IRISH MEDICINES BOARD ACTS 1995 AND 2006

MEDICINAL PRODUCTS(CONTROL OF PLACING ON THE MARKET)REGULATIONS,2007

(S.I. No.540 of 2007)

PA0568/001/001
Case No: 2066568

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

Les Laboratoires Servier

22, rue Garnier, **92200 Neuilly-sur-Seine**, **France**

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

Artexal 5 mg 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 **31/08/2009**.

Signed on behalf of the Irish Medicines Board this

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A person authorised in that behalf by the said Board.

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Artexal 5 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Tertatolol hydrochloride 5 mg per tablet.

Excipients: contains Lactose Monohydrate 37.0mg

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Film coated tablet.

White, oblong, film-coated tablets scored on one face.

The tablet can be divided into equal halves.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

As a beta adrenoceptor blocker for the treatment of essential hypertension.

4.2 Posology and method of administration

Oral administration

Adults Only:
The usual daily dose is 5 mg in single or divided doses.

Hypertension:
The usual daily dose is 5 mg as a single dose. This can be increased to 10 mg daily if required for control, but should only be done after the effects of the initial dose have been achieved (1 to 2 weeks). Tertatolol may be combined with a diuretic if required, or other antihypertensive agents.

4.3 Contraindications

- Hypersensitivity to tertatolol hydrochloride or to any of the excipients.
- 2nd or 3rd degree atrioventricular block.
- Severe bradycardia.
- Uncontrolled or digitalis/diuretic-refractory heart failure.
- Use in patients with asthma or a history of asthma.

- Cardiogenic shock.
- Renal failure with creatinine clearance below 10 ml/min.
- Use in hepatic insufficiency in absence of clinical studies.

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 development of either condition should be regarded as a signal to discontinue therapy.
- The beta-blocker can be administered to patients with obstructive respiratory disorders provided that adequate supervision is maintained to permit any necessary adjustment of dosage of the bronchodilator employed.
- 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 dosage may require adjustment. In patients with hepatic dysfunction, dosage should be reduced and if the prothrombin time is less than 70% the drug should be discontinued.
- Some cases of ocular changes (conjunctivitis and 'dry eye') and/or skin rashes (including a 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

- 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.
- The beta-blocker should only be used with great caution in patients who are receiving concomitant myocardial depressants such as halogenated hydrocarbon anaesthetics, lignocaine, procainamide, beta-adrenoceptor stimulants such as isoprenaline, or verapamil or alpha-adrenoceptor stimulants such as noradrenaline.
- Adrenergic-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.
- The beta-blocker may mask some of 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 tachycardia of hypoglycaemia may be modified.
- If the beta-blocker and clonidine are given concurrently the clonidine should not be discontinued until several days after withdrawal of the beta-blocker.
- Care should be taken in prescribing a β-adrenoceptor blocker in conjunction with antidysrhythmics, particularly those in Class I such as disopyramide.

4.6 Pregnancy and lactation

Pregnancy
Although the drug crosses the placental barrier and is present in cord blood, there is no evidence up to the present time of foetal abnormalities. Nonetheless the possibility cannot be excluded and the drug should only be used if considered essential and with the patient under close supervision.

Lactation
The drug is excreted in breast milk. The risk of hypoglycaemia and bradycardia occurring has not been evaluated. Consequently, and as a precaution, breast-feeding is inadvisable throughout treatment.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machine have been performed.

4.8 Undesirable effects

The following undesirable effects could be observed during treatment and ranked under the following frequency: very common (≥1/10); common (≥1/100, <1/10); uncommon (≥1/1000, <1/100); rare (≥1/10000, <1/1000), very rare (<1/10000), including isolated reports.

- Metabolism and nutrition disorders:
  - Very rare: Hypoglycaemia
- Psychiatric disorders
  - Rare: insomnia and nightmares
- Cardiac disorders
  - Common: bradycardia, severe at times
  - Uncommon: heart failure
  - Very rare: slowing down of atrioventricular conduction or increase in existing atrioventricular block
- Vascular disorders
  - Common: cold extremities
  - Uncommon: drop in blood pressure
  - Very rare: aggravation of existing intermittent claudication, Raynaud's syndrome
- Respiratory, thoracic and mediastinal disorders
  - Common: bronchospasm
- Gastrointestinal disorders
  - Uncommon**:** gastrointestinal disorders (gastralgia, nausea and vomiting)
- Skin and subcutaneous tissue disorders
  - Uncommon: miscellaneous skin reactions, including psoriasiform eruptions
- Reproductive system and breast disorders
  - Uncommon: impotence
- General disorders and administration site conditions
  - Common: asthenia

Effects on laboratory parameters:
In rare cases, antinuclear antibodies have been observed. These are only very rarely accompanied by clinical signs such as systemic lupus erythematosus which subside when treatment is discontinued.

4.9 Overdose

The following should be administered in cases of bradycardia or an excessive drop in blood pressure:
- atropine, 1 to 2 mg I. V.,
- glucagon 10 mg, to be repeated as required,
- followed, if necessary, by isoprenaline 25 µg by slow injection, or dobutamine 5 to 10 µg/kg/min.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Code: C07AA16 Beta Blocking agents, non-selective
Non-selective β-adrenoceptor blocker.
Some clinical studies have shown that ARTEXAL® maintains or improves renal haemodynamics, particularly renal plasma flow and glomerular filtration, in patients with and without renal failure.

5.2 Pharmacokinetic properties

Tertatolol is well absorbed after oral dosing and excreted unchanged (and as hydroxymetabolite) through the kidneys with a plasma elimination half life of about 3 hours.

5.3 Preclinical safety data

No findings in the preclinical testing which could be of relevance for the prescriber.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Stearic acid
Sodium starch glycollate
Microcrystalline cellulose
White beeswax
Glycerol
Calcium hydrogen phosphate dihydrate
Hypromellose
Lactose monohydrate
Sodium Laurilsulfate
Titanium dioxide
Macrogol 6000
Colloidal anhydrous silica
Magnesium stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

3 years.

6.4 Special precautions for storage

Store below 25°C.

6.5 Nature and contents of container

Blister strip (PVC/Aluminium) of 30 tablets. One strip per carton.

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

Les Laboratoires Servier
22, rue Garnier
92200 Neuilly - sur - Seine
France

8 MARKETING AUTHORISATION NUMBER

PA568/1/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 13th April 1988
Date of last renewal: 13th April 2008

10 DATE OF REVISION OF THE TEXT

August 2009