1. NAME OF THE MEDICINAL PRODUCT

VIMPAT® 50 mg film-coated tablets
VIMPAT® 100 mg film-coated tablets
VIMPAT® 150 mg film-coated tablets
VIMPAT® 200 mg film-coated tablets
VIMPAT® 15 mg/ml syrup
VIMPAT® 10 mg/ml solution for infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Tablets:
Film-coated tablet:
Each film-coated tablet contains 50 mg lacosamide, 100 mg lacosamide, 150 mg lacosamide or 200 mg lacosamide and 0.17 mg, 0.34 mg, 0.50 mg or 0.67 mg, respectively, of the excipient soya-lecithin.
Syrup:
Each ml of syrup contains 15 mg lacosamide.

Each bottle of 200 ml contains 3000 mg lacosamide.

3. PHARMACEUTICAL FORM

Film-coated tablet:
Each film-coated tablet contains 50 mg lacosamide, with 'SP' on one side and '50' on the other side.

100 mg: Dark yellow, oval film-coated tablet debossed with 'SP' on one side and '100' on the other side.

150 mg: Salmon, oval film-coated tablet debossed with 'SP' on one side and '150' on the other side.

200 mg: Blue, oval film-coated tablet debossed with 'SP' on one side and '200' on the other side.

Syrup:
Clear solution, slightly yellow to yellow-brown in colour.

Solution for infusion:
Each ml of solution for infusion contains 10 mg lacosamide.

1 vial of 20 ml solution for infusion contains 200 mg lacosamide.

For a full list of excipients, see section 6.1.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

VIMPAT® is indicated as adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation in patients aged 16 years and older.

4.2 Posology and method of administration

VIMPAT® must be taken twice a day. The recommended starting dose is 50 mg twice a day which should be increased to an initial thera-

peutic dose of 100 mg twice a day after one week.

Depending on response and tolerability, the maintenance dose can be further increased by 50 mg twice a day every week, to a maximum recommended daily dose of 400 mg (200 mg twice a day). VIMPAT® may be taken with or without food.

VIMPAT® therapy can be initiated with either oral or i.v. administration.

In accordance with current clinical practice, if VIMPAT® has to be discontinued, it is recommended this be done gradually (e.g. taper the daily dose by 200 mg/week).

Tablets:
VIMPAT® treatment initiation pack contains 4 different packages (one for each tablet strength) with 14 tablets each, for the first 2 to 4 weeks of therapy depending on the patient’s response and tolerability. The packages are marked with ‘week 1 (2, 3 or 4)’.

On the first day of treatment the patient starts with VIMPAT® 50 mg tablets twice a day. During the second week, the patient takes VIMPAT® 100 mg tablets twice a day. Depending on response and tolerability, VIMPAT® 150 mg tablets may be taken twice a day during the third week and VIMPAT® 200 mg tablets twice a day during the fourth week.

Syrup:
VIMPAT® syrup is provided with a measuring cup with graduation marks and instructions for use in the package leaflet.

Solution for infusion:
Each ml of solution for infusion contains 10 mg lacosamide.

1 vial of 20 ml solution for infusion contains 200 mg lacosamide.

For a full list of excipients, see section 6.1.

5.4 Special warnings and precautions for use

Treatment with lacosamide has been associated with dizziness which could increase the occurrence of accidental injury or falls. Therefore, patients should be advised to exercise caution until they are familiar with the potential effects of the medicine (see section 4.6).

Prolongations in PR interval with lacosamide have been observed in clinical studies. Lacosamide should be used with caution in patients with known conduction problems or severe cardiac disease such as a history of myocardial infarction or heart failure. Caution should especially be exerted when treating elderly patients as they may be at an increased risk of cardiac disorders or when lacosamide is used in combination with products known to be associated with PR prolongation.

Syrup:
VIMPAT® syrup contains sodium propylhydroxybenzoate (E217) and sodium methylhydroxybenzoate (E219), which may cause allergic reactions (possibly delayed). It contains 3.7 g sorbitol (E420) per dose (200 mg lacosamide), corresponding to a caloric value of 9.7 kcal. Patients with rare hereditary problems of fructose intolerance should not take this medicine. The syrup contains aspartame (E951), a source of phenylalanine, which may be harmful for people with phenylketonuria. It contains 1.06 mmol (or 25.2 mg) sodium per dose (200 mg lacosamide). To be taken into consideration for patients on a controlled sodium diet.

