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	Eptinezumab for preventing migraine		
Available at	https://www.nice.org.uk/guidance/ta871		
Date of issue	1 March 2023	**Implementation deadline**	31st March 2023

Medicine details[1]	
Name and brand name	Eptinezumab - VYEPTI® 100 mg concentrate for solution for infusion.
Manufacturer	Lundbeck Limited
Mode of action	Eptinezumab is a humanized monoclonal antibody produced in Pichia pastoris yeast cells. Eptinezumab is a recombinant humanized immunoglobulin G1 (IgG1) antibody that binds to α- and β- forms of human calcitonin gene-related peptide (CGRP) ligand. Eptinezumab prevents the activation of the CGRP receptors and hence the downstream cascade of physiological events linked to initiation of migraine attacks.
Licensed indication	VYEPTI® is indicated for the prophylaxis of migraine in adults who have at least 4 migraine days per month.
Formulation	Concentrate for solution for infusion Each vial of concentrate contains 100 mg eptinezumab per mL. Following dilution, infusion is over approximately 30 minutes. Eptinezumab can be administered as a 300 mg dose, but a 300 mg vial is not available and will not be commercialised in the UK.
Dosage	The treatment should be initiated by a healthcare professional experienced in the diagnosis and treatment of migraine. The infusion of VYEPTI® should be initiated and supervised by a healthcare professional. Posology The recommended dose is 100 mg administered by intravenous infusion every 12 weeks. Some patients may benefit from a dosage of 300 mg administered by intravenous infusion every 12 weeks. The need for dose escalation should be assessed within 12 weeks after initiation of the treatment. When switching dosage, the first dose of the new regimen should be given on the next scheduled

	dosing date. Overall benefit and continuation of treatment should be assessed 6 months after initiation of the treatment. Any further decision to continue the treatment should be made on an individual patient basis.
Comparison of NICE TA with Summary of Product Characteristics (SmPC)[2]	Eptinezumab is indicated for 'the prophylaxis of migraine in adults who have at least 4 migraine days per month'. NICE have specified that it may be used if at least 3 preventative drug treatments have failed and have specified a stop criterion after 12 weeks (the SmPC recommends assessment of overall benefit and continuation of treatment at 6 months after initiation of the treatment. *The 300mg dose is not currently licensed in the UK and did not form part of the NICE resource calculation. Therefore, the recommendations are based only on the 100mg dose.* *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

1.1 Eptinezumab is recommended as an option for preventing migraine in adults, only if:
• they have 4 or more migraine days a month
• at least 3 preventive drug treatments have failed and
• the company provides it according to the commercial arrangement.

1.2 Stop eptinezumab after 12 weeks of treatment if:
• in episodic migraine (fewer than 15 headache days a month), the frequency does not reduce by at least 50%
• in chronic migraine (15 headache days a month or more with at least 8 of those having features of migraine), the frequency does not reduce by at least 30%.

1.3 If people with the condition and their clinicians consider eptinezumab to be 1 of a range of suitable treatments (including erenumab, fremanezumab and galcanezumab), discuss the advantages and disadvantages of the available treatments. After that discussion, if more than 1 treatment is suitable, choose the least expensive. Take account of administration costs, dosage, price per dose and commercial arrangements.

1.4 These recommendations are not intended to affect treatment with eptinezumab 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 31st March 2023.

Clinical effectiveness

Treatments for preventing chronic or episodic migraines include erenumab, fremanezumab

and galcanezumab when they have not responded to at least 3 oral preventive drug treatments. These treatments are already recommended in NICE's technology appraisal guidance on erenumab, fremanezumab and galcanezumab. They are all administered as injections under the skin. Eptinezumab is another treatment option that works in a similar way but is administered as an infusion into a vein.

There are no clinical trials directly comparing eptinezumab with erenumab, fremanezumab or galcanezumab. An indirect comparison suggests that eptinezumab works as well as these treatments.

A cost comparison suggests that eptinezumab has similar costs and overall health benefits to erenumab, fremanezumab and galcanezumab. So, eptinezumab is recommended for preventing migraine if it is used in the same population as these treatments.

Patient safety

- The product should be used within its product license.
- This is a Black Triangle drug – all suspected adverse reactions should be reported.

Patient factors

- It was agreed that eptinezumab would likely improve access to specialist treatment for people with difficulty self-injecting the CGRP inhibitors administered subcutaneously.

Environmental impact

No statement on environmental impact was made in the NICE TA.

- Patients will be required to travel to the hospital to receive their treatment.

Equality & diversity

Stakeholders raised several potential equality issues during the evaluation. This included that migraine is more common in women, particularly in those of childbearing age. But it was agreed that issues relating to differences in prevalence or incidence of a condition cannot be addressed in a technology evaluation.

A stakeholder commented that appropriate treatments should be available for everyone including people who cannot self-administer available treatments because of a physical, cognitive or other disability. It was agreed that eptinezumab would likely improve access to specialist treatment for people with difficulty self-injecting the CGRP inhibitors administered subcutaneously. This is because it would be administered in a hospital setting intravenously.

A stakeholder commented that there should be equality of access to treatment for people with migraine and that best supportive care should not be the default option because of where someone lives.

The decision making took into account any obligations in relation to the Equality Act 2010 and that eptinezumab can only be recommended for use within its marketing authorisation. It was noted that issues about healthcare implementation could not be addressed in the evaluation.

It was agreed that there were no equality issues relevant to the recommendations.

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

This is the fourth CGRP inhibitor – it differs from the others as it is an intravenous infusion given in hospital every 12 weeks (the others are subcutaneous injections). So, it offers another option.

The current migraine pathway has been adopted from NHS Kent and Medway ICS and is currently being updated to include this latest NICE TA. This will be shared on completion and

taken through the usual consultation and governance process for SH.

Stakeholder views

The paper was sent out for consultation, and comments are included in the front sheet.

Cost-effectiveness

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

Section 1: cost of the technology

The price of eptinezumab is £1,350 for a 100 mg per ml vial (excluding VAT; BNF online accessed January 2023).

a. Annual cost per patient (or complete course if shorter) for both primary and secondary care:

Dose	Annual cost of medicine only
100mg every 12 weeks	£5,400
300mg every 12 weeks	£16,200

b. Availability of CAP/PAS price:

The company has a commercial arrangement. This makes eptinezumab 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:

People with migraine first try a range of oral preventive drug treatments before considering more specialist treatment, such as botulinum toxin type A (for chronic migraine) or erenumab, fremanezumab or galcanezumab (for episodic or chronic migraine). Usual practice in the NHS is that there is an insufficient response to at least 3 oral preventive drug treatments before more specialist treatment is considered.

Erenumab, fremanezumab and galcanezumab are CGRP inhibitors and are recommended in their respective NICE TA guidance for preventing chronic or episodic migraines after at least 3 oral preventive drug treatments have failed. These treatments are available as subcutaneous injections that can be self-administered at home.

Technology	NICE TA	Administration frequency	Cost (as per TA)	Annual cost*
Erenumab	TA682 March 2021	4-weekly	£386.50 per 70 mg or 140 mg injection	£5,025
Fremanezumab	TA764 Feb 2022	Monthly	£450.00 per 225-mg injection (£1,350 per 675 mg)	£5,400
Galcanezumab	TA659 Nov 2020	Monthly or 3-monthly	£450.00 per 120-mg injection	£5,850
Eptinezumab	TA871 Mar 2023	12-weekly	£1,350 for a 100 mg per ml vial	£5,400

*Commercial arrangements and administration costs associated with eptinezumab are NOT included.

Eptinezumab is another CGRP inhibitor that works in a similar way, but it is administered by intravenous infusion every 12 weeks in hospital.

When taking account of administration costs, dosage, price per dose and commercial arrangements for all treatments, the total cost associated with eptinezumab 100 mg every 12 weeks was similar to or lower than that with erenumab (140 mg 4-weekly), fremanezumab (225 mg monthly or 675 mg 3-monthly) or galcanezumab (120 mg monthly after a 240 mg initial loading dose). The exact results are confidential and cannot be reported here.

It was agreed that, after people with the condition and their clinicians have discussed the advantages and disadvantages of the available treatments, if more than 1 treatment is suitable, it would be appropriate to choose the least expensive option. So, the decision was made to recommend eptinezumab for preventing migraine in line with the previous recommendations for erenumab, fremanezumab and galcanezumab.

Of the three current CGRP inhibitors available, the most cost-effective is erenumab.

Clinical opinion suggests that eptinezumab would therefore be reserved for people with severe migraine attacks or who are unable to use the CGRP inhibitors administered subcutaneously.

In their submission, the company did not identify any evidence directly comparing eptinezumab with the relevant comparators. The results of the network meta-analysis suggested that eptinezumab has *similar clinical effectiveness* to erenumab, fremanezumab and galcanezumab in reducing migraine frequency in people with chronic or episodic migraines. Clinical opinion also suggested that the treatments are similar.

Section 2: NICE resource impact statement and template

The NICE resource impact template is an updated template for all three CGRP inhibitors. It states that in year 5 based on an adult population of 851,080 in SH, the number of people accessing treatment (CGRP inhibitors and botulinum toxin A) will be 285 out of an eligible population of 3,096.

People who continue treatment	140
People who stop treatment at 12 weeks	89
People who stopped treatment in previous years and who receive best supportive care	56
Total	**285**

Currently, there are 121 patients in SH receiving a CGRP inhibitor.

Technology	2021	2022	2023 (to date)	Total
Erenumab		25	10	35
Fremanezumab	1	42	15	58
Galcanezumab	5	13	10	28
Grand Total	**6**	**80**	**35**	**121**

Interestingly, of the 121 SH patients, 58% were initiated at trusts outside of SH and 42% were initiated by one of the trusts within SH.

Potential patient numbers per 100,000:
The NICE resource impact template states this is 27 per 100,000 population.

a. NICE resource impact statement
NICE state:

'No significant resource impact is anticipated.

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 (or approximately £9,000 per 100,000 population, based on a population for England of 56.3m people).

This is because eptinezumab is another treatment option that works in a similar way to other

CGRP inhibitors but is administered as an infusion into a vein. We do not think practice will change substantially as a result of this guidance. Therefore, the overall incremental cost of treatment is low.'

b. NICE resource impact template

Drug costs for Surrey Heartlands:
This is another option for patients who require a CGRP inhibitor and will be reserved for people with severe migraine attacks or who are unable to use the CGRP inhibitors administered subcutaneously.

Given the small patient numbers and the rates of discontinuation, it is unlikely that costs will exceed £100,000 per Place.

Commentary:
NICE states that a significant impact on resources is not expected, as this will be below the £9,000 per 100,000 population threshold for NICE.

At £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	£17,418	£20,951	£28,502	£34,962	£101,832

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

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.

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

Implementation

NICE TA implementation must be within 30 days of publication.

Actions to implement:

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.

Secondary care

- Providers are NHS hospital trusts.
- Eptinezumab will be administered in hospital every 12 weeks as it is an intravenous

infusion, with implications for administration costs, capacity and staffing.
- Trusts to follow internal governance procedures to add to their formulary.
- 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.

ICS
- This technology is commissioned by integrated care systems.

PAD and Joint Formulary
- The current migraine pathway has been adopted from NHS Kent and Medway ICS and is currently being updated. This will be shared on completion and taken through the usual governance process for SH.

Proposed tick box forms

Blueteq® forms have been developed and included below.

References:

1 Summary of Product Characteristics. emc. VYEPTI 100 mg concentrate for solution for infusion. Available at: https://www.medicines.org.uk/emc/product/13243 Accessed <7.3.23>

2 NICE Technology Appraisal Guidance: Eptinezumab for preventing migraine. Technology appraisal guidance [TA871] Published: 01 March 2023. Available at: https://www.nice.org.uk/guidance/ta871 Accessed <6.3.23>

3 NICE Resource Impact Report: Eptinezumab for preventing migraine. Technology appraisal guidance [TA871] Published: 01 March 2023. Available at: https://www.nice.org.uk/guidance/ta871/resources Accessed <7.3.>

4 NICE Resource Impact Template: Eptinezumab for preventing migraine. Technology appraisal guidance [TA871] Published: 01 March 2023. Available at: https://www.nice.org.uk/guidance/ta871/resources Accessed <7.3.23>

Declaration of interest:

	Name	Role	Date	Declaration of interests (please give details below)
Prepared by	Tejinder Bahra	Medicines Resource Unit Lead Pharmacist	9.3.23	None
Supported by				
Reviewed by				

Explanation of declaration of interest:
None.

Version control sheet:

Version	Date	Author	Status	Comment
1	9.3.23	Tejinder Bahra	Draft	Out for consultation

2	2.3.23	Tejinder Bahra	Final	With comments

Blueteq® form: