
Available at	Overview | Risankizumab for previously treated moderately to severely active Crohn's disease | Guidance | NICE		
Date of issue	17 May 2023	**Implementation deadline**	24th August 2023

Medicine details[1]	
Name and brand name	**Risankizumab (Skyrizi)**
Manufacturer	AbbVie Ltd
Mode of action	www.medicines.org.uk 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. IL-23 is a cytokine that is involved in inflammatory and immune responses. By blocking IL-23 from binding to its receptor, risankizumab inhibits IL-23-dependent cell signalling and release of proinflammatory cytokine Risankizumab is a humanised immunoglobulin G1 (IgG1) monoclonal antibody selective to the interleukin (IL)-23 protein produced in Chinese Hamster Ovary cells using recombinant DNA technology.
Licensed indication	www.nice.org.uk Therapeutic indications (link in NICE guidelines provided) Risankizumab is indicated for the treatment of patients 16 years and older with moderately to severely active Crohn's disease who have had an inadequate response to, lost response to, or were intolerant to conventional therapy or a biologic therapy, or if such therapies are not advisable.
Formulation	PHARMACEUTICAL FORM (link in NICE guidelines provided) Concentrate for solution for infusion (infusion) The solution is colourless to slightly yellow and clear to slightly opalescent.
Dosage	Posology (link in NICE guidelines provided) The recommended dose is 600 mg administered by intravenous infusion at Week 0, Week 4, and Week 8, followed by 360 mg administered by subcutaneous injection at Week 12, and every 8 weeks thereafter. For the posology of the subcutaneous regimen, see section 4.2 of the Skyrizi 360 mg solution for injection in cartridge.

Comparison of NICE TA with Summary of Product Characteristics (SmPC)[2]	No mention of intolerance to conventional therapy in the NICE The dose is as above. 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

1.1Risankizumab is recommended as an option for treating moderately to severely active Crohn's disease in people 16 years and over, only if:

- the disease has not responded well enough or lost response to a previous biological treatment, or
- a previous biological treatment was not tolerated, or
- tumour necrosis factor (TNF)-alpha inhibitors are not suitable.

Risankizumab is only recommended if 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, after discussing the advantages and disadvantages of all the options, use the least expensive. Take account of 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 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. For young people, this decision should be made jointly by the clinician, the young person, and their parents or carers.

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 the date that the on-body device receives CE marking (if this is later). The CE mark was awarded 24th August 2023.

Clinical effectiveness

Standard treatments for moderately to severely active Crohn's disease when conventional treatments stop working are biological treatments (such as TNF-alpha inhibitors [adalimumab and infliximab], ustekinumab and vedolizumab). Risankizumab is another biological treatment.

Clinical trial evidence suggests that risankizumab reduces symptoms and increases the likelihood of disease remission compared with placebo. Results from indirect comparisons of risankizumab with other biological treatments are uncertain. But there is enough evidence to suggest it is as effective as vedolizumab, a treatment recommended by NICE for use after a TNF-alpha inhibitor or when TNF-alpha inhibitors are not suitable.

A cost comparison of risankizumab with vedolizumab suggests that risankizumab has similar or lower costs than vedolizumab. NICE considers risankizumab an acceptable use of NHS resources. This is when it is used after a biological treatment has not worked well enough, has stopped working, or was not tolerated, or TNF-alpha inhibitors are unsuitable. So, risankizumab is recommended.

Patient safety

- Concomitant immunosuppressive therapy the safety and efficacy of risankizumab in combination with immunosuppressants, including biologics, have not been evaluated. The product should be used within its product license.
- Paediatric population the safety and efficacy of Skyrizi for the treatment of Crohn's disease in children and adolescents younger than 16 years of age have not yet been established. No data are available.
- BLACK TRIANGLE DRUG This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.
- 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.

Patient factors

- An additional treatment option would be valued by patients because it's a new mode of action. Therefore, a new line of treatment added to the Crohn's pathway.
- 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.
- Patient educational and training will be given (training materials)
- First 3 doses are given by IV infusion in Secondary Care

Environmental impact

- Additional packaging will be generated and will be an environmental impact with regards to waste management.
- Patients will be travelling into hospital for their 1st 3 Infusions (additional carbon and footfall)
- Homecare deliveries – patients' home (additional carbon – increase air pollution)
- Discharge into wastewater (post metabolism unknown effect)
- Sharps waste

Equality & diversity

No equality or social value judgement issues were identified by the NICE TA committee

- Paediatric population the safety and efficacy of Skyrizi for the treatment of Crohn's disease in children and adolescents younger than 16 years of age have not yet been established. No data are available.
- Patient with learning or physical disabilities may not be able to self-inject
- Religion/Beliefs/Vegan – drug is of biologic origin. It is also worth pointing out that no **medicines** are 100% vegan friendly as they will have been **tested** on **animals** at some point.

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

Risankizumab is a of a novel class of drugs and therefore will constitute a new line of treatment in the pathway which will be updated accordingly

Stakeholder views

Specialist clinicians who sit in the Gastro network and the wider APC audience have been consulted on process. See comments below

Cost-effectiveness

www.nice.org.uk

NICE considers that risankizumab was:

- not cost saving compared with all comparators
- not cost saving compared with all adalimumab and infliximab comparators
- cost saving when compared with ustekinumab and vedolizumab in the biological treatment failure population.

