1. NAME OF THE MEDICINAL PRODUCT

Cinfaval cinfa 40 mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Cinfaval 40 mg film-coated tablets
Each tablet contains 40 mg of valsartan.

Excipients:
contains sorbitol.....4.63 mg
contains lactose.....0.54 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet.

Cinfaval 40 mg tablets are coated, cylindrical, yellow, scored tablets.
The tablet can be divided into equal doses.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Recent myocardial infarction
Treatment of clinically stable patients with symptomatic heart failure or asymptomatic left-ventricular systolic dysfunction after a recent myocardial infarction (12 hours – 10 days), (see sections 4.4 and 5.1.).

Heart failure
Treatment of symptomatic heart failure when ACE inhibitors cannot be used or as add-on treatment to ACE inhibitors when beta-blockers cannot be used (see sections 4.4 and 5.1).

4.2 Posology and method of administration

Posology

Recent myocardial infarction
In clinically stable patients, the treatment can be initiated 12 hours after the myocardial infarction. After an initial dose of 20 mg twice daily, valsartan should be titrated to 40 mg, 80 mg and 160 mg twice daily over the next few weeks. The starting dose is obtained from the divisible 40 mg tablet.
The maximum target dose is 160 mg twice daily. In general, it is recommended that patients reach the 80 mg twice-daily dose two weeks after initiating treatment and the maximum target dose, 160 mg twice daily, by about three months, depending on the patient's tolerability. Reducing the dose of **Cinfaval** should be considered in cases of symptomatic hypotension or altered renal function.
Valsartan can be used concomitantly by patients taking other post-myocardial infarction treatments, e.g. thrombolytics, acetylsalicylic acid, beta blockers, statins and diuretics. Combination with ACE inhibitors is not recommended (see sections 4.4 and 5.1).
Assessment of post-myocardial infarction patients must always include an evaluation of renal function.

Heart failure
The recommended starting dose of **Cinfaval** is 40 mg twice a day. Uptitration to 80 mg and 160 mg twice daily should be performed at intervals of at least two weeks, based on patient tolerance. Reducing the dose of the diuretics taken concomitantly should be considered. The maximum daily dose administered during clinical trials is 320 mg in divided doses.
Valsartan may be administered concomitantly with other treatments for heart failure. Nevertheless, it should not be used concomitantly with an ACE inhibitor and a beta blocker (see sections 4.4 and 5.1).
The assessment of patients with heart failure should always include the evaluation of renal function.
Cinfaval can be administered independently from food and should be administered with liquid.

Method of administration
Cinfaval may be taken independently of a meal and should be administered with water.

Additional information on special populations

Renal impairment
No dosage adjustment is required for patients with a creatinine clearance >10 ml/min (see sections 4.4 and 5.2)

Hepatic impairment
In patients with mild to moderate hepatic impairment without cholestasis, the dose of valsartan should not exceed 80 mg. valsartan is contraindicated in patients with severe hepatic impairment and in patients with cholestasis (see sections 4.3, 4.4 and 5.2).

Elderly
Elderly patients can be administered the same dose as younger patients.

Paediatric patients
Cinfaval is not recommended for children under 18 years of age due to the lack of safety and efficacy data.

4.3 Contraindications

- Hypersensitivity to valsartan or to any of its excipients.
- Severe hepatic impairment, biliary cirrhosis and cholestasis.
- Second and third trimester of pregnancy (see sections 4.4 and 4.6).

4.4 Special warnings and precautions for use

Hyperkalaemia
The concomitant use of potassium supplements, potassium-sparing diuretics, salt substitutes containing potassium or other agents that may increase potassium levels (heparin, etc.) is not recommended, and potassium levels should be monitored as appropriate.

Sodium and/or volume depleted patients
Patients with severe sodium and/or volume depletion, such as those receiving high doses of diuretics, may occasionally experience symptomatic hypotension after starting therapy with **Cinfaval**. Therefore, sodium and/or volume depletion should be corrected before commencing treatment with **Cinfaval**, for example, by reducing the dose of the diuretic.

Renal artery stenosis
The safety of **Cinfaval** has not been established in patients with bilateral renal artery stenosis or stenosis in patients with a single kidney.
Short term administration of **Cinfaval** in 12 patients with renovascular hypertension secondary to unilateral renal artery stenosis did not induce any significant changes in renal haemodynamics, serum creatinine or blood urea nitrogen (BUN). However, other agents that affect the renin-angiotensin system can increase blood urea and serum creatinine in patients with unilateral renal artery stenosis, it is recommended to monitor these parameters in patients with unilateral renal artery stenosis for safety reasons.

