

Xonvea®

doxylamine succinate/
pyridoxine hydrochloride



XONVEA® is the only licensed
treatment of NVP in the UK¹

Effectiveness of delayed-release doxylamine and pyridoxine for nausea and vomiting of pregnancy: a randomised placebo controlled trial

Koren G *et al.* Effectiveness of delayed-release doxylamine and pyridoxine for nausea and vomiting of pregnancy: a randomized placebo controlled trial. *Am J Obstet Gynecol.* 2010 Dec;203(6):571.e1-7. doi: 10.1016/j.ajog.2010.07.030. Epub 2010 Sep 16

XONVEA® is indicated for the treatment of nausea and vomiting of pregnancy (NVP) in pregnant women ≥ 18 years who do not respond to conservative management.²

Adverse events should be reported.
Reporting forms and information can be found at
www.mhra.gov.uk/yellowcard or search for MHRA Yellow
Card in the Google Play or Apple App store. Adverse events
should also be reported to Exeltis UK Limited by email to
pharmacovigilance.uk@exeltis.com

Care should be taken when prescribing in pregnancy as
medicines can cross the placenta and may affect the foetus



Objective:

Evaluate the effectiveness of XONVEA®* compared to placebo for controlling nausea and vomiting of pregnancy

*delayed-release combination of doxylamine succinate (10 mg) and pyridoxine hydrochloride (10 mg). Note, in this paper XONVEA® is referred to as Diclectin, the brand name used in Canada

Primary endpoint:

Change from baseline to Day 15 in the pregnancy unique quantification of emesis (PUQE) score for those patients receiving XONVEA® vs placebo

- PUQE incorporates number of daily vomiting episodes, number of daily retching episodes, and length of daily nausea in hours, for an overall score of symptoms rated from 3 (no symptoms) to 15 (most severe)

XONVEA® met its primary symptom control endpoint – demonstrating a significant reduction in PUQE symptom domain score from baseline to Day 15 compared to placebo (P=0.006)²

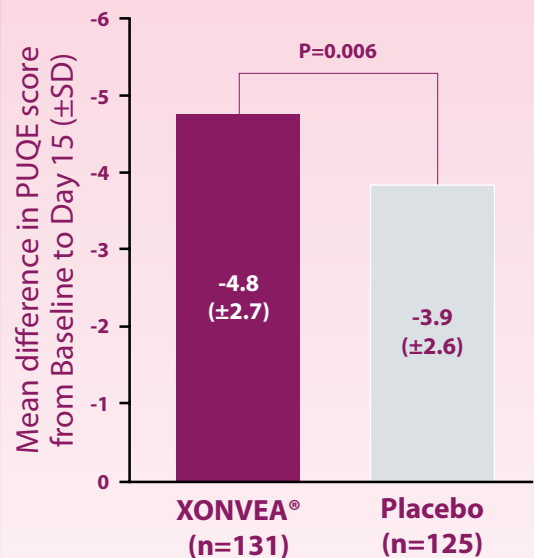
- XONVEA® delivered a **4.8-point reduction in the PUQE symptom domain score**

Table as shown in the Summary of Product Characteristics²

PUQE score	XONVEA®	Placebo	Treatment difference [95% Confidence Interval]
Baseline	9.0±2.1	8.8±2.1	
Change from baseline at Day 15	-4.8±2.7	-3.9±2.6	-0.9 [-1.2, -0.2]

The PUQE score incorporates the number of daily vomiting episodes, number of daily retching episodes, and length of daily nausea in hours, for an overall score of symptoms rated from 3 (no symptoms) to 15 (most severe).

Change in PUQE score from Baseline to Day 15 Primary endpoint



Adapted from Koren *et al.* 2010

Data shown are the ITT population, inclusive of any subject who took at least one dose of study medication and had at least one post-baseline PUQE measurement.

Other endpoints:

All endpoints compare outcomes for patients receiving XONVEA® vs those on placebo

Secondary effectiveness endpoints

- Change from baseline to Day 15 in quality of life
 - global assessment of well-being score, a patient report of present well-being, from zero (worst possible) to 10 (best possible)
- Day-by-day area under the curve for change in PUQE from baseline
- Time lost from employment between baseline and Day 15
- Number of women who continued with (blinded) compassionate use of medication after Day 15 (XONVEA® or placebo)



Other endpoints

- Number of patients who reported concurrent use of alternate therapy for nausea and vomiting of pregnancy (NVP) during the study (to Day 15)
 - Therapies included management strategies such as nutritional modifications, teas, aromatherapy, massage, and yoga
- Frequency and severity of all adverse events (AEs) during the study (to Day 15)

Method:

- Design:** double-blind, randomised, multicentre, placebo-controlled trial
- Inclusion:** pregnant women, ≥ 18 years of age, gestational age range of 7-14 weeks, suffering from nausea and vomiting of pregnancy with a PUQE score ≥ 6 , and had not responded to conservative management consisting of dietary/lifestyle advice
- Exclusion:** treatment with other antiemetics, chronic medical conditions, inability to communicate in English or Spanish
- Dosage:** minimum dose: 2 tablets daily at bedtime. Maximal dose: 4 tablets daily (dose increased dependent on symptom control)
- Protocol:** 15-day study, with study drug administered for 14 days

