PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

PROSTASAN®

COMPLEMENTARY MEDICINE

Western Herbal Medicine

This unregistered medicine has not been evaluated by the South African Health Products Regulatory Authority for its quality, safety or intended use.

SCHEDULING STATUS

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1 NAME OF THE MEDICINE

A.VOGEL PROSTASAN® (capsules)
Serenoa repens (BARTRAM) SMALL

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains:

Serenoa repens (BARTRAM) SMALL = *Sabal serrulata* (MICHAUX) NICHOLS (Saw palmetto) ..... 320 mg

[Dried fruit, 9 – 12:1 extract providing dry plant equivalent: 2,9 – 3,8 g herbal drug per capsule]

Contains sugar: Sorbitol (70 %) ..... 6,93 – 8,47 mg

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Oval-shaped, dark brown coloured soft capsules containing a clear, green-brown coloured oil.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

A.VOGEL PROSTASAN® is a herbal medicine for the chronic supportive treatment and prevention of benign prostatic hypertrophy and associated lower urinary tract symptoms including sexual dysfunction.

A.VOGEL PROSTASAN® is indicated for the following symptoms associated with benign prostatic hypertrophy:

- dysuria, nocturia and polyuria
- urinary retention
- frequent, difficult, and incomplete, daytime, and night-time urination
- poor urinary flow
- dribbling
- associated sexual dysfunction

4.2 Posology and method of administration

Posology

Adults (Males 18 years and over):
Take 1 capsule daily with a meal.

Special populations
Elderly population:
No dosage adjustment is required for this population.

Paediatric population:
This product is not indicated in patients younger than 18 years.

Method of administration
For oral use only.

Duration of use
For long-term use, there is no evidence for restriction of the length of time the medication should be taken.
Should the complaints of the disease persist, please seek the advice of a healthcare provider.

4.3 Contraindications

- A.VOGEL PROSTASAN® should not be used in patients who have a hypersensitivity to the active substances, *Serenoa repens* fruit (Saw palmetto), or to any of the excipients listed in section 6.1.
- A.VOGEL PROSTASAN® is not indicated for use in women.

4.4 Special warnings and precautions for use

- Prior to treatment other serious conditions should have been ruled out by a healthcare provider.
- If the condition worsens or does not improve after 8 weeks, consult a healthcare provider.
- If symptoms are accompanied by blood in the urine or fever, medical advice should be sought urgently.
- A.VOGEL PROSTASAN® may cause minor stomach upsets. These symptoms may be avoided by taking the medication with meals.
- Hepatic and renal impairment: The safety of Saw palmetto has not been studied in patients with hepatic and/or renal impairment.

Sorbitol warning:
Patients with the rare hereditary condition of sorbitol intolerance should not take A.VOGEL PROSTASAN®.

4.5 Interaction with other medicines and other forms of interaction

None known.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential/Contraception in males and females
No information available.

Pregnancy
A.VOGEL PROSTASAN® is not indicated for use in women.
The safety of this product during pregnancy has not been established. In the absence of sufficient data, the use of A.VOGEL PROSTASAN® during pregnancy is not recommended.

Breastfeeding
A.VOGEL PROSTASAN® is not indicated for use in women.
The safety of this product during breastfeeding has not been established. In the absence of sufficient data, the use of A.VOGEL PROSTASAN® during breastfeeding is not recommended.

Fertility
Fertility studies have not been performed.

4.7 Effects on ability to drive and use machines

A.VOGEL PROSTASAN® has no known effect on mental and/or physical ability to perform or execute tasks or activities requiring mental alertness, judgment and/or sound coordination and vision.

4.8 Undesirable effects

If symptoms of hypersensitivity or allergic reactions (itching, rash, urticaria) occur, discontinue use of product, and contact a healthcare professional immediately. The frequency of these symptoms is rare.

Gastrointestinal symptoms (e.g., eructation and gastrointestinal discomfort) may also occur rarely.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

None known.
Treatment of overdosage should be symptomatic and supportive.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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Pharmacotherapeutic group and ATC code:
Other drugs used in benign prostatic hypertrophy / L03AW05

Pre-clinical studies:
The effect of an ethanolic extract of *Serenoa repens* extract (PROSTASAN®) was tested on hormone-sensitive LNCaP, MCF-7 and hormone-insensitive DU 145, MDA MB231 prostate, breast carcinoma cell lines, renal Caki-1, urinary bladder 182, colon HCT 116 and lung A 549 cancer cells. The subsequent impact on growth inhibition and the ability to induce apoptosis was measured using the WST-1 assay and flow cytometry (Annexin V/PI stain) and/or by colourimetric assay (APO Percentage assay™). A dose-dependent antiproliferative effect was displayed by PROSTASAN® against all cell lines tested with GI50 values between 107 and 327 ug/ml. In hormone-sensitive prostate LNCaP and breast MCF-7 cell lines, the effect of extract expressed in GI50 was 2,2- and 2,5-fold more potent (p<0,01) than in hormone insensitive DU 145 and MDA MB231 cells. Apoptosis was induced in all cell lines with the exception of NSCLC A 549 with the degree of apoptosis achieved comparable to genistein and quercetin (positive controls), apoptosis was achieved within 24 hours with the exception of breast ER-MDA MB231 which required 48 hours to reach comparable levels.
Researchers concluded that the *Serenoa repens* extract prevented exponential growth of various cancer cell lines and induced apoptosis therein including hormone-sensitive and insensitive prostate cancer cell lines with low levels of toxicity. (Hostanska, Suter *et al.* 2007)

In a subsequent study, the biological effects of *Serenoa repens* extract (PROSTASAN®) on prostate cells beyond its known antiandrogenic actions were determined *in vitro* using human prostate cancer PC-3 cell lines. PROSTASAN® inhibited epidermal growth factor (EGF) and lipopolysaccharide (LPS) induced proliferation of the prostatic epithelial, androgen-independent cell line PC-3. At effective concentrations of 50 µg/mL, PROSTASAN® partly displaced EGF from EGF receptor (EGFR) but fully blocked EGF-induced cell proliferation of PC-3 cells. Similarly, PROSTASAN® inhibited LPS-induced proliferation of PC-3 cells without affecting LPS activation of the NFκB pathway via toll-like receptor-4 (TLR-4). Additionally, PROSTASAN® reduced the constitutive secretion of monocyte chemotactic protein-1 (MCP-1), the LPS-induced secretion of IL-12 and inhibited MCP-1 and granulocyte-macrophage colony-stimulating factor (GM-CSF) production in the presence of LPS on PC-3 cells. The results suggested that in addition to other reported effects on BPH development and prostatitis, PROSTASAN® also inhibits EGF-dependent growth and proinflammatory responses of the prostate epithelial cells, thus inhibiting prostate growth in both androgen-dependent and independent settings (seen in the present study) by interfering with function of 5-alpha-reductase, altering cell membrane organization and competing with ligands binding to receptors. (Iglesias-Gato, Carsten *et al.* 2012)

Clinical studies:
In an open multicentre trial, 69 men with moderate BPH and concomitant sexual dysfunction were treated with PROSTASAN® 1 capsule daily for 8 weeks. International Prostate Symptom Scores were reduced by 52 % from 14,4 ± 4,7 to 6,9 ± 5,2 (p<0,0001); sexual dysfunction measured with the Brief Sexual Function Inventory improved by 40 % from 22,4 ± 7,2 to 31,4 ± 9,2 (p<0,0001), and the Urolife BPH QoL-9 total score improved by 35 % from 162,7 ± 47,9 to 105,0 ± 56,3 (p<0,0001). Investigators' and patients' assessments confirmed good efficacy, and treatment was very well tolerated and accepted by the patients. Correlation analyses confirmed the relationship between improved BPH symptoms and reduced sexual dysfunction. The degree of reduction in BPH symptoms achieved was comparable to that demonstrated by alpha-blockers or 5-alpha-reductase inhibitors in previous trials with simultaneous improvement in sexual dysfunction and quality of life. (Suter, Saller *et al.* 2013)

A subsequent trial conducted on 72 men (40-85 years, mean 62,7 ± 8,54) with moderate benign prostatic enlargement and lower urinary tract symptoms determined similar findings to Suter *et al.* 2012. The subsequent trial applied PROSTASAN® 1 capsule daily for 12 months. IPSS scores and quality of life were reduced from 14,46 ± 5,36 to 11,08 ± 3,92 (p=0,0000) and from 2,72 ± 0,96 to 2,25 ± 1,05 (p=0,0001) respectively after 12 months of treatment. The uroflow increased from 13,94 ± 5,00 to 15,34 ± 4,07 ml/s (p=0,0005). Prostate volume also reduced significantly after 12 months by 3 % (p=0,0392). (Tršinar, Lovšin *et al.* 2014)

5.2 Pharmacokinetic properties
Since the total extract is regarded as active constituent, pharmacokinetic studies on selected components provide some information but remain inconclusive in regard of the total extract.

Plasma concentrations of Saw Palmetto fruit extract-components were measured from blood samples of 23 healthy abstinent male volunteers. A mean value of 2,6 mg/l was reached 1,5 hours after oral intake. The elimination rate amounted 8,2 mg/l/h and the eliminated half-life was 1,9 hours. Tissue distribution patterns in rats showed that the uptake of the extract was much higher in the prostate than either the liver or genitourinary regions. (De Bernardi Di Valserra *et al.* 1994)

5.3 Preclinical safety data
No data are available on acute toxicity, repeated dose toxicity, embryotoxicity, teratogenicity, and anaphylaxis for the current extract. Documented clinical long-term studies for up to 3 years and extensive post marketing experience report that Saw Palmetto fruit extract are well tolerated in humans.
No mutagenic effects of PROSTASAN® were detected in Ames' test (with or without metabolic activation).

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Ferric oxide black E172
Ferric oxide red E172
Ferric oxide yellow E172
Gelatin (porcine)
Glycerol
Purified water
Sorbitol 70 %

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
60 months unopened.
Use within 5 months of opening.

6.4 Special precautions for storage
No special storage conditions.
Store at or below 25 °C in a cool, dry place.
Store in the original package/container.

6.5 Nature and contents of container
Amber glass bottles (type III glass) closed with pilfer proof screw caps fitted with a polyethylene liner.

Pack size: 30 capsules

6.6 Special precautions for disposal of a used medicine or waste materials derived from such medicine and other handling of the product
No special requirements.

7 THE HOLDER OF THE CERTIFICATE OF REGISTRATION

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8 REGISTRATION NUMBER(S)/REFERENCE NUMBER

Listing number: 134577

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

To be allocated.

10 DATE OF REVISION OF TEXT

January 2021