Briefing Paper for Surrey Heartlands Integrated Care System (ICS) Area Prescribing Committee (APC)

Surrey Downs, Guildford & Waverley, North West Surrey, East Surrey Places & associated partner organisations.

NICE Technology Appraisals: Local implementation

NICE TA Guidance name and number	Fremanezumab for preventing migraine Technology appraisal guidance 764 This guidance replaces TA631 which only considered the use of fremanezumab in chronic migraine. This new NICE TA is for use in both chronic and episodic migraine.		
Available at	www.nice.org.uk/guidance/ta764		
Date of issue	2 February 2022	**Implementation deadline**	2 May 2022

Medicine details[1]	
Name, brand name and manufacturer	Fremanezumab - Ajovy® Teva Pharmaceuticals
Mode of action	Fremanezumab is a humanised monoclonal antibody produced in Chinese Hamster Ovary (CHO) cells by recombinant DNA technology. It is one of three currently available anti-calcitonin gene-related peptides (CGRPs) monoclonal antibody treatments for use in preventing migraine: the others are galcanezumab and erenumab.
Licensed indication	Prophylaxis of migraine in adults who have at least 4 migraine days per month.
Formulation	One pre-filled syringe contains 225 mg fremanezumab. One pre-filled pen contains 225 mg fremanezumab. For subcutaneous injection
Usual dosage	Two dosing options are available: • 225 mg once monthly (monthly dosing) or • 675 mg every three months (quarterly dosing)
Comparison with NICE TA use[2]	Licensed dosage and strength same as the NICE TA. *This is the current dose considered by NICE as part of the 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.*

Disease and potential patient group	
Brief description of disease[2]	Migraine attacks usually last between 4 hours and 72 hours and involve throbbing head pain of moderate to severe intensity, which can be highly disabling. The patient experts explained that they are often accompanied by nausea, vomiting, sensitivity to light, sensitivity to sound or other sensory stimuli, numbness, confusion, loss of concentration and

	speech issues. Migraine can adversely affect quality of life, affecting people's ability to do their usual activities, including work. Some people with migraine have severe depression and suicidal thoughts. All of these can slow personal and professional development so that people feel they have unachieved potential. **Chronic migraine** is defined as 15 or more headache days a month with at least 8 of those having features of migraine. **Episodic migraine** is defined as less than 15 headache days a month. A clinical expert explained that the severity of the condition can vary over time. The committee concluded that migraine, particularly chronic migraine, is a debilitating condition that substantially affects both physical and psychological aspects of quality of life and employment.
Potential patient numbers per 100,000[4]	See appendix 1 for patient numbers by ICS and Place. The potential patients per 100,000 adults is 135.

SUMMARY

Guidance[2]

Recommendations

1.1 Fremanezumab 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 fremanezumab 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 These recommendations are not intended to affect treatment with fremanezumab 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.

Why the committee made these recommendations

Treatments for preventing chronic or episodic migraine include beta-blockers, antidepressants and anticonvulsant drugs. If chronic migraine does not respond to at least 3 preventive drug treatments, botulinum toxin type A or best supportive care (treatment for the migraine symptoms) is offered. If episodic migraine does not respond to at least 3 preventive drug treatments, best supportive care is offered.

For people whose migraine has not responded to at least 3 oral preventive treatments, clinical trial evidence shows that fremanezumab works better than best supportive care in both episodic and chronic migraine. However, it is unclear if fremanezumab works better than botulinum toxin type A.

For chronic migraine, assuming fremanezumab works better than botulinum toxin type A, the most likely cost-effectiveness estimates are within the range NICE normally considers an acceptable use of NHS resources. So it is recommended for chronic migraine. For episodic migraine, the estimates of cost effectiveness are even lower, so it is recommended for episodic migraine. Fremanezumab treatment should be stopped if it is not working well enough after 12 weeks.

Cost implications* [2,3,4]

Cost:
The price of fremanezumab is £450.00 per 225-mg injection (£1,350 per 675 mg) excluding VAT; BNF online, accessed November 2021.

Availability of PAS and details (if appropriate):
The company has a commercial arrangement. This makes fremanezumab available to the NHS with a discount. The size of the discount is commercial in confidence.

The PAS price only applies to trusts.

Availability of homecare service (if appropriate):
Yes.

Annual or monthly cost per patient:
The average cost for each patient per year is estimated based on the list price.

Monthly dosing: 12 doses @ £450 each = £5,400
Quarterly dosing: 4 doses @ £1,350 each = £5,400

Has dose escalation been considered as part of the NICE costing template?
No

1. NICE resource impact statement:

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 £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.

The resource impact assumptions made are unchanged for both chronic and episodic migraine, further details on how these were arrived at were in the previous resource impact report for this topic. The population assumptions for episodic migraine are different. These are set out clearly in the assumptions input sheet of the resource impact template. The rapid review of TA631, which has now published as TA764, has resulted in fremanezumab being recommended for the episodic migraine population. It was only recommended for the chronic migraine population in TA631'.

