



BEDFORDSHIRE AND LUTON JOINT PRESCRIBING COMMITTEE (JPC)

18th September 2019

Review: October 2022

Bulletin 283 : Doxylamine succinate and pyridoxine for nausea and vomiting in pregnancy

JPC Recommendations:

The JPC agreed to support the East of England Advisory Committee Bulletin and the set of interim recommendations:

- Prescribing of doxylamine and pyridoxine (Xonvea®) for nausea and vomiting in pregnancy is NOT recommended in primary care.
- There is insufficient information for clinical superiority or cost effectiveness for doxylamine and pyridoxine in comparison with other recognised non-pharmacological and pharmacological ways to manage nausea and vomiting in pregnancy.
- Patients presenting with nausea and vomiting in pregnancy should be managed in line with current Royal College of Obstetricians and Gynaecologists (RCOG) guidelines.
- These recommendations will be reviewed in the light of new evidence and/or publication of new national guidance (including from the RCOG and the RMOCs).

NB : Full EoEPAC bulletin is attached .

GUIDANCE STATEMENT

Doxylamine succinate 10mg and pyridoxine hydrochloride 10mg delayed-release (Xonvea®) for the treatment of nausea and vomiting in pregnancy

PAC interim recommendations

- Prescribing of doxylamine and pyridoxine (Xonvea®) for nausea and vomiting in pregnancy is NOT recommended in primary care.
- There is insufficient information for clinical superiority or cost effectiveness for doxylamine and pyridoxine in comparison with other recognised non-pharmacological and pharmacological ways to manage nausea and vomiting in pregnancy.
- Patients presenting with nausea and vomiting in pregnancy should be managed in line with current Royal College of Obstetricians and Gynaecologists (RCOG) guidelines.
- These recommendations will be reviewed in the light of new evidence and/or publication of new national guidance (including from the RCOG and the RMOCs).

Background

Xonvea® contains doxylamine succinate (10mg), an antihistamine, and pyridoxine hydrochloride, also known as vitamin B6, (10mg), in a delayed release tablet. Xonvea is indicated for the treatment of Nausea and Vomiting of Pregnancy (NVP) in women who do not respond to conservative management and was launched in the UK in October 2018.^{1,2}

Xonvea® is the only product licensed in the UK for use in pregnancy. All existing treatment options are licensed for the management of nausea and vomiting, with general advice to avoid use in pregnancy. However, they have been widely used off label for many years in line with Royal College of Obstetrics and Gynaecology (RCOG) guidelines.³

Current National Institute for Health and Care Excellence (NICE) and Department of Health (DoH) guidance encourages non pharmacological strategies to manage NVP as first line interventions such as rest, drinking little and often to avoid dehydration, eating small, frequent meals that are high in carbohydrates and low in fat, eating plain biscuits 20 minutes before getting up in the morning and avoiding triggers such as specific odours and foods.⁴⁻⁷

Pharmacological anti-emetics should be reserved for more severe cases of NVP. If an anti-emetic is warranted for patients experiencing severe NVP, the current RCOG guideline recommended antiemetic therapies for treating NVP are cyclizine, prochlorperazine, and promethazine first line, then metoclopramide, domperidone and ondansetron second line based on the available data relating to safety and efficacy.^{3,6}

The Drugs and Therapeutics Bulletin published a review of doxylamine with pyridoxine for the treatment of nausea and vomiting in pregnancy in March 2019. The reviewers did not identify any high quality evidence that shows that the combination of doxylamine and pyridoxine is more effective than other antiemetics.⁸

Doxylamine succinate and pyridoxine hydrochloride (Xonvea®) is not recommended for use within NHS Scotland as the submitting company did not present a sufficiently robust clinical or economic analysis to gain acceptance by the Scottish Medicines Consortium (SMC).⁹

Doxylamine succinate and pyridoxine hydrochloride (Xonvea®) is not recommended for use within NHS Wales as the cost-effectiveness data presented in the submission were insufficient for the All Wales Medicines Strategy Group to recommend its use.¹⁰

NICE Evidence summary ES20, Doxylamine/pyridoxine (Xonvea) for treating nausea and vomiting of pregnancy concluded that there is no evidence to show how the safety and efficacy of doxylamine/pyridoxine compares with current first-line treatment options such as antihistamines and phenothiazines.¹¹

The combination of doxylamine and pyridoxine is considerably more expensive than other antiemetics that have long been used off-label for NVP. Currently there is insufficient evidence for clinical superiority or cost effectiveness over existing treatments and therefore it is not recommended for prescribing in primary care. It is recommended that patients presenting with nausea and vomiting in pregnancy should be managed in line with current RCOG guidelines.

