

## USE OF ONDANSETRON IN PREGNANCY

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A corresponding **bumps** patient information leaflet on ondansetron use in pregnancy is available at [www.medicinesinpregnancy.org](http://www.medicinesinpregnancy.org)

**SUMMARY:** Ondansetron is a selective 5-HT<sub>3</sub> serotonin antagonist used in the treatment of chemotherapy-induced and post-operative nausea and vomiting, and off-licence for nausea and vomiting in pregnancy (NVP) and hyperemesis gravidarum (HG).

The currently available data do not provide evidence that ondansetron use in the first trimester of pregnancy is associated with an increase in the overall malformation rate.

Although small numbers of studies have described statistically significant increased risks of both overall and specific cardiac malformations, namely septal defects, these data are conflicting. Furthermore, most of these studies did not utilise disease-matched ondansetron-unexposed control groups, therefore the possibility of confounding cannot be excluded.

Several studies have suggested that associations may exist between maternal ondansetron use and fetal orofacial clefts, specifically cleft palate alone. Whilst the available data are conflicting, should a true association exist, the absolute risk is likely to remain small (background rate ~0.11% vs. ondansetron-exposed rate ~0.14%).

Four studies which utilised data from three unique datasets have also suggested possible associations with overall or specific renal malformations. These observations require further investigation before adequate conclusions can be drawn.

Studies investigating the risk of miscarriage, intrauterine death/stillbirth, low birth weight, preterm delivery and neurodevelopmental impairment are more limited than those investigating malformation risks, but do not currently provide evidence suggestive of an increased risk of these outcomes following maternal ondansetron use in pregnancy.

Ondansetron should only be used during pregnancy where the benefits of treatment are considered to outweigh any potential fetal risks. Exposure to ondansetron at any stage in pregnancy would not usually be regarded as medical grounds for termination of pregnancy or

any additional fetal monitoring. However, other risk factors may be present in individual cases which may independently increase the risk of adverse pregnancy outcome. Clinicians are reminded of the importance of consideration of such factors when performing case-specific risk assessments.

**Related document:**      **Treatment of nausea and vomiting in pregnancy**

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Ondansetron is a selective 5-HT<sub>3</sub> serotonin antagonist used in the treatment of chemotherapy-induced and post-operative nausea and vomiting,<sup>[1]</sup> and increasingly as an off-licence medication in the treatment of nausea and vomiting in pregnancy (NVP) and hyperemesis gravidarum (HG).<sup>[2]</sup>

### **Preclinical (animal) data**

The frequency of malformations was not increased among the offspring of pregnant rats or rabbits treated respectively with 1.6-62 or 1-47 times the maximum human dose of ondansetron.<sup>[3]</sup> However, in some studies, reduced fetal weight, delayed skeletal ossification, and increased rates of fetal death were seen among the offspring of pregnant rabbits treated with four or more times the maximum human dose.<sup>[3]</sup>

A 2018 *in vitro* study which exposed gestational day 13 rat embryos to increasing doses of ondansetron identified that such exposures were associated with decreased embryonic heart rate in a dose-dependent manner, and ventricular arrhythmias at the highest doses.<sup>[4]</sup> As previously published, animal teratology studies had suggested ondansetron exposure to be related to arrhythmia-related anomalies (including cardiovascular and skeletal defects); the authors of this *in vitro* study suggested that these results provided a plausible biological mechanism (induction of fetal ventricular arrhythmia) by which fetal ondansetron exposure could produce cardiac defects. The relevance of these findings to human embryogenesis is unclear, especially given that the most recently available epidemiological data call into question the previously suggested association between gestational ondansetron exposure and congenital heart defects.

### **Human data**

Often, data from observational sources or case reports, including data collected by UKTIS, may be confounded by maternal co-ingestion of a number of drugs, at varying doses, and for a range of indications. The severity of the underlying maternal condition, where relevant, is frequently unknown and information on other potential confounding variables may be incomplete. These factors should be considered when interpreting observational human pregnancy data.

Only controlled studies which utilise statistical tests to compare rates of adverse outcomes between ondansetron-exposed and unexposed control groups have been considered in this monograph. The available data concerning fetal outcomes following gestational ondansetron use in pregnancy therefore consist of 15 controlled studies and a meta-analysis which collectively describe more than 168,000 unique exposed pregnancies. The findings of these studies are summarised in the relevant sections below.

### **Pharmacokinetic data**

Transplacental passage of ondansetron has been demonstrated at term, and pregnancy has not been demonstrated to alter the maternal distribution.<sup>[5]</sup> Another study described decreased maternal plasma concentrations with increasing gestational age in a single patient, which the authors thought likely due to increased CYP3A4 and CYP2D6 activity.<sup>[6]</sup> As this result was described in a single patient, additional pharmacokinetic and pharmacodynamic data are needed to confirm the findings, and these data cannot currently be used to support recommendations concerning dose alterations in pregnancy.

### ***Miscarriage***

Studies investigating relationships between gestational exposures and the occurrence of miscarriage should be interpreted with caution. Miscarriage prior to the recognition of pregnancy, or the pregnancy being reported to a clinician, is likely to be common; as such, observational studies likely underestimate true rates of early pregnancy loss. Additionally, the risk of miscarriage decreases as pregnancy progresses and elective termination acts as a competing risk. Correction for exposed and control group differences in stage of pregnancy at recruitment, and variation in the rate of elective termination, is therefore essential, but rarely performed.

The risk of miscarriage has been assessed in a collective total of more than 3,000 ondansetron-exposed pregnancies from three studies,<sup>[7-9]</sup> two of which utilised disease-matched ondansetron-unexposed comparator groups. All of these studies reported much lower rates of miscarriage than the expected background rate of 10-20%, and none identified statistically significant increased risks following maternal ondansetron use.<sup>[7-9]</sup>

### ***Congenital malformations/anomalies***

The available data concerning malformation risks following maternal first trimester ondansetron exposure are provided from 13 controlled studies (including three retrospective case-control studies, two retrospective cohort studies and eight prospective cohort studies) which collected data from 11 unique data sources to report the outcomes of more than 167,000 unique exposed pregnancies, only a small number of which were not confirmed to have been exposed in the first trimester (n=165). A 2019 meta-analysis also combined data from up to eight of these studies (published between 2004 and 2016 only).

### **Overall malformation rates**

Ten studies, including one meta-analysis of data from five studies, collectively including more than 91,000 unique first trimester-exposed pregnancies have assessed the overall malformation rate following maternal ondansetron use in pregnancy.<sup>[7-16]</sup> The majority of these studies,<sup>[7-9, 12-15]</sup> including the largest and most statistically robust (>88,000 first trimester exposures)<sup>[14]</sup> and the primary analysis of the meta-analysis<sup>[16]</sup>, did not identify increased risks in comparison with disease-matched and/or healthy or population unexposed controls.

Given the wealth of evidence available, on the whole these data do not suggest that ondansetron use in the first trimester increases the overall malformation rate.

### **Heart defects**

Seven studies, including one meta-analysis of data pooled from five studies, which collectively included more than 168,000 unique first trimester-exposed pregnancies, have assessed overall and specific heart malformation rates following maternal ondansetron use in pregnancy.<sup>[9, 10, 13, 14, 16-18]</sup> Although the available data consist of a very large number of ondansetron-exposed pregnancies, the data remain limited as the majority of the available studies include exposure at any time in the

first trimester rather than during the critical period of fetal heart development (<10 weeks gestational age).

### *Overall heart defects*

Available data are conflicting, with three<sup>[10, 13, 18]</sup> of six studies investigating overall heart malformation rates,<sup>[9, 10, 13, 14, 16, 18]</sup> suggesting statistically significant increased risks (2, 1.6 and 1.4-fold) following maternal ondansetron use. However, the meta-analysis, which included data from five studies, did not identify an increased risk for overall cardiac malformations in the primary analysis<sup>[16]</sup>, and the findings from one of the primary data studies<sup>[18]</sup> (not included in the meta-analysis) were likely influenced by the severity of the condition, which was not adequately controlled for. Finally, the largest of the available studies, which included more than 88,000 ondansetron-exposed pregnancies and utilised a propensity score method to account for data confounding, did not describe a statistically significant increased risk.<sup>[14]</sup> In this study, the authors also performed sensitivity analyses and restricted their dataset to only include ondansetron-exposed pregnancies if the medication was used during a period considered to be relevant for inducing heart defects (six to 12 weeks of gestation). This restricted analysis also did not identify a statistically significant increased risk following maternal ondansetron use.<sup>[14]</sup>

Overall, the available data does not provide robust evidence to suggest that ondansetron use in pregnancy increases the overall heart malformation rate.

### *Specific heart defects*

Four studies have investigated the risk of specific cardiac defects following maternal ondansetron use in pregnancy.<sup>[13, 14, 17, 18]</sup>

Both studies, which assessed the risk of any septum defect, described statistically significant increased risks.<sup>[13, 18]</sup> However, it is important to consider that neither of these studies utilised a disease-matched control group and, as such, a possibility of confounding by indication cannot be excluded.

Three studies<sup>[14, 17, 18]</sup> have assessed the risks of both atrial septal defects (ASD) and, separately, ventricular septal defects (VSD), with two not describing statistically significant increased risks for either defect.<sup>[14, 17]</sup> The study, which provided evidence of an association with ASD and VSD, utilised two exposed groups.<sup>[18]</sup> The first consisted of women who had been administered ondansetron in a clinical setting (n>5,000) and the analysis of this data suggested approximate 1.5 and 1.3-fold statistically significant increased risks of ASD and VSD respectively. However, when the second and larger exposure group was analysed, which also included ondansetron exposures defined by pharmacy dispensing records (n>76,000), the findings were no longer statistically significant. Furthermore, it is important to consider that the study which reported a significant increased risk did not utilise a disease-matched control group. Therefore data confounding cannot be excluded.

Two very large studies assessed the risk of atrioventricular septal defects (AVSD) with conflicting results. The first did not provide evidence of a statistically significant increased risk.<sup>[14]</sup> The second described a statistically significant approximate 2.7-fold increased risk for women exposed to ondansetron in a clinical setting, and a statistically significant approximate 1.25-fold increased risk for women clinically exposed or with dispensing records indicating exposure.<sup>[18]</sup> However, it is

important to consider that the second of these studies did not utilise a disease-matched control group and, as such, a possibility of data confounding cannot be excluded.

Overall, the available data does not provide robust evidence to suggest that ondansetron use in pregnancy increases the risk of specific cardiac malformations, but given that some point-estimates are elevated and statistically significant, further research is required.

### Orofacial clefts

Six studies, including one meta-analysis of data from three studies, have investigated the risk of overall or specific orofacial clefts following maternal ondansetron use in pregnancy.<sup>[14, 16-20]</sup>

#### *Overall orofacial clefts*

A 2019 meta-analysis, which included some previously unpublished data (derived from author communication) from three studies published up to 2016<sup>[16]</sup>, described no significant increase in the overall orofacial cleft rate following maternal ondansetron use in the first trimester.

Two additional studies published after the meta-analysis was performed have investigated the overall orofacial cleft rate following exposure to ondansetron, and have reported conflicting findings. The first of these studies included up to >76,000 ondansetron-exposed pregnancies and described non-significant 1.3 (exposure defined by medical administration only) and 1.12-fold (exposure defined by medical administration and dispensing data) increased risks.<sup>[18]</sup> However, the second study, which utilised a highly robust statistical analysis technique which controlled for a large number of confounding factors, described a statistically significant 1.3-fold increased risk.<sup>[14]</sup>

It is unclear if a true association exists between maternal first trimester ondansetron use and orofacial clefting. Should such an association exist, the absolute risk may still be quite small, equating to approximately three additional cases of oral cleft in every 10,000 ondansetron-exposed pregnancies relative to the expected background rate (11.1 per 10,000).

#### *Specific orofacial clefts*

Six studies, including one meta-analysis<sup>[16]</sup> of data from two studies which utilised an overlapping dataset,<sup>[17, 20]</sup> have investigated the risk of cleft palate following maternal first trimester ondansetron use.<sup>[10, 14, 16-18, 20]</sup> Three of these studies have provided possible evidence of an association.<sup>[14, 17, 19]</sup> However, in one study, which reported data from two unique datasets, a statistically significant association was observed in one dataset but not in the other.<sup>[17]</sup> These conflicting results produced a significant heterogeneity in the meta-analysis which meant that the combined results were not useful for determining risk.<sup>[16]</sup> Furthermore, in the largest and most statistically robust study, the primary analysis found no statistically significant increased risk of cleft palate alone following maternal first trimester ondansetron use.<sup>[14]</sup> However, a secondary analysis, which employed a high-dimensional propensity score method to account for potential residual confounding, described a statistically significant 1.3-fold increased risk.

Given the available data are currently conflicting, it is unclear if a true association exists between maternal first trimester ondansetron use and fetal cleft palate. Should such an association exist, the absolute risk may still be quite small, equating to approximately two additional cases of cleft palate in every 10,000 ondansetron-exposed pregnancies relative to the expected background rate (5.7 per 10,000).

Other studies have investigated the risk of cleft lip<sup>[14, 18]</sup> and cleft lip with or without cleft palate<sup>[14, 17-19]</sup>, with none finding any statistically significant increased risks or associations between exposure and outcome.

#### ***Other specific defects***

Several studies have also reported associations with other specific congenital malformations. These have included ear<sup>[14]</sup> and respiratory anomalies<sup>[14]</sup>, and more specifically, laryngeal clefts<sup>[18]</sup> and craniosynostosis<sup>[18]</sup>. For the majority of these findings, associations have only ever been described in single studies and therefore could have resulted from chance observations. As such, further studies are required to confirm or refute these observations. However, two studies have reported possible associations with diaphragmatic hernia<sup>[17, 18]</sup> and four studies have described possible associations with renal anomalies.<sup>[12, 17, 18, 20]</sup>

#### ***Intrauterine death/stillbirth***

The risk of intrauterine death/stillbirth has been investigated in a collective total of more than 3,000 ondansetron-exposed pregnancies from four studies<sup>[7-9, 15]</sup>, three of which utilised disease-matched ondansetron-unexposed comparator groups.<sup>[7, 8, 15]</sup> None of these studies described increased risks of intrauterine death and/or stillbirth following maternal ondansetron use.

#### ***Low birth weight/SGA***

Two studies have compared the incidence of small for gestational age among the infants of more than 1,800 unique women who used ondansetron in pregnancy, with neither describing statistically significant increased risks in comparison with healthy unexposed controls.<sup>[9, 21]</sup>

#### ***Preterm delivery***

Four studies, which collectively included more than 3,200 ondansetron-exposed pregnancies, have investigated the risk of preterm delivery (<37 weeks). Whilst the majority of these studies do not report a statistically significant increased risk<sup>[9, 12, 21]</sup>, one large study, which included 1,070 ondansetron-exposed pregnancies, has described an approximate 2-fold increased risk in comparison with both disease-matched and healthy ondansetron-unexposed controls.<sup>[8]</sup> However, these findings may have been influenced by retrospective enrolment which could have resulted in a sampling bias. As such, the available data do not currently provide conclusive evidence that maternal ondansetron use in pregnancy increases the risk of preterm delivery.

#### ***Neonatal complications***

No studies were located which investigated neonatal outcome following maternal exposure to ondansetron during pregnancy.

#### ***Neurodevelopment***

Two studies, which collectively included more than 350 ondansetron-exposed pregnancies, have investigated infant neurodevelopment following *in utero* exposure.<sup>[21, 22]</sup> Although available data remain limited, neither of these studies have demonstrated adverse effects.

The first study compared neurobehavioural outcomes between a cohort of children who had been exposed to either ondansetron or promethazine *in utero* (n=143) and a group of unexposed children (n=407). No significant differences were observed when the children were assessed at

seven days old, and subsequently between 17 and 66 months of age, however the ondansetron-exposed children were not analysed separately.<sup>[21]</sup>

The second study utilised a case-control design to compare gestational ondansetron exposure rates between children with and without neurodevelopmental impairments (gender and age matched), all of whom had mothers who experienced HG in pregnancy. The rates of ondansetron exposure did not significantly differ between the two groups.<sup>[22]</sup>

### **Carcinogenicity**

No studies were located which investigated cancer in the offspring following maternal exposure to ondansetron during pregnancy.

### **Paternal exposure**

Only studies which examine the effects of paternal exposure on offspring congenital malformation rate, development, cancer and reproductive potential are included here. Effects on sperm quality and the reproductive health of the exposed father are NOT included.

There were no reports found regarding paternal exposure to ondansetron.

### **Lactation**

For information on the therapeutic use of medicines during breastfeeding please consult the UKMi online lactation database ([www.sps.nhs.uk](http://www.sps.nhs.uk)) or contact the UKMi service enquiry line ([details can be found here](#)).

If you have concerns regarding toxicity in the child as a consequence of exposure to a drug or chemical during lactation please consult TOXBASE or contact the National Poisons Information Service on 0344 892 0111.

### **UKTIS data**

UKTIS has followed up 79 cases of ondansetron exposure during pregnancy. There were 70 prospective therapeutic exposures and nine retrospective cases.<sup>[23]</sup>

### **Prospective therapeutic exposure data**

The frequency of live-born infants with one or more major congenital malformation (1/63, 1.59%, 95% CI; 0.0829 to 9.68) was not significantly higher than the background rate (2-3%). However, due to the small number of exposed and affected cases, and the consequent wide confidence intervals, the conclusions that can be drawn from these data are limited.

<b>Trimester</b>	<b>Total pregnancies/ Total live born</b>	<b>Normal infants</b>	<b>Neonatal problems</b>	<b>Congenital malformations</b>		<b>ETOP</b>	<b>SA</b>	<b>IUD</b>
				<b>Minor</b>	<b>Major</b>			
1 <sup>st</sup>	20/17*	16*	-	-	1 <sup>a</sup>	2	3	-
1 <sup>st</sup> & 2 <sup>nd</sup>	6/6	4	1 <sup>b</sup>	1 <sup>c</sup>	-	-	-	-
2 <sup>nd</sup>	6/6	5	1 <sup>d</sup>	-	-	-	-	-
2 <sup>nd</sup> & 3 <sup>rd</sup>	2/2	-	1 <sup>e</sup>	1 <sup>f</sup>	-	-	-	-
3 <sup>rd</sup>	4/4	4	-	-	-	-	-	-
Throughout	12/12	10	1 <sup>g</sup>	1 <sup>h</sup>	-	-	-	-
Unknown	20/16 <sup>+</sup>	13 <sup>+</sup>	2 <sup>ij</sup>	1 <sup>k</sup>	-	1	1	3
<b>Total</b>	<b>70/63*<sup>+</sup></b>	<b>52*<sup>+</sup></b>	<b>6</b>	<b>4</b>	<b>1</b>	<b>3</b>	<b>4</b>	<b>3</b>

ETOP – elective termination of pregnancy, SA – spontaneous miscarriage, IUD – intrauterine death

\* - one set of triplets, <sup>+</sup> - one set of twins

<sup>a</sup> Exposure to ondansetron at 12/40, and sterculia and lactulose at an unknown stage of pregnancy. The outcome was an infant with a birthmark on the face and neck.

<sup>b</sup> Exposure to unreported doses of ondansetron, promethazine, cyclizine, metoclopramide and prochlorperazine from 8-14/40, and unreported doses of prochlorperazine suppositories at an unreported stage of pregnancy. The infant was born at term (38/40) but had a low birth weight (2,200 g) and developed hypoglycaemia for 2 days post-delivery.

<sup>c</sup> Exposure to 8mg ondansetron tds, 20mg omeprazole od and 30mg prednisolone from 10/40 to an unreported stage of the second trimester, 25mg amitriptyline daily at an unreported stage in the first and second trimester, and an overdose of amitriptyline (150mg) at 13/40. The infant was born preterm at 34/40 and required admission to NICU for one night. The infant also had ankyloglossia.

<sup>d</sup> Exposure to unreported doses of ondansetron, metoclopramide, cyclizine and prochlorperazine at 16/40, unreported doses of citalopram and 400mcg folic acid daily throughout the first trimester, 5mg folic acid daily from 16/40 to an unreported stage of pregnancy, and unreported doses of fluoxetine from 21-25/40. The infant was born at term but developed breathing problems which required admission to NICU; no cause was found and the infant was later discharged.

<sup>e</sup> Exposure to unreported doses of ondansetron from 24/40 to an unreported stage of pregnancy, unreported doses of metoclopramide and cyclizine from 9-24/40, unreported doses of amoxicillin at 17/40, and unreported doses of folic acid at an unreported stage of pregnancy. The infant was delivered preterm (34/40) and was born with pulmonary stenosis and a low birth weight (2,380 g), the infant also experienced hypoglycaemia and neonatal jaundice.

<sup>f</sup> Exposure to ondansetron between 13-28/40. The outcome was an infant with positional talipes.

<sup>g</sup> Exposure to ondansetron, diamorphine, cyclizine, and dalteparin throughout pregnancy, total parenteral nutrition (TPN) from 13/40, and fentanyl at an unreported stage of pregnancy. The outcome was a premature infant born at 33/40 requiring treatment on a neonatal unit for 3 weeks.

<sup>h</sup> Exposure to 4mg ondansetron daily, 200mg quinine tds, 10mg nifedipine bd, 5mg bisacodyl bd and 5mg levocetirizine daily throughout pregnancy, in addition to unreported doses of folic acid at an unreported stage of pregnancy. The infant was born with bilateral positional talipes.

<sup>i</sup> Exposure to unreported doses of ondansetron, zopiclone, prochlorperazine, metoclopramide and heparin at an unknown stage of pregnancy, and fluoxetine at 20/40. The outcome was an infant with intermittent twitching and eyes rolling upwards at 4 days of life.

