Urostemol Prosta capsules

THR 02855/0241

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UROSTEMOL PROSTA CAPSULES

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LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Jenson R+ Ltd a Traditional Herbal Registration Certificate for the traditional herbal medicinal product Urostemol Prosta capsules (Traditional Herbal Registration number: THR 41188/0009) on 24 April 2015. Ownership of this Traditional Herbal Registration Certificate was transferred from Jenson R+ Ltd to Omega Pharma Ltd on 29 May 2015 (Traditional Herbal Registration number: THR 02855/0241). This product is available without prescription and can be bought from pharmacies and other outlets.

The active ingredient of Urostemol Prosta capsules comes from Pumpkin (*Cucurbita pepo* L. convar. *citrullina* I. Greb. var. *styriaca* I. Greb) seed. Urostemol Prosta capsules is a traditional herbal medicinal product used for the relief of lower urinary tract symptoms in men related to an overactive bladder, such as urgency to urinate and frequent urination, or who have a confirmed diagnosis of benign prostatic hyperplasia (BPH), based on traditional use only.

This registration is based exclusively upon the longstanding use of Pumpkin seed as a traditional herbal medicine and not upon data generated from clinical trials. There is no requirement under the Traditional Herbal Registration scheme to prove scientifically that a product works.

No new or unexpected safety concerns arose from this application and it was, therefore, decided that a Traditional Herbal Registration Certificate could be granted.

UROSTEMOL PROSTA CAPSULES

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SCIENTIFIC DISCUSSION

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INTRODUCTION

The MHRA granted a Traditional Herbal Registration Certificate for the traditional herbal medicinal product Urostemol Prosta capsules (41188/0009) on 24 April 2015. Ownership of this THR Certificate was transferred from Jenson R+ Ltd to Omega Pharma Ltd on 29 May 2015 (Traditional Herbal Registration number: THR 02855/0241). This product is on the general sales list (GSL).

This application was submitted according to Article 16.c of Directive 2001/83 EC, as amended, as part of the Traditional Herbal Medicines Registration Scheme. The product is used for the relief of lower urinary tract symptoms in men related to an overactive bladder, such as urgency to urinate and frequent urination, or who have a confirmed diagnosis of benign prostatic hyperplasia (BPH), based on traditional use only.

The data supplied by the Applicant demonstrate 30 years of traditional use of Pumpkin seed, including at least 15 years of use in the European Community. A satisfactory review of the available safety data on Pumpkin seed has also been provided, together with an Expert Safety Report supporting the proposed product.

PHARMACEUTICAL ASSESSMENT

HERBAL SUBSTANCE: **PUMPKIN SEED**

Scientific name of the plant: *Cucurbita pepo* L. convar. *citrullina* I. Greb. var. *styriaca* I. Greb
Family: Cucurbitaceae

The Pumpkin plants used in this product are cultivated in Hungary and Austria. Following harvesting, the seeds are dried gently followed by a brief purification (aspiration) step in which the loose skins are removed.

Confirmation has been provided that the herbal substance is produced in line with the Guideline on Good Agricultural and Collection Practice (GACP) EMEA/HMPC/246816/2005 and that the herbal substance has not been fumigated or treated with ionising radiation.

Control of Herbal Substance
An appropriate specification based on the German Pharmacopeia monograph for Pumpkin seed is applied and is acceptable. The specification is supported by the batch data provided.

Container Closure System
Satisfactory details of the container closure system are provided and confirmation has been given that all components of the container closure system comply with Directive 2008/39/EC relating to plastic materials and articles intended to come into contact with foodstuffs.

Stability
Confirmation is given that the herbal substance will be tested prior to being used to make the herbal preparation. A shelf-life for the herbal substance is not appropriate because it is only a precursor of the active substance, the herbal preparation. The actual guideline requires stability testing data for the herbal preparation and the herbal product in the application documents and not for the herbal substance.

HERBAL PREPARATION: **PUMPKIN SEED SOFT EXTRACT**

Part of the plant used: Seed
Ratio of the herbal substance to the herbal preparation (native): 15-25: 1
Extraction solvent: Ethanol 92% (m/m)

Manufacture
A satisfactory description of the manufacturing process of the herbal substance and flow diagram has been provided. The in-process controls are satisfactorily detailed. The manufacture of the herbal preparation is considered a standard procedure.