Cost of the technology

Annual cost per patient
Costs in secondary care:
The list price of Risankizumab 360mg solution for injection in cartridge is ££3,326.09 (Hospital only) minus VAT if supplied via homecare.
The list price of Risankizumab 600mg concentrate for solution for infusion is £ £3,326.09 (Hospital only) + infusion costs
Annual treatment costs - £29,934.81 per year (Yr1), and £23,282.63 in subsequent years (using list price above) +/- VAT

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. It is the company's responsibility to let relevant NHS organisations know details of the discount.

Price relative to comparable medicines:
This is the first IL23 protein available to treat Crohn's disease and is a new mode of action for this pathway. There are now 4 modes of action for this pathway and Risankizumab constitutes a new treatment line for this pathway.

Treatment requests: 2293 – note that 15 of these patients have since deceased.
Information from the Blueteq Database (since 2008) The treatment with the most initiations (at any line) within each mode of action has been highlighted below

Mode of action	Drug name	Patient nos (Blueteq)	4th line requests
TNF-Alpha inhibitors	Adalimumab*	859	0
	Infliximab*	924	2
	Golimumab	3	0
A4B7 integrin receptor	Vedolizumab	208	8
Interleukin (IL)12/23 inhibitor	Ustekinumab	295	4

*now available as a biosimilar

To date Surrey Heartlands ICB patients have received 1st, 2nd 3rd & 4th line treatments. To date there are no patients (on Blueteq) being treated for 5th or subsequent lines.
Sequential use of biosimilars is permitted currently in the Surrey Heartlands geography. This was permitted due to the limited options available to IBD patients at the time.
For those patients being treated at 4th line (14 patients) treatments have been proposed and agreed by the gastroenterology MDT.

NICE resource impact statement - www.nice.org.uk
Resource impact statement
NICE has recommended risankizumab as an option for treating moderately to severely

active Crohn's disease in people 16 years and over, only if:

- the disease has not responded well enough or lost response to a previous biological treatment, or
- a previous biological treatment was not tolerated, or
- tumour necrosis factor (TNF)-alpha inhibitors are not suitable.
- Risankizumab is only recommended if the company provides it according to the commercial arrangement (see section 2 of the guidance).

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 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. For young people, this decision should be made jointly by the clinician, the young person, and their parents or carers.

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 56.6 million people).

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

Risankizumab and the other treatment options have discounts that are commercial in confidence. For enquiries about the patient access schemes contact the manufacturers.

This technology is commissioned by integrated care boards for people aged 18 and over and by NHS England for people aged 16 to 17. Providers are NHS hospital trusts.

The payment mechanism for the technology appraisal is determined by the responsible commissioner and depends on the technology being classified as high cost.

The first 3 doses of risankizumab are administered by intravenous (IV) infusion in a secondary care setting, thereafter it is administered by subcutaneous injection by people themselves in their home.

Where risankizumab displaces the use of IV vedolizumab there will be capacity savings in the maintenance phase.

Where risankizumab displaces the use of ustekinumab there will be capacity increase in the induction period. Ustekinumab is administered for one dose by IV infusion in a secondary care setting and thereafter by subcutaneous injection by people themselves in their home.

At £8,800 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	**£17,031**	**£20,485**	**£27,869**	**£34,185**	**£99,570**

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

The drug costs for Risankizumab treatment for Crohn’s disease is not expected to exceed the £100,000 per Place threshold.

Commentary:

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:

1. RED – APC decision making criteria (Colour classification) Red Point 8 - Medicines for which the funding is levied outside of hospital tariff

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

Implementation

Section 7 of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires integrated care boards, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this evaluation within 3 months of its date of publication or the date that the on-body device receives CE marking (if this is later). Because risankizumab has been available through the early access to medicines scheme, NHS England and integrated care boards have agreed to provide funding to implement this guidance 30 days after publication or the date that the on-body device receives CE marking (if this is later) – CE mark was awarded 24th August 2023.

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.
- Homecare arrangements will be managed by the trust.

c. ICS

- This technology is commissioned by integrated care systems.
- Blueteq forms have been developed for use
- Pathway to be discussed at the next Gastroenterology network, to consider:
    - Place in pathway

d. PAD and Joint Formulary

- Remove current IBD pathway from all treatments for this condition from PAD and replace with revised pathway
- New PAD profile for Risankizumab for Crohn's disease will be required

Proposed tick box forms

Blueteq® forms have been developed.

References:

1. Summary of Product Characteristics. emc. Microsoft Word - 447634659800168917 7_spc-doc.doc (windows.net) 05/06/2023
2. NICE Technology Appraisal Guidance: . Available at: Overview | Risankizumab for previously treated moderately to severely active Crohn's disease | Guidance | NICE 05/06/2023
3. NICE Resource Impact Report: . Available at: Accessed <insert date here>
4. NICE Resource Impact Template: . Available at: Accessed <insert date here>

Declaration of interest:

	Name	Role	Date	Declaration of interests (please give details below)
Prepared by	Lorraine Kelly	Senior Pharmacy Technician, MRU	May23	None
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Reviewed by	Tejinder Bahra	Lead Pharmacist, MRU	Sep-23	None

Explanation of declaration of interest:
None.

Version control sheet:

Version	Date	Author	Status	Comment
1			Draft	Out for consultation
			Final	Out for clinical comment

Blueteq® form: