SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Tensipine MR 10

Tensipine MR 20

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Tensipine MR 10
One film-coated tablet contains 10mg nifedipine.

Tensipine MR 20
One film-coated tablet contains 20mg nifedipine.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Modified release tablets for oral administration.

Tensipine MR 10
Pink-grey lacquered, modified release tablets each containing 10mg nifedipine, one side marked TMR and the reverse side marked 10.

Tensipine MR 20
Pink-grey lacquered, modified release tablets each containing 20mg nifedipine, one side marked TMR and the reverse side marked 20.

4. CLINICAL PARTICULARS

4.1. Therapeutic Indications

For the prophylaxis of chronic stable angina pectoris and the treatment of hypertension.

4.2 Posology and method of administration

Method of Administration
Oral use.

As a rule, tablets are swallowed whole with a little liquid, either with or without food.

Tensipine MR should not be taken with grapefruit juice (see Section 4.5).

Dosage regimen

The recommended starting dose of Tensipine MR is 10mg every 12 hours swallowed with water with subsequent titration of dosage according to response. The dose may be adjusted to 40mg every 12 hours, to a maximum daily dose of 80mg.

Co-administration with CYP 3A4 inhibitors or CYP 3A4 inducers may result in the recommendation to adapt the nifedipine dose or not to use nifedipine at all (see Section 4.5).

Duration of treatment
Treatment may be continued indefinitely.

Additional information on special populations

Children and adolescents
The safety and efficacy of nifedipine in children below 18 years of age has not been established. Currently available data for the use of nifedipine in hypertension are described in section 5.1.

Elderly patients
The pharmacokinetics of nifedipine are altered in the elderly so that lower maintenance doses of nifedipine may be required compared to younger patients.

Patients with hepatic impairment
Nifedipine is metabolized primarily by the liver and therefore patients with liver dysfunction should be carefully monitored and in severe cases, a dose reduction may be necessary.

Patients with renal impairment
Based on pharmacokinetic data, no dosage adjustment is required in patients with renal impairment.

4.3 Contraindications

Tensipine MR must not be administered to patients with known hypersensitivity to the active substance, or to other dihydropyridines because of the theoretical risk of cross-reaction, or to any of the excipients listed in section 4.4 and 6.1.

Tensipine MR is contraindicated in pregnancy before week 20 and during breastfeeding (see sections 4.4, 4.6 and 5.3).

Tensipine MR must not be used in cases of cardiogenic shock, clinically significant aortic stenosis, unstable angina, or during or within one month of a myocardial infarction.

Tensipine MR should not be used for the treatment of acute attacks of angina.

The safety of Tensipine MR in malignant hypertension has not been established.

Tensipine MR should not be used for secondary prevention of myocardial infarction.

Tensipine MR must not be administered concomitantly with rifampicin since effective plasma levels of nifedipine may not be achieved owing to enzyme induction (see section 4.5).

4.4 Special warnings and precautions for use

Tensipine MR is not a beta-blocker and therefore gives no protection against the dangers of abrupt beta-blocker withdrawal; any such withdrawal should be by gradual reduction of the dose of beta-blocker preferably over 8 - 10 days.

Tensipine MR may be used in combination with beta-blocking drugs and other antihypertensive agents but the possibility of an additive effect resulting in postural hypotension should be borne in mind. Tensipine MR will not prevent possible rebound effects after cessation of other antihypertensive therapy.

Care must be exercised in patients with very low blood pressure (severe hypotension with systolic pressure less than 90mm HG), in cases of manifest heart failure and in the case of severe aortic stenosis.

Tensipine MR should not be used during pregnancy unless the clinical condition of the woman requires treatment with nifedipine. Tensipine MR should be reserved for women with severe hypertension who are unresponsive to standard therapy (see section 4.6).

Nifedipine is not recommended for use during breastfeeding because nifedipine has been reported to be excreted in human milk and the effects of oral absorption of small amounts of nifedipine are not known (see section 4.6)

Careful monitoring of blood pressure must be exercised, also when administering nifedipine with I.V. magnesium sulfate, owing to the possibility of an excessive fall in blood pressure, which could harm both mother and foetus. For further information regarding use in pregnancy, refer to section 4.6.

In patients with impaired liver function, careful monitoring, and in severe cases, a dose reduction may be necessary.

