ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Flagentyl 500 mg scored film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Secnidazole ..... 500.00 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Scored film-coated tablets.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

- Urethritis and vaginitis due to *Trichomonas vaginalis.*
- Intestinal amebiasis.
- Hepatic amebiasis.
- Giardiasis.

4.2 Posology and method of administration

Urethritis and vaginitis due to *Trichomonas vaginalis*

Adults: 2 g taken as a single dose at the beginning of a meal.

Intestinal amebiasis

Symptomatic acute amebiasis (*E.histolytica* form):

- adults: 2 g taken as a single dose at the beginning of a meal.
- children: 30 mg/kg/day taken as a single dose. Duration of treatment: one day only.

Asymptomatic amebiasis (minuta and cyst forms): same daily dose for 3 days.

Hepatic amebiasis

- adults: 1.5 g daily taken as one or several doses at the beginning of a meal for 5 days.
- children: 30 mg/kg/day taken as one or several doses at the beginning of a meal for 5 days.

Note: during the suppurative phase of hepatic amebiasis, pus or abscess drainage should be carried out at the same time as secnidazole administration.

Giardiasis

- children: 30 mg/kg/day taken as a single dose. Duration of treatment: one day only.

The oral solution is recommended for children aged under 6 years.

4.3 Contraindications

- Hypersensitivity to imidazole derivatives or to any of the ingredients in the medicinal product.
- Lactation.
- Wheat allergy (a condition that is different from celiac disease).

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4.4 Special warnings and precautions for use

Drinking alcoholic beverages should be avoided during treatment with secnidazole.

This medicine should not be administered in patients with a history of blood dyscrasia.

This medicinal product can be administered in patients with celiac disease. Wheat starch can contain gluten, but only traces, and is therefore considered safe for patients with celiac disease.

4.5 Interaction with other medicinal products and other forms of interaction

Inadvisable combinations

- Disulfiram: acute transient delusional disorder (*bouffées délirantes*), mental confusion.
- Alcohol: antabuse effect (heat sensation, redness, vomiting, tachycardia). Alcoholic drinks or medicinal products containing alcohol should be avoided.

Combinations requiring precautions for use

Oral anticoagulants (described for warfarin): potentiation of the oral anticoagulant effect, with increased risk of bleeding, due to decreased hepatic catabolism. Prothrombin times should be checked more frequently and INR monitored. The oral anticoagulant dosage should be adjusted during treatment with secnidazole and for 8 days after its discontinuation.

4.6 Fertility, pregnancy and lactation

Pregnancy

Animal studies have not demonstrated any teratogenic effects, therefore no malformative effect is expected in humans. This is because, to date, substances that cause malformations in man have been shown to be teratogenic in animals during controlled studies in two species.

There are currently not enough relevant clinical data to evaluate possible teratogenic or fetotoxic effects of secnidazole when administered during pregnancy.

Therefore, as a precautionary measure, secnidazole should preferably not be used during pregnancy.

Lactation

No data are available concerning excretion of the medicinal product in breast milk. However, excretion in breast milk has been documented with other imidazole derivatives, and cases of oral and anal candidiasis and diarrhea have been described in breast-fed infants whose mothers were treated with other imidazole derivatives.

Therefore, clinical monitoring of the neonate or even discontinuation of breast-feeding is required during treatment.

4.7 Effects on ability to drive and use machines

Rare cases of dizziness have been reported following administration of imidazole derivatives.

4.8 Undesirable effects

The undesirable effects that may be observed are those of imidazole derivatives:

- most frequent: gastrointestinal disorders with gastric pain, taste alteration (metallic taste), glossitis, stomatitis,
- moderate leukopenia, reversible on treatment discontinuation,
- rare: dizziness, coordination disorders and ataxia, paresthesia, sensorimotor polyneuropathy.

The following have been reported with secnidazole:

- rare gastrointestinal disorders (nausea, vomiting, gastric pain),
- rare immediate hypersensitivity reactions: fever, erythema, urticaria and angioedema.

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Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization 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 French national reporting system, i.e. *Agence Nationale de Sécurité du Médicament et des Produits de Santé* (ANSM) under "*Réseau des Centres de Pharmacovigilance*" (Network of Pharmacovigilance Centers) - Website: www.ansm.sante.fr.

4.9 Overdose

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ANTIPARASITIC PRODUCT - ANTIPROTOZOAL

TISSUE AMEBICIDE - CONTACT AMEBICIDE

(P: Parasitology)

Pharmacodynamic effects

Synthetic derivative of the nitroimidazole group.

Amebicidal effect on *Entamoeba histolytica*.

Secnidazole is also active against *Giardia lamblia* and *Trichomonas vaginalis*.

5.2 Pharmacokinetic properties

After oral administration of 2 g of secnidazole, peak plasma concentrations are reached within 3 hours. Plasma half-life is about 25 hours. Elimination is slow and mainly via the urinary route (about 50% of the administered dose is excreted over 120 hours). Secnidazole crosses the placental barrier and is excreted in breast milk.

5.3 Preclinical safety data

Not applicable.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Calcium hydrogen phosphate, microcrystalline cellulose, wheat starch, hydrated silica, sodium starch glycolate, gelatin, magnesium stearate, hypromellose.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

4 years.

6.4 Special precautions for storage

Not applicable.

6.5 Nature and contents of container

4 tablets in (PVC/Aluminum) blisters.

6.6 Special precautions for disposal and other handling

No special requirements.

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7. MARKETING AUTHORIZATION HOLDER

SANOFI AVENTIS FRANCE
82, avenue Raspail
94250 Gentilly
France

8. MARKETING AUTHORIZATION NUMBER

- 322 819-8: 4 tablets in (PVC/Aluminum) blisters; box of 4.

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION

August 20, 1979

August 23, 2004

10. DATE OF REVISION OF THE TEXT

September 18, 2015

11. DOSIMETRY

Not applicable.

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Not applicable.

GENERAL CLASSIFICATION FOR SUPPLY

List I.

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