SUMMARY OF PRODUCT CHARACTERISTICS
Last update May 2014

1. TRADENAME OF THE MEDICINAL PRODUCT

PERMIXON 160 mg, hard capsules

2. QUALITATIVE & QUANTITATIVE COMPOSITION

Each hard capsule contains 160 mg lipidosterolic extract of *Serenoa repens**/

* Oil extract originated from fruits of *Serenoa repens* (Bartram) Small.

Drug extract ratio 7-11:1

Extraction solvent : hexanic solvent

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

The hard capsules are pale green and contain a greenish yellow paste with a characteristic odour.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

PERMIXON is indicated in male adult for treatment of moderate micturition disorders related to benign prostatic hypertrophy.

4.2. Dosage and method of administration

Posology:
Adult:
One capsule, two times a day, at mealtimes.

Method of administration
Take with a glass of water.

Paediatric population
This medicine should not be used in children.

4.3. Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1

4.4. Special warnings and special precautions for use

During treatment, as routine surveillance of benign prostatic hypertrophy, the patient must be under continuous medical supervision.
This medicinal product may cause nausea if taken on an empty stomach.

4.5. Interactions with other medicinal products or other forms of interactions

Experimental studies with PERMIXON do not show any negative interference with the therapeutic groups commonly associated with this condition (antibiotics for urinary tract infections, antiseptics and anti-inflammatory medicines).
Results from dedicated in vitro studies demonstrated the absence of inhibition and induction potential of lipidosterolic extract of Serenoa repens.
No pharmacokinetic interactions are expected with co-administered treatments.

4.6. Pregnancy and lactation

Not relevant, as this medicinal product is not indicated in women.

4.7. Effects on ability to drive and use machines

PERMIXON has no influence on the ability to drive and use machines.

4.8. Undesirable effects

The following table shows the undesirable effects observed in seven clinical studies with a total of 3593 patients: 2127 taking PERMIXON, for which the assessment of causality was not "excluded".
The undesirable effects classified by organs or systems (according to MedDRA) are listed below as very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1000 to < 1/100), rare (≥ 1/10,000 to < 1/1000), very rare (< 1/10,000) and frequency unknown (it cannot be estimated on the basis of the data available).
No adverse drug reactions were "very rare", "rare" or "very common" in frequency and therefore theses columns were not presented in the table.

Common (≥ 1/100 to < 1/10)	**Uncommon (≥ 1/1000 to < 1/100),**
Nervous system disorders	
Headache	
Gastrointestinal disorders	
Abdominal pain	Nausea
Hepatobiliary disorders	
	Gamma-glutamyltransferase increased Transaminases increased
Skin and subcutaneous tissue disorders	
	Rash
Reproductive system and breast disorders	
	Gynecomastia

During clinical trials, only moderate increases in transaminases were recorded and the increase of liver function tests were without clinical significance.
Moreover, oedema was reported in post-marketing experience with an unknown frequency (it cannot be estimated on the basis of the data available).
Gynecomastia has been observed, but was reversible after treatment discontinuation.

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 national reporting system.

4.9. Overdose

In the event of overdose, the patient may show transient gastrointestinal disorders. Studies in animals did not indicate any specific toxicity of this medicine.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Drugs used in benign prostatic hypertrophy, ATC code: G04CX02.

The lipidosterolic extract of *Serenoa repens* has anti-inflammatory, antiandrogenic and antiproliferative properties that act on benign prostatic hypertrophy.

Anti-inflammatory properties are expressed by an inhibition
- of phospholipase A2 (reduction of arachidonic acid synthesis),
- of cyclooxygenase (reduction of prostaglandins)
- of lipoxygenase (reduction of leukotrienes.)

This action on the arachidonic acid cascade and the effect observed on some inflammatory cytokines explain the anti-inflammatory activity found both in animal models and benign prostatic hypertrophy.

Antiandrogenic properties are mainly due to an inhibition of the 5 alpha reductases responsible for transforming testosterone into its active metabolite dihydrotestosterone (DHT). This antiandrogenic activity is also increased by a

reduction of the prolactin-dependent penetration of testosterone into the cell, an inhibition of oestrogen-dependent androgen receptor formation and finally an inhibition of DHT binding to its receptors.
This activity has been confirmed in an experimental rat model of benign prostatic hypertrophy.

Antiproliferative properties are explained by the fact that the lipidosterolic extract of *Serenoa repens* slows the proliferation of the glandular epithelium (estimated using the tritium-labelled thymidine index) induced by growth factors in human prostate organotypic cells.
It reduces protein synthesis in prostate cell cultures, stimulated by a combination of testosterone and prolactin, the latter of which regulates prostatic volume.

5.2. Pharmacokinetic properties

It is impossible to fully evaluate the pharmacokinetic profile of medicines of this type as it is impossible to determine the levels of all plant extract's components in the blood and, additionally, as some of these components already exist in the blood.

5.3. Preclinical safety studies

Non-clinical data reveal no special hazard for humans based on nonclinical studies of single and repeated dose toxicity, genotoxicity, and toxicity to reproduction.

No study was performed to assess the safety pharmacology and the carcinogenic potential.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Capsule content:
Macrogol 10 000
Body and cap of the capsule:
Gelatin, yellow iron oxide E 172, indigotin E 132, titanium dioxide E 171

6.2. Incompabilities

Not applicable.

6.3. Shelf-life

3 years in blister pack (PVC-Aluminium)

6.4. Special precautions for storage

Do not store above 25°C.

6.5. Nature and content of container

Packs of 30 or 60 hard capsules, in PVC/Aluminium blister. Not all pack sizes may be registered.

6.6. Instructions for use/handling

No special requirements.

Any unused product and all materials that have been in contact with it should be disposed of in accordance with local requirements.

6.7. Marketing authorization holder

Pierre Fabre Medicament
45, Place Abel Gance
92100 Boulogne – France

6.8. Date of revision of the text

May 2014.