Kidney transplantation
There is currently no experience on the safe of **Cinfaval** in patients who have recently undergone kidney transplantation.

Primary hyperaldosteronism
Patients with primary hyperaldosteronism should not be treated with **Cinfaval** as the renin-angiotensin system is not activated.

Aortic and mitral valve stenosis, obstructive hypertrophic cardiomyopathy
As with all vasodilators, special caution is recommended in patients with aortic or mitral stenosis, or with hypertrophic obstructive cardiomyopathy (HOCM).

Impaired renal function
No dosage adjustments is required for patients with a creatinine clearance >10 ml/min. There is currently no experience on the safe use in patients with a creatinine clearance <10 ml/min and patients undergoing dialysis, therefore valsartan should be used with caution in these patients (see sections 4.2 and 5.2)..

Hepatic impairment
In patients with mild to moderate hepatic impairment without cholestasis, valsartan should be used with caution. (see sections 4.2 and 5.2).

Recent myocardial infarction
The combination of captopril and valsartan has shown no additional clinical benefit; instead the risk of adverse event increased compared to treatment with the respective therapies (see sections 4.2 and 5.1). Therefore, the combination of valsartan with an ACE inhibitor is not recommended.
Caution is required when starting the treatment in post-myocardial infarction patients. Evaluation of post-myocardial infarction patients must always include assessment of renal function (see section 4.2).
The use of **Cinfaval** in patients after myocardial infarction usually causes a blood pressure reduction, but discontinuation of therapy because of continuing symptomatic hypotension is not usually necessary provided dosing instructions are followed (see section 4.2)..

Heart failure
In patients with heart failure, the triple combination of an ACE inhibitor, a beta blocker and valsartan has shown no clinical benefit (see section 5.1). This combination apparently increases the risk of adverse events and is therefore not recommended.
CinfavalCaution should be taken when starting treatment in patients with heart failure. Evaluation of patients with heart failure should always include assessment of renal function (see section 4.2).
The use of **Cinfaval** in patients with heart failure usually causes a reduction in blood pressure, but discontinuation of therapy because of continuing symptomatic hypotension is not usually necessary provided dosing instructions are followed (see section 4.2).
In patients whose renal function could be dependent on the activity of the renin-angiotensin system (e.g. patients with severe congestive heart failure), treatment with angiotensin-converting enzyme inhibitors has been associated with oliguria and/or progressive azotaemia and rarely with acute renal failure and/or death. As valsartan is an angiotensin II receptor antagonist, it has an inhibitory effect on the renin-angiotensin system and therefore an association between the use of valsartan and impaired renal function cannot be excluded.

Pregnancy
Treatment with angiotensin II receptor antagonists (AIIRAs) should not be started during pregnancy. Unless it is considered essential to continue treatment with AIIRAs, patients planning pregnancy should change to an alternative antihypertensive treatment with a known safety profile for use during pregnancy. When pregnancy is diagnosed, treatment with AIIRAs should be stopped immediately and an alternative therapy should be started if appropriate (see sections 4.3 and 4.6).

Warning about the excipients:
This medicinal product contains sorbitol. Patients with hereditary intolerance to fructose should not take this medicinal product.
This medicinal product contains lactose. Patients with hereditary intolerance to galactose, Lapp lactase deficiency (deficiency seen in some populations in Lapland) or glucose or galactose absorption problems should not take this medicinal product.

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant use not recommended

Lithium
Reversible increases in serum lithium concentrations and toxicity have been reported during concurrent use of ACE inhibitors. Due to the lack of experience with concomitant use of valsartan and lithium, this combination is not recommended. If the combination proves necessary, careful monitoring of serum lithium levels is recommended.

Potassium-sparing diuretics, potassium supplements, salt substitutes containing potassium and other substances that may increase potassium levels
If a medicinal product that affects potassium levels is considered necessary in combination with valsartan, monitoring of potassium plasma levels is advised.

Caution required with concomitant use

Non-steroidal anti-inflammatory medicines (NSAIDs), including selective COX-2 inhibitors, acetylsalicylic acid >3 g/day), and non-selective NSAIDs
When angiotensin II antagonists are administered simultaneously with NSAIDs, attenuation of the antihypertensive effect may occur. Furthermore, concomitant use of angiotensin II antagonists and NSAIDs may lead to an increased risk of worsening of renal function and an increase in serum potassium. Therefore,

monitoring of renal function at the beginning of the treatment is recommended, as well as adequate hydration of the patient.

