

## Use of Ondansetron (“Zofran”) in pregnancy:

Ondansetron is a drug used to treat nausea and vomiting. It is widely used all over Australia and in many other first world countries to treat vomiting in pregnancy, including in Hyperemesis Gravidarum. It is used orally as wafers or tablets, or with severe hyperemesis with dehydration, intravenously. Many women seem to find that it is much better than anything else they have tried – often the only thing that works for them. Most Maternity Units in Australia use this drug in certain pregnant women; for example, the current South Australian Perinatal Practice Guidelines from Adelaide note that:

*“Ondansetron – may be prescribed for cases of severe hyperemesis gravidarum, in association with intravenous rehydration, thiamin and electrolyte correction. Give 4 – 8 mg intravenously or orally, 8 – 12 hourly, available as wafers to dissolve in the mouth”.*

At present in Australia, this drug is listed as Category B1, which means:

*“The safety of Ondansetron for use in human pregnancy has not been established. Evaluation of experimental animal studies does not indicate direct or indirect harmful effects with respect to the development of the embryo or fetus, the course of gestation, and perinatal and postnatal development. However, as animal studies are not always predictive of human response, the use of ondansetron in pregnancy is not recommended.”*

In the PBS (Pharmaceutical Benefits Scheme) in Australia, the only approved use of Ondansetron is for management of nausea and vomiting in cancer patients having Radiotherapy and/or Chemotherapy. Ondansetron is not approved by the PBS for the treatment of nausea and vomiting in pregnancy. Therefore, such use in pregnancy is a so-called “off-label” use of a medicine. (It should be noted that several other drugs are also used in pregnant women in an “off-label” use setting). So, if a woman is to use this drug in pregnancy, she should do so in this knowledge. This is a Prescription-only medicine.

As with all new drugs, it takes some time, typically years, to fully assess the safety and/or risks of using that (new) drug in pregnancy for both mothers and babies. However, Ondansetron has now been used for more than twenty-five (25) years in pregnant women. Several small studies over the years have raised some concerns about the possibility that this drug may increase the risk of fetal malformations in the exposed infants – especially fetal heart malformations and oral clefts (cleft lip and/or cleft palate).

However, recently (last year) a very important new study has been published – “Association of Maternal First-Trimester Ondansetron Use With Cardiac Malformations and Oral Clefts in Offspring (JAMA. 2018;320(23):2429-2437. doi:10.1001/jama.2018.18307). This study, involving 1.8 million women (a huge number) looked at the use of Ondansetron and concluded:

“Among offspring of mothers enrolled in Medicaid, first-trimester exposure to Ondansetron was not associated with cardiac malformations or congenital malformations overall after accounting for measured confounders but was associated with a small increased risk of oral clefts”. This increase in risk for oral clefts was small - accounting for about three (3) additional cases of oral clefts per 10,000 women taking Ondansetron in the study.

**While this is of some concern, the major finding of this study, that use of Ondansetron in the first-trimester (the time of greatest risk of a drug causing fetal malformations in general) was NOT associated with an increased risk of congenital malformations overall is very reassuring about the safety of this drug in pregnancy.**

**NB. There is no good information about the safety or risks of long-term Ondansetron use – that is for a prolonged time, extending well into the second and third trimesters.**

(SO'C Aug 2019).