Solution for infusion:
This medicinal product contains 2.6 mmol (or 59.8 mg) sodium per vial. To be taken into consideration for patients on a controlled sodium diet.

5.5 Interaction with other medicinal products and other forms of interaction

Lacosamide should be used with caution in patients treated with medicinal products known to be associated with PR prolongation (e.g. carbamazepine, lamotrigine, pregabalin) and in patients treated with class I antiarrhythmic drugs. However, subgroup analysis did not identify an increased magnitude of PR prolongation in patients with concomitant administration of carbamazepine or lamotrigine in clinical trials.

Data generally suggest that lacosamide has a low interaction potential. In vitro studies indicate that the enzymes CYP1A2, 2B6, and 2C9 are not induced and that CYP1A1, 1A2, 2A6, 2B6, 2C8, 2C9, 2D6, and 2E1 are not inhibited by lacosamide at plasma concentrations observed in clinical trials. An in vitro study indicated that lacosamide is not transported by P-glycoprotein
in the intestine. Lacosamide does not inhibit or induce the enzyme CYP2C19 in vivo.

In vitro studies indicate that lacosamide may be a weak inhibitor and inducer of CYP3A4A. The clinical relevance of this is presently unknown. An interaction study with carbamazepine does not indicate a marked inhibitory effect of lacosamide on CYP3A4A catalysed metabolism at therapeutic/toxic doses. Strong enzyme inducers such as rifampicin or St John’s wort (Hypericum perforatum) may moderately reduce the systemic exposure of lacosamide. Therefore, starting or ending treatment with these enzyme inducers should be done with caution.

Anti-epileptic drugs

In interaction trials lacosamide did not significantly affect the plasma concentrations of carbamazepine and valproic acid. Lacosamide plasma concentrations were not affected by carbamazepine and by valproic acid. A population PK analysis estimated that concomitant treatment with other anti-epileptic drugs known to be enzyme inducers (carbamazepine, phenytoin, phenobarbital, in various doses) decreased the overall systemic exposure of lacosamide by 25%.

Oral contraceptives

In an interaction trial there was no clinically relevant interaction between lacosamide and the oral contraceptives ethinylestradiol and levonorgestrel. Progesterone concentrations were not affected when the medicinal products were co-administered.

Others

Interaction trials showed that lacosamide had no effect on the pharmacokinetics of digoxin. There was no clinically relevant interaction between lacosamide and metformin. Omeprazole 40 mg q.d. increased the AUC of lacosamide by 19%. The effect probably lacks clinical relevance. Lacosamide did not affect the single-dose pharmacokinetics of omeprazole. No data on the interaction of lacosamide with alcohol are available.

Lacosamide has a low protein binding of less than 15%. Therefore, clinically relevant interactions with other drugs through competition for protein binding sites are considered unlikely.

4.6 Pregnancy and lactation

Pregnancy

Risk related to epilepsy and antiepileptic medicinal products in general

For all anti-epileptic drugs, it has been shown that in the offspring of women treated with epilepsy, the prevalence of malformations is two to three times greater than the rate of approximately 3% in the general population. In the treated population, an increase in malformations has been noted with polytherapy; however, the extent to which the treatment and/or the illness is responsible has not been elucidated.

Moreover, effective anti-epileptic therapy must not be interrupted, since the aggravation of the illness is detrimental to both the mother and the foetus.

Risk related to lacosamide

There are no adequate data from the use of lacosamide in pregnant women. Studies in animals did not indicate any teratogenic effects in rats or rabbits, but embryotoxicity was observed in rats and rabbits at maternal toxic doses (see section 5.3). The potential risk for humans is unknown.

Lacosamide should not be used during pregnancy unless clearly necessary (if the benefit to the mother clearly outweighs the potential risk to the foetus). If women decide to become pregnant, the use of this product should be carefully re-evaluated.

Lactation

It is unknown whether lacosamide is excreted in human breast milk. Animal studies have shown excretion of lacosamide in breast milk. For precautionary measures, breast-feeding should be discontinued during treatment with lacosamide.

