



Annex I: Summary of Product Characteristics for Quinapril

Section 4.3 Contraindication

Second and third trimesters of pregnancy (see sections 4.4 and 4.6).

[Comment: No contraindication in Section 4.3 for lactation.]

Section 4.4 Special warnings and precautions for use

Pregnancy: ACE inhibitors should not be initiated during pregnancy. Unless continued ACE inhibitor therapy is considered essential, patients planning pregnancy should be changed to alternative antihypertensive treatments which have an established safety profile for use in pregnancy. When pregnancy is diagnosed, treatment with ACE inhibitors should be stopped immediately, and, if appropriate, alternative therapy should be started (see sections 4.3 and 4.6).

Section 4.6 Pregnancy and lactation

Pregnancy:

The use of ACE inhibitors is not recommended during the first trimester of pregnancy (see section 4.4). The use of ACE inhibitors is contraindicated during the 2nd and 3rd trimester of pregnancy (see sections 4.3 and 4.4).

Epidemiological evidence regarding the risk of teratogenicity following exposure to ACE inhibitors during the first trimester of pregnancy has not been conclusive; however a small increase in risk cannot be excluded. Unless continued ACE inhibitor therapy is considered essential, patients planning pregnancy should be changed to alternative antihypertensive treatments which have an established safety profile for use in pregnancy. When pregnancy is diagnosed, treatment with ACE inhibitors should be stopped immediately, and, if appropriate, alternative therapy should be started.

Exposure to ACE inhibitor therapy during the second and third trimesters is known to induce human fetotoxicity (decreased renal function, oligohydramnios, skull ossification retardation) and neonatal toxicity (renal failure, hypotension, hyperkalaemia). (See section 5.3.) Should exposure to ACE inhibitor have occurred from the second trimester of pregnancy, ultrasound check of renal function and skull is recommended. Infants whose mothers have taken ACE inhibitors should be closely observed for hypotension (see sections 4.3 and 4.4).

Lactation:

Limited pharmacokinetic data demonstrate very low concentrations in breast milk (see section 5.2). Although these concentrations seem to be clinically irrelevant, the use of [Product] in breastfeeding is not recommended for preterm infants and for the first few weeks after delivery, because of the hypothetical risk of cardiovascular and renal effects and because there is not enough clinical experience.

In the case of an older infant, the use of [Product] in a breast-feeding mother may be considered if this treatment is necessary for the mother and the child is observed for any adverse effect.

Section 5.2 Pharmacokinetic properties

Lactation:

After a single oral dose of 20 mg of quinapril in six breast-feeding women, the M/P (milk to plasma ratio) for quinapril was 0.12. Quinapril was not detected in milk after 4 hours after the

dose. Quinalaprilat milk levels were undetectable ($<5 \mu\text{g/L}$) at all time points. It is estimated that a breastfed infant would receive about 1.6% of the maternal weight-adjusted dosage of quinapril.

Annex II: Package Leaflet for Quinapril

Before you take [Product]

Do not take [Product]

If you are more than 3 months pregnant. (It is also better to avoid [Product] in early pregnancy – see pregnancy section.)

Take special care with [Product]

You must tell your doctor if you think you are (or might become) pregnant. [Product] is not recommended in early pregnancy, and must not be taken if you are more than 3 months pregnant, as it may cause serious harm to your baby if used at that stage (see pregnancy section).

Pregnancy and breast feeding

Pregnancy

You must tell your doctor if you think you are (or might become) pregnant. Your doctor will normally advise you to stop taking [Product] before you become pregnant or as soon as you know you are pregnant and will advise you to take another medicine instead of [Product]. [Product] is not recommended in early pregnancy, and must not be taken when more than 3 months pregnant, as it may cause serious harm to your baby if used after the third month of pregnancy.

Breastfeeding

Tell your doctor if you are breast-feeding or about to start breast-feeding. Breast-feeding newborn babies (first few weeks after birth), and especially premature babies, is not recommended whilst taking [Product].

In the case of an older baby your doctor should advise you on the benefits and risks of taking [Product] whilst breast-feeding, compared with other treatments.