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	Mirikizumab for treating moderately to severely active ulcerative colitis Technology appraisal guidance 925		
Available at	https://www.nice.org.uk/guidance/ta925		
Date of issue	25 October 2023	**Implementation deadline**	30 days – 25 November 2023

Medicine details[1]	
Name and brand name	Mirikizumab Omvoh®
Manufacturer	Eli Lilly
Mode of action	Mirikizumab is a humanised IgG4 monoclonal, anti-interleukin-23 (anti-IL-23) antibody.
Licenced indication	Mirikizumab (Omvoh, Eli Lilly) is indicated for: 'the treatment of adult patients with moderately to severely active ulcerative colitis who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a biologic treatment.'
Formulation	1. Each vial contains 300 mg mirikizumab in 15 mL (20 mg/mL) solution. 2. Each pre-filled syringe or pen contains 100 mg mirikizumab in 1 mL solution.
Dosage	The recommended mirikizumab dose regimen has 2 parts. <u>Induction dose:</u> The induction dose is 300 mg by *intravenous infusion* for at least 30 minutes at weeks 0, 4 and 8. <u>Maintenance dose:</u> The maintenance dose is 200 mg (i.e., two pre-filled syringes or two pre-filled pens) by *subcutaneous injection* every 4 weeks after completion of induction dosing. <u>Transition to maintenance dosing</u> Patients should be evaluated after the 12-week induction dosing and if there is adequate therapeutic response, transition to maintenance dosing. <u>Extended Induction Therapy</u> For patients who do not achieve adequate therapeutic benefit at week 12 of induction dosing, mirikizumab 300 mg by intravenous infusion may be continued at weeks 12, 16 and 20 (extended

	induction therapy). If therapeutic benefit is [then] achieved with the additional intravenous therapy, patients may initiate mirikizumab subcutaneous maintenance dosing (200 mg) every 4 weeks, starting at week 24. Mirikizumab should be discontinued in patients who do not show evidence of therapeutic benefit to extended induction therapy by week 24. <u>Loss of Therapeutic Response</u> Patients with loss of therapeutic response during maintenance treatment may receive 300 mg mirikizumab by intravenous infusion every 4 weeks, for a *total of 3 doses (re-induction).* If clinical benefit is achieved from this additional intravenous therapy, patients may resume mirikizumab subcutaneous dosing every 4 weeks. The efficacy and safety of repeated re-induction therapy have not been evaluated. In case of a missed dose, instruct patients to inject as soon as possible. Thereafter, resume dosing every 4 weeks.
Comparison of NICE TA with Summary of Product Characteristics (SmPC)[2]	<u>Notes for dose optimisation:</u> 1. Extended induction therapy - after the induction dose at week 12, if patients do not achieve adequate therapeutic benefit, the 300mg induction dose (by intravenous infusion) may be continued at weeks 12,16 and 20. 2. Loss of therapeutic response - if during maintenance treatment there is a loss of therapeutic effect, then patients may receive 300mg mirikizumab by intravenous infusion every 4 weeks, for a total of 3 doses (re-induction). The efficacy and safety of repeated re-induction therapy have not been evaluated. These dose optimisation regimens are included in the NICE TA. 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 Mirikizumab 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 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
• a TNF-alpha inhibitor 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 mirikizumab to be 1 of a range of suitable treatments (including vedolizumab and 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 mirikizumab 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.

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 30 days.
- The implementation deadline is 25th November 2023.

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, usually people are offered vedolizumab or ustekinumab. Mirikizumab is another biological treatment that would be offered to the same population as these 2 treatments.

Clinical trial evidence shows that mirikizumab is more effective than placebo for treating moderately to severely active ulcerative colitis. But there are no clinical trials directly comparing mirikizumab with vedolizumab or ustekinumab. An indirect comparison Mirikizumab for treating moderately to severely active ulcerative colitis (TA925) suggests that all 3 treatments are similarly effective.

Patient safety

- The product should be used within its product licence.
- Mirikizumab is a Black Triangle drug – all suspected adverse reactions should be reported to the MHRA. This is normally in place for 5 years (but may be extended if needed.
- Although the patient is able to use a sub-cut preparation dose during the maintenance period, mirikizumab requires three intravenous induction doses in hospital.

Patient factors

- An additional treatment option would be valued by patients. However, another IL inhibitor, ustekinumab is already available. Ustekinumab only requires one intravenous infusion in hospital before patients start the sub-cutaneous injections at home (mirikizumab requires three intravenous induction doses in hospital).
- Mirikizumab in the maintenance phase is given as two subcutaneous injections self-administered by the patient on a monthly basis. The patient must be capable of self-administration or make carers able to do so.
- This medicine is available under a homecare service so will be delivered directly to the patient.
- Patients must adhere to the storage requirements.

Environmental impact

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

Equality & diversity

No equality or social value judgement issues were identified by the NICE TA committee, however ICB implications are as follows:

- Paediatric population – the NICE TA is only applicable to adults. See note 1 below.
- Patient with learning or physical disabilities may not be able to self-inject.
- Religion/beliefs/vegan – drug is of biologic origin.

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

There are two IL inhibitors now available in ulcerative colitis - mirikizumab is an IL-23 inhibitor and ustekinumab is an IL-12 and IL-23 inhibitor.

Ustekinumab is well established with a good evidence base of efficacy. Patent expiry is due in early to mid-2024 when biosimilars are expected to be available.

