

**IRISH MEDICINES BOARD ACT 1995**

**MEDICINAL PRODUCTS(LICENSING AND SALE)REGULATIONS, 1998**

**(S.I. No.142 of 1998)**

**PA0540/125/003**

Case No: 2029151

The Irish Medicines Board in exercise of the powers conferred on it by the above mentioned Regulations hereby grants to

**sanofi-aventis Ireland Limited**

**Citywest Business Campus, Dublin 24, Ireland**

an authorisation, subject to the provisions of the said Regulations, in respect of the product

**Sectral 400mg Tablets**

The particulars of which are set out in Part I and Part II of the attached Schedule. The authorisation is also subject to the general conditions as may be specified in the said Regulations as listed on the reverse of this document.

This authorisation, unless previously revoked, shall continue in force from **26/10/2006** until **15/03/2008**.

Signed on behalf of the Irish Medicines Board this

\_\_\_\_\_

A person authorised in that behalf by the said Board.

## Part II

### Summary of Product Characteristics

#### 1 NAME OF THE MEDICINAL PRODUCT

Sectral 400mg Tablets

#### 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains Acebutolol Hydrochloride equivalent to 400 mg of acebutolol.  
For excipients, see 6.1.

#### 3 PHARMACEUTICAL FORM

Film-coated tablet.

Circular white to off-white, biconvex, film-coated tablets with bevel edges, one face impressed 'SECTRAL 400', plain reverse.

#### 4 CLINICAL PARTICULARS

##### 4.1 Therapeutic Indications

1. For the management of cardiac tachyarrhythmias.
2. For the management of angina pectoris.
3. For the management of mild and moderate hypertension.

##### 4.2 Posology and method of administration

Oral.

##### Recommended Dosage

###### *Cardiac Arrhythmias*

Oral dosage of 100 to 200mg can be given initially but may take up to three hours to achieve its effect. The usual dosage for maintenance of the  $\beta$ -adrenoceptor blocking action is 400 to 1200mg daily preferably in divided doses.

###### *Angina Pectoris*

The usual daily dosage is 400mg in single or divided doses. Up to 1200mg daily has been used in severe forms.

###### *Hypertension*

The initial oral dosage is 400mg once or 200mg twice daily. This may be gradually increased by increments of 100mg at weekly intervals until a satisfactory response has been obtained, up to 800mg daily in single or divided doses.

If combination is contemplated of this drug with other anti-hypersensitive agents, including thiazide diuretics, the dosage of these can usually be reduced.

In renal insufficiency dosage may be at lower levels.

Nifedipine may be usefully combined with acebutolol for hypertension.

### 4.3 Contraindications

1. 2<sup>nd</sup> or 3<sup>rd</sup> degree atrioventricular block
2. Severe bradycardia
3. Uncontrolled or digitalis/diuretic-refractory heart failure
4. Cardiogenic Shock
5. Hypersensitivity to acebutolol or  $\beta$ -blockers.
6. As with all beta blockers, these should be avoided in patients with obstructive airways disease unless there are compelling clinical reasons for their use.

### 4.4 Special warnings and precautions for use

Sudden withdrawal of beta-adrenoceptor blocking agents in patients with ischaemic heart disease may result in the appearance of anginal attacks of increased frequency or severity or deterioration in cardiac state. Discontinuation of therapy should be gradual.

The beta blocker should only be used with caution in patients with controlled congestive cardiac failure or with a family history of asthma. Evidence of recrudescence of either condition should be regarded as a signal to discontinue therapy.

Although some patients have developed anti-nuclear factor titres, the incidence of associated clinical symptoms is rare and when present, these clear promptly on discontinuation of treatment.

The beta-blocker may mask the symptoms of thyrotoxicosis and of hypoglycaemia by inhibition of sympathetic nerve functions. The effects of hypoglycaemic agents may be increased, particularly by the non-cardioselective beta-blockers.

The initial treatment of severe malignant hypertension should be so designed as to avoid sudden reduction in diastolic blood pressure with impairment of autoregulatory mechanisms.

When this agent is administered to patients in renal failure, the interval between doses may need to be increased or the dosage reduced to avoid accumulation of the drug. As a guide, the dose of acebutolol should be reduced by 50% and 75% when glomerular filtration rates are 25-50 ml/min and less than 25 ml/min respectively.

Some cases of ocular changes (conjunctivitis and 'dry eye') and/or skin rashes (including psoriasiform type) have been reported in association with the use of beta-adrenoceptor blockers. Until their significance is known it is recommended that consideration be given to discontinuing such therapy if these effects appear.

### 4.5 Interaction with other medicinal products and other forms of interaction

1. This product should only be used with great caution in patients who are receiving concomitant myocardial depressants such as chloroform, lignocaine, procainamide, beta-adrenoceptor stimulants such as isoprenaline, or alpha-adrenoceptor stimulants such as noradrenaline, adrenaline (which reverse the effects and increase the vasoconstrictor activities). The product should not be used with verapamil or within several days of verapamil therapy (and vice versa).
2. Neurone blocking agents such as guanethidine, reserpine, diuretics and other anti-hypertensive agents, including the vasodilator group, will have an additive effect on the hypotensive action of the drug.
3. If the beta-blocker and clonidine are given concurrently, the clonidine should not be discontinued until several days after withdrawal of the beta-blocker.
4. In the event that a patient receiving the beta-blocker requires anaesthesia the anaesthetist should be informed of the use of the medication prior to the use of a general anaesthetic to permit his taking the necessary precautions. If treatment is continued special care should be taken using anaesthetic agents such as either cyclopropane and trichloroethylene.

5. In patients with labile and insulin dependent diabetes, receiving this product, the dosage of the hypoglycaemic agent may need to be reduced, however, beta-blockers have also been known to blunt the effect of glibenclamide.
6. Concurrent use of digoxin and beta-blockers may occasionally induce serious bradycardia.
7. The anti-hypertensive effects of beta-blockers may be attenuated by non-steroidal anti-inflammatory agents, cross reactions due to displacement of other drugs from plasma protein binding sites are unlikely due to the low degree of plasma protein binding of this product.
8. Acebutolol is a cardioselective beta-blocker and it may antagonise the effect of sympathomimetic and xanthine bronchodilators, but to a lesser extent than non-cardioselective beta-blockers.
9. There is theoretical risk that concurrent administration of monoamine oxidase inhibitors and high doses of beta-blockers, even if they are cardioselective, can produce hypertension.

## 4.6 Pregnancy and lactation

The beta blocker should not be given during pregnancy or lactation unless it is considered essential by the physician.

Sectral should not be administered to female patients during the first trimester of pregnancy unless the physician considers it essential. Animal studies have shown no teratogenic hazard. Beta-blockers administered in late pregnancy may give rise to bradycardia, hypotension and hypoglycaemia in the foetus/neonate.

Acebutolol and its active metabolite are excreted in breast milk, the half-life of acebutolol in the neonate is double that in adults. In view of this, the use of Sectral in nursing mothers requires careful assessment of the risk to the suckling infant.

## 4.7 Effects on ability to drive and use machines

None.

## 4.8 Undesirable effects

Side effects include bradycardia, hypotension, gastrointestinal disturbances, cold extremities, dizziness, headaches, breathlessness, nightmares, loss of libido and lethargy have been reported. Sleep disturbances and depression have been reported rarely.

There have been reports of skin rashes and/or dry eyes associated with the use of beta-adrenoceptor blocking drugs. The reported incidence is small and in most cases the symptoms have cleared when treatment was withdrawn. Discontinuation of the drug should be considered if any reaction is not otherwise explicable. Although some patients have developed anti-nuclear factor titres, the incidence of associated clinical symptoms is rare and when present, these clear promptly on discontinuation of treatment.

Bronchospasm has occurred rarely during treatment with acebutolol.

Cases of Pneumonitis have been reported with acebutolol. (e.g. Pneumonitis appears to be rare but a potentially serious complication of beta-blockade therapy. Cases of pneumonitis have been reported with acebutolol.

## 4.9 Overdose

In the rare event of excessive bradycardia or hypotension, 1 mg 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 micrograms per minute) with constant monitoring until a response occurs. In severe cases of self-poisoning 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 overdose 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

Mode of action: Sectral is a beta adrenoceptor antagonist which is cardioselective, i.e. acts preferentially on beta-1 adrenergic receptors in the heart. Its principal effects are to reduce heart rate especially on exercise and to lower blood pressure in hypertensive subjects.

Sectral and its equally active metabolite, diacetolol have anti-arrhythmic 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. Sectral blocks the effects of excessive catecholamine stimulation resulting from stress.

### 5.2 Pharmacokinetic properties

After oral administration, acebutolol is rapidly and almost completely absorbed. Absorption appears to be unaffected by the presence of food in the gut. There is rapid formation of a major equiactive metabolite, diacetolol, which possesses a similar pharmacological profile to acebutolol. 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 Sectral 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. Both acebutolol and diacetolol are hydrophilic and exhibit poor penetration of the CNS.

### 5.3 Preclinical safety data

Not relevant.

## 6 PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Maize starch  
Colloidal anhydrous silica  
Magnesium stearate  
Lactose monohydrate  
Talc  
Povidone K30  
Opadry OY-L-28900 (contains titanium dioxide (E171), lactose monohydrate, hypromellose and macrogol 4000).

### 6.2 Incompatibilities

Not applicable.

### **6.3 Shelf Life**

3 years.

### **6.4 Special precautions for storage**

Do not store above 25°C.  
Store in the original container.

### **6.5 Nature and contents of container**

HDPE tablet container with polyethylene tamper proof cap, containing 100 tablets.

AL/PVC blisters in strips (2 x 14) packed in outer carton, containing 28 tablets.

### **6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product**

No special requirements.

## **7 MARKETING AUTHORISATION HOLDER**

sanofi-aventis Ireland Ltd.  
Citywest Business Campus  
Dublin 24.

## **8 MARKETING AUTHORISATION NUMBER**

PA 540/125/3

## **9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date of first authorisation: 15<sup>th</sup> March 1978

Date of last renewal: 15<sup>th</sup> March 2003

## **10 DATE OF REVISION OF THE TEXT**

October 2006