Tensipine MR should be used with caution in patients whose cardiac reserve is poor. Deterioration of heart failure has occasionally been observed with nifedipine.

Diabetic patients taking Tensipine MR may require adjustment of their control.

In dialysis patients with malignant hypertension and hypovolaemia, a marked decrease in blood pressure can occur.

Nifedipine is metabolised via the cytochrome P450 3A4 system. Drugs that are known to inhibit or to induce this enzyme system may therefore alter the first pass or the clearance of nifedipine (see section 4.5).

Drugs that are known inhibitors of the cytochrome P450 3A4 system, and which may therefore lead to increased plasma concentrations of nifedipine include, for example:

- macrolide antiobiotics (e.g. erythromycin)
- anti-HIV protease inhibitors (e.g. ritonavir)
- azole anti-mycotics (e.g. ketoconazole)
- the antidepressants, nefazodone and fluoxetine
- quinupristin/dalfopristin
- valproic acid
- cimetidine

Upon co-administration with these drugs, the blood pressure should be monitored and, if necessary, a reduction of the nifedipine dose should be considered (see section 4.5).

Since this medicinal product contains lactose, patients with rare heriditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

For use in special populations see section 4.2.

4.5 Interaction with other medicinal products and other forms of interaction

Drugs that affect nifedipine:

Nifedipine is metabolised via the cytochrome P450 3A4 system, located both in the intestinal mucosa and in the liver. Drugs that are known to either inhibit or to induce this enzyme system may therefore alter the first pass (after oral administration) or the clearance of nifedipine (see section 4.4).

The extent as well as the duration of interactions should be taken into account when administering nifedipine together with the following drugs:

Rifampicin: Rifampicin strongly induces the cytochrome P450 3A4 system. Upon co-administration with rifampicin, the bioavailability of nifedipine is distinctly reduced and this its efficacy weakened. The use of nifedipine in combination with rifampicin is therefore contraindicated (see section 4.3)

Upon co-administration of the following weak to moderate inhibitors of the cytochrome P450 3A4 system the blood pressure should be monitored and, if necessary, a reduction in the nifedipine dose considered (see sections 4.2 and 4.4). In the majority of these cases, no formal studies to assess the potential for a drug interaction between nifedipine and the drug(s) listed have been undertaken, thus far

Macrolide antiobiotics (e.g. erythromycin)
No interaction studies have been carried out between nifedipine and macrolide antibiotics. Certain macrolide antibiotics are known to inhibit the P450 3A4 mediated metabolism of other drugs. Therefore the potential for an increase of

nifedipine plasma concentrations upon co-administration of both drugs cannot be excluded (see section 4.4).
Azithromycin, although structurally related to the class of macrolide antibiotics is void of CYP3A4 inhibition.

anti-HIV protease inhibitors (e.g. ritonavir)
A clinical study investigating the potential of a drug interaction between nifedipine and certain anti-HIV protease inhibitors has not yet been performed. Drugs of this class are known to inhibit the cytochrome P450 3A4 system. In addition, drugs of this class have been shown to inhibit *in vitro* the cytochrome P450 3A4 mediated metabolism of nifedipine. When administered together with nifedipine, a substantial increase in plasma concentrations of nifedipine due to a decreased first pass metabolism and a decreased elimination cannot be excluded (see section 4.4).

Azole anti-mycotics (e.g. ketoconazole)
A formal interaction study investigating the potential of a drug interaction between nifedipine and certain azole anti-mycotics has not yet been performed. Drugs of this class are known to inhibit the cytochrome P450 3A4 system. When administered orally together with nifedipine, a substantial increase in systemic bioavailability of nifedipine due to a decreased first pass metabolism cannot be excluded (see section 4.4).

Fluoxetine
A clinical study investigating the potential of a drug interaction between nifedipine and fluoxetine has not yet been performed. Fluoxetine has been shown to inhibit in vitro the cytochrome P450 3A4 mediated metabolism of nifedipine. Therefore an increase of nifedipine plasma concentrations upon co-administration of both drugs cannot be excluded (see section 4.4).

Nefazodone
A clinical study investigating the potential of a drug interaction between nifedipine and nefazodone has not yet been performed. Nefazodone is known to inhibit the cytochrome P450 3A4 mediated metabolism of other drugs. Therefore an increase of nifedipine plasma concentrations upon co-administration of both drugs cannot be excluded (see section 4.4).

