

DRUG INFORMATION

Bob Buckham
Pamela Buffery
Judy Dalrymple
Sharon Gardiner



CLINICAL PHARMACOLOGY

Murray Barclay
Evan Begg
Petra Lowe
Jane Vella-Brincat
Mei Zhang

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QUESTION:

What is the safety of omeprazole in pregnancy?

BACKGROUND:

When omeprazole was first available, our ability to assess the safety during pregnancy was limited by a lack of human data. Therefore we recommended that alternatives with more data to support safety during pregnancy be used (such as ranitidine). More data is available now describing the safety of omeprazole in pregnancy, such that omeprazole can be considered relatively safe in this context. AstraZeneca, who marketed the original brand of omeprazole (Losec®), changed their datasheet in September 2006 to say "results from three prospective epidemiological studies indicate no adverse effects of omeprazole on pregnancy or on the health of the foetus/newborn child. Losec can be used during pregnancy" [1].

ANSWER:

The use of omeprazole during pregnancy does not increase the risk of fetal malformations according to several reports.

Clinical studies, a population-based cohort study and case reports conducted in the 1990s suggest that pregnant women exposed to omeprazole do not have a significantly higher rate of malformations compared with controls (pregnant women who received H2-antagonists or other known nonteratogens) [2-7]. These studies included limited data regarding the use of omeprazole during the first trimester of pregnancy.

A meta-analysis examining 593 proton pump inhibitor-exposed infants (including several of the studies already discussed [2,4,6,7]) found no significant correlation between first trimester fetal exposure and teratogenicity [8]. The combined relative risk of major fetal malformation with any proton pump inhibitor exposure was 1.18 (95% confidence interval: 0.72-1.94, $p=0.7$). The most common proton pump inhibitor taken was omeprazole. The median omeprazole dose was 20 mg daily, with a mean duration of therapy of 15.3 weeks (range 3 days to 42 weeks) [8].

More recently, a study of 955 infants born to mothers from the Swedish Medical Birth Registry who used omeprazole in first trimester ($n=863$) and/or second and third trimester ($n=131$) of pregnancy, reported five stillbirths and a total of 22 infants with malformations (including eight infants with cardiac defects) [9]. The overall risk of malformations was 2.3% (less than the population rate) [10] and omeprazole was therefore not associated with an increased fetal risk [9].

In a multicenter, prospective, controlled study comparing pregnancies exposed to proton pump inhibitors and those exposed to known non-teratogens, there was no difference in the rate of major malformations between omeprazole and the control groups [11]. There

were 233 cases of omeprazole (median daily dose of 20 mg for a median duration 22 days of treatment) during the first trimester. Of all the omeprazole exposures, there were 247 live births, 3 stillbirths, 24 spontaneous abortions and 26 elective abortions. Two of the the elective abortions were related to prenatal diagnosis of anomalies. Major congenital anomaly rate was 3.6% in the omeprazole group compared to 3.8% in the control group (p=0.9) [11].

CONCLUSION:

We are aware of nine studies looking at 1766 women who have taken omeprazole during pregnancy. More than 1000 of these involved first trimester use. The available data suggest that omeprazole is not associated with an increased risk of fetal malformations.

As with all drugs in pregnancy we would advise careful assessment of the risks and benefits prior to commencing therapy, particularly in the first trimester. When acid-suppression is required during pregnancy, we favour initial treatment with simple antacids such as calcium carbonate (Titalac®) and ranitidine due to longer experience with these agents. However, where these treatments have not provided adequate symptom relief, omeprazole use is probably reasonable.

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