Amendment of recommendation 1.3.15 about the use of metoclopramide and prochlorperazine in Headaches in over 12s: diagnosis and management (NICE guideline CG150)

August 2021

Amendment proposal

We propose changing recommendation 1.3.15 in headaches over 12s: diagnosis and management to a 'consider' recommendation. Currently it recommends to 'offer a non-oral preparation of metoclopramide or prochlorperazine' in people in whom oral or nasal treatments for acute migraine are ineffective or not tolerated. We propose changing the recommendation from 'offer' to 'consider' to better reflect the benefits and harms associated with these drugs. Additionally, we propose adding wording to the recommendation that reminds healthcare professionals to check the specific product characteristics (SPCs) of these drugs for any warnings or precautions.

The following wording is proposed:

For people in whom oral preparations (or nasal preparations in young people aged 12 to 17 years) for the acute treatment of migraine are ineffective or not tolerated:

- *consider a non-oral preparation of metoclopramide or prochlorperazine and*
- *if non-oral metoclopramide or prochlorperazine is used, consider adding a non-oral NSAID or triptan if they have not been tried. [2012]*

Note the special warnings and precautions for use in the summaries of product characteristics for metoclopramide and prochlorperazine and discuss the benefits and risks with the person (or their parents or carers).

In November 2015, only a buccal preparation of prochlorperazine was licensed for this indication (prochlorperazine was licensed for the relief of nausea and vomiting); nasal sumatriptan was the only triptan licensed for this indication in under 18s. This was an off-label use of metoclopramide in children and young people. See NICE's information on prescribing medicines.

Reasons for the proposal

The recommendation to offer the anti-emetics metoclopramide and prochlorperazine was developed in 2012 based on moderate to very low-quality evidence of their effectiveness for pain relief from migraine irrespective of whether a person is experiencing nausea. The evidence for prochlorperazine included children in the study population (5-18 years), none of the evidence for metoclopramide included people under 18 years. The committee agreed that there were no additional considerations to be made about this drug for people 12 to 17 years.

It was noted by the committee there is a small risk that anti-emetic drugs of this type (dopamine receptor antagonists) can trigger extrapyramidal side-effects which is higher in people less than 20 years old. The committee agreed that these side-effects are rare and reversible; that the benefits of metoclopramide or prochlorperazine justify their use with consideration of the side-effects; and made an ‘offer’ recommendation. NICE uses 'offer' to reflect a strong recommendation, usually where there is clear evidence of benefit (see 'Developing NICE guidelines: the manual section 9.2 wording the recommendations').

An MHRA drug safety update (2014) (DSU) about the use of metoclopramide that post-dates recommendation 1.3.15 development provides further

evidence of its association with extrapyramidal side-effects and that this risk is higher in paediatric populations.

We carried out small focussed PubMed searches for the risks associated with metoclopramide and other anti-emetics in children and young people and identified a systematic review that indicated a small risk in paediatric populations associated with metoclopramide that was generally reversible (*Lau Moon Lin M et al., 2016*). We also identified an observational study (Kirkpatrick et al., 2020) that reports a small risk of dystonic reactions for metoclopramide and prochlorperazine and that the risk is relatively higher for prochlorperazine.

The European Medicines Agency report that informs the MHRA DSU considers benefit and harm data from various indications of metoclopramide and reports that rates of extrapyramidal side-effects are 6 times higher for children compared to adults. It concludes that in paediatric populations metoclopramide should only be used as a second-line option for prevention of delayed chemotherapy-induced nausea and vomiting and treatment of established post-operative nausea and that use should be short-term (up to 5 days).

When recommendation 1.3.15 was developed in 2012 the guideline committee were confident in making an 'offer' recommendation about metoclopramide and prochlorperazine. At that time the DSU was not available to the committee, and whilst it is not direct evidence for harm in the population covered by recommendation 1.3.15, it confirms the risks associated with metoclopramide particularly in paediatric populations. The report's conclusion is assessed as acting to reduce the certainty around the benefit-harm balance of metoclopramide in paediatric populations and by extension reduces the certainty of the original benefit-harm assessment made by the committee.

Therefore, it is proposed to reduce the strength of recommendation 1.3.15 by making it a 'consider' recommendation. It is also proposed to add advice about checking SPCs to alert practitioners, particularly those who may not be pain management or headache specialists, to the safety issues associated

with metoclopramide. NICE uses 'consider' to reflect a recommendation for which the evidence of benefit is less certain (see 'Developing NICE guidelines: the manual section 9.2 wording the recommendations').

Prochlorperazine is also a dopamine receptor antagonist and is known to be associated with extrapyramidal side-effects. An observational study (Kirkpatrick et al., 2020) identified during this assessment reported that the risk of extra pyramidal side-effects associated with prochlorperazine, although small, may be relatively higher compared with metoclopramide. It is assessed as appropriate therefore for ‘consider’ to also apply to use of this drug.

Equalities

No equalities issues were identified.

Overall proposal

We propose amending recommendation 1.3.15 about the use of metoclopramide and prochlorperazine for the treatment of acute migraine to make it a ‘consider’ recommendation to better reflect the balance between the benefits and harms associated with their use. We also propose adding wording that reminds healthcare professionals to check the SPCs of these drugs for any warnings or use precautions.