<sup>j</sup> Exposure to ondansetron at an unreported stage of pregnancy. The infant was delivered at term in distress due to nuchal cord.

<sup>k</sup> Exposure to unreported doses of ondansetron, bisoprolol, metoclopramide, ferrous sulphate and prochlorperazine at an unknown stage of pregnancy, and domperidone between 0-9/40. The outcome was an infant with pyloric stenosis.

### **Retrospective therapeutic exposure data**

UKTIS occasionally receives retrospective information on the outcome of pregnancies. Although retrospective reports are biased in that adverse outcomes are more likely to be reported, these data may be useful in identifying patterns of malformations that may be suggestive of a teratogenic syndrome and are therefore analysed periodically. No specific pattern has been observed for ondansetron..

UKTIS have retrospective follow up data for nine pregnancies following therapeutic exposure to ondansetron. Two pregnancies resulted in healthy infants, details for the remaining cases are provided below.

<sup>a</sup> Exposure to ondansetron, fentanyl, morphine, midazolam, propofol, diclofenac, rocuronium and neostigmine at 5/40. The outcome was an infant with a cleft lip and palate and a large head.

<sup>b</sup> Exposure to ondansetron, metoclopramide and domperidone between 6-36/40. The outcome was a premature infant born at 36/40 with a very flat nasal bridge and congenital deafness.

<sup>c</sup> Exposure to ondansetron and prednisolone at an unknown stage of pregnancy. The outcome was an infant subsequently diagnosed with autism.

<sup>d</sup> Exposure to ondansetron, IV frusemide, domperidone, omeprazole, folic acid and allopurinol at an unknown stage of pregnancy, methotrexate at 20/40, and unspecified chemotherapeutic agents at an unknown stage of pregnancy. The outcome was a premature infant born at 34/40 with IUGR and subsequently diagnosed with cerebral palsy at 1 year of age.

<sup>e</sup> Exposure to ondansetron at an unknown stage of pregnancy and atovaquone/proguanil during the first trimester. The outcome was a premature infant born at 35/40 with scaphocephaly and red patches on the face and head.

<sup>f</sup> Exposure to ondansetron during the first and second trimesters. The outcome was a spontaneous abortion. No further details provided.

<sup>g</sup> Exposure to unreported doses of ondansetron and cyclizine in the first and second trimester, and 10mg prednisolone daily from 14-18/40. The large for gestational age infant (4,200 g) was delivered at term

### **Conclusions**

The currently available data do not provide evidence that ondansetron use in the first trimester of pregnancy is associated with an increase in the overall malformation rate.

Although small numbers of studies have described statistically significant increased risks of both overall and specific cardiac malformations, namely septal defects, these data are conflicting. Furthermore, most of these studies did not utilise disease-matched ondansetron-unexposed control groups and therefore the possibility of confounding cannot be excluded.

Several studies have suggested that associations may exist between maternal ondansetron use and fetal orofacial clefts, specifically cleft palate alone. Whilst the available data are conflicting, should a true association exist, the absolute risk is likely to remain small (background rate ~0.1% vs. ondansetron-exposed rate ~0.14%).

Four studies, which utilised data from three unique datasets, have also suggested possible associations with overall or specific renal malformations. These observations require further investigation before adequate conclusions can be drawn.

Studies investigating the risk of miscarriage, intrauterine death/stillbirth, low birth weight, preterm delivery and neurodevelopmental impairment are more limited than those investigating malformation risks but do not currently provide evidence suggestive of an increased risk of these outcomes following maternal ondansetron use in pregnancy.

Ondansetron should only be used during pregnancy where benefits of treatment are considered to outweigh any potential risks.

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**Disclaimer:** Every effort has been made to ensure that this monograph was accurate and up-to-date at the time of writing, however it cannot cover every eventuality and the information providers cannot be held responsible for any adverse outcomes of the measures recommended. There is a background incidence of major congenital malformations (2-3%), miscarriage (10-20%) and stillbirths (0.5%) irrespective of any drug or chemical exposure. **This information is intended for use by healthcare professionals only and may require expert clinical interpretation: such cases should be discussed with UKTIS.** The final decision regarding which treatment is used for an individual patient remains the clinical responsibility of the prescriber. This material may be freely reproduced for education and not for profit purposes within the UK National Health Service, however no linking to this website or reproduction by or for commercial organisations is permitted without the express written permission of this service. This document is regularly reviewed and updated. Only use UKTIS monographs downloaded directly from TOXBASE.org or UKTIS.org to ensure you are using the most up-to-date version.

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