Others
In drug interaction studies with valsartan, no interactions of clinical significance have been found with valsartan or any of the following substances: cimetidine, warfarin, furosemide, digoxin, atenolol, indometacin, hydrochlorothiazide, amlodipine, glibenclamide.**CinfavalCinfaval**

4.6 Pregnancy and lactation

Pregnancy

Pregnancy: Use of Angiotensin II Receptor Antagonists AIIRAs is not recommended during the first trimester of pregnancy (see section 4.4). The use of AIIRAs is contraindicated during the second and third trimester of pregnancy (see Section 4.3 and 4.4).

Epidemiological evidence on the risk of teratogenicity after exposure to ACE inhibitors during the first trimester of pregnancy has not been conclusive; however, a small increase in risk cannot be excluded. Despite having no specific epidemiological data on the risk of administering angiotensin II receptor antagonists (AIIRAs) during pregnancy, there may be similar risks for this type of medicinal products. Unless it is considered essential to continue treatment with AIIRAs, patients planning pregnancy should change to an alternative antihypertensive treatment with a known safety profile for use during pregnancy. When pregnancy is diagnosed, treatment with AIIRAs should be stopped immediately and an alternative treatment started if appropriate.

Exposure to AIIRAs in the second and third trimester is known to induce human fetotoxicity (decreased renal function, oligohydramnios, skull ossification retardation) and neonatal toxicity (renal failure, hypotension, hyperkalaemia). (See also section 5.3).

If there is AIIRAs exposure from the second trimester of pregnancy, an ultrasound check of renal function and skull is recommended.

Infants whose mothers have been treated with AIIRAs should be carefully monitored in case hypotension occurs (see sections 4.3 and 4.4).

Lactation

Because no information relating to the use of this medicinal product during breast-feeding is available, administration of **Cinfaval** is not recommended during this period. It is preferable to change to a treatment with a better known safety profile for breast-feeding, especially in nursing a new-born or preterm infant.

4.7 Effects on ability to drive and use machines

No studies have been made of the effects on the ability to drive and use machines. When driving or using machinery, it should be taken into account that occasionally dizziness or weariness may occur.

4.8 Undesirable effects

In controlled clinical trials in patients with hypertension, the total incidence of adverse reactions was comparable with placebo and is consistent with the pharmacology of valsartan. The incidence of adverse

reactions did not appear to be related to the dose or treatment duration and also showed no association with gender, age or race.

The adverse reactions reported from clinical trials, post-marketing experience and laboratory findings are listed below according to system organ class

Adverse reactions are ranked by frequency, the most frequent first, using the following convention: very common (>1/10); common (>1/100, <1/10); uncommon (>1/1,000, <1/100); rare (>1/10,000, < 1/1,000), very rare (<1/10,000), including isolated reports, within each frequency grouping, adverse reactions are ranked in order of decreasing seriousness.
For all the adverse reactions reported from post-marketing experience and laboratory findings, it is not possible to apply any adverse reaction frequency and therefore they are mentioned with a "not known" frequency.

- **Hypertension**

Blood and lymphatic system disorders
Not known: Decrease in haemoglobin, decrease in haematocrit, neutropenia, Thrombocytopenia

Immune system disorders
Not known: Hypersensitivity including serum sickness

Metabolism and nutrition disorders
Not known: Increase of serum potassium

Ear and labyrinth system disorders
Uncommon: Vertigo

Vascular disorders
Not known: Vasculitis

Respiratory, thoracic and mediastinal disorders
Uncommon: Cough

Gastrointestinal disorders
Uncommon: Abdominal pain

Hepato-biliary disorders
Not known Elevation of liver function values including increase of serum bilirubin

Skin and subcutaneous tissue disorders
Not known: Angioedema, rash, pruritus

Musculoskeletal and connective tissue disorders
Not known: Myalgia

Renal and urinary disorders
Not known: Renal failure and impairment, elevation of serum creatinine

General disorders and administration site conditions
Uncommon: Fatigue

The safety profile seen in controlled-clinical studies in patients with post-myocardial infarction and/or heart failure varies from the overall safety profile seen in hypertensive patients. This may relate to the patients underlying disease. ADRs that occurred in post-myocardial infarction and/or heart failure patients are listed below.