Quinupristin / Dalfopristin
Simultaneous administration of quinupristin / dalfopristin and nifedipine may lead to increased plasma concentrations of nifedipine (see section 4.4).

Valproic acid
No formal studies have been performed to investigate the potential interaction between nifedipine and valproic acid. As valproic acid has been shown to increase the plasma concentrations of the structurally similar calcium channel blocker nimodipine due to enzyme inhibition, an increase in nifedipine plasma concentrations and hence an increase in efficacy cannot be excluded (see section 4.4).

Cimetidine

Due to its inhibition of cytochrome P450 3A4, cimetidine elevates the plasma concentrations of nifedipine and may potentiate the antihypertensive effect (*see section 4.4)*.

Further Studies:

- **Diltiazem**

- **Cisapride**
  Simultaneous administration of cisapride and nifedipine may lead to increased plasma concentrations of nifedipine.

- **Cytochrome P450 3A4 system inducing anti-epileptic drugs, such as phenytoin, carbamazepine and phenobarbitone**
  Phenytoin induces the cytochrome P450 3A4 system. Upon co-administration with phenytoin, the bioavailability of nifedipine is reduced and thus its efficacy weakened. When both drugs are concomitantly administered, the clinical response to nifedipine should be monitored and, if necessary, an increase of the nifedipine dose considered. If the dose of nifedipine is increased during co-administration of both drugs, a reduction of the nifedipine dose should be considered when the treatment with phenytoin is discontinued.

  No formal studies have been performed to investigate the potential interaction between nifedipine and carbamazepine or phenobarbitone. As both drugs have been shown to reduce the plasma concentrations of the structurally similar calcium channel blocker nimodipine due to enzyme induction, a decrease in nifedipine plasma concentrations and hence a decrease in efficacy cannot be excluded.

Effects of nifedipine on other drugs:

Blood pressure lowering drugs

Nifedipine may increase the blood pressure lowering effect of concomitant applied antihypertensives, such as:

- Diuretics,
- β-blockers,
- ACE-inhibitors,
- Angiotensin 1 (AT1) receptor-antagonists
- Other calcium antagonists
- α-adrenergic blocking agents,
- PDE5 inhibitors
- α-methyldopa

When nifedipine is administered simultaneously with β-receptor blockers the patient should be carefully monitored, since deterioration of heart failure is also known to develop in isolated cases.

Digoxin: The simultaneous administration of nifedipine and digoxin may lead to reduced digoxin clearance and, hence, an increase in the plasma concentrations

of digoxin. The patient should therefore be checked for symptoms of digoxin overdosage as a precaution and, if necessary, the glycoside dose should be reduced taking account of the plasma concentration of digoxin.

Quinidine: When nifedipine and quinidine have been administered simultaneously, lowered quinidine or, after discontinuation of nifedipine, a distinct increase in plasma concentrations of quinidine has been observed in individual cases. For this reason, when nifedipine is either additionally administered or discontinued, monitoring of the quinidine plasma concentration and, if necessary, adjustment of the quinidine dose are recommended. Some authors reported increased plasma concentrations of nifedipine upon co-administration of both drugs, while others did not observe an alteration in the pharmacokinetics of nifedipine. Therefore, the blood pressure should be carefully monitored, if quinidine is added to an existing therapy with nifedpine. If necessary, the dose of nifedipine should be decreased.

Tacrolimus: Tacrolimus has been shown to be metabolised via the cytochrome P450 3A4 system. Published data indicate that the dose of tacrolimus administered simultaneously with nifedipine may be reduced in individual cases. Upon co-administration of both drugs, the tacrolimus plasma concentrations should be monitored and, if necessary, a reduction in the tacrolimus dose considered.

Drug food interactions:

Grapefruit juice

Grapefruit juice inhibits the cytochrome P450 3A4 system. Administration of nifedipine together with grapefruit juice thus results in elevated plasma concentrations and prolonged action of nifedipine due to a decreased first pass metabolism or reduced clearance. As a consequence, the blood pressure lowering effect of nifedipine may be increased. After regular intake of grapefruit juice, this effect may last for at least three days after the last ingestion of grapefruit juice. Ingestion of grapefruit/grapefruit juice is therefore to be avoided while taking nifedipine (see section 4.2).

Other forms of interaction

Nifedipine may cause falsely increased spectrophotometric values of urinary vanillylmandelic acid. However, measurement with HPLC is unaffected.