Ustekinumab only requires one intravenous infusion before patients start the sub-cutaneous injections at home where as mirikizumab requires three intravenous induction doses (as a minimum) in hospital.

The preferred IL-inhibitor is therefore ustekinumab.

Stakeholder views

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

Cost-effectiveness

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

There are no savings shown in the NICE resource template see below for limitations of the calculator.

Section 1: cost of the technology

a. Annual cost per patient (or complete course if shorter)

The list price is £2,056.56 (excluding VAT; emc med data browser accessed August 2023) per:

• 300 mg vial of concentrate for solution for infusion
• 2 pack of 100 mg per 1 ml solution for injection pre-filled syringes.

Costs may vary in different settings because of negotiated procurement discounts.

b. Availability of CAP/PAS price:
The company has a commercial arrangement. This makes mirikizumab 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:
The NICE TA states that a cost comparison suggests the costs of mirikizumab (IL-23 inhibitor) are similar or lower to those of vedolizumab (integrin α4β7 receptor antagonist) and ustekinumab (IL-12/23 inhibitor). These are possible choices after TNF-alpha inhibitors.

Section 2: NICE resource impact statement and template

Potential patient numbers per 100,000:
It is estimated that 33 patients per 100,000 patients would be eligible for treatment of which mirikizumab is an option i.e., with moderately to severely active ulcerative colitis. This would be 347 patients within the Surrey Heartlands geography.

a. NICE resource impact statement
NICE has recommended mirikizumab 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 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
• a TNF-alpha inhibitor cannot be tolerated or is not suitable and

• the company provides it according to the commercial arrangement.

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 mirikizumab is a further treatment option and the overall cost of treatment for this patient group will be similar.

The previously published template for this patient group has been updated and replaced to include mirikizumab and all other treatment options for moderately to severely active ulcerative colitis.

Organisations should complete both current and future uptake based on local practice in order to assess the financial impact.

The company has a commercial arrangement. This makes mirikizumab 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. The other treatment options have discounts that are commercial in confidence.

b. NICE resource impact template

Drug costs for Surrey Heartlands:
The drug costs do not exceed the £100,000 per Place threshold.

The template predicts that the impact of change on costs of future practice is £80,558 across all of the Surrey Heartlands geography in year 5 (this includes drug and administration costs).

Commentary:
There are severe limitations of the NICE resource impact template.

- All the options available in UC are included, with an assumption that mirikizumab will account for 5% of the number of people treated for UC in year 5 and the number of people on ustekinumab will fall.
- It does not account for the patent expiry of ustekinumab (due early-mid 2024, with biosimilars expected). This is currently one of the most expensive options, so the availability of biosimilars will reduce the costs.
- It assumes that the number of people treated with ozanimod will change from 7.5% to 7.15%. Currently there is no use of ozanimod and very little interest, as confirmed at the last GN meeting.
- It does not account for the increase in costs of mirikizumab for extended induction therapy and loss of therapeutic response (where patients may receive 300mg mirikizumab by intravenous infusion every 4 weeks, for a total of 3 doses).
- It does not account for the use of vedolizumab subcutaneous which reduces administration costs compared to using infusions.
- The weighted average drug cost is for the maintenance costs and does not include initiation.
- Biosimilar costs continue to fall and new biosimilars are coming to the market.

Please note: the NICE resource impact template is not specific for mirikizumab but covers all medicines available with a NICE TA. This includes:

Technology	TA	Indication
Infliximab, adalimumab and golimumab	TA329	Moderately to severely active UC after

		the failure of conventional therapy
Vedolizumab	TA342	Moderately to severely active UC
Tofacitinib	TA547	Moderately to severely active UC
Ustekinumab	TA633	Moderately to severely active UC
Filgotinib	TA792	Moderately to severely active UC
Ozanimod	TA828	Moderately to severely active UC
Upadacitinib	TA856	Moderately to severely active UC
Mirikizumab	TA925	Moderately to severely active UC

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: see NHS England » 2023-25 NHS Payment Scheme
Yes.

Recommended traffic light status and rationale:
RED – Specialist ONLY drugs - treatment initiated and continued by specialist clinicians.

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

Implementation

NICE TA implementation must be within 30 days of 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 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.
- Pathway to be discussed at the next Gastroenterology Network

d. PAD and Joint Formulary
  - Addition of mirikizumab to the IBD pathway
  - A new PAD profile is 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 <6.11.23>

2 NICE Technology Appraisal Guidance: Mirikizumab for treating moderately to severely active ulcerative colitis. Available at: Overview | Mirikizumab for treating moderately to severely active ulcerative colitis | Guidance | NICE Accessed <6.11.23>

3 NICE Resource Impact Report: Mirikizumab for treating moderately to severely active ulcerative colitis. Available at: Tools and resources | Mirikizumab for treating moderately to severely active ulcerative colitis | Guidance | NICE Accessed <6.11.23>

4 NICE Resource Impact Template: Mirikizumab for treating moderately to severely active ulcerative colitis. Available at: Tools and resources | Mirikizumab for treating moderately to severely active ulcerative colitis | Guidance | NICE Accessed <6.11.23>

Declaration of interest:

	Name	Role	Date	Declaration of interests (please give details below)
Prepared by	Tejinder Bahra	Lead Pharmacist MRU - Operational	6.11.23	None
Supported by				
Reviewed by				

Explanation of declaration of interest:
None.

Version control sheet:

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1	6.11.23	Tejinder Bahra	Draft	Out for consultation
			Final	Out for clinical comment