- Post-myocardial infarction and/or heart failure

Blood and lymphatic system disorders
Not known: Thrombocytopenia

Immune system disorders
Not known: Hypersensitivity including serum sickness

Metabolism and nutrition disorders
Uncommon Hyperkalaemia
Not known: Increase of serum potassium

Nervous system disorders
Common: Dizziness, Postural dizziness
Uncommon: Syncope, Headache

Ear and labyrinth system disorders
Uncommon: Vertigo

Cardiac disorders
Uncommon: cardiac failure

Vascular disorders
Common Hypotension, Orthostatic hypotension
Not known: Vasculitis

Respiratory, thoracic and mediastinal disorders
Uncommon: Cough

Gastrointestinal disorders
Uncommon: Nausea, Diarrhoea

Hepato-biliary disorders
Not known Elevation of liver function values

Skin and subcutaneous tissue disorders
Uncommon Angioedema
Not known: Rash, Pruritus

Musculoskeletal and connective tissue disorders
Not known: Myalgia

Renal and urinary disorders
Common: Renal failure and impairment
Uncommon Acute renal failure, elevation of serum creatinine
Not known: Increase in Blood Urea Nitrogen

General disorders and administration site conditions
Uncommon: Asthenia, Fatigue

4.9 Overdose

Symptoms
An overdose of **Cinfaval** may result in marked hypotension that could cause a depressed level of consciousness, circulatory collapse and/or shock.

Treatment
The therapeutic measures depend on the time of ingestion and the type and severity of the symptoms; stabilisation of the circulatory state is of prime importance.
If hypotension occurs, the patient should be placed in a supine position and blood volume correction should be undertaken.
Valsartan is unlikely to be removed by haemodialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: angiotensin II antagonists, plain. ATC code: C09C A03.
Cinfaval is an orally, potent, and specific antagonist II (Ang II) receptor antagonist. This substance acts selectively on the AT_1 subtype receptor, which is responsible for the known mechanisms of action of angiotensin II. An increase in angiotensin II levels after AT_1 receptor blockade with valsartan can stimulate the unblocked AT2 receptor, which appears to compensate the effect of the AT_1 receptor. Valsartan does not possess any partial agonist activity at the AT_1 receptor and shows a much greater affinity (approximately 20,000 fold) for the AT_1 receptor than for the AT_2 receptor. Valsartan is not known to bind to or block other hormone receptors or ion channels known to be important in cardiovascular regulation. Valsartan does not inhibit ACE, (also known as kininase II), that converts Ang I into Ang II and degrades bradykinin. Since there is no effect on ACE and no potentiation of bradykinin or substance P, angiotensis II antagonists are unlikely to be associated with coughing. In a clinical trial, in patients with a history of dry cough during treatment with an ACE inhibitor, 19.5% and 19.0% of patients who received valsartan or a thiazide diuretic, respectively, experienced cough, compared with 68.5% of patients treated with the ACE inhibitor ($p < 0.05$).
Cinfaval

Recent myocardial infarction
The VALsartan In Acute myocardial iNfarcTion trial (VALIANT) was a randomised, controlled, multinational double blind study conducted in 14,703 patients with acute myocardial infarction and signs, symptoms or radiological evidence of congestive heart failure and/or evidence of left ventricular systolic dysfunction (manifested as an ejection fraction ≤40 % by radionuclide ventriculography, or ≤35 % by echocardiography or ventricular contrast angiography). The patients were randomised between 12 hours and 10 days after the onset of the symptoms of myocardial infarction to valsartan, captopril or the combination of both. The mean duration of treatment was two years. The primary endpoint was time to all-cause mortality.

Valsartan was as effective as captopril in reducing all-cause mortality after myocardial infarction. All-cause mortality was similar in the groups taking valsartan (19.9 %), captopril (19.5 %) and valsartan + captopril (19.3 %). groups The combination of valsartan and captopril had no additional benefit to captopril alone. No differences were observed between valsartan and captopril in all-cause mortality based on age, gender, race, baseline therapies or underlying disease. Valsartan efficacy was also demonstrated in prolonging time to