4.7 Effects on ability to drive and use machines

VIMPAT™ may have minor to moderate influence on the ability to drive and use machines. VIMPAT™ treatment has been associated with dizziness or blurred vision. Accordingly, patients should be advised not to drive a car or to operate other potentially hazardous machinery until they are familiar with the effects of VIMPAT™ on their ability to perform such activities.

4.8 Undesirable effects

Based on the analysis of pooled placebo-controlled clinical trials in 1,308 patients with partial-onset seizures, a total of 61.9% of patients randomized to lacosamide and 35.2% of patients randomized to placebo reported at least 1 adverse reaction. The most frequently reported adverse reactions with lacosamide treatment were dizziness, headache, nausea and diplopia. They were usually mild to moderate in intensity. Some were dose-related and could be alleviated by reducing the dose. Incidence and severity of CNS and gastrointestinal (GI) adverse reactions usually decreased over time.

System organ class

Very common

Common

Psychiatric disorders

Dizziness

Depression

Nervous system disorders

Headache

Balance disorder

Coordination abnormal

Memory impairment

Cognitive disorder

Somnolence

Tremor

Nystagmus

Eye disorders

Diplopia

Vision blurred

Vertigo

Ear and larynx disorders

Nausea

Vomiting

Constipation

Flatulence

Gastrointestinal disorders

Skin and subcutaneous tissue disorders

General disorders and administration site conditions

Injury, poisoning and procedural complications

Other

Over all controlled studies, the discontinuation rate due to adverse reactions was 12.2% for patients randomized to lacosamide and 1.8% for patients randomized to placebo. The most common adverse reaction resulting in discontinuation of lacosamide therapy was dizziness.

The table below shows the frequencies of adverse reactions which have been reported in placebo-controlled clinical trials (≥1/100).

System organ class

Very common

Common

Psychiatric disorders

Dizziness

Depression

Nervous system disorders

Headache

Balance disorder

Coordination abnormal

Memory impairment

Cognitive disorder

Somnolence

Tremor

Nystagmus

Eye disorders

Diplopia

Vision blurred

Vertigo

Ear and larynx disorders

Nausea

Vomiting

Constipation

Flatulence

Gastrointestinal disorders

Skin and subcutaneous tissue disorders

General disorders and administration site conditions

Injury, poisoning and procedural complications

Other

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: other antiepileptics, ATC code: N03AX18

The active substance, lacosamide (R-2-acetamido-N-benzyl-3-methoxypropionamide) is a functionalised amino acid.

Mechanism of action

The precise mechanism by which lacosamide exerts its antiepileptic effect in humans remains to be fully elucidated. Two observations that may be of relevance for the observed therapeutic effects are: In vitro electrophysiological studies have shown that lacosamide selectively enhances slow inactivation of voltage-gated sodium channels, resulting in stabilization of hyperexcitable neuronal membranes. Further, lacosamide binds to collapsin response mediator protein-2 (CRMP-2), a phosphoprotein which is mainly expressed in the nervous system and is involved in neuronal differentiation and control of axonal outgrowth.

Pharmacodynamic effects

Lacosamide protected against seizures in a broad range of animal models of partial and primary generalized seizures and delayed kindling development.

5.2 Pharmacokinetic properties

Lacosamide is rapidly and almost completely absorbed after oral administration. The absolute bioavailability is approximately 70%. Absorption is not significantly affected by food. The mean time to reach maximum plasma concentration (tmax) following oral administration of 100mg, 200mg, 400mg or 600mg is 2 hours, with little variation among the doses. Mean maximum plasma concentration (Cmax) increases proportionally with increasing dose, with a dose proportionality index of 0.73 (90% confidence interval 0.63 to 0.86).

The plasma clearance (Cl) of lacosamide is approximately 30% higher in women than in men. In elderly patients, the exposure of lacosamide (AUC) is increased by approximately 16%.

The mean elimination half-life (t1/2) of lacosamide is approximately 7 hours, and decreases to approximately 4 hours in elderly patients. The apparent volume of distribution (Vd) is 1.5 L/kg.

Lacosamide undergoes extensive metabolism in the liver, predominantly by cytochrome P450 3A4 (CYP3A4) and to a lesser extent by CYP2C9. Two major metabolites of lacosamide have been identified: a glucuronide conjugate and a monohydroxy metabolite. Less than 2% of the dose is excreted as unchanged lacosamide in the urine. Lacosamide is extensively bound to plasma proteins (97–99%).