4.6 Fertility, pregnancy and lactation

Pregnancy

Nifedipine is contra-indicated in pregnancy before week 20 (see section 4.3.) and should not be used during pregnancy unless the clinical condition of the woman requires treatment with nifedpine. Nifedipine should be reserved for women with severe hypertension who are unresponsive to standard therapy (see section 4.4).

In animal studies, nifidepine has been shown to produce embryotoxicity, foetoxicity and teratogenicity (see section 5.3 Preclinical safety data).

There are no adequate and well-controlled studies in pregnant women.

The available information is inadequate to rule out adverse drug effects on the unborn and newborn child. Therefore any use in pregnancy after week 20 requires a very careful individual risk benefit assessment and should only be considered if all other treatment options are either not indicated or have failed to be efficacious.

From the clinical evidence available a specific prenatal risk has not been identified. Although an increase in perinatal asphyxia, caesarean delivery, as well as prematurity and intrauterine growth retardation has been reported. It is unclear whether these reports are due to the underlying hypertension, its treatment, or to a specific drug effect.

Acute pulmonary oedema has been observed when calcium channel blockers, among others nifedipine, have been used as a tocolytic agent during pregnancy (see section 4.8), especially in cases of multiple pregnancy (twins or more), with the intravenous route and/or concomitant use of beta-2 agonists

Breast-feeding
Nifedipine is excreted in the breast milk. The nifedipine concentration in the milk is almost comparable with mother serum concentration. As there is no experience of possible effects on infants, breastfeeding should first be stopped if nifedipine treatment becomes necessary during the breastfeeding period.

Fertility
In single cases of in vitro fertilization calcium antagonists like nifedipine have been associated with reversible biochemical changes in the spermatozoa's head section that may result in impaired sperm function. In those men who are repeatedly unsuccessful in fathering a child by in vitro fertilization, and where no other explanation can be found, calcium antagonists like nifedipine should be considered as possible causes.

4.7 Effects on ability to drive and use machines

Reactions to the drug, which vary in intensity from individual to individual, may impair the ability to drive or to operate machinery (see section 4.8). This applies particularly at the start of treatment, on changing the medication and in combination with alcohol.

4.8 Undesirable effects

Ischaemic pain has been reported in a small proportion of patients within one to four hours of the introduction of Tensipine MR therapy. Although a "steal" effect has not been demonstrated, patients experiencing this effect should discontinue Tensipine MR.

Adverse drug reactions (ADRs) based on placebo-controlled studies with nifedipine sorted by CIOMS III categories of frequency (clinical trial data base: nifedipine n = 2,661; placebo n = 1,486; status: 22 Feb 2006 and the ACTION study: nifedipine n = 3,825; placebo n = 3,840) are listed below:
ADRs listed under 'common' were observed with a frequency below 3% with the exception of oedema (9.9%) and headache (3.9%).

The frequencies of ADRs reported with nifedipine-containing products are summarized in the table below. Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness. Frequencies are defined as common (≥ 1/100 to <1/10), uncommon (≥ 1/1,000 to <1/100) and rare (≥1/10,000 to <1/1,000). The ADRs identified only during the ongoing postmarketing surveillance, and for which a frequency could not be estimated, are listed under 'Not known'.

System Organ Class (MedDRA)	**Common**	**Uncommon**	**Rare**	**Not Known**
Blood and Lymphatic System Disorders				Agranulocytosis Leucopenia
Immune System Disorders		Allergic reaction Allergic oedema/ angioedema (inc. larynx oedema*)	Pruritus Urticaria Rash	Anaphylatic/ anaphylactoid reaction
Psychiatric Disorders		Anxiety reactions Sleep disorders		Depression
Metabolism and Nutrition Disorders				Hyperglycaemia
Nervous System Disorders	Headache	Vertigo Migraine Dizziness Tremor	Par-/Dysaesthesia	Hypoaesthesia Somnolence
Eye Disorders		Visual disturbances		Eye pain
Cardiac Disorders		Tachycardia Palpitations		Chest pain (Angina Pectoris)
Vascular Disorders	Oedema (inc. peripheral oedema) Vasodilatation	Hypotension Syncope		Pulmonary oedema**
Respiratory, Thoracic, and Mediastinal Disorders		Nasal congestion Nosebleed		Dyspnea
Gastrointestinal Disorders	Constipation	Gastrointestinal and abdominal pain Nausea Dyspepsia Flatulence Dry mouth	Gingival hyperplasia	Vomiting Gastroesophageal sphincter insufficiency
Hepatobiliary Disorders		Transient increase in liver enzymes		Jaundice
Skin and Subcutanenous		Erythema		Toxic Epidermal Necrolysis