- Subjects completed PUQE score and study diary every morning before study dose at approximately the same time each day
- Subjects completed global assessment of wellbeing scale of PUQE on Day 1, 8, and 14, at the same time PUQE score was completed
- Telephone contact on Day 2, 6, 12, and 14 assessed diary information, AEs, concomitant medications, and compliance with study medication
- Patients returned to the clinic prior to their morning dose on Day 4, Day 8, and Day 15 (all ± 1 day) to collect diary reports and complete all study-related assessments
- Day 15 marked the end of study visit
- A follow-up phone call was conducted 30 days after final dosing for patients completing treatment period or early termination
- AEs and concomitant medications were recorded at all visits and follow-up phone calls

Compassionate use:

- Following final study visit (Day 15), patients were offered ongoing compassionate use of the product they had received (XONVEA® or placebo)
- If compassionate use was commenced, drug accountability and dispensing was conducted at clinic visits and AEs were reported during the compassionate use period
- All AEs and concomitant medications reported and recorded on the case report form for first 30 days of compassionate use. After first 30 days, only serious AEs were recorded

Results:

Patients included 298 pregnant women who were assessed for eligibility. 261 received ≥ 1 dose of study medication. 256 had ≥ 1 post-baseline PUQE and were included in the intent to treat (ITT) population (131 XONVEA[®], 125 placebo)

There were no significant differences between treatment groups in any demographic or baseline medical characteristic assessed

Over the treatment period, 19% of XONVEA[®]-treated patients remained on two tablets daily, 21% three tablets daily, and 60% received four tablets daily³

Table: Baseline characteristics for the ITT population

Characteristic, mean \pm SD	XONVEA [®] (n=131)	Placebo (n=125)	P value
Gestational age at enrolment, weeks	9.3 \pm 2.0	9.3 \pm 1.8	0.75
PUQE score at enrolment	9.0 \pm 2.1	8.8 \pm 2.1	0.44
Global assessment of well-being	5.0 \pm 2.3	5.4 \pm 2.2	

Primary endpoint:

XONVEA® led to significantly greater improvements from baseline to Day 15 vs placebo in PUQE score:

- **XONVEA®: -4.8 ± 2.7 , vs placebo: -3.9 ± 2.6 (p=0.006)**

Other endpoints (from baseline to Day 15)

- Global assessment of well-being: significantly greater improvements for XONVEA® vs placebo
 - **XONVEA®: 2.8 ± 2.8 , vs placebo: 1.8 ± 2.2 (p=0.005)**
- Mean area under the curve for change in PUQE from baseline as measured day-by-day: significantly greater improvements with XONVEA® vs placebo
 - **XONVEA®: 61.5 ± 36.9 , vs placebo: 53.5 ± 37.5 (p< 0.0001)**
- Time lost from employment: trend toward more time lost in placebo group vs XONVEA®
 - **XONVEA®: 0.92 ± 3.86 , vs placebo: 2.37 ± 10.23 (not significant, p=0.06)**
- Continuation of compassionate use: after Day 15, significantly more women receiving XONVEA® asked to continue compassionate use, vs placebo
 - **XONVEA®: 48.9%, vs placebo: 32.8% (p=0.009)**
- Alternate therapies: significantly more women receiving placebo than XONVEA® used alternate therapies for NVP symptoms concomitantly
 - **XONVEA®: n=31, 23.7%; vs placebo: n=46, 36% (p=0.04)**

Tolerability:

- Use of XONVEA® was not associated with an increased rate of any AE as compared with placebo (all differences were non-significant)

Table: Treatment emergent adverse events for the ITT population

Adverse event, n (%)	XONVEA® (n=131)	Placebo (n=125)	P value
Somnolence	19 (14.5%)	15 (2.0%)	0.54
Dry mouth	4 (3.0%)	1 (0.8%)	0.37
Hypersensitivity	1 (0.8%)	0	>0.99
Dizziness	8 (6.0%)	8 (6.4%)	0.94
Headache	17 (13.0%)	20 (16.0%)	0.51
Loss of consciousness	0	1 (0.8%)	0.49

Limitations:

Study length: 15-day trial, including 10 potential business days

- Analysis of time lost from employment showed non-significant trend in favour of XONVEA®
- There is a greater likelihood that this difference might have translated into a significant economic impact if a longer study had extended to the typical 6–8-week duration of NVP symptoms

Timing of medication initiation:

- NVP symptoms tend to subside spontaneously in most women by end of first trimester
- In this study, NVP symptoms typically started at 6 weeks of gestation, but average recruitment into the trial was around Week 9 of gestation, when symptoms may begin to subside

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Prescribing information
can be accessed [HERE](#)

[CLICK HERE](#) to visit the XONVEA[®] promotional website

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References:

1. Nelson-Piercy et al; Royal College of Obstetricians and Gynaecologists. The Management of Nausea and Vomiting in Pregnancy and Hyperemesis Gravidarum (Green-top Guideline No. 69). BJOG. 2024.
2. Xonvea 10 mg/10 mg gastro-resistant tablets. Summary of Product Characteristics.
3. Koren, G., Clark, S., Hankins, G. D., Caritis, S. N., Miodovnik, M., Umans, J. G., & Mattison, D. R. (2010). Effectiveness of delayed-release doxylamine and pyridoxine for nausea and vomiting of pregnancy: a randomized placebo controlled trial. American journal of obstetrics and gynecology, 203(6), 571.e1–571.e5717.



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