death due to cardiovascular causes, hospitalisation due to heart failure, recurrent myocardial infarction, resuscitated cardiac arrest, and non- fatal stroke (secondary composite endpoint).
The safety profile of valsartan was consistent with the clinical course of patients treated in the post-myocardial infarction setting. Regarding renal function, doubling of serum creatinine was observed in 4.2% of valsartan-treated patients, 4.8% of valsartan+captopril-treated patients, and 3.4% of captopril-treated patients. Discontinuations due to various types of renal dysfunction occurred in 1.1% of valsartan-treated patients, 1.3% in valsartan+captopril patients, and 0.8% of captopril patients. An assessment of renal function should be included in the evaluation of patients post-myocardial infarction.
No differences were observed in all-cause mortality, cardiovascular mortality or morbidity when beta-blockers were administered along with the combination valsartan + captopril, valsartan alone or captopril alone. Regardless of the study drug therapy, mortality was lower in the patient group treated with a beta-blocker, suggesting that the known benefit of the beta-blocker in this population was maintained in this trial.

Heart failure
Val-HeFT was a randomised, controlled, multinational clinical trial of valsartan compared with placebo on morbidity and mortality in 5,010 NYHA class II (62 %), III (36 %) and IV (2 %) heart failure patients receiving usual treatment with LVEF < 40 % and internal left ventricular diastolic diameter (LVIDD) > 2.9 cm/cm^2. The underlying treatment included ACE inhibitors (93 %), diuretics (86 %), digoxin (67 %) and beta blockers (36 %). The mean duration of the follow-up was nearly two years. The mean daily dose of valsartan in Val-HeFT was 254 mg.
The study had 2 primary endpoints: all-cause mortality (time to death) and composite mortality and heart failure morbidity (time to the first morbid event) defined as death, sudden death with resuscitation, hospitalisation for heart failure or administration of intravenous inotropic or vasodilator drugs for at least four hours without hospitalisation.
All-cause mortality was similar (p=NS) in valsartan (19.7%) and placebo (19.4%) groups. The primary benefit was a reduction in risk of 27.5 % (95% CI: 17 to 37%) for the time to the first hospital admission for heart failure (13.9 % vs 18.5 %). Results were observed that appeared to favour placebo in patients who received the triple combination of an ACE inhibitor, a beta-blocker and valsartan. In a subgroup of patients not receiving an ACE inhibitor (n=366), the morbidity benefits were greatest. N this subgroup all cause-mortality was significantly reduced with valsartan compared to placebo by 33% (95% CI: -6% to 58%) (17.3% valsartan vs. 27.1% placebo) and the composite mortality and morbidity risk was significantly reduced by 44% (24.9% valsartan vs. 42.5% placebo). In patients receiving an ACE inhibitor without a beta-blocker, all-cause mortality was similar (p=NS) in the valsartan (21.8%) and placebo (22.5%) groups. Composite mortality and morbidity risk was significantly reduced by 18.3% (95% CI: 8% to 28%) with valsartan compared with placebo (31.0% vs. 36.3%).
In the overall Val-HeFT population, patients treated with valsartan experienced a significant improvement in the NYHA class and in the signs and symptoms of heart failure, including dyspnoea, fatigue, oedema and rales when compared with placebo. Patients treated with valsartan had a better quality of life, demonstrated by the change in the Minnesota Living with Heart Failure Quality of Life score from baseline at endpoint than placebo. Ejection fraction in patients treated with valsartan increased significantly and LVIDD significantly reduce from baseline at endpoint compared to placebo.

5.2 Pharmacokinetic properties

Absorption
Following oral administration of valsartan alone, peak plasma concentrations of valsartan are reached in 2-4 hours. The mean absolute bioavailability is 23 %. Food decreases exposure (as measured by AUC) to valsartan by about 40% and peak plasma concentration (C_{max}) by about 50%, although from about 8 h post dosing plasma valsartan concentrations are similar for the fed and fasted groups. This reduction in AUC is not, however, accompanied by a clinically significant reduction in the therapeutic effect, and valsartan can therefore be given either with or without food.

Distribution:
The steady-state volume of distribution of valsartan after intravenous administration is about 17 litres, indicating that valsartan does not distribute into tissues extensively. Valsartan is highly bound to serum proteins (94–97%), mainly serum albumin.

Biotransformation:
Valsartan is not bio transformed to a high extent as only about 20% of dose is recovered as metabolites. A hydroxy metabolite has been identified in plasma at low concentrations (less than 10% of the valsartan AUC). This metabolite is pharmacologically inactive.