5.3 Postmarketing observations

Omeprazole 40 mg q.d. increased the AUC of lacosamide by 19%. The effect probably lacks clinical relevance. Lacosamide did not affect the single-dose pharmacokinetics of omeprazole. No data on the interaction of lacosamide with alcohol are available.
In non-clinical experiments lacosamide in combination with levetiracetam, carbamazepine, phenytin, valproate, lamotrigine, topiramate or gabapentin showed synergistic or additive anti-convulsant effects.

**Clinical experience**

The efficacy of VIMPAT® as adjunctive therapy at recommended doses (200 mg/day; 400 mg/day) was established in 3 multicenter, randomized, placebo-controlled clinical trials with a 12-week maintenance period. VIMPAT® 600 mg/day was also shown to be effective in controlled adjunctive therapy trials, although the efficacy was similar to 400 mg/day and patients were less likely to tolerate this dose because of CNS- and gastrointestinal-related adverse reactions. Thus, the 600 mg/day dose is not recommended. The maximum recommended dose is 400 mg/day. These trials, involving 1308 patients with a history of an average of 23 years of partial-onset seizures, were designed to evaluate the efficacy and safety of lacosamide when administered concomitantly with 1-3 antiepileptic drugs in patients with uncontrolled partial-onset seizures with or without secondary generalization. Overall the proportion of subjects with a 50% reduction in seizure frequency was 23%, 34%, and 40% for placebo, lacosamide 200 mg/day and lacosamide 400 mg/day.

There is insufficient data regarding the withdrawal of concomitant antiepileptic medicinal products to achieve monotherapy with lacosamide.

**5.2 Pharmacokinetic properties**

**Absorption**

**Tablets and Syrup:**

Lacosamide is rapidly and completely absorbed after oral administration. The oral bioavailability of lacosamide tablets is approximately 100%. Following oral administration, the plasma concentration of unchanged lacosamide increases rapidly and reaches C<sub>max</sub> about 0.5 to 4 hours post-dose. VIMPAT® tablets and oral syrup are bioequivalent. Food does not affect the rate and extent of absorption.

**Solution for infusion:**

After i.v. administration, C<sub>max</sub> is reached at the end of infusion. The plasma concentration increases proportionally with dose after oral (100-800 mg) and i.v. (50-300 mg) administration.

**Distribution**

The volume of distribution is approximately 0.6 L/kg. Lacosamide is less than 15% bound to plasma proteins.

**Metabolism**

95% of the dose is excreted in the urine as drug and metabolites. The metabolism of lacosamide has not been completely characterised. The major compounds excreted in urine are unchanged lacosamide (approximately 40% of the dose) and its O-desmethyl metabolite less than 30%.

A polar fraction proposed to be serine derivatives accounted for approximately 20% in urine, but was detected only in small amounts (0-2%) in human plasma of some subjects. Small amounts (0.5-2%) of additional metabolites were found in the urine. CYP2C19 is mainly responsible for the formation of the O-desmethyl metabolite. However, no clinically relevant difference in lacosamide exposure was observed comparing its pharmacokinetics in extensive metabolisers (EMs, with a functional CYP2C19) and poor metabolisers (PMs, lacking a functional CYP2C19). Further-more an interaction trial with omepazole (CYP2C19-inhibitor) demonstrated no clinically relevant increase in lacosamide plasma concentrations indicating that the importance of this pathway is minor. No other enzymes have been identified to be involved in the metabolism of lacosamide.

The plasma concentration of O-desmethyl-lacosamide is approximately 15% of the concentration of lacosamide in plasma. This major metabolite has no known pharmacological activity.

**Elimination**

Lacosamide is primarily eliminated from the systemic circulation by renal excretion and biotransformation. After oral and intravenous administration of radiolabeled lacosamide, approximately 95% of radioactivity administered was recovered in the urine and less than 0.5% in the feces. The elimination half-life of the unchanged drug is approximately 13 hours. The pharmacokinetics is dose-proportional and constant over time, with low intra- and intersubject variability. Following twice daily dosing, steady state plasma concentrations are achieved after 3 days. The plasma concentration increases with an accumulation factor of approximately 2.

**Pharmacokinetics in special patient groups**

**Gender**

Clinical trials indicate that gender does not have a clinically significant influence on the plasma concentrations of lacosamide.

