NHS
Pan Mersey
Area Prescribing Committee

DOXYLAMINE/PYRIDOXINE gastro-resistant tablets (Xonvea®) for the treatment of nausea and vomiting of pregnancy

The Pan Mersey Area Prescribing Committee recommends the prescribing of DOXYLAMINE/PYRIDOXINE gastro-resistant tablets (Xonvea®) as an option for the treatment of nausea and vomiting of pregnancy

GREEN

Doxylamine/pyridoxine is indicated for the treatment of nausea and vomiting of pregnancy (NVP) in women who do not respond to conservative management. It is taken every day and not on an as needed basis. [1]

NICE guideline (NG201) for Antenatal care (19 August 2021) includes a chapter on Interventions for common problems during pregnancy and includes a table containing the advantages and disadvantages of different pharmacological treatments for nausea and vomiting in pregnancy in which doxylamine/pyridoxine is included. When considering pharmacological treatments for nausea and vomiting in pregnancy, NG201 highlights the importance of discussing the advantages and disadvantages of different antiemetics with the woman and taking into account her preferences and her experience with treatments in previous pregnancies to support shared decision making.

The Royal College of Obstetricians and Gynaecologists' (RCOG) guideline on the management of nausea and vomiting of pregnancy (22 June 2016) predates the availability of doxylamine/pyridoxine in the UK.

The MHRA noted that, because of prescribing hierarchy, the use of other medicines that do not have a specific licence over a medicine that does, would need to be justified. [2]

Note: Patients who are not eligible for treatment under this statement may be considered on an individual basis where their GP or consultant believes exceptional circumstances exist that warrant deviation from the rule of this policy. In this situation, follow locally defined processes.

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This recommendation has been designated suitable for inclusion on the Pan Mersey APC static list and will only be reviewed if significant new evidence becomes available.
APC administration provided by Midlands and Lancashire Commissioning Support Unit

Prescribing policy statement
Version: 3.0
STATIC

DOXYLAMINE/PYRIDOXINE gastro-resistant tablets (Xonvea®) for the treatment of nausea and vomiting of pregnancy

Effectiveness

Xonvea® is a gastro-resistant tablet containing doxylamine succinate 10 mg (a first-generation antihistamine that selectively binds H1 receptors in the brain) and pyridoxine hydrochloride 10 mg (vitamin B6). Its mode of action is not well established because the aetiology of NVP is not well known. The delayed action of the product allows the night time dose to work the following morning, when some women may need treatment most. [3]

Symptoms of nausea and vomiting [2]

At day 15, Koren et al. (2010) found a small but statistically significant improvement in the mean Pregnancy unique quantification of emesis (PUQE) symptom score (a measure of the severity of nausea and vomiting) in the doxylamine/pyridoxine group compared with the placebo group (−4.8 compared with −3.9 respectively, p=0.006). Post hoc analyses obtained similar results at days 3, 4 and 5 (all differences around −1.0 point on a scale from 3 to 15 points, all p≤0.002). The MHRA concluded that these small but statistically significant improvements in PUQE score are clinically important for women suffering from NVP.

The DESI study was undertaken in 1975 but not published because it was an FDA regulatory study for which publication was not routine at that time. Zhang et al. obtained the data and published their report in 2017. Over 7 days, statistically significant improvements (classed as moderate or excellent) were seen with doxylamine/ pyridoxine compared with placebo in doctors' evaluations of effectiveness (78% compared with 57%, p<0.01) and improvement in nausea (75% compared with 52%, p<0.001). However, there was no statistically significant improvement in vomiting (73% compared with 66%, p=0.17).

Global assessment of wellbeing [2]

Koren et al. (2010) also found a small statistically significant improvement in the global assessment of wellbeing score at 15 days (a second primary outcome) with doxylamine/pyridoxine compared with placebo (2.8 compared with 1.8, difference 1.0 point on a scale from 0 to 10 points, p=0.005).

Safety [1]

Contraindications

Hypersensitivity to doxylamine succinate, other ethanolamine derivative antihistamines or pyridoxine hydrochloride. Concomitant use with monoamine oxidase inhibitors. Anticholinergic effects of doxylamine/pyridoxine may be prolonged and intensified by monoamine oxidase inhibitors.

Special Warnings

Not recommended if a woman is concurrently using central nervous system depressants including alcohol. Doxylamine/pyridoxine has anticholinergic properties and, therefore, should be used with caution in patients with: asthma, increased intraocular pressure, narrow angle glaucoma, stenosing peptic ulcer, pyloroduodenal obstruction and bladder-neck obstruction. Doxylamine/pyridoxine contains traces of azo colouring agent Allura Red AC Aluminium Lake (E129) which may cause allergic reactions.

There is limited evidence in cases of hyperemesis gravidarum for the combination doxylamine/pyridoxine. These patients should be treated by a specialist.

Side effects

Somnolence (very common); dizziness, dry mouth, fatigue (common).

Safety in Pregnancy and Breast Feeding[1]

A large amount of data on pregnant women indicates no malformative nor feto/neonatal toxicity of doxylamine succinate and pyridoxine hydrochloride. Pyridoxine hydrochloride is excreted into breast milk and the molecular weight of doxylamine succinate is low enough that passage into breast milk can be expected. A risk to breastfed infants cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from doxylamine/pyridoxine therapy, taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.

For full information, please refer to the SPC.

Patient factors [1]

Doxylamine/pyridoxine has a moderate to major influence on the ability to drive and use machines. Women should avoid engaging in activities requiring complete mental alertness, such as driving or operating heavy machinery, while using doxylamine/pyridoxine. False positive urine drug screens for methadone, opiates, and phencyclidine phosphate can occur with doxylamine/pyridoxine use.

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Cost [4]

*6 week treatment duration

Drug	Daily dose	Cost*	Additional cost* of using doxylamine/pyridoxine
Doxylamine/Pyridoxine tabs	2 tablets	£119.70	-
Cyclizine 50mg tabs	50mg x 3	£6.17	£113.53
Prochlorperazine 5mg tabs	10mg x 3	£13.95	£105.75
Promethazine hydrochloride 25mg tabs	50mg	£8.25	£111.45

The estimated annual cost of prescribing doxylamine/pyridoxine for treatment of NVP will depend on the uptake of the new drug. The budget impact per 100,000 population of using doxylamine/pyridoxine as a first-line agent instead of current treatment options, based on various uptake scenarios is shown below: [5]

	Uptake level of doxylamine/pyridoxine (as first-line drug treatment option after conservative measures)				
	10%	**30%**	**50%**	**75%**	**100%**
Budget impact per 100,000 population*	**£432**	**£1,297**	**£2,161**	**£3,242**	**£4,323**

*Budget impact taken from the NICE Budget Impact template: ES20 doxylamine and pyridoxine for the treating nausea and vomiting in pregnancy, and based on dm+d browser [4] drug costs on 11 March 2022. NICE assumes that 22% of women who are pregnant are prescribed medicines for NVP. Costs assume the number of patients progressing to second-line treatment options, and the choice of second-line treatment used, remain the same and that no effect on hospital admissions is seen when using doxylamine/pyridoxine as the first-line agent.

Prescribing information [1]

The recommended starting dose is two tablets at bedtime (Day 1). If this dose adequately controls symptoms the next day, the patient can continue taking two tablets at bedtime. However, if symptoms persist into the afternoon of Day 2, the patient should continue the usual dose of two tablets at bedtime (Day 2) and on Day 3 take three tablets (one tablet in the morning and two tablets at bedtime). If these three tablets do not adequately control symptoms on Day 3, the patient can take four tablets starting on Day 4 (one tablet in the morning, one tablet mid-afternoon and two tablets at bedtime). The maximum recommended daily dose is four tablets (one in the morning, one in the mid-afternoon and two at bedtime). Doxylamine/pyridoxine should be taken as a daily prescription and not on an as needed basis. Continued need for doxylamine/pyridoxine should be reassessed as the pregnancy progresses. Tablets should be taken on an empty stomach, with a glass of water. To prevent a sudden return of nausea and vomiting of pregnancy symptoms, a gradual tapering dose is recommended at the time of discontinuation.

References

1. Alliance Pharmaceuticals. Summary of Product Characteristics: Xonvea 10 mg/10 mg gastro-resistant tablets, 01 December 2019. Accessed 15 December 2021.
2. National Institute for Health and Care Excellence. Evidence Summary [ES20]: Doxylamine/pyridoxine (Xonvea) for treating nausea and vomiting of pregnancy. 24 June 2019. Accessed 29 December 2021.
3. National Institute for Health and Care Excellence. Evidence review: ES20 Doxylamine/pyridoxine (Xonvea) for treating nausea and vomiting of pregnancy, 24 June 2019. Accessed 29 December 2021.
4. NHS Business Services Authority. dm + d browser. Accessed 11 March 2022.
5. National Institute for Health and Care Excellence. Budget impact report: ES20 Doxylamine and pyridoxine for treating nausea and vomiting of pregnancy. 24 June 2019. Accessed 15 December 2021.