Tissue Disorders				Photosensitivity allergic reaction Palpable purpura
Musculoskeletal and Connective Tissue Disorders		Muscle cramps Joint swelling		Arthralgia Myalgia
Renal and Urinary Disorders		Polyuria Dysuria		
Reproductive System and Breast Disorders		Erectile dysfunction		
General Disorders and Administration Site Conditions	Feeling unwell	Unspecific pain Chills		

* = may result in life-threatening outcome
** = cases have been reported when used as tocolytic during pregnancy (see section 4.6)

In dialysis patients with malignant hypertension and hypovolaemia a distinct fall in blood pressure can occur as a result of vasodilation.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard

4.9 Overdose

Symptoms
The following symptoms are observed in cases of severe nifedipine intoxication:

Disturbances of consciousness to the point of coma, a drop in blood pressure, tachycardiac / bradycardiac heart rhythm disturbances, hyperglycaemia, metabolic acidosis, hypoxia, cardiogenic shock with pulmonary oedema.

Management of Overdose
As far as treatment is concerned, elimination of nifedipine and the restoration of stable cardiovascular conditions have priority. Elimination must be as complete as possible, including the small intestine, to prevent the otherwise inevitable subsequent absorption of the active substance.

The benefit of gastric decontamination is uncertain.

1. Consider activated charcoal (50 g for adults, 1g/kg for children) if the patient presents within 1 hour of ingestion of a potentially toxic amount.

Although it may seem reasonable to assume that late administration of activated charcoal may be beneficial for sustained release (SR, MR) preparations there is no evidence to support this.

2. Alternatively, after oral ingestion, consider thorough gastric lavage in adults within 1 hour of a potentially life-threatening overdose, if necessary in combination with irrigation of the small intestine

3. Consider further doses of activated charcoal every 4 hours if a clinically significant amount of a sustained release preparation has been taken.

4. Asymptomatic patients should be observed for at least 4 hours after ingestion and for 12 hours if a sustained release preparation has been taken.

Haemodialysis serves no purpose as nifedipine is not dialysable, but plasmapheresis is advisable (high plasma protein binding, relatively low volume of distribution).

Bradycardiac heart rhythm disturbances may be treated symptomatically with beta-sympathomimetics, and in life-threatening bradycardiac disturbances of heart rhythm, temporary cardiac pacemaker therapy can be advisable.

Hypotension as a result of cardiogenic shock and arterial vasodilatation can be treated with calcium (10 -20 ml of a 10% calcium gluconate solution administered slowly intraveneously over 5-10 minutes). As a result the serum calcium can reach the upper normal range to slightly elevated levels. If the effects are inadequate, the treatment can be continued, with ECG monitoring. If an insufficient increase in blood pressure is achieved with calcium, vasoconstricting sympathomimetics such as dopamine or noradrenaline should be additionally administered. The dosage of these drugs is determined solely by the effect obtained / by the patient's response.

Additional liquid or volume must be administered with caution because of the danger of overloading the heart.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC code: C08CA05

Nifedipine is a specific and potent calcium antagonist of the 1,4-dihydropyridine type. Calcium antagonists reduce the transmembranal influx of calcium ions through the slow calcium channel into the cell. Nifedipine acts particularly on the cells of myocardium and the smooth muscle cells of the coronary arteries and the peripheral resistance vessels.

In hypertension, the main action of Tensipine MR is to cause peripheral vasodilatation and thus reduce peripheral resistance.

In angina, Tensipine MR reduces peripheral and coronary vascular resistance, leading to an increase in coronary blood flow, cardiac output and stroke volume, whilst decreasing after-load.

Additionally, nifedipine dilates submaximally both clear and atherosclerotic coronary arteries, thus protecting the heart against coronary artery spasm and improving perfusion to the ischaemic myocardium.

Nifedipine reduces the frequency of painful attacks and the ischaemic ECG changes irrespective of the relative contribution from coronary artery spasm or atherosclerosis.

