Northern (NHS) Treatment Advisory Group

Treatment Appraisal: Decision Summary

Date	26th February 2019
Appraisal & Details	The Northern (NHS) Treatment Advisory Group considered an appraisal of **Doxylamine/Pyridoxine (Xonvea®) for nausea & vomiting in pregnancy**
Recommendation	**The Northern (NHS) Treatment Advisory Group <u>does not</u> currently recommend the use of Doxylamine/Pyridoxine (Xonvea®) for the management of nausea & vomiting in pregnancy.** It was noted that a NICE Evidence Summary or TA is not yet available, and the drug has been referred to Regional Medicines Optimisation Committee (RMOC) for a national recommendation. This NTAG recommendation will be reviewed in light of publication of a NICE and/or RMOC recommendation, or updated clinical guidelines from the Royal College of Obstetricians and Gynaecologists. The group recognised that current treatment options are unlicensed in pregnancy but felt that guidance from RCOG was sufficient to justify current practice until such time that a national recommendation from RMOC is available, or RCOG guidelines are updated.
Clinical evidence summary	Despite widespread clinical use, there is limited evidence from randomised controlled trials demonstrating the efficacy and safety of this combination in the treatment of NVP. A single randomised 15-day trial compared Doxylamine/Pyridoxine (Diclectin®) to placebo in women with symptoms of NVP. At day 15, Doxylamine/Pyridoxine (Diclectin®) treatment was associated with a significantly greater improvement in symptoms of NVP compared with placebo, as assessed using the PUQE score (-0.9; p=0.006). The clinical significance of such a modest improvement in the PUQE score, less than one point on a 13-point scale has not been clearly established. However, the MHRA Assessment Report on Doxylamine/Pyridoxine (Xonvea®) states that the statistical differences represent improvements that are clinically meaningful for women suffering from NVP, and could represent a change from three hours of nausea per day to one hour or less.
Safety	Doxylamine succinate is a sedating antihistamine, and safety concerns with Xonvea® are expected to be primarily related to this component. Pyridoxine hydrochloride is generally recognized as having no adverse effects. No new or unexpected safety concerns were identified in the pivotal study. There is extensive post-marketing experience (>33 million pregnancies worldwide) regarding the use of the combination of doxylamine succinate and pyridoxine hydrochloride (with or without dicyclomine hydrochloride) in women with NVP. The safety and efficacy in women with hyperemesis gravidarum has not been assessed.
Patient Perspective	Xonvea® is the only drug specifically licensed in the UK for the treatment of NVP. It is intended for use in women with symptoms of NVP that do not respond to conservative management. When conservative management has failed, the RCOG recommends antihistamines (H1 receptor antagonists) and phenothiazines as firstline antiemetics for NVP, as there are adequate safety

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<table>
<tr><td></td><td>and efficacy data to support this recommendation. Combinations of different drugs should be used in women who do not respond to a single antiemetic. Although none of these medicines are specifically licensed to treat NVP, there is reasonable experience with their (off-label) use in clinical practice, usually at doses consistent with their licensed use.
NICE guidance on antenatal care for uncomplicated pregnancies states that antihistamines appear to be effective in reducing symptoms of nausea and vomiting in early pregnancy.</td></tr>
<tr><td>Cost analysis summary</td><td>The list price of Xonvea® is £28.50 for 20 tablets (exc. VAT). Assuming an average dose of three tablets daily, Xonvea® costs £29.92 per patient per week, which equates to a total cost of around £180 per patient, for a 6-week course. The estimated weekly cost of RCOG recommended oral antiemetic therapies prescribed off-label for NVP are shown in the table below:
<table>
<tr><th>Intervention</th><th>Estimated weekly cost at lowest dose</th><th>Estimated weekly cost at maximum dose</th></tr>
<tr><td colspan="3">First line</td></tr>
<tr><td>Cyclizine 50 mg 8 hourly</td><td>£1.33</td><td>£1.33</td></tr>
<tr><td>Prochlorperazine 5–10 mg 6–8 hourly</td><td>£0.53</td><td>£1.40</td></tr>
<tr><td>Promethazine 12.5–25 mg 4–8 hourly</td><td>£1.46</td><td>£5.85</td></tr>
<tr><td colspan="3">Second line</td></tr>
<tr><td>Metoclopramide 5–10 mg 8 hourly</td><td>£0.21</td><td>£0.42</td></tr>
<tr><td>Ondansetron 4–8 mg 6–8 hourly</td><td>£1.79</td><td>£4.84</td></tr>
</table></td></tr>
<tr><td>Financial impact

PbR: In tariff</td><td>The financial impact of this recommendation is expected to be nil.</td></tr>
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