SUMMARY OF PRODUCT CHARACTERISTICS,
LABELLING AND PACKAGE LEAFLET

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1. NAME OF THE MEDICINAL PRODUCT

ARCALION 200 mg, coated tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Sulbutiamine ..... 200 mg per coated tablet.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Coated tablet.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Treatment of certain physical or mental inhibition states involving reduced activity and apathy. In confirmed depressive states, this medicine does not eliminate the need for specific antidepressant treatment.

4.2. Posology and method of administration

FOR ADULT USE ONLY.
2 to 3 tablets daily.
Tablets should be swallowed whole with a large glass of water, dividing the doses between the morning and midday meals.
Duration of treatment is limited to 4 weeks.

4.3. Contraindications

ARCALION is contra-indicated in the case of past-history of hypersensibility to one of the ingredients of the tablet.

4.4. Special warnings and special precautions for use

Due to the presence of lactose, patients with rare hereditary problems of galactose intolerance, glucose-galactose malabsorption, or the Lapp lactase deficiency should not take this medicinal product.

Due to the presence of glucose and sucrose, patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption, or sucrase-isomaltase insufficiency should not take this medicinal product.

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

Not applicable.

4.6. Pregnancy and lactation

Pregnancy:

There have been no teratogenic studies in animals.

Clinically, no foetal toxicity or malformation has been reported. However, follow-up of women exposed to ARCALION during pregnancy is insufficient to exclude such a risk.

Therefore, as a precautionary measure, it is preferable not to use ARCALION during pregnancy.

Lactation:

Due to the absence of data concerning the excretion of ARCALION in breast milk, its use should be avoided in breastfeeding women.

4.7. Effects on ability to drive and use machines

Not applicable.

4.8. Undesirable effects

The following adverse effects or events have been reported and are ranked using the following frequency: 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 form the available data).

Gastrointestinal disorders:

Uncommon (>1/1000; <1/100): nausea, vomiting.

Nervous system disorders:

Uncommon (>1/1000; <1/100): agitation, headache, tremor.

Cutaneous and subcutaneous tissue disorders:

Uncommon (>1/1000; <1/100): rash.

Due to the presence of sunset yellow FCF (E110), risk of allergic reactions.

4.9. Overdose

In cases of massive absorption, there may be agitation with euphoria and tremor of the extremities. These disorders are transient and rapidly resolved.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: 2.13.1 Medicinal products used in the symptomatic treatment of cognitive function disturbances,
ATC code: A11DA02

Sulbutiamine is an original substance resulting from important structural modifications of the thiamine nucleus: formation of a disulphide bridge, introduction of a lipophilic ester, and opening of the thiazole ring.
These various modifications explain:
• its liposolubility, promoting rapid gastrointestinal absorption and allowing it to cross the blood-meningeal barrier;
• its specific neurotropism for the reticular substance, hippocampus and folds, as well as for Purkinje cells and the glomeruli of the cerebellar granular layer, as demonstrated by histofluorescence, whilst thiamine produces no fluorescence under the same conditions;

In animals:
• administration of ARCALION to animals has led to improved motor coordination and resistance to muscular fatigue, particularly in tests where motor deficit was induced by neuroleptics;
• ARCALION improved the resistance of the cerebral cortex sensitized by repeated anoxia. The state of wakefulness of the animals was, however, increased by ARCALION;
• during learning tests in animals, a beneficial effect on motor performance and on memory was observed.

In man:
ARCALION has been studied in functional asthenia by means of controlled studies (against placebo or reference products) using psychometric tests (Wechsler), evaluation scales (Middlesex Hospital Questionnaire, Crocq Scale for the evaluation of nonpsychotic depressive conditions, Lipman auto-evaluation scale), with statistical analysis of the results.
These studies provide evidence of the activity of ARCALION in the symptomatic treatment of functional asthenia.

5.2. Pharmacokinetic properties

Sulbutiamine is rapidly absorbed both in animals and in man and the blood concentration is maximum between one and two hours after administration. The blood concentration then decreases exponentially. The product is rapidly distributed in the body, with considerable cerebral binding being observed in animals. It is then eliminated with a biological half-life of around five hours. Maximum urinary excretion is reached two to three hours after administration.

5.3. Preclinical safety data

Sulbutiamine showed no special hazards for clinical use on the basis of studies of acute, subchronic and chronic toxicity and reproduction toxicity. Sulbutiamine was not mutagenic in the Ames test. No studies of carcinogenicity have been carried out.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

TABLET:
Glucose anhydrous, lactose monohydrate, magnesium stearate, maize starch, starch pregelatinised, talc.

COATING:
Beeswax white, carmellose sodium, ethylcellulose, glycerol mono-oleates, polysorbate 80, povidone, silica colloidal anhydrous, sodium hydrogen carbonate, sucrose, sunset yellow FCF (E110) aluminium lake, talc, titanium dioxide (E171).

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

3 years.

6.4. Special precautions for storage

Below 25°C.

6.5. Nature and contents of container

15, 20, 30, 60, and 100 tablets in heat-sealed blister packs (PVC/aluminium).

Not all pack sizes may be marketed.

6.6. Instructions for use and handling

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Les Laboratoires Servier
50, rue Carnot
92284 Suresnes cedex
France

8. MARKETING AUTHORISATION NUMBER

MA 066/00201

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

November 17th 2005

10. DATE OF REVISION OF THE TEXT

05/2012