NHS
Greater Glasgow and Clyde

CLINICAL GUIDELINE

Calcitonin Gene-Related Peptide (CGRP) Monoclonal antibodies in Chronic Migraine, Neurology

A guideline is intended to assist healthcare professionals in the choice of disease-specific treatments.

Clinical judgement should be exercised on the applicability of any guideline, influenced by individual patient characteristics. Clinicians should be mindful of the potential for harmful polypharmacy and increased susceptibility to adverse drug reactions in patients with multiple morbidities or frailty.

If, after discussion with the patient or carer, there are good reasons for not following a guideline, it is good practice to record these and communicate them to others involved in the care of the patient.

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Lead Author:	Krishna Dani
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Important Note:

The Intranet version of this document is the only version that is maintained.
Any printed copies should therefore be viewed as 'Uncontrolled' and as such, may not necessarily contain the latest updates and amendments.

NHS Greater Glasgow and Clyde	**NHS Greater Glasgow and Clyde** **Neurology** **Migraine: Protocol for use of Calcitonin Gene-Related Peptide (CGRP) Monoclonal antibodies in Chronic Migraine**
Background:	Erenumab (Aimovig®), Fremanezumab (Ajovy®), Galcanezumab (Emgality®) and Eptinezumab (Vyepti®) are calcitonin gene-related peptide (CGRP) monoclonal antibodies (mAbs)which are indicated for the prophylaxis of chronic migraine in adults. CGRP is associated with vasodilation, inflammation and modulation of the transmission of pain. Levels of CGRP increase significantly during migraine and return to baseline levels with headache relief.
Agent and route:	Erenumab, Fremanezumab, Galcanezumab Subcutaneous solution for injection in pre-filled pen or pre-filled syringe Eptinezumab Concentrate for solution for intravenous infusion
Patient population applicable to:	In line with the Scottish Headache Interest Group, experts in NHS GGC propose that CGRP mAbs should be restricted to specialist use in patients with chronic migraine (i.e. headaches occurring on 15 or more days per month of which ≥ 8 are migraine days) for whom at least four prior prophylactics (+/- flunarizine) have failed and the patient has failed to respond to, or not tolerated, an adequate trial of botulinum toxin A (Botox®). CGRP mAbs may be considered if Botox® is contraindicated.
Authorised and Designated Areas applicable to:	Erenumab, Fremanezumab, Galcanezumab Homecare prescription will be initiated by a Headache Specialist Nurse/ GPSI/ Consultant/ Pharmacist. Products require storage in a refrigerator and Homecare Company will supply sharps box. Eptinezumab A prescription and patient checklist will be completed by Headache specialist nurse/GPSI/Consultant/Pharmacist for administration in the neurology day ward of QEUH. The patient's General Practitioner will be informed that this medicine is being prescribed for the patient. Within General Practice it is beneficial for patient and prescriber safety to ensure that a patient's medicine record includes medicines that may be prescribed and supplied outwith the GP practice.

Indication and place in therapy:	CGRP mAbs should only be considered once patient has received an adequate trial (>6 weeks at therapeutic dose unless side effects or contraindicated) of the following medicines: • Beta blockers (e.g. propranolol) • Tricyclic antidepressant drug (e.g. amitriptyline) • Candesartan • Topiramate (we do not recommend initiation of this drug in patients of child bearing potential, see MHRA advice for more detail) • Atogepant (only following adequate trial of three prophylactics as per formulary restrictions) • Botulinum toxin A (Botox®) • +/- Flunarizine Medication overuse must be addressed prior to initiating CGRP mAbs. Cost-effectiveness should be considered when choosing a first line CGRP mAb. Erenumab (Aimovig®) contains latex in the needle cap and should be avoided in patients with a latex allergy. <u>First line therapy</u> One of the three subcutaneous CGRP mAbs (erenumab, fremanezumab or galcanezumab) should be considered first line. <u>Second line therapy</u> If erenumab is used first line, either fremanezumab or galcanezumab should be considered second line. If fremanezumab or galcanezumab are used first line, erenumab should be considered as second line (unless patient has latex allergy). <u>Third line therapy</u> A trial of eptinezumab given by IV infusion could be considered if patient fails to respond to first and second line therapies. A trial of a third subcutaneous mAb may also be considered at this stage. Eptinezumab may be considered at an earlier stage in patients who cannot self-inject or those for whom there are concerns surrounding potential intolerance of other CGRP mAbs. This must be subject to multidisciplinary team (MDT) agreement. Clinical studies have demonstrated that the majority of patients responding to therapy showed clinical benefit within 3 months. Patients who do not respond to treatment will discontinue after 12 weeks. It is estimated that between 40-60% of patients will be non-responders at the 12 week assessment. Patients must complete headache diaries and bring these to their appointment.
Dose, duration and administration:	<u>Erenumab</u> 140mg every 4 weeks