2. NICE resource impact template

The resource impact template covers all treatment options and updates and replaces the previous NICE resource impact templates that were published for these topics.

The resource impact template relates to the use of fremanezumab in episodic migraine. If

future practice remained unchanged, the impact of the use of fremanezumab in episodic migraine in NHS Surrey Heartlands in 5 years would result in:

a. an additional £10,095 in appointment activity.

Fremanezumab follow up activity and costs	Unit cost	Activity current practice	Activity future practice	Activity change	Cost of current practice	Cost of future practice	Impact of change on cost
People who continue treatment (2 appointments per year)	£ 187	0	48	48	0	£ 8,996	£ 8,996
People who stop treatment at 12 weeks and revert to BSC	£ 187	0	6	6	0	£ 1,099	£ 1,099
Total		0	54	54	0	£ 10,095	£ 10,095

b. an additional £101,671 in drug costs.

	Cost of current practice	Cost of future practice	Impact of change on cost
Total Resource impact episodic and chronic	698,926	800,597	101,671
Total Resource impact episodic	**142,128**	**243,799**	**101,671**
Total Resource impact chronic	556,798	556,798	0

Alternative treatments and cost per patient per year

Other NICE recommended products:

1. **NICE Botulinum toxin type A for the prevention of headaches in adults with chronic migraine. Technology appraisal guidance. Published: 27 June 2012**

This NICE TA is for chronic migraine only.

The current annual cost per patient is £1,419, as described below:

	Dose mg/vial	Frequency (weeks)	Price per vial	Annual cost
Drug costs	200	12	£238.8	£955

	Cost per appointment	Annual number of appointments	Annual cost
Administration costs	£116	4	£464

Although botulinum toxin type A is recommended by NICE, there are lengthy waiting lists and it is not always available in some areas of the country.

Botulinum toxin type A treatment requires a 30-minute hospital appointment every 12 weeks for administration).

Treatment consists of between 31 to 39 injections of the medication in the head and neck

region, a procedure that may be viewed as relatively invasive.

According to The Migraine Trust and local intelligence, there is only one NHS migraine clinic within the APC geography, which is at Surrey and Sussex NHS Healthcare Trust, headed by a local trust neurologist. This clinic currently offers botulinum toxin type A. There are others in Brighton (both BSUH and Royal Sussex Hospital) and in London. Most patients are referred to the London trusts including St George's, Guy's and St Thomas' and King's College Hospital.

There is currently no alternative medical therapy to patients who do not respond to botulinum toxin type A.

Information from St George's Hospital is that 'patients who have intractable headache refractory to multiple medications and botulinum toxin type A, would eventually be referred to a quaternary unit such as the National Hospital for Neurology and Neurosurgery for consideration of invasive treatments. These interventions cost the NHS in the region of £20,000 and have significant side effects'.

2. **NICE Galcanezumab for preventing migraine. Technology appraisal guidance 659. Published: 18 November 2020**
3. **NICE Erenumab for preventing migraine. Technology appraisal guidance 682. Published: 10 March 2021**

Galcanezumab and erenumab are both anti-calcitonin gene-related peptides (CGRPs) monoclonal antibody treatments (as is fremanezumab):

Anti-CGRP	Annual cost
Fremanezumab (Ajovy®) - both monthly and quarterly dosing	£5,400
Galcanezumab (Emgality®) - monthly dosing	£5,850
Erenumab (Aimovig® - 4 weekly dosing	£5,024.50

The NICE TA for galcanezumab and erenumab support use in both episodic and chronic migraine.

Options not reviewed by NICE but used in standard practice:
Treatment options for preventing chronic or episodic migraine include beta-blockers, antidepressants and anticonvulsant drugs.

Impact to patients

- An additional treatment option for patients with episodic migraine would be valued.
- Choice of monthly or quarterly dosing is available.
- Available under a homecare service so will be delivered directly to the patient.
- Patients in primary care headache services would need to be referred to the trust as a RED drug and in order to access the PAS price.
- Training may be required before a person can self-administer the treatment.
- Carers may have to help administer the sc injection if the patient has issues with dexterity or needle-phobia.

Impact to primary care prescribers

- This is a PbRe drug and is commissioned by CCGs 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.

Impact to secondary care

• Providers are NHS hospital trusts. • The initiation, administration and on-going treatment is managed by secondary care. • Homecare arrangements will be managed by the trust. • An additional treatment option would be valued by clinicians.
Impact to CCGs
• The technology is commissioned by integrated care systems/clinical commissioning groups (CCGs) and they are required to comply with the recommendations in the NICE TA within 3 months of its date of publication.
Implementation
• NICE TA implementation must be within 90 days of publication. • Blueteq forms to be developed. • Trusts to follow internal governance procedures to add to their formulary and initiate Homecare. • Migraine pathway to be amended to allow use in episodic migraine
Recommendation to APC
PbRe: Yes **Recommended traffic light status (see attached guidelines):** Red See proposed Blueteq forms.