Excretion:
Valsartan shows multiexponential decay kinetics ($t_{½\alpha}$ <1 h and $t_{½\beta}$ about 9 h). Valsartan is primarily eliminated by biliary excretion in faeces (about 83% of dose) and renally in urine (about 13% of dose), mainly as unchanged drug. Following intravenous administration, plasma clearance of valsartan is about 2 l/h and its renal clearance is 0.62 l/h (about 30% of total clearance). The half-life of valsartan is 6 hours.**Cinfaval**

In heart failure patients:
The average time to the peak concentration and the elimination half-life of valsartan in patients with heart failure is similar to that seen in healthy volunteers. The AUC and C_{max} values of valsartan are almost proportional with increasing dose over the clinical dosing range (40 to 160 mg twice a day). Average accumulation factor is approximately 1.7. Apparent clearance of valsartan after oral administration is approximately 4.5 L/h. Age does not affect apparent clearance in patients with heart failure.

Special populations
Elderly
Some elderly people show a somewhat higher systemic exposure to valsartan than young individuals; however, this difference has not been shown to be clinically significant.

Impaired renal function
As expected for a compound with a renal clearance of only 30% of the total plasma clearance, no correlation was seen between renal function and systemic exposure to valsartan. Therefore, no dose adjustment is required in patients with renal impairment (creatinine clearance > 10 ml/min). there is currently no experience on the safe use in patients with a (creatinine clearance < 10 ml/min) or those undergoing dialysis, therefore valsartan is highly bound to plasma protein and is unlikely to be removed by dialysis.

Hepatic impairment
Approximately 70% of the dose absorbed is eliminated in the bile, essentially in the unchanged form. valsartan does not undergo any noteworthy biotransformation. A doubling of exposure (AUC) was observed in patients with mild to moderate hepatic impairment compared to healthy subjects. However, no correlation was observed between plasma valsartan concentration versus degree of hepatic dysfunction No data are available on the use of valsartan in patients with severe liver dysfunction (see sections 4.2, 4.3 and 4.4).

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity and carcinogenic potential.

In rats, maternally toxic doses (600 mg/kg/day) during the last days of gestation and lactation led to lower survival, lower weight gain and delayed development (pinna detachment and ear-canal opening) in the offspring (see section 4.6). These doses in rats (600 mg/kg/day) are approximately 18 times the maximum recommended human dose on a mg/m^2 basis (calculations assume an oral dose of 320 mg/day and a 60-kg patient).

In non-clinical safety studies, high doses of valsartan in rats (200 to 600 mg/kg body weight) caused a reduction of red blood cell parameters (erythrocytes, haemoglobin, haematocrit) and evidence of changes in renal haemodynamic (slight raised plasma urea, renal tubular hyperplasia and basophilia in males). These doses in rats (200 to 600 mg/kg/day) are approximately 6 and 18 times the maximum recommended human dose on a mg/m^2 basis (calculations assume an oral dose of 320 mg/day and a 60-kg patient)

In marmosets at similar doses, the changes were similar although more severe, particularly in the kidney, where they developed nephropathy which included raised in urea and creatinine.
Hypertrophy of renal juxtaglomerular cells was also observed in both species. It was considered that these changes were caused by the pharmacological action of valsartan that causes prolonged hypotension, particularly in marmosets. At therapeutic doses of valsartan in humans, hypertrophy of juxtaglomerular renal cells does not appear to be relevant.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core: microcrystalline cellulose (E-460), colloidal anhydrous silica, sorbitol (E-420), magnesium carbonate (E-504), pregelatinised starch, povidone (E-1201), sodium stearyl fumarate, sodium lauryl sulphate and crospovidone.

Coating: Opadry OY-L-28900 (lactose monohydrate, hypromellose (E-464), titanium dioxide (E-171) and macrogol) and yellow iron oxide (E-172).

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store at a temperature less than 30ºC.

6.5 Nature and contents of container

The tablets are supplied in PVC-PE-PVDC (Triplex)/Aluminium blister packs.

Cinfaval 40 mg is supplied in packages containing 14 tablets.

6.6 Special precautions for disposal

Any unused medicinal product and all materials that have come into in contact with it should be disposed of in accordance with local regulations.

7. MARKETING AUTHORISATION HOLDER

LABORATORIOS CINFA, S.A.
Olaz-Chipi, 10 – Polígono Areta
31620 Huarte-Pamplona (Navarra)

8. MARKETING AUTHORISATION NUMBER(S)

Pending

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT