SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Acebutolol 400 mg film-coated tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 400 mg of acebutolol (as acebutolol hydrochloride)

Excipients with known effect
Each 400 mg film-coated tablet contains 52 mg lactose monohydrate

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet.

White to off-white, oblong shaped biconvex film coated tablets having the length approximately 17.15 mm, diameter of body approximately 8.42 mm debossed with ‘AC’ and ‘4’ separated with breakline on one side and plain on the other side.

The tablet can be divided into equal doses

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

The management of hypertension, angina pectoris and the control of tachyarrhythmias.

4.2 Posology and method of administration

Posology

The dose and treatment duration should be based on the individual response and should be adequately monitored by the treating physician.

If long-term treatment will be discontinued, withdrawal of treatment by betablockers should be achieved by gradual dosage reduction.

Hypertension:
The usual initial daily dose is 400 mg. Based on pharmacokinetic studies it is recommended to administer the entire dose at once in the morning. In exceptional cases, the daily dose can be divided into two separate doses of 200 mg administered in the morning and evening.
If response is not adequate within two weeks, dosage may be increased up to 400 mg orally twice daily; in some patients 1200 mg orally daily, given as 800 mg at breakfast and 400 mg in the evening may be required. A further reduction in blood pressure may be obtained by the concurrent administration of a thiazide diuretic or other antihypertensive agent .

Angina pectoris: Initial dosage of 400 mg orally once daily at breakfast or 200 mg twice daily. In severe forms up to 300 mg three times daily may be required. Up to 1200 mg daily has been used.

Cardiac Arrhythmias: When given orally, an initial dose of 200 mg is recommended. The daily dose requirement for long term anti arrhythmic activity should lie between 400 and 1200 mg daily. The dose can be gauged by response, and better control may be achieved by divided doses rather than single doses. It may take up to three hours for maximal antiarrhythmic effect to become apparent.

Renal impairment:
Dosage in patients with renal impairment should be based on creatinine clearance.
Creatinine clearance 25-50 ml / min, the dose should be reduced in 50%.
Creatinine clearance < 25 ml / min, the dose should be reduced in 75% (see section 4.4).

Elderly: There are no specific dosage recommendations for the elderly with normal glomerular filtration rate. Dose reduction is necessary if moderate to severe renal impairment is present (see Section 4.4)

Paediatric population
Paediatric dose has not been established.
The safety and efficacy of Acebutolol in children has not been established.
No data are available

Method of administration
Oral use
For all indications, it is advised that the lowest recommended dosage be used initially.
Acebutolol tablets are swallowed with a glass of water and not chewed or crushed.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1 or to beta blockers.

Cardiogenic shock is an absolute contraindication. Extreme caution is required in patients with blood pressures of the order of 100/60 mmHg or below.

Acebutolol is also contraindicated in patients with

- Asthma and chronic obstructive pulmonary disease in their severe forms,
- Second and third degree heart block,
- Prinzmetal angina
- Sick sinus syndrome
- Marked bradycardia (< 45 – 50 bpm)
- Raynaud's phenomenon and peripheral arterial disease in their severe forms,
- Decompensated heart failure
- Metabolic acidosis
- Severe peripheral circulatory disorders
- Untreated phaeochromocytoma.
- Combination with floctafenine or sultopride (see section 4.5),
- History of anaphylaxis,
- Breastfeeding (see section 4.6).

4.4 Special warnings and precautions for use

Renal impairment:

Renal impairment is not contraindicated to the use of Acebutolol which has both renal and non-renal excretory pathways. Some caution should be exercised when administering high doses to patients with severe renal impairment as accumulation could possibly occur in these circumstances.

The dosage frequency should not exceed once daily in patients with renal impairment. As a guide, the dosage should be reduced by 50% when glomerular filtration rates are between 25-50 ml/ min and by 75% when they are below 25 ml/min (see section 4.2). Monitoring for heart rate could further guide on the appropriate dose in clinical practice, and should be reduced if excessive bradycardia appears (< 50-55 beats/min at rest).

Asthma and chronic obstructive pulmonary disease:

Drug-induced bronchospasm is usually at least partially reversible by the use of a suitable agonist.

Although cardio-selective beta blockers may have less effect on lung function than nonselective beta blockers as with all beta blockers these should be avoided in patients with obstructive airways disease unless there are compelling clinical reasons for their use. Where such reasons exist, cardio-selective β-blockers should be used with the utmost care.

Acebutolol can only be administered to mild forms of bronchospastic disease or bronchial asthma, but the initial dose is low. Respiratory function tests are recommended before starting treatment.

If bronchospasm occurs during treatment, beta-mimetic bronchodilators may be used.

Bradycardia:

Betablockers may induce bradycardia. In such cases (< 50-55 beats/min at rest), the dosage should be reduced. They may be used with patients with controlled heart failure (see Section 4.3).

Heart failure:

In treatment-compensated heart failure, acebutolol should be given at very low, gradually increasing doses and under strict medical supervision if necessary.

Atrioventricular block first degree:

Given their dromotropic negative effect, beta-blockers should be administered with caution to patients with atrioventricular block first degree.

Prinzmetal angina:

Beta-blockers may increase the number and duration of seizures in patients with variant angina.

Peripheral circulatory disorders:

In patients with peripheral arterial disorders (Raynaud's disease or syndrome, arteritis or chronic occlusive arterial disease of the lower limbs), beta-blockers can cause aggravation of these disorders.

In such situations, cardioselective beta blocker with partial agonist activity (e.g. acebutolol) are preferred, although this should be administered with caution.

Pheochromocytoma:

The use of beta-blockers in the treatment of hypertension due to pheochromocytoma treated requires close monitoring of blood pressure.

They should only be used in patients with pheochromocytoma with concomitant alpha-adrenoreceptor therapy.

Elderly

In the elderly, the absolute respect of contraindications is imperative. Care should be taken to initiate treatment with a low dose and be closely monitored.

Diabetic patients:

Warn the patient and reinforce glycemic self-monitoring at the start of treatment. The warning signs of hypoglycaemia may be masked, particularly tachycardia, palpitations and sweating.

Thyrotoxicosis:

Acebutolol may mask signs of thyrotoxicosis.

Psoriasis:

Aggravation of the disease has been reported with beta-blockers. Patients with known psoriasis should take betablockers only after careful consideration.

Sensitivity to antigens and anaphylactic reactions:

Beta-blockers may increase the sensitivity to allergens and the severity of anaphylactic reactions. In patients susceptible to severe anaphylactic reactions, whatever its origin, particularly with iodine contrast products or floctafenin or during desensitizing treatments, the beta-blocker treatment may lead to worsening of the reaction and resistance to treatment by adrenaline in usual doses.

Discontinuation of treatment

Withdrawal of treatment by betablockers should be achieved by gradual dosage reduction: i.e. over 1-2 weeks this is especially important in patients with ischaemic heart disease.

If necessary replacement therapy should be initiated at the same time, to prevent exacerbation of angina pectoris.

Abrupt withdrawal of beta-blockers is to be avoided. Abrupt discontinuation of treatment may result in severe cardiac arrhythmias, myocardial infarction or sudden death.

General anesthesia:

Beta blockers will cause an attenuation of the reflex tachycardia and increased risk of hypotension. Continued treatment with beta-blocker reduces the risk of arrhythmia, myocardial ischemia and hypertensive crisis. The anaesthesiologist should be informed when the patient is receiving beta-blockers.

- If discontinuation of treatment is deemed necessary, a suspension of at least 24 hours may be considered sufficient for the reappearance of sensitivity to catecholamines.
- In some cases, beta-blocker treatment cannot be interrupted:

  o in patients with coronary insufficiency, it is desirable to continue treatment until surgery, given the risk associated with abrupt discontinuation of beta blockers,

  o Emergency stop or failure, the patient should be protected from vagal predominance by adequate atropine premedication renewed as needed.

  Anesthesia will make use of products as little as possible myocardial depressant and blood loss must be compensated.

  - Anaphylactic risk should be taken into account.

Myasthenia gravis

In patients with myasthenia gravis can lead to aggravation of symptoms.

Depression

Caution should be exercised in patients with depression.

Information about excipient

This medicine contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Combinations not recommended

+ diltiazem, verapamil

Disorders of automatism (excessive bradycardia, sinus arrest), sinoatrial and atrioventricular conduction disorders and cardiac failure.

Such an association should only be done under close clinical and electrocardiographic supervision and, especially in the elderly or at the beginning of treatment.

Acebutolol should not be used with verapamil or in the days after taking verapamil (or vice versa).

Great attention should be paid when combining with any other calcium antagonist, especially with diltiazem.

An increased risk of depression has been reported when beta-blockers are co-administered with diltiazem. (See section 4.8 undesirable effects).

+ **fingolimod**

Concomitant use of fingolimod with beta blockers may potentiate bradycardic effects with possible fatal outcomes and is not recommended. Beta blockers are most at risk as they prevent adrenergic compensation mechanisms. Where such coadministration is considered necessary, appropriate monitoring and ECG continuously for 24 hours at treatment initiation, i.e. at least overnight monitoring, is recommended.

+ floctafenine

In case of shock or hypotension due to floctafenine, the cardiovascular compensatory response is reduced by beta-blockers and therefore co-administration is contraindicated (see section 4.3).

+ sultopride

Concomitant administration of sultopride and acebutolol may lead to autoimmune disorders (excessive bradycardia) due to the addition of bradycardia effects. This combination is contraindicated (see section 4.3).

Combinations requiring precautions for use

+ halogenated volatile anesthetics

Reduction of cardiovascular compensation reactions by beta-blockers. The beta-adrenergic inhibition may be removed during surgery by beta-mimetics.

As a general rule, do not stop the beta-blocking treatment and, in any case, avoid abrupt cessation. If treatment is continued, special care should be taken when using anaesthetic agents such as ether, cyclopropane and trichlorethylene. Inform the anesthesiologist of this treatment (see section 4.4).

+ amiodarone

Disorders of automatism and conduction (suppression of compensatory sympathetic mechanisms). ECG and clinical monitoring are required.

Antiarrhythmics of class I (eg disopyramide) and amiodarone may increase atrial conduction time and induce negative inotropic effects when used in combination with beta-blockers.

+ central antihypertensives

significant increase in blood pressure in case of abrupt discontinuation of the central antihypertensive agent. Avoid the sudden discontinuation of the central antihypertensive therapy. Clinical monitoring required.

If a beta-blocker is used in combination with clonidine, the gradual withdrawal of beta-blocker should first be considered before the withdrawal of clonidine.

+Bronchodilators

Acebutolol may antagonize the effect of sympathomimetic and xanthine bronchodilators.

+Digoxin

Concurrent use of digoxin and beta-blockers may occasionally induce serious bradycardia.

+ insulin, meglitinides, sulfonylureas and gliptins

All beta-blockers may mask certain symptoms of hypoglycemia: palpitations and tachycardia. Warn the patient and strengthen, especially at the beginning of treatment, the self-monitoring glycemic (see section 4.4.)

In patients with unstable diabetes or insulin-dependent diabetes, the dosage of hypoglycemic medication (eg insulin or oral antidiabetic) may be decreased. In addition, beta-blockers are also known to decrease the effect of glibenclamide.

+Monoamine oxidase inhibitors

There is a theoretical risk that concurrent administration of monoamine oxidase inhibitors and high doses of beta-blockers, even if they are cardio-selective can produce hypertension.

+Baclofen

Baclofen may potentiate the antihypertensive effect. Arterial pressure monitoring and dose adjustment of antihypertensives should be considered if necessary.

+ lidocaine used intravenously

Increased plasma concentrations of lidocaine with possibility of neurological and cardiac side effects (decreased hepatic clearance of lidocaine).

Clinical monitoring, ECG and possibly control of plasma concentrations of lidocaine during the association and after discontinuation of beta-blocker.

Adaptation if necessary of dosage of lidocaine.

+ drugs likely to give torsades de pointes

Increased risk of ventricular arrhythmias, including torsades de pointes.

Clinical and electrocardiographic monitoring required.

+ Class I antiarrhythmic drugs (except lidocaine)

Disorders of contractility, automatism and conduction (suppression of compensatory sympathetic mechanisms). ECG and clinical monitoring.

Antiarrhythmics of class I (eg disopyramide) and amiodarone may increase atrial conduction time and induce negative inotropic effects when used in combination with beta-blockers.

To be taken into account

+ nonsteroidal anti-inflammatory

Reduced the antihypertensive effect (inhibition of vasodilator prostaglandins by nonsteroidal anti-inflammatory and fluid retention with phenylbutazone).

+ alpha blockers for urologic purposes

Increase of the hypotensive effect. Increased risk of orthostatic hypotension.

+ alpha-blocker antihypertensives

Increase of the hypotensive effect. Increased risk of orthostatic hypotension.

+ other bradycardia

Risk of excessive bradycardia (additive effects).

+ Dapoxetine

Risk of increased adverse effects such type of dizziness or syncope.

+ dihydropyridine

Hypotension, heart failure in patients with latent heart failure or uncontrolled (addition of negative inotropic effects). The beta-blocker can further minimize the reflex sympathetic reaction involved in case of excessive haemodynamic repercussion.

+ dipyridamole (IV route)

Increased antihypertensive effect.

+ pilocarpine

Risk of excessive bradycardia (additive effects bradycardia).

+ drugs causing orthostatic hypotension (including antihypertensives, nitrates, phosphodiesterase type 5 inhibitors, urological alpha-blockers, imipraminic antidepressants, phenothiazine neuroleptics, dopaminergic agonists, levodopa)

Risk of increase of hypotension including orthostatic.

+ **Plasma binding**

Cross reactions due to displacement of other drugs from plasma protein binding sites are unlikely due to the low degree of plasma protein binding exhibited by Acebutolol and Diacetolol.

+ Iodine X-ray contrast media

When iodinated contrast agents cause shock or hypotension, beta-blockers reduce cardiovascular compensatory responses. Therefore, beta-blocker therapy should be discontinued, if possible, prior to X-ray contrast testing. If not, the radiologist must have resuscitation treatment options.

+ Corticosteroids, tetracosactide

Corticosteroids and tetracosactide cause sodium retention and reduce the antihypertensive effect of beta-blockers.

+ Mefloquine

Mefloquine increases the risk of bradycardia.

4.6 Fertility, pregnancy and lactation

Pregnancy:

Acebutolol should not be administered to female patients during the first trimester of pregnancy unless the physician considers it essential. In such cases the lowest possible dose should be used.

Beta blockers administered in late pregnancy may give rise to bradycardia, hypoglycaemia and cardiac or pulmonary complications in the foetus/neonate.

Beta-blockers can reduce placental perfusion, which may result in intrauterine foetal death, immature and premature deliveries, small-for-gestational-age newborn.

Therefore, this drug, under normal conditions of use, can be prescribed during pregnancy if necessary. In case of treatment until delivery, close monitoring of the neonate (heart rate and blood glucose during the first 3 to 5 days of life) is recommended.

Clinically, no teratogenic effects have been reported to date and the results of controlled prospective studies with some beta-blockers have not reported birth defects.

Animal studies have shown no teratogenic hazard. In the absence of teratogenic effects in animals, a malformative effect in humans is not expected. Indeed, to date, the substances responsible for malformations in humans have proved to be teratogenic in animals during well-conducted studies in two species.

Breastfeeding

Acebutolol and its active metabolites are excreted in human milk and effects have been shown in breastfed newborns/infants of treated mothers. Acebutolol should not be used during breastfeeding.

Fertility

There is no human data available. Animal studies have not revealed adverse effects on fertility (see section 5.3).

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. As with all betablockers, dizziness or fatigue may occur occasionally. This should be taken into account when driving or operating machinery.

4.8 Undesirable effects

Summary of safety profile

Adverse reactions associated with acebutolol during controlled clinical trials in patients with hypertension, angina pectoris or arrhythmia (1002 patients exposed to acebutolol) are presented by system organ class and by decreasing order of frequency.

The frequency of the events “antinuclear antibody” and “lupus like syndrome” was found from 1440 patients suffering from hypertension, angina pectoris or arrhythmia and exposed to acebutolol in open or double blind studies performed in the United States.

Frequencies are defined as: very common (≥1/10), common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000), Not known (cannot be estimated from the available data)

When the exact frequency of the event was not reported, the frequency category assigned is “not known” (ADRs with *).

Adverse reactions reported from post marketing experience are also listed. These adverse reactions are derived from spontaneous reports and therefore, the frequency of these adverse reactions is “not known” (cannot be estimated from the available data).

The most frequent and serious adverse reactions of acebutolol are related to the beta adrenergic blocking activity. The most frequent reported clinical adverse reactions are fatigue and gastrointestinal disorders. Among the most serious adverse reactions are cardiac failure, atrioventricular block and bronchospasm. Abrupt withdrawal as for all betablockers may exacerbate angina pectoris and precaution is especially required in patients with ischaemic heart disease (see Section 4.4).

Tabulated list of adverse reactions:

Immune system disorders	Very common	Antinuclear antibody
	Uncommon	Lupus like syndrome
	Rare	Although antinuclear factor titres have increased in some patients, the incidence of associated clinical syndromes is rare and, if present, an immediate discontinuation of treatment is required.
Metabolism and nutrition disorders	Uncommon	Hypoglycemia

Psychiatric disorders	Common	Depression, nightmare
	Not known	Psychoses, hallucinations, confusion, loss of libido*, sleep disorder
Nervous system disorders	Very common	Fatigue
	Common	Dizziness, headache
	Not known	Paraesthesia*, central nervous system disorder
Eye disorders	Common	Visual impairment
	Not known	Dry eye*
Cardiac disorders	Not known	Cardiac failure*, atrioventricular block first degree, increase of an existing atrioventricular block, bradycardia*
Vascular disorders	Uncommon	Postural hypotension
	Not known	Intermittent claudication, Raynaud's syndrome, cyanosis peripheral and peripheral coldness, hypotension*
Respiratory, thoracic and mediastinal disorders	Common	Dyspnoea
	Not known	Pneumonitis, lung infiltration, bronchospasm
Gastrointestinal disorders	Very common	Gastrointestinal disorders
	Common	Nausea, diarrhoea
	Not known	Vomiting*
Hepatobiliary disorders	Not known	Hepatic enzymes increased, liver injury mainly hepatocellular
Skin and subcutaneous tissue	Common	Rash

disorders	Uncommon	Skin manifestations including psoriasiform skin changes or psoriasis exacerbations (see section 4.4)
	Not known	Alopecia
General disorders and administration site condition	Not known	Withdrawal syndrome (see Section 4.4)

**Stopped after the end of the treatment

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 national reporting system the national reporting system listed in Yellow Card Scheme, Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

In the event of excessive bradycardia or hypotension, 1mg atropine sulphate administered intravenously should be given without delay. If this is insufficient it should be followed by a slow intravenous injection of isoprenaline (5 mcg per minute) with constant monitoring until a response occurs. In severe cases of selfpoisoning with circulatory collapse unresponsive to atropine and catecholamines the intravenous injection of glucagon 10-20 mg may produce a dramatic improvement. Cardiac pacing may be employed if bradycardia becomes severe.

Judicious use of vasopressors, diazepam, phenytoin, lidocaine, digoxin and bronchodilators should be considered depending on the presentation of the patient. Acebutolol can be removed from blood by haemodialysis. Other symptoms and signs of over dosage include cardiogenic shock, AV block, conduction defects, pulmonary oedema, depressed level of consciousness, bronchospasm, hypoglycaemia and rarely hyperkalaemia.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Beta Blocker agents; Beta blocker agents, selective, ATC code: C07AB04.

Mode of action: Acebutolol is a beta adrenoceptor antagonist which is cardio selective, i.e. acts preferentially on beta1 adrenergic receptors in the heart. Its principal effects are to reduce heart rate especially on exercise and to lower blood pressure in hypertensive subjects. Acebutolol and its active metabolite, diacetolol have antiarrhythmic activity, the combined plasma half-life of the active drug and metabolite being 7-10 hours. Both have partial agonist activity (PAA) also known as intrinsic sympathomimetic activity (ISA). This property ensures that some degree of stimulation of beta receptors is maintained. Under conditions of rest, this tends to balance the negative chronotropic and negative inotropic effects. Acebutolol blocks the effects of excessive catecholamine stimulation resulting from stress.

5.2 Pharmacokinetic properties

Absorption

After oral administration, acebutolol is rapidly and almost completely absorbed from the gastrointestinal tract. A maximum plasma concentration of ± 925 ng/ml was observed 2-4 hours after oral administration of 400 mg of acebutolol. Absorption appears to be unaffected by the presence of food in the gut.

Distribution

The plasma protein binding of acebutolol is weak (20%).

Both Acebutolol and diacetolol are hydrophilic and exhibit poor penetration of the CNS.

Biotransformation

There is rapid formation of a major equiactive metabolite, diacetolol, which possesses a similar pharmacological profile to acebutolol. Acebutolol undergoes a significant first pass metabolism: absolute bioavailability after oral administration is 30% -51%. Acebutolol is converted into diacetolol in the liver. This metabolite is pharmacologically active and in steady state the plasma concentration of diacetolol is 2.5 times that of Acebutolol.

Elimination

Peak plasma concentrations of active material (i.e. acebutolol plus diacetolol) are achieved within 2-4 hours and the terminal plasma elimination half-life is around 8-10 hours.

Because of biliary excretion and direct transfer across the gut wall from the systemic circulation to the gut lumen, more than 50% of an oral dose of acebutolol is recovered in the faeces with acebutolol and diacetolol in equal proportions; the rest of the dose is recovered in the urine, mainly as diacetolol.

Populations at risk

Renal impairment

Urinary elimination is reduced and the half-lives of acebutolol, and even more of diacetolol, increase. There is a very significant correlation between creatinine clearance and renal clearance of diacetolol.

The risks of accumulation exist during renal insufficiency, in particular in the event of twice-daily intake. Reduce the doses, if necessary, by exercising careful clinical supervision, for example on the bradycardic effect (see section 4.4).

Elderly

Physiological decline in renal function may lead to increased half-lives of acebutolol and diacetolol.

Pregnancy

Acebutolol passes into the placenta. Mean cord/maternal blood concentration ratios of acebutolol and its active metabolite, diacetolol, are approximately 1.6 for doses of 200 and 400 mg. The maximum concentrations are observed, for acebutolol, 4 to 5 hours after the last dose, for diacetolol, 5 to 7 hours later.

Breast-feeding

Acebutolol is excreted in breast milk; the concentration of acebutolol in milk is maximum between 4:30 and 6 hours after intake. The mean ratios of breast milk/mother blood concentrations vary in a ratio of 4 to 5.5 for doses of 200 and 400 mg respectively. For diacetolol, these ratios vary between 3 and 4, the maximum concentration being observed 7 hours after taking 200 mg and 12 hours after taking 400 mg.

5.3 Preclinical safety data

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

Fertility and generic reproduction capacity were investigated in rats on a two-generational study. The rats were submitted to maximum daily doses of 220 mg of acebutolol hydrochloride/kg of body weight in the diet. No undesirable effects were observed.

Embryo toxicity and teratogenicity studies were performed on rats and rabbits after oral and intravenous administration. Acebutolol did not show embryo toxicity and teratogenicity on those two species by oral route, from gestation day 6 to 16, on doses up to 54 mg/kg/day. When administered by intravenous route from gestation day 5 to 17 (rat) and from gestation day 5 to 20 (rabbit), acebutolol also did not wield embryotoxic and teratogenic effects.

Increase in post-natal mortality on all treated groups was observed on female rat pups treated orally with 50-240 mg/kg/day. Gestation extension and decreased lactation were observed on the mothers.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:

Lactose monohydrate
Maize starch
Povidone (K-30)
Talc
Silica colloidal Anhydrous
Magnesium Stearate

Tablet coat:

Hypromellose 6 cp
Macrogol 6000
Titanium dioxide (E171)

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store below 30 ºC

6.5 Nature and contents of container

Acebutolol film-coated tablets are available in Clear PVC– Aluminium foil blister packs.

Pack sizes:

Blister packs: 28, 30, 90 and 100 tablets

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER(S)

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