SSRIs (fluvoxamine, citalopram, escitalopram, fluoxetine and sertraline, paroxetine) and Possible increased risk of male infertility due to sperm impairment

Final SmPC and PL wording agreed by PhVWP March 2012

Doc.Ref.: CMDh/PhVWP/050/2012
March 2012, Rev0

SUMMARY OF PRODUCT CHARACTERISTICS & PACKAGE LEAFLET

Substance	SmPC wording section 4.6	SmPC wording section 5.3	PL wording
Fluvoxamine	Animal data have shown that fluvoxamine may affect sperm quality (see section 5.3). Human case reports with some SSRIs have shown that an effect on sperm quality is reversible. Impact on human fertility has not been observed so far.	Animal studies on fertility revealed reduction of mating performance, decreased sperm count, and fertility index at levels higher than human exposure.	Fluvoxamine has been shown to reduce the quality of sperm in animal studies. Theoretically, this could affect fertility, but impact on human fertility has not been observed as yet.
Citalopram	Animal data have shown that citalopram may affect sperm quality (see section 5.3). Human case reports with some SSRIs have shown that an effect on sperm quality is reversible. Impact on human fertility has not been observed so far.	Animal data have shown that citalopram induces a reduction of fertility index and pregnancy index, reduction in number in implantation and abnormal sperm at exposure well in excess of human exposure.	Citalopram has been shown to reduce the quality of sperm in animal studies. Theoretically, this could affect fertility, but impact on human fertility has not been observed as yet.
Escitalopram	Animal data have shown that citalopram may affect sperm quality (see section 5.3). Human case reports with some SSRIs have shown that an effect on sperm quality is reversible. Impact on human fertility has not been observed so far.	Animal data have shown that citalopram induces a reduction of fertility index and pregnancy index, reduction in number in implantation and abnormal sperm at exposure well in excess of human exposure. No animal data related to this aspect are available for escitalopram.	Citalopram, a medicine like escitalopram, has been shown to reduce the quality of sperm in animal studies. Theoretically, this could affect fertility, but impact on human fertility has not been observed as yet.
Fluoxetine	Animal data have shown that fluoxetine may affect sperm quality (see section 5.3). Human case reports with some SSRIs have shown that an effect on sperm quality is reversible. Impact on human fertility has not been observed so far.	Adult animal studies In a 2-generation rat reproduction study, fluoxetine did not produce adverse effects on the mating or fertility of rats, was not teratogenic, and did not affect growth, development, or reproductive parameters of the offspring. The concentrations in the diet provided doses approximately equivalent to 1.5, 3.9, and 9.7 mg fluoxetine/kg body weight. Male mice treated daily for 3 months with fluoxetine in the diet at a dose approximately equivalent to 31 mg/kg showed a decrease in testis weight and hypospermatogenesis. However, this dose level exceeded the maximum-tolerated dose (MTD) as significant signs of toxicity were seen.	Fluoxetine has been shown to reduce the quality of sperm in animal studies. Theoretically, this could affect fertility, but impact on human fertility has not been observed as yet.

		[Above data from adult animal studies in addition to the existing wording on juvenile animal studies]	
Sertraline	Animal data did not show an effect of sertraline on fertility parameters (see section 5.3.). Human case reports with some SSRIs have shown that an effect on sperm quality is reversible. Impact on human fertility has not been observed so far.	Animal data from rodents and non-rodents does not reveal effects on fertility.	Some medicines like sertraline may reduce the quality of sperm in animal studies. Theoretically, this could affect fertility, but impact on human fertility has not been observed as yet.
Paroxetine	Animal data have shown that paroxetine may affect sperm quality (see section 5.3). In vitro data with human material may suggest some effect on sperm quality, however, human case reports with some SSRIs (including paroxetine) have shown that an effect on sperm quality appears to be reversible. Impact on human fertility has not been observed so far.	Reproduction toxicity studies in rats have shown that paroxetine affects male and female fertility by reducing fertility index and pregnancy rate. In rats, increased pup mortality and delayed ossification were observed. The latter effects were likely related to maternal toxicity and are not considered a direct effect on the foetus/neonate.	Paroxetine has been shown to reduce the quality of sperm in animal studies. Theoretically, this could affect fertility, but impact on human fertility has not been observed as yet.