Certificates of analysis for all materials used in the manufacture of the herbal preparation have been provided.

Control of Herbal Preparation
A satisfactory specification with appropriate tests and limits has been provided for the herbal preparation.

Satisfactory analytical procedures are used to control the quality of the herbal preparation. Analytical procedures have been validated, as appropriate.

Certificates of analysis have been provided for production batches of the herbal preparation, demonstrating satisfactory compliance with the proposed specification.

Container Closure System
Confirmation is provided that all components of the container closure system used to store the herbal preparation comply with Directive 2008/39/EC relating to plastic materials and articles intended to come into contact with foodstuffs.

Stability
Stability studies have been performed in accordance with current guidelines. The proposed re-test period for the Pumpkin seed soft extract is acceptable.

HERBAL PRODUCT: UROSTEMOL PROSTA CAPSULES

Description and Composition of the Herbal Product
Urostemol Prosta capsules are hard, brown, gelatin capsules. Each capsule contains 500 mg of soft extract from Pumpkin seed and the excipients hydrophobic colloidal silica, gelatin, black iron oxide (E 172), red iron oxide (E 172) and yellow iron oxide (E 172).

The compatibility of the herbal preparation with the excipients is demonstrated by the stability testing results. The hydrophobic colloidal silica and gelatin are controlled in line with the respective Ph Eur monographs and representative certificates of analysis are provided to demonstrate full compliance with the Ph Eur. The black iron oxide (E 172), red iron oxide (E 172) and yellow iron oxide (E 172) comply with EU regulation 231/2012 and are controlled in line with suitable specifications, in the absence of Ph Eur monographs for these excipients this is acceptable.

A certificate of suitability has been provided for the gelatin.

Manufacture of Herbal Product
A flow diagram outlining the various stages of the manufacturing process and the in-process controls is provided.

In-process controls are appropriate considering the nature of the product and the method of manufacture. Process validation has been carried out on a commercial batch and the results are acceptable.

Control of Herbal Product
The finished product specifications are satisfactory. Acceptance limits have been justified with respect to conventional pharmaceutical requirements and, where appropriate, safety. Test methods have been described and have been adequately validated, as appropriate. Batch data have been provided and comply with the release specification.

Container Closure System
The herbal product is stored in PVC/PVdC-aluminium-blister packs. Packs sizes of 20, 40, 80 or 140 hard capsules have been authorised, although not all pack sizes may be marketed.

Suitable specifications have been provided by the packaging suppliers and it has been confirmed that all primary packaging materials comply with Directive 2002/72/EC.

Stability
Finished product stability studies have been conducted in accordance with current guidelines. Based on the results, a product shelf-life of 3 years is appropriate.

Product Literature
All product literature is satisfactory.

A package leaflet has been submitted to the MHRA along with results of consultations with target patient groups ("user testing"), in accordance with Article 59 of Council Directive 2001/83/EC. The results indicate that the package leaflet is well-structured and organised, easy to understand and written in a comprehensive manner. The test shows that the patients/users are able to act upon the information that it contains.

CONCLUSION
There are no objections to granting of a Traditional Herbal Registration from a quality point of view.

NON-CLINICAL ASSESSMENT

NON-CLINCIAL OVERVIEW

The applicant has submitted a literature review with this application. An Expert Safety Report was provided, which included reviews of some non-clinical data. The Expert Safety Report was written by a suitably qualified professional.

The overview submitted in support of this application is satisfactory.

Due to a shortage of published data on Pumpkin seed, it is not possible to assess if the safety package for the phytochemical constituents of these active ingredients is acceptable to the standards of today's GLP and safety testing requirements. However, the information supplied demonstrating traditional use is acceptable and thus the lack of provision of a complete standard safety package is acceptable and in compliance with guideline EMEA/HMPC/32116/05.

Assurance was provided that the results of genotoxicity testing will be provided before renewal of the registration.

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

The SmPC for this product is satisfactory from a non-clinical point of view.

ENVIRONMENTAL RISK ASSESSMENT

An environmental risk assessment is not required for herbal medicinal products according to guidance CPMP/SWP/4447/00.

CONCLUSION

There are no objections to granting of a Traditional Herbal Registration from a non-clinical point of view.

CLINICAL ASSESSMENT

INDICATIONS

The applicant has submitted the following therapeutic indication:

"A traditional herbal medicinal product used for the relief of lower urinary tract symptoms in men related to an overactive bladder, such as urgency to urinate and frequent urination, or who have a confirmed diagnosis of benign prostatic hyperplasia (BPH), based on traditional use only.

Prior to treatment, other serious conditions should have been ruled out by a doctor."

The indication is acceptable.

POSOLOGY AND METHOD OF ADMINISTRATION

The applicant has submitted the following:

"For oral use only.

Adults and the elderly:
One capsule to be taken twice a day.

The use in children and adolescents under 18 years of age is not recommended (see section 4.4 'Special warnings and precautions for use.').

Method of administration
The capsules should be taken with water, ideally before meals.

Duration of use
Long-term use is possible on the advice of a doctor or qualified healthcare practitioner (see section 4.4 'Special warnings and precautions for use'). "

This is acceptable.

EFFICACY

No clinical efficacy data is required for registration of Traditional Herbal Medicinal Products (THMP).

EVIDENCE OF TRADITIONAL USE

Article 16 c 1 (c) requires the applicant to provide bibliographic or expert evidence to show that the medicinal product in question, or a corresponding product, has been in medicinal use throughout a period of at least 30 years, including at least 15 years within the EU.

The published HMPC assessment report and Community Monograph for Pumpkin seed adopted by the HMPC adequately cover the evidence for traditional use of the herbal preparation in the product under assessment in the EU for at least 30 years. The requirements of the Directive are considered to be met.

SAFETY REVIEW

Article 16 c 1 (d) requires the applicant to provide a bibliography of the safety data together with an expert report.

The HMPC Assessment Report for Pumpkin seed covers the bibliographic data available and the safety of Pumpkin seed has been demonstrated. The SmPC is in line with the HMPC monograph.

PRODUCT LITERATURE

The SmPC, PIL and labelling for this product are medically satisfactory.

RECOMMENDATIONS

A Traditional Herbal Registration may be granted.

OVERALL CONCLUSION AND RISK ASSESSMENT

QUALITY
The quality data submitted with this application are satisfactory.

NON-CLINICAL
No new non-clinical data were submitted with this application. However, assurance was provided that the results of genotoxicity testing will be provided before renewal of this registration. This is satisfactory.

EFFICACY AND SAFETY
No clinical efficacy data are required for registration of Traditional Herbal Medicinal Products (THMP).

The published HMPC assessment report and Community Monograph for Pumpkin seed adopted by the HMPC adequately cover the evidence for traditional use of the extract in the product under assessment in the EU for at least 30 years and the non-clinical and clinical safety issues associated with Pumpkin seed.

The SmPC, PIL and labelling are satisfactory.

RISK ASSESSMENT
The quality of the product is acceptable and no new non-clinical or clinical safety concerns have been identified. The risk: benefit balance is acceptable and a Traditional Herbal Registration may be granted.

UROSTEMOL PROSTA CAPSULES

THR 02855/0241

STEPS TAKEN FOR ASSESSMENT

1	The MHRA received the Traditional Herbal Registration application on 2 August 2013
2	Following standard checks and communication with the applicant the MHRA considered the application valid on 16 August 2013
3	Following assessment of the application the MHRA requested further information relating to the quality dossier on 24 September 2013 and the clinical dossier on 30 September 2013
4	The applicant responded to the MHRA's requests, providing further information on the quality and clinical dossiers on 25 March 2014
5	Following assessment of the response the MHRA requested further information relating to the quality dossier on 28 April 2014 and the clinical dossier on 13 June 2014
6	The applicant responded to the MHRA's request, providing further information on the quality dossier on 14 May 2013
7	Following assessment of the response the MHRA requested further information relating to the clinical dossier on 30 September 2014
8	The applicant responded to the MHRA's request, providing further information on the clinical dossier on 20 February 2015
9	Following assessment of the response the MHRA requested further information relating to the clinical dossier on 5 March 2015
10	The applicant responded to the MHRA's request, providing further information on the clinical dossier on 19 March 2015
11	A THR was granted on 24 April 2015

STEPS TAKEN AFTER INITIAL REGISTRATION

Date submitted	Application type	Scope	Outcome
29/04/2015	Change of Ownership	Change of Ownership of THR from Jenson R+ Ltd to Omega Pharma Ltd	Granted - 29/05/2015

SUMMARY OF PRODUCT CHARACTERISTICS