	<u>Galcanezumab</u> 240mg loading dose followed by 120mg once monthly <u>Fremanezumab</u> Two dosing options are available: • 225mg once monthly (monthly dosing) or • 675mg every three months (quarterly dosing) Eptinezumab 100mg every 12 weeks* *In exceptional circumstances a dose of 300mg could be considered subject to MDT approval. Patients will be reviewed in clinic prior to commencing treatment and after a 3 month trial to assess for efficacy and side effects. A positive response is defined as either a: • 30% reduction in the number of headache days based on analysis of baseline headache diaries • 50% reduction in migraine days (i.e. severe headaches which are at least 7/10 in severity) Following a positive response, treatment will be continued for a further 9 months until patient has received treatment for up to 1 year. Patient will have a 3-month treatment break and then be reviewed by their Consultant, GPSI, specialist nurse or pharmacist. If patient reverts to chronic migraine, the CGRP mAb may be re-started or an alternative therapy commenced. A treatment holiday will be considered if chronic migraine becomes episodic (i.e. <15 days/month with headache for 3 consecutive months). Treatment will be stopped if: • Treatment has failed to reduce the number of headache days by at least 30% or severe headache days reduce by at least 50% • Patient becomes pregnant or is breast feeding. • Patient becomes refractory to treatment (headache days per month rise to comparable levels pre-CGRP mAb) In line with expert opinion, a treatment break of 3 months is recommended before switching from one CGRP mAb to another. Note that for eptinezumab this means another CGRP mAb should not be given for six months following the last dose of eptinezumab.
Strength of preparation used:	Erenumab 140mg s/c injection (Auto-injector) Fremanezumab 225mg s/c injection (Auto-injector) Galcanezumab 120mg s/c injection (Auto-injector) Eptinezumab 100mg/ml concentrate for solution for infusion vials

Licensed status:	Licensed Medicines
Authorised prescribers:	Consultant Neurologists with Specialist Interest in Headache Designated General Practitioners with Specialist Interest in Headache Designated non-medical prescribers (e.g. Clinical Nurse Specialists, Specialist Pharmacists)
Authorised for administration	Erenumab, Fremanezumab, Galcanezumab Patient will be educated and trained on injection technique at initial clinic appointment. Eptinezumab Administered by Intravenous infusion by nursing staff on the neurology day ward at QEUH
Authorised for storage in clinical areas:	Yes. Store in a refrigerator
References:	Scottish Medicines Consortium https://www.scottishmedicines.org.uk/medicines-advice/erenumab-aimovig-full-submission-smc2134/ https://www.scottishmedicines.org.uk/medicines-advice/fremanezumab-ajovy-full-smc2226/ https://www.scottishmedicines.org.uk/medicines-advice/galcanezumab-emgality-full-smc2313/ eptinezumab (Vyepti) (scottishmedicines.org.uk) Aimovig® Summary of Product Characteristics https://www.medicines.org.uk/emc/product/9380/smpc Ajovy® Summary of Product Characteristics https://www.medicines.org.uk/emc/product/11630/smpc Emgality® Summary of Product Characteristics https://www.medicines.org.uk/emc/product/10478/smpc Vyepti® Summary of Product Characteristics https://www.medicines.org.uk/emc/product/13243
Prepared by:	Laura Stobo (Senior Pharmacist) on behalf of NHS GGC Headache Team
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