Tensipine MR administered twice-daily provides 24-hour control of raised blood pressure. Tensipine MR causes reduction in blood pressure such that the percentage lowering is directly related to its initial level. In normotensive individuals, Tensipine MR has little or no effect on blood pressure.

Paediatric population:
Limited information on comparison of nifedipine with other antihypertensives is available for both acute hypertension and long-term hypertension with different formulations in different dosages. Antihypertensive effects of nifedipine have been demonstrated but dose recommendations, long term safety and effect on cardiovascular outcome remain unestablished. Paediatric dosing forms are lacking.

5.2 Pharmacokinetic properties

Absorption
After oral administration nifedipine is rapidly and almost completely absorbed. The systematic availability of orally administered nifedipine is 45 – 56% owing to a first pass effect. Maximum plasma and serum concentrations are reached at 1.5 to 4.2 hours with Tensipine MR (20mg tablets). Simultaneous food intake leads to delayed, but not reduced absorption.

Distribution
Nifedipine is about 95% bound to plasma protein (albumin). The distribution half-life after intraveneous administration was determined to be 5 to 6 minutes.

Biotransformation
After oral administration nifedipine is metabolized in the gut wall and in the liver, primarily by oxidative processes. These metabolites show no pharmacodynamic activity. Nifedipine is excreted in the form of its metabolites predominantly via the kidneys and about 5 – 15% via the bile in the faeces. The unchanged substance is recovered only in traces (below 0.1%) in the urine.

Elimination
The terminal elimination half-life is 6 – 11 hours (Tensipine MR), because of delayed absorption. No accumulation of the substance after the usual dose was reported during long-term treatment. In cases of impaired kidney function no substantial changes have been detected in comparison with healthy volunteers. In cases of impaired liver function the elimination half-life is distinctly prolonged and the total clearance is reduced. A dose reduction may be necessary in severe cases.

5.3 Preclinical safety data

Preclinical data reveal no special hazard for humans based on conventional studies of single and repeated dose toxicity, genotoxicity and carcinogenic potential.

Reproduction toxicology
Nifedipine has been shown to produce teratogenic findings in rats, mice and rabbits, including digital anomalies, malformation of the extremities, cleft palates, cleft sternum and malformation of the ribs. Digital anomalies and malformation of the extremities are possibly as a result of compromised uterine blood flow, but have also been observed in animals treated with nifedipine solely after the end of the organogenesis period.

Nifedipine administration has been associated with a variety of embryotoxic, placentotoxic and fetotoxic effects, including stunted fetuses (rats, mice and rabbits), small placentas and underdeveloped chorionic villi (monkeys), embryonic and foetal deaths (rats, mice, rabbits) and prolonged pregnancy/decreased neonatal survival (rats; not evaluated in other species). The risk to humans cannot be ruled out if a significantly high systematic exposure is achieved, however, all of the doses associated with the teratogenic, embryotoxic or fetotoxic effects in animals were maternally toxic and several times the recommended maximum dose for humans (see Section 4.6)..

6. PHARMACEUTICAL PARTICULARS

6.1. List of Excipients

Tensipine MR tablets contain the following excipients:

Microcrystalline cellulose, maize starch, lactose, polysorbate 80, magnesium stearate, hydroxypropyl methylcellulose, polyethylene glycol 4000, iron oxide red and titanium dioxide.

6.2. Incompatibilities

Not applicable.

6.3. Shelf-Life

PVC blister strips: 48 months
PP blister strips: 30 months

6.4. Special Precautions for Storage

The tablets should be protected from strong light and stored in the manufacturer's original container.

6.5. Nature and Contents of Container

Blister strips of 14 tablets in a cardboard outer container, packs of 56 tablets.

Blister strips are composed of red polypropylene foil (0.3mm) with aluminium backing foil (0.02mm) or red PVC foil (0.3mm) with aluminium backing foil (0.02mm).

6.6. Instructions for Use, Handling and Disposal

No additional information.

7 MARKETING AUTHORISATION HOLDER

Genus Pharmaceuticals Limited

T/A Genus Pharmaceuticals

Linthwaite,

Huddersfield,

HD7 5QH, UK

8. MARKETING AUTHORISATION NUMBER(S)

Tensipine MR 10
PL 06831/0048

Tensipine MR 20
PL 06831/0049

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Tensipine MR 10
19/02/2009

Tensipine MR 20
23/02/2009

10 DATE OF REVISION OF THE TEXT

09/03/2023