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	Ozanimod for treating moderately to severely active ulcerative colitis TA828		
Available at	https://www.nice.org.uk/guidance/TA828		
Date of issue	05 October 2022	**Implementation deadline**	05 January 2023
Medicine details[1]			
Name and brand name	Ozanimod (Zeposia)		
Manufacturer	Celgene (Bristol Myers Squibb)		
Mode of action	Ozanimod is a potent sphingosine 1-phosphate (S1P) receptor modulator, which binds with high affinity to sphingosine 1-phosphate receptors 1 and 5. Ozanimod has minimal or no activity on S1P2, S1P3, and S1P4. In vitro, ozanimod and its major active metabolites demonstrated similar activity and selectivity for S1P1 and S1P5. The mechanism by which ozanimod exerts therapeutic effects in MS and UC is unknown, but may involve the reduction of lymphocyte migration into the central nervous system (CNS) and intestine. The ozanimod-induced reduction of lymphocytes in the peripheral circulation has differential effects on leucocyte subpopulations, with greater decreases in cells involved in the adaptive immune response. Ozanimod has minimal impact on cells involved in innate immune response, which contribute to immunosurveillance.		
Licensed indication	Zeposia is indicated for the treatment of adult patients with moderately to severely active ulcerative colitis (UC) who have had an inadequate response, lost response, or were intolerant to either conventional therapy or a biologic agent.		
Formulation	Hard capsules		
Dosage	The recommended dose is 0.92 mg ozanimod once daily. The initial dose escalation regimen of ozanimod from Day 1 to Day 7 is required and shown below in Table 1. Following the 7-day dose escalation, the once daily dose is 0.92 mg, starting on Day 8. **Table 1: Dose escalation regimen** Days 1 – 4: 0.23 mg once daily Days 5 – 7: 0.46 mg once daily Days 8 and thereafter: 0.92 mg once daily		
Comparison of NICE TA with Summary of Product Characteristics (SmPC)2	• No differences noted between NICE and product licence at time of publication. Although the NICE TA does specifically mention that it may be used if infliximab is not suitable. • No narrower indication in NICE and no specific dose schedule is recommended by NICE other than as per SPC at time of		

	publication. Dose escalation is not included in current licence.

NICE TA recommendations[2]

Recommendations

1.1 Ozanimod is recommended as an option for treating moderately to severely active ulcerative colitis in adults, only if:

- conventional treatment cannot be tolerated or is not working well enough, and infliximab is not suitable, or
- biological treatment cannot be tolerated or is not working well enough, and
- the company provides it according to the commercial arrangement.

1.2 This recommendation is not intended to affect treatment with ozanimod 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 assigned an implementation deadline of 90 days.
- The implementation deadline is 05 January 2023.

Clinical effectiveness

- Standard treatments for moderately to severely active ulcerative colitis after conventional treatments are biological treatments (adalimumab, golimumab, infliximab, ustekinumab or vedolizumab) or the targeted synthetic immunomodulators (JAK inhibitors), tofacitinib and filgotinib.
- Clinical trial evidence shows that ozanimod is more effective than placebo for treating moderately to severely active ulcerative colitis. There is no direct evidence comparing ozanimod with standard treatments that are offered after conventional treatment, but indirect comparisons suggest that it is likely to be as effective as some of them.
- When conventional treatment is not tolerated or not working well enough, infliximab is more cost effective than ozanimod. But the most likely cost-effectiveness estimates for ozanimod compared with most other treatments are within the range that NICE normally considers an acceptable use of NHS resources. So, ozanimod is recommended, but only if conventional treatment cannot be tolerated or is not working well enough, and only if infliximab is not suitable. Ozanimod is also recommended if a biological treatment cannot be tolerated or is not working well enough.

Patient safety

- The product should be used within its product license. There are no additional safety concerns identified outside those already recognised and described in BNF / SPC.
- Ozanimod is licensed for this indication in the UK. It is to be taken by mouth only.
- As with all systemic immunosuppressants, prescribers should be aware of patient risk of reduced immune response to infection, and this should be considered when triaging patient exhibiting symptoms. GP practice records should be maintained accordingly (this should be reiterated in the PAD narrative).

Patient factors

- Ozanimod constitutes an alternative option for those patients who are unable to receive or tolerate biological agents and/or are unable to receive or tolerate JAK inhibitors.
- Ozanimod (as a new class of drug) adds a further therapeutic line to the current treatment pathway. Patients will now have 5 lines of treatment available within the IBD high-cost immune modulator pathway for ulcerative colitis.
- Patient education materials are provided.
- 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.

Environmental impact

- **Packaging waste** from ozanimod would be additional to usual municipal waste recycling or landfill. Although it should be noted that as an oral treatment, it is likely that less waste would be generated compared to a subcutaneous preparation.
- Discharge into the **wastewater** system (post-metabolism) from an individual patient is unlikely to have a significant impact short term, however the long-term impact to the water ecosystem is unknown.

Equality & diversity

- NICE considered that for some religious groups the impact of active disease and the effects of surgery may interfere with religious practices and cause distress, but ultimately did not consider this an equality issue that could be resolved by this appraisal. No other equality or social value judgement issues were identified.
- **Age** – Ozanimod is only licensed for adult patients – younger patients will not be able to access this treatment under this TA. 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. This includes drugs normally commissioned by CCGs/ICS in adults (e.g. adalimumab, etanercept, infliximab, etc). Please note that medicines funded under the NHS England Medicines for Children Policy may have additional criteria with respect to access.

Place in therapy relative to available treatments

- Ozanimod, as a new class of treatment, constitutes an additional line of treatment. The current treatment pathway will be amended accordingly.

Stakeholder views

- Specialist clinicians who sit in the Surrey Gastroenterology Network and the wider APC audience have been consulted on this paper. Comments to be included in the front sheet.

Cost-effectiveness

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

Are there any savings shown in the calculator? No savings shown

Section 1: cost of the technology

Annual cost per patient (or complete course if shorter) for both primary and secondary care: £17,849 (year 2 onwards) at list, but PAS price is available.

b. Availability of CAP/PAS price: Yes

c. Price relative to comparable medicines:
Using the CAP/PAS price (if applicable), indication of relative cost, compared to other available treatments in primary/secondary care at Year 2.

1. Infliximab IV
2. Adalimumab
3. Filgotinib
4. Tofacitinib
5. Ozanimod
6. Infliximab subcut
7. Ustekinumab
8. Vedolizumab subcut
9. Golimumab
10. Vedolizumab IV

Section 2: NICE resource impact report and template
Number of patients Year 1 and Year 5: NICE calculator assumed no change in patient numbers over 5 years.

Potential patient numbers per 100,000: According to NICE, 19 per 100,000 population will have Ulcerative Colitis (203 for Surrey Heartlands).

a) NICE resource impact report

NICE does 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 (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.

There is a possible a cost pressure even though this may be below the £9,000 per 100,000 population threshold for NICE, as this TA represents a new additional line of treatment.
At a maximum of £9,000 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 per Place	£ 17,418	£ 20,951	£ 28,502	£ 34,962	£ 101,832

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

b) NICE resource impact template

The NICE calculator provided with the TA publication was unsuitable for use, and a complaint to NICE about the quality of the calculator was raised by the MRU on behalf of the APC.

Based on local intelligence sources and experience, the above costings would seem reasonable. It is likely that ozanimod would be mainly used as a 3rd or 4th line drug option, after infliximab, adalimumab and tofacitinib.

Traffic light recommendation to APC

Hospital National Tariff excluded high-cost drug: Yes

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

Recommended traffic light status and rationale: RED, because of the following colour-classification criteria:

Criterion 1: Specialist assessment to enable patient selection, initiation and continuation of treatment
Criterion 4: Specifically designated as being “specialist” or “hospital only” by product license, Department of Health, NICE or BNF)
Criterion 8: Medicines for which the funding is levied outside of tariff e.g. PBR excluded drugs

Implementation

NICE TA implementation must be within **90** days of publication.

Actions to implement:

- Blueteq forms to be developed.
- Trusts to follow internal governance procedures to add these drugs to their formulary, so that prescribers can initiate use as per NICE TA.
- Trusts to ensure that these drugs are available to prescribe to patients via the homecare route as appropriate.

- IBD high-cost drugs pathway to be discussed at Gastroenterology Network (attached pathway as example).

Primary care

- This is a hospital 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.

Secondary care

- Providers are NHS hospital trusts.
- Trusts to follow internal governance procedures to add to their formulary and initiate homecare as appropriate.
- 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.
- It is not yet known how keen clinicians are to use this new mode of action, so uptake might be faster or slower than anticipated.
- Homecare arrangements if used will be managed by the trust.
- Patients eligible for these treatments will already be known to the gastroenterology clinics, so there will be very low impact to clinic capacity from current levels.

ICS

- The technology is commissioned by integrated care systems, and they are required to comply with the recommendations of this NICE TA within 90 days of its date of publication. Providers are NHS hospital trusts.
- This guidance introduces another line of treatment into the current treatment pathway i.e. there will now be 5 lines of treatment available to patients.
- Pathway to be discussed at the next Gastroenterology Network to consider:
    - Placement of ozanimod into current treatment pathway
    - Ranking of medicines by efficacy and cost
    - Evolution of current 4th line MDT process into 5th line process

PAD and Joint Formulary

- Ozanimod is already on PAD with a "holding" statement, this will now be refreshed with the APC narrative, along with a link to the NICE TA webpage and a copy of the refreshed IBD HCD immune modulator treatment pathway.
- Ozanimod does not need to be linked to any other documents already on PAD, however the refreshed IBD HCD pathway will need to be re-linked to all other drugs on that pathway which are also on PAD.
- No impact on other traffic light statuses of other drugs on PAD.
- Joint Formulary is a work in progress.

Proposed tick box forms

- Blueteq® forms have been developed and included below.

References:

1 Specification of Product Characteristics. emc. Available at: https://www.medicines.org.uk/emc/product/11908/smpc Accessed 28/10/2022

2 NICE Technology Appraisal Guidance: Available at: https://www.nice.org.uk/guidance/ta828 Accessed 28/10/2022

3 NICE Resource Impact Report: Available at: https://www.nice.org.uk/guidance/ta828/resources Accessed 28/10/2022

4 NICE Resource Impact Template: Available at: https://www.nice.org.uk/guidance/ta828/resources Accessed 28/10/2022

Declaration of interest:

	Name	Role	Date	Declaration of interests (please give details below)
Author	G. Randall	Senior Technician, MRU	28/10/22	None
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QA check	S. Watkin	Associate Director of Pharmacy	07/12/22	None

Explanation of declaration of interest:
None.

Version control sheet:

Version	Date	Author	Status	Comment
1	07/12/22	G. Randall	Draft	Out for consultation
			Final	Out for clinical comment

Blueteq® form:

Please indicate whether patient meets the following NICE criteria:	**Please tick**
1. Ozanimod is recommended as an option for treating moderately to severely active ulcerative colitis in adults Please provide Mayo Score for this patient and date this score was taken Mayo Score (more than or equal to 6): _____ Date taken: _____ If this marker does not apply please provide alternative score (such as partial mayo) Score: _____ Date taken: _____	○ Yes ○ No
2. only if: CONVENTIONAL treatment cannot be tolerated or is not working well enough Please indicate which conventional therapies have been trialled below ○ Mesalazine ○ Corticosteroids ○ Azathioprine** (with or without Allopurinol) ○ Ciclosporin ○ Tacrolimus Please provide details of any medical contraindications here::	○ Yes ○ No
3. and Infliximab is not suitable, or BIOLOGICAL treatment cannot be tolerated or is not working well enough Please provide details here:	○ Yes ○ No
4. FOR INFORMATION Funding will be approved for induction of ozanimod. Objective evidence of a response to ozanimod should be provided following induction (8-12 weeks after initiation) using the appropriate continuation form on blueteq. At 12 months another continuation form will need to be completed if the patient continues to have active disease and trial withdrawal of treatment is considered to be inappropriate	