

IRISH MEDICINES BOARD ACTS 1995 AND 2006

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

(S.I. No.540 of 2007)

PA0812/004/002

Case No: 2039380

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

Recordati Industria Chimica e Farmaceutica SpA

Via Matteo Civitali, 20148, Milan, Italy

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

Gynoxin 600 mg Vaginal Capsules

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 **05/02/2008**.

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

Gynoxin 600 mg Vaginal Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vaginal capsule contains 600 mg of the active ingredient fenticonazole nitrate.

Excipients: Also contains ethyl parahydroxybenzoate sodium (E215) 1mg per vaginal capsule, and sodium propyl parahydroxybenzoate (E217) 0.5mg per vaginal capsule.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Vaginal capsule, soft. (Vaginal capsule)

Ivory white, opaque, soft gelatin capsules.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

In the topical treatment of vulvo vaginal infections due to superficial dermatophytes of *C. albicans*, sensitive to the drug.

4.2 Posology and method of administration

Dosage

One 200 mg vaginal capsule at bedtime for 3 days or one 600 mg vaginal capsule at bedtime once only.

If necessary treatment may be repeated after 3 days.

Administration

Intravaginal, inserted deeply into vagina.

4.3 Contraindications

Use in patients hypersensitive to imidazoles.

4.4 Special warnings and precautions for use

1. Side effects include local irritation.
2. If there is no improvement or there is aggravation of the condition, the physician should be consulted.

4.5 Interaction with other medicinal products and other forms of interaction

Not investigated. Since systemic absorption of fenticonazole after application is low, interactions with other drugs are unlikely.

4.6 Pregnancy and lactation

Reproduction studies showed embryotoxic effects at high oral dosage in one species (rat) of two tested.

Although the results of oral dosage are unlikely to be relevant for topical application in women, use during pregnancy or lactation should be avoided unless deemed essential by the physician. There is no experience of use during pregnancy or lactation in human beings.

4.7 Effects on ability to drive and use machines

None.

4.8 Undesirable effects

Side effects include local irritation.

4.9 Overdose

Overdosage has never been encountered.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC code: G01A F12

Fenticonazole is a broad-spectrum antimycotic agent.

- *In vitro*: high fungistatic and fungicidal activity against dermatophytes (all species of Trichophyton, Microsporum and Epidermophyton), against Candida albicans and against the other agents responsible for mycotic infections of skin and mucous membranes.
- *In vivo*: healing of vaginal mycoses due to Candida within 5 days in mice.

Fenticonazole also shows antibacterial activity against Gram-positive micro-organisms. Supposed mode of action: block of oxidative enzymes leading to accumulation of peroxides and necrosis of fungal cells; direct action on the membrane.

5.2 Pharmacokinetic properties

Pharmacokinetic studies have revealed no transcutaneous absorption either in man or in animals and a very low vaginal absorption.

5.3 Preclinical safety data

LD50 mice: oral >3000mg/kg; i.p 1276mg/kg (M), 1265mg/kg (F)

LD50 rats: oral >3000mg/kg; s.c. >750mg/kg; i.p. 440mg/kg (M), 309mg/kg (F)

Chronic toxicity: following oral administration of 40-80-160mg/kg/day for 6 months in rats and dogs, fenticonazole was well tolerated, although some evidence of light and moderate general toxicity occurred (increase in liver weight at 160mg/kg without histopathological alterations in rats, and a transient increase in serum SGPT at 80 and 160mg/kg, together with an increase in liver weight in dogs).

Fenticonazole does not interfere with the function of male and female gonads, and does not modify the first phases of reproduction. Studies in reproductive toxicology revealed, as for other imidazole derivatives, an embryo-lethal effect at

high dosages (>20mg/kg). Fenticonazole has shown no teratogenic effects in rats and rabbits and has revealed no mutagenic potential in six mutagenicity tests.

Satisfactory results were obtained in tolerability tests performed in guinea pigs, rabbits as well as in mini-pigs, the skin of which is similar to that of humans, as far as morphology, functionality and sensitivity to irritating agents are concerned.

Fenticonazole has shown no evidence of sensitisation, phototoxicity and photoallergy.

Pharmacokinetic studies have revealed no transcutaneous absorption either in man or in animals and a very low vaginal absorption.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Liquid paraffin
White soft paraffin
Soya lecithin

Shell constituents:

Gelatin
Glycerol
Titanium dioxide
Ethyl Parahydroxybenzoate Sodium (E215)
Sodium propyl Parahydroxybenzoate (E217)

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

3 years

6.4 Special precautions for storage

Do not store above 30°C. Do not refrigerate or freeze. Store in the original package.

6.5 Nature and contents of container

Blister pack of PVC/PVdC + aluminium foil, in packs of 3.

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

Recordati Industria Chimica e Farmaceutica SpA
Via M. Civitali
1-20148 Milano
Italy

8 MARKETING AUTHORISATION NUMBER

PA 812/4/2

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 24th February 1992

Date of last renewal: 23rd February 2007

10 DATE OF REVISION OF THE TEXT

October 2007