References:

1. Specification of Product Characteristics. Ajovy (fremanezumab) 225 mg Pre-filled Pen for Injection. Available at: https://www.medicines.org.uk/emc/product/11630/smpc Accessed <2.3.22>

2. NICE Technology appraisal: Fremanezumab for preventing migraine. Technology appraisal guidance [TA764] Published: 02 February 2022. Available at: https://www.nice.org.uk/guidance/ta764 Accessed <2.3.22>

3. NICE Resource impact report. Available at: https://www.nice.org.uk/guidance/ta764/resources Accessed <2.3.22>

	Name	Role	Date	Declaration of interests (please give details below table)
Prepared by	Tejinder Bahra	Lead Commissioning Pharmacist	1.3.22	None
Reviewed by:				

Explanation of declaration of interest:

VERSION CONTROL SHEET

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

2		Tejinder Bahra	Final	Inclusion of comments and resource template information
3		Tejinder Bahra	Final	Blueteq forms added to document for consultation with specialist teams

Appendix 1: Patient numbers by ICS and Place.

	% of people	Surrey Heartlands	East Surrey	G&W	NW Surrey	Surrey Downs
Total population for area selected (all ages)	-	1,049,170	188,122	210,122	350,153	294,255
Population of people aged 18 or over	-	815,884	146,293	163,401	272,295	228,827
Prevalence of migraine	0.143	116,671	20,920	23,366	38,938	32,722
People who have episodic migraine	0.88	102,671	18,409	20,562	34,266	28,796
People who have preventative therapy	0.28	28,748	5,155	5,757	9,594	8,063
People who have had 3 or more prior treatment failures	0.093	2,674	479	535	892	750
Total number of people eligible for treatment with erenumab, fremanezumab or galcanezumab	**1**	**2,673**	**479**	**535**	**892**	**750**
Chronic migraine	**% of people**	**Surrey Heartlands**	**East Surrey**	**G&W**	**NW Surrey**	**Surrey Downs**
Population of people aged 18 or over	-	815,884	146,293	163,401	272,295	228,827
Prevalence of migraine	0.143	116,671	20,920	23,366	38,938	32,722
People who have chronic migraine	0.12	14,001	2,510	2,804	4,673	3,927
People who have preventative therapy	0.28	3,920	703	785	1,308	1,099
People who have had 3 or more prior treatment failures	0.28	1,098	197	220	366	308
Total number of people eligible for treatment with erenumab, fremanezumab or galcanezumab	**1**	**1,098**	**197**	**220**	**366**	**308**

Appendix 2 – Blueteq forms

FREMANEZUMAB - for prevention of migraine TA764 (225 mg once monthly (monthly dosing) or 675 mg every three months (quarterly dosing)

Please indicate whether patient meets the following NICE criteria:	**Please tick**
1. The patient has 4 or more migraine days per month? Please identify below if the patient has episodic or chronic migraine ☐ Episodic Migraine (fewer than 15 headache days a month) Number of episodic migraine days per month?: ☐ Chronic Migraine (15 headache days a month or more with at least 8 of those having features of migraine)? Number of chronic migraine days per month?:	○ Yes ○ No
2. At least 3 preventative drug treatments have been tried and failed. Please provide details below:	○ Yes ○ No
3. Fremanezumab will be stopped after 12 weeks if: - In episodic migraine the frequency does not reduce by at least 50%. - In chronic migraine the frequency does not reduce by at least 30%.	○ Yes ○ No
4. FOR INFORMATION: Funding will be approved for an INITIAL induction of 12 weeks. Funding will only be re-approved for a further 9 months (up to 1st year of treatment) if: The patient has responded adequately to treatment at 12 weeks (see above in question 3):	
SUBMISSION FOR FUNDING BY TRUST	
Form completed by Name	Date

Continuation form

Please indicate whether patient meets the following NICE criteria:	**Please tick**
1. Please provide the following information Current number of headache/migraine days per month:	
3. Continuation of funding will be approved for either (Please check which applies in this patient's case): ☐ 9 months in the very first year of treatment after the initial review, which would give 1 year of treatment. I can confirm that there has been an adequate response to treatment (in line with NICE criteria 1.2) after the initial 12 weeks of treatment. **OR** ☐ A further 12 months funding for patients that have been on treatment for more than 12 months **OR** ☐ After a drug holiday has been trialled and the treatment is being restarted. (if this box is checked, please provide next review date for this patient so that appropriate funding can be provided)	
4. FOR INFORMATION: Stop fremanezumab 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%. Funding will be approved as above.	

SUBMISSION FOR FUNDING BY TRUST	
Form completed by Name	Date