Cost impact

The list price for Xonvea® at the time of writing is £28.50 for 20 tablets.¹²

An audit conducted in Canada (where this drug combination is marketed as Diclectin) found that the average number of tablets taken per day was 4, with an average treatment duration of 5.27 weeks (37 days).¹³

Estimated number of tablets per course: 148

Estimated average cost per patient: £211 per patient

Current anti-emetic choices are usually taken on an as required basis to minimise possible exposure of the foetus as much as possible. Xonvea® needs to be administered as a course of treatment and is not recommended on an as required basis. Table 1 shows comparative costs of treatment options assuming that they are taken on a regular basis over a period of 37 days.

Table 1: Comparative costs of treatment options.¹²

Drug	Cost per pack	Dose	Cost if taken regularly for 37 days
Xonvea®	£28.50 for 20	4 tablets per day regularly	£210.90
Cyclizine 50mg tablets	£6.81 for 100	50mg tds prn	£7.56
Promethazine teoclate 25mg tablets	£3.13 for 28	25mg qds prn	£16.54
Prochlorperazine 5mg tablets	£0.73 for 28	10mg tds prn	£2.89
Metoclopramide 10mg tablets	£0.61 for 28	10mg tds prn	£2.42

National guidance

Current RCOG and NICE guidelines do not include recommendations on the use of doxylamine and pyridoxine for NVP.^{3,5} Doxylamine and pyridoxine is listed as an item for review by the RMOCs, but at the time of writing, there was no expected date for publication for the RMOCs guidelines.¹⁴ These recommendations will be reviewed in the light of new evidence and/or publication of new national

guidance (including from the RCOG and the RMOCs).

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Document history

PAC approval date	14th June 2019
Version	1
Consultation process	PAC members East of England clinicians via PAC members
QA process	Katie Smith, Senior Clinical Pharmacist, PrescQIPP. 17th June 2019

References

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Assessment against ethical and commissioning principles

Treatment assessed

Doxylamine succinate 10mg and pyridoxine hydrochloride 10mg delayed-release (Xonvea®) for nausea and vomiting in pregnancy.

East of England Priorities Advisory Committee interim recommendations

- Prescribing of doxylamine and pyridoxine (Xonvea®) for nausea and vomiting in pregnancy is NOT recommended in primary care.
- There is insufficient information for clinical superiority or cost effectiveness for doxylamine and pyridoxine in comparison with other recognised non-pharmacological and pharmacological ways to manage nausea and vomiting in pregnancy.
- Patients presenting with nausea and vomiting in pregnancy should be managed in line with current Royal College of Obstetrician RCOG guidelines.
- These recommendations will be reviewed in the light of new evidence and/or publication of new national guidance (including from the RCOG and the RMOCs).

Clinical effectiveness

Doxylamine and pyridoxine has been shown to improve symptoms of NVP compared with placebo however, there is no high-quality evidence that shows that the combination of doxylamine and pyridoxine is more effective than other antiemetics.

Cost effectiveness

There is no cost-effectiveness data for Xonvea®. There is currently no evidence that the use of Xonvea® will prevent progression of less severe NVP or that it will reduce hospital admissions.

Xonvea® needs to be administered as a course of treatment over a few days and is not recommended on an as required basis. An average course of 37 days is estimated to cost £211. Costs for current anti-emetic options taken regularly over the same duration range from £2.42 to £16.54, however, current anti-emetic choices are usually taken on an as required basis to minimise possible exposure of the fetus as much as possible, and therefore actual costs are likely to be less.

Equity

None identified.

Needs of the community

The needs of the community are considered to be low as well established alternative treatments exist.

Need for healthcare (incorporates patient choice and exceptional need)

Non pharmacological treatment is preferable and where deemed necessary, well established alternative treatments exist.

Policy drivers

None

Disinvestment

Xonvea® is significantly more expensive than existing established treatments and use may result in funding being diverted from other healthcare priorities.