SPC and PL Wording for Non-Steroidal Anti-inflammatory Drugs (NSAIDs) with regard to disturbances of female fertility as agreed by the PhVWP in September 2001 and revised by the PhVWP for ibuprofen non-prescription in January and March 2003 and revised by the PhVWP for ketoprofen and naproxen non-prescription in May 2004 and for acetyl-salicylic acid > 500mg / day and equipotent derivates as agreed by PhVWP in May 2004

for COX I and/or II inhibiting NSAIDs, excluding salicylic acid and its derivates and non-prescription ibuprofen, ketoprofen and naproxen:

Summary of Product Characteristics (SPC) - 4.4 Special warnings and precautions for use

The use of <INN> may impair female fertility and is not recommended in women attempting to conceive. In women who have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of <INN> should be considered.

Package Leaflet (PL)

<INN> may make it more difficult to become pregnant. You should inform your doctor if you are planning to become pregnant or if you have problems to become pregnant.

for non-prescription formulations of ibuprofen, ketoprofen and naproxen and acetylsalicylic acid > 500 mg/d and equipotent acetyl-salicylic acid derivates:

Summary of Product Characteristics (SPC) - 4.4 Special warnings and precautions for use

There is some evidence that drugs which inhibit cyclo-oxygenase / prostaglandin synthesis may cause impairment of female fertility by an effect on ovulation. This is reversible on withdrawal of treatment.

Package Leaflet (PL)

The product belongs to a group of medicines (NSAIDs) which may impair the fertility in women. This effect is reversible on stopping the medicine.

Note: For acetyl-salicylic acid "(NDAIDs)" need to be omitted.
ACETYLSALICYLIC ACID ≥ 100 mg/unit

4.3 Contraindication

Doses > 100 mg/day during the third trimester of pregnancy

4.6 Pregnancy and lactation

Pregnancy

Low doses (up to 100 mg/day):
Clinical studies indicate that doses up to 100 mg/day for restricted obstetrical use, which require specialised monitoring, appear safe.

Doses of 100-500 mg/day:
There is insufficient clinical experience regarding the use of doses above 100 mg/day up to 500 mg/day. Therefore, the recommendations below for doses of 500 mg/day and above apply also for this dose range.

Doses of 500 mg/day and above:
Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/foetal development. Data from epidemiological studies suggest an increased risk of miscarriage and of cardiac malformation and gastroschisis after use of a prostaglandin synthesis inhibitor in early pregnancy. The absolute risk for cardiovascular malformation was increased from less than 1%, up to approximately 1.5%. The risk is believed to increase with dose and duration of therapy. In animals, administration of a prostaglandin synthesis inhibitor has been shown to result in increased pre- and post-implantation loss and embryo-foetal lethality. In addition, increased incidences of various malformations, including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during the organogenetic period. During the first and second trimester of pregnancy, acetyl salicylic acid should not be given unless clearly necessary. If acetylsalicylic acid is used by a woman attempting to conceive, or during the first and second trimester of pregnancy, the dose should be kept as low and duration of treatment as short as possible.

During the third trimester of pregnancy, all prostaglandin synthesis inhibitors may expose the foetus to:
- cardiopulmonary toxicity (with premature closure of the ductus arteriosus and pulmonary hypertension);
- renal dysfunction, which may progress to renal failure with oligo-hydroamnios;

the mother and the neonate, at the end of pregnancy, to:
- possible prolongation of bleeding time, an anti-aggregating effect which may occur even at very low doses.
- inhibition of uterine contractions resulting in delayed or prolonged labour.

Consequently, acetylsalicylic acid at doses of 100 mg/day and higher is contraindicated during the third trimester of pregnancy.
NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (incl Selective COX II-Inhibitors)

4.3 Contraindication

Third trimester of pregnancy

4.6 Pregnancy and lactation

Pregnancy

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- cardiopulmonary toxicity (with premature closure of the ductus arteriosus and pulmonary hypertension);
- renal dysfunction, which may progress to renal failure with oligo-hydroamniosis;

the mother and the neonate, at the end of pregnancy, to:
- possible prolongation of bleeding time, an anti-aggregating effect which may occur even at very low doses.
- inhibition of uterine contractions resulting in delayed or prolonged labour.

Consequently, <INN> is contraindicated during the third trimester of pregnancy.