

Evidence Review for Prescribing Clinical Network

Treatment: Migraine prophylaxis: flunarizine

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Summary page

Flunarizine is a calcium channel blocker that reduces arterial and arteriolar smooth muscle spasm. While flunarizine is unlicensed in the UK, it is licensed in other countries, including Ireland, for the prophylaxis of migraine in adults aged 18 years and older. For adults aged 18 to 64 years the starting dose is 10 mg at night, and for adults aged 65 years and older the starting dose is 5 mg at night

- How strong is the evidence for claimed efficacy?

Overall, the studies suggest that flunarizine is as effective as propranolol or topiramate at reducing the frequency of migraines in adults (1 RCT v propranolol n= 783 and 1 RCT v topiramate n=150). In children, flunarizine was more effective than placebo at reducing migraine frequency, and as effective as nimodipine, aspirin, propranolol or dihydroergotamine. However, all of the studies in children were small and of poor quality

- Potential advantages in terms of: efficacy, compliance, pharmacokinetics, drug interactions and adverse effects?

NICE CG 150 (diagnosis and management of headaches in young people and adults) recommends that topiramate or propranolol should be offered for the prophylactic treatment of migraine according to the person's preference, comorbidities and risk of adverse events, with other treatments recommended if both of these are unsuitable or ineffective.

- Is there a clear place in therapy / treatment pathway?
(E.g. patient type / characteristics, and relationship to other therapies)

Flunarizine is an unlicensed special and is not included within NICE CG 150. Potentially might be an option for patients who are unable to tolerate / CI to the recommended prophylactic treatment options in NICE CG 150.

- Is monitoring for toxicity required? No

- Is monitoring for efficacy required? No:

For people whose condition responds to initial treatment, the summary of product characteristics recommends that maintenance treatment should continue at the same daily dose but that there should be 2 successive drug-free days every week. It further recommends that flunarizine treatment should be stopped after 6 months and that it should only be re-started if the person's condition relapses. In addition, it recommends that treatment should be stopped if no significant improvement is seen after 2 months of treatment.

- Financial implications:

No price is listed for flunarizine and the cost will differ depending on the source. NHS prescription cost analysis for England 2013 reported that flunarizine hydrochloride 5 mg capsules cost £115.42 per item (with the average quantity per item of 68.92). The cost of alternative treatment options for migraine prophylaxis (not all of which are licensed

specifically for this use) varies depending on the treatment used and the dosage. Propranolol tablets 40 mg 3 times a day costs £9.06 for 30 days' treatment. Topiramate tablets 50 mg twice a day cost £3.52 for 30 days' treatment. However as an unlicensed special the price in primary care can fluctuate considerably.

- National Guidance available –
 - NICE CG 150 (Sept 2012) Headaches: diagnosis and management of headaches in young people and adults
 - NICE ESUOM 33 (Sept 2014) Migraine prophylaxis: flunarizine
 - NICE TA260 (June 2012): Botulinum Toxin type A for the prevention of headaches in adults with chronic migraine.

Recommendation to PCN:

Flunarizine should be reserved as a treatment option for the prophylactic treatment of migraine in patients who do not respond / are unable to tolerate other available treatment options. NICE CG 150 states under prophylactic treatment:

- *Discuss the benefits and risks of prophylactic treatment for migraine with the person, taking into account the person's preference, comorbidities, risk of adverse events and the impact of the headache on their quality of life.*
- *Offer topiramate or propranolol for the prophylactic treatment of migraine according to the person's preference, comorbidities and risk of adverse events. Advise women and girls of childbearing potential that topiramate is associated with a risk of fetal malformations and can impair the effectiveness of hormonal contraceptives. Ensure they are offered suitable contraception.*
- *If both topiramate and propranolol are unsuitable or ineffective, consider a course of up to 10 sessions of acupuncture over 5–8 weeks or gabapentin (up to 1200 mg per day) according to the person's preference, comorbidities and risk of adverse events.*
- *For people who are already having treatment with another form of prophylaxis such as amitriptyline, and whose migraine is well controlled, continue the current treatment as required.*
- *Review the need for continuing migraine prophylaxis 6 months after the start of prophylactic treatment.*
- *Advise people with migraine that riboflavin (400 mg once a day) may be effective in reducing migraine frequency and intensity for some people.*

As flunarizine is an unlicensed drug which will be used only for a small number of patients with migraines that are refractory to standard treatment options it should be considered as RED on the traffic light system

• **VERSION CONTROL SHEET**

Version	Date	Author	Status	Comment
1	2/10/14	Linda Honey		

For full information and review of available evidence please refer to:

- NICE Evidence Summary: unlicensed or off-label medicine (ESUOM) 33 Sept 20141: Migraine prophylaxis: flunarizine
AND

- NICE CG 150 Sept 2012: Diagnosis and management of headaches in young people and adults.

which are circulated together with this summary document.

Additional information:

- **Current use:** ePACT data for the CCGs shows that to date there have been no prescriptions for flunarizine in G&W, NW Surrey, Surrey Heath, Surrey Downs, NE Hamps & Farnham and Crawley CCGs. There have been 5 prescriptions only in Horsham & Mid Sussex over the last 12 months.
- **Other areas policies:** limited information available. Information available:
 - Approved by Leeds DTG for use in migraine prophylaxis as red hospital only
 - Nottinghamshire formulary – named patient use only in hospital