IRISH MEDICINES BOARD

Fluoxetine and possible small risk of congenital cardiac defects

The Irish Medicines Board wishes to communicate the outcome of an EU review of recent epidemiological evidence which suggests a possible small increased risk of congenital cardiac defects in association with fluoxetine in early pregnancy, similar to that seen with paroxetine. There are insufficient data to draw conclusions on whether there is a similar risk for other antidepressants in the same class (i.e. selective serotonin reuptake inhibitors or SSRIs). The potential risks should be considered in the context of the benefits of treatment.

Fluoxetine is a commonly prescribed antidepressant belonging to the SSRI class of medicines. Following publication of a study and review which suggested a possible causal association between cardiovascular birth defects and the use of fluoxetine during the first three months of pregnancy, the Pharmacovigilance Working Party of the European Medicines Agency (PhVWP) considered the review and requested that the original marketing authorisation holder for fluoxetine conduct a systematic critical meta analysis of all available epidemiological data regarding the effects of first trimester fluoxetine exposure and the risk of congenital malformations with a particular focus on cardiac defects. The meta-analysis included data from nine studies.

The results suggest that fluoxetine is not associated with a risk of non-cardiac defects, and that any increased risk of malformations appears to be driven by a possible excess cardiac risk. The cardiac defects reported in the studies included in the meta analysis were varied, and ranged in severity from reversible ventricular septal defects to transposition of the great vessels. The background incidence of congenital cardiac defects is approximately 1/100. The meta-analysis results for fluoxetine are consistent with an increased absolute risk to less than 2/100 pregnancies. The current evidence indicates that the risk of congenital cardiac defects for fluoxetine is similar to that for paroxetine. The mechanism is unknown and it is possible that the effects may be a class-related phenomenon; however data are insufficient at present to issue advice about the risk with other SSRIs.

The PhVWP also considered that the small increase in risk of cardiovascular congenital malformations must be weighed against the risks of untreated depression during pregnancy. Untreated depression in pregnancy is associated with a variety of adverse outcomes, including low birth weight, preterm delivery, and lower Apgar scores.

The current Summary of Product Characteristics (SmPCs) and Package Leaflets (PLs) are being revised to reflect this information for fluoxetine-containing products.

Advice for Healthcare Professionals

- When prescribing fluoxetine to treat depression during pregnancy, prescribers should be aware that there may be a small increased risk of congenital cardiac defects in infants exposed in early pregnancy, similar to that seen with paroxetine.
- There are insufficient data to draw conclusions on the risk of congenital anomalies with other SSRIs, but the possibility of a class effect cannot be excluded.
- The potential increased risk should be considered in the context of the benefits of treating depression in pregnancy.

References available on request from the Irish Medicines Board