**Renal impairment**

The AUC of lacosamide was increased by approximately 30% in mildly and moderately and 60% in severely renal impaired patients and patients with end-stage renal disease requiring haemodialysis compared to healthy subjects, whereas C<sub>max</sub> was unaffected.

Lacosamide is effectively removed from plasma by haemodialysis. Following a 4-hour haemodialysis treatment, AUC of lacosamide is reduced by approximately 50%. Therefore dosing supplementation following haemodialysis is recommended (see section 4.2). The exposure of the O-desmethyl metabolite was several-fold increased in patients with moderate and severe renal impairment. In absence of haemodialysis in patients with endstage renal disease, the levels were increased and continuously rising during the 24-hour sampling. It is unknown whether the increased metabolite exposure in endstage renal disease subjects could give rise to adverse effects but no pharmacological activity of the metabolite has been identified.

**Hepatic impairment**

Subjects with moderate hepatic impairment (Child-Pugh B) showed higher plasma concentrations of lacosamide (approximately 50% higher AUC<sub>norm</sub>). The higher exposure was partly due to a reduced renal function in the studied subjects. The decrease in non-renal clearance in the patients of the study was estimated to give a 20% increase in the AUC of lacosamide. The pharmacokinetics of lacosamide has not been evaluated in severe hepatic impairment (see section 4.2).

**Elderly (over 65 years of age)**

In a study in elderly men and women including 4 patients >75 years of age, AUC was about 30 and 50% increased compared to young men, respectively. This is partly related to lower body weight. The body weight normalized difference is 25 and 23%, respectively. An increased variability in exposure was also observed. The renal clearance of lacosamide was only slightly reduced in elderly subjects in this study.

A general dose reduction is not considered to be necessary unless indicated due to reduced renal function (see section 4.2).

**5.3 Preclinical safety data**

In the toxicity studies, the plasma concentrations of lacosamide obtained were similar or only marginally higher than those observed in patients, which leaves room for non-existing margins to human exposure. A safety pharmacology study with intravenous administration of lacosamide in anesthetized dogs showed transient increases in PR interval and QRS complex duration and decreases in blood pressure most likely due to a cardiodepressant action. These transient changes started in the same concentration range as after maximum recommended clinical dosing. In anesthetized dogs and Cynomolgus monkeys, at intravenous doses of 15-60 mg/kg, slowing of atrial and ventricular conductivity, atrioventricular block and atrioventricular dissociation were seen. In the repeated dose toxicity studies, mild reversible liver changes were observed in rats starting at about 3 times the clinical exposure. These changes included an increased organ weight, hypertrophy of hepatocytes, increases in serum concentrations of liver enzymes and increases in total cholesterol and triglycerides. Apart from hepatomegaly, no other histopathologic changes were observed. In reproductive and developmental toxicity studies in rodents and rabbits, no teratogenic effects but an increase in numbers of stillborn pups and pup deaths in the peripartum period, and slightly reduced live litter sizes and pup body weights were observed at maternal toxic doses in rats corresponding to systemic exposure levels similar to the expected clinical exposure. Since higher exposure levels could not be tested in animals due to maternal toxicity, data are insufficient to fully characterise the embryofetotoxic and teratogenic potential of lacosamide.

Studies in rats revealed that lacosamide and/or its metabolites readily crossed the placental barrier.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

**Tablets:**

**Tablet core:**

- microcrystalline cellulose
- hydroxypropylcellulose
- hydroxypropylcellulose (low substituted)
- silica, colloidal, anhydrous
- crospovidone
- magnesium stearate

**Tablet coat:**

- polyvinyl alcohol
- polyethylene glycol 400, 3350 and 8000
talc
- soya-lecithin
- hypromellose
- titanium dioxide (E171)

50 mg tablet: red iron oxide (E172), black iron oxide (E172), indigo carmine aluminium lake (E132)

100 mg tablet: yellow iron oxide (E172)

150 mg tablet: yellow iron oxide (E172), red iron oxide (E172), black iron oxide (E172)

200 mg tablet: indigo carmine aluminium lake (E132)

**Syrup:**

- glycerr (E422)
- carmellose sodium
sorbitol liquid (crystallizing) (E420)
polyethylene glycol 4000
sodium chloride
citric acid, anhydrous
acesulfame potassium (E950)
sodium propylparahydroxybenzoate (E217)
sodium methylparahydroxybenzoate (E219)
strawberry flavour (contains propylene glycol,
maltol)
masking flavour (contains propylene glycol,
aspartame (E951), acesulfame potassium
(E950), maltol, deionised water)
purified water

Solution for infusion:
water for injection
sodium chloride
hydrochloric acid (for pH adjustment)

6.2 Incompatibilities
Tablets and Syrup:
Not applicable.

Solution for infusion:
This medicinal product must not be mixed with
other medicinal products except those
mentioned in section 6.6.

6.3 Shelf life
Tablets:
3 years.
Syrup:
2 years.
After first opening: 4 weeks.

Solution for infusion:
3 years.
Chemical and physical in-use stability has been
demonstrated for 24 hours at temperatures up
to 25°C for product mixed with the diluents
mentioned in 6.6.

From a microbiological point of view, the prod-
uct should be used immediately. If not used
immediately, in-use storage times and condi-
tions prior to use are the responsibility of the
user and would not be longer than 24 hours at 2
to 8°C, unless dilution has taken place in con-
trolled and validated aseptic conditions.

6.4 Special precautions for storage
Tablets:
This medicinal product does not require any
special storage conditions.

Syrup:
Do not store above 30°C.

Solution for infusion:
Do not store above 25°C.

6.5 Nature and contents of container
Tablets:
PVC/PVDC blister sealed with an aluminium
foil.

50 mg & 100 mg: Packs of 14, 56 and 168 film-
coated tablets.
150 mg & 200 mg: Packs of 14, 56 and 168
film-coated tablets (multipacks containing 3
packs of 56 tablets).
The treatment initiation pack contains 4 cartons,
each carton with 14 tablets of 50 mg, 100 mg,
150 mg and 200 mg
Not all pack sizes may be marketed.

Syrup:
200 ml and 465 ml amber type III glass or
polyethylene terephthalate (PET) bottles with a
polypropylene screw cap and a measuring cup.
Not all pack sizes may be marketed.

Solution for infusion:
1x20 ml colourless type I glass vial with a
chlorobutyl rubber closure coated with a
fluoropolymer.

6.6 Special precautions for disposal
Tablets and Syrup:
No special requirements.

Solution for infusion:
This medicinal product is for single use only,
any unused solution should be discarded.
Product with particulate matter or discolouration
should not be used. VIMPAT® solution for infu-
sion was found to be physically compatible and
chemically stable when mixed with the following
diluents for at least 24 hours and stored in glass
or PVC bags at temperatures up to 25°C.

Diluents:
sodium chloride 9 mg/ml (0.9%) solution for
injection
glucose 50 mg/ml (5%) solution for injection
lactated Ringer’s solution for injection.

7. MARKETING AUTHORISATION
HOLDER
UCB Pharma S.A.
Allée de la Recherche 60
B-1070 Bruxelles
Belgium

8. MARKETING AUTHORIZATION
NUMBER(S)
50 mg x 14 tabs: EU/1/08/470/001
50 mg x 56 tabs: EU/1/08/470/002
50 mg x 168 tabs: EU/1/08/470/003
100 mg x 14 tabs: EU/1/08/470/004
100 mg x 56 tabs: EU/1/08/470/005
100 mg x 168 tabs: EU/1/08/470/006
150 mg x 14 tabs: EU/1/08/470/007
150 mg x 56 tabs: EU/1/08/470/008
150 mg x 168 tabs: EU/1/08/470/009
200 mg x 14 tabs: EU/1/08/470/010
200 mg x 56 tabs: EU/1/08/470/011
200 mg x 168 tabs: EU/1/08/470/012
Treatment initiation pack: 50/100/150/200 mg x
14/14/14/14 tabs: EU/1/08/470/013
Syrup (15 mg/ml) x 200 ml: EU/1/08/470/014
Syrup (15 mg/ml) x 465 ml: EU/1/08/470/015
Syrup for Infusion (10 mg/ml) x 20 ml:
EU/1/08/470/016

9. DATE OF FIRST
AUTHORISATION/RENEWAL OF
THE AUTHORISATION
29.08.2008

10. DATE OF REVISION OF THE TEXT
02.09.2008

Detailed information on this medicine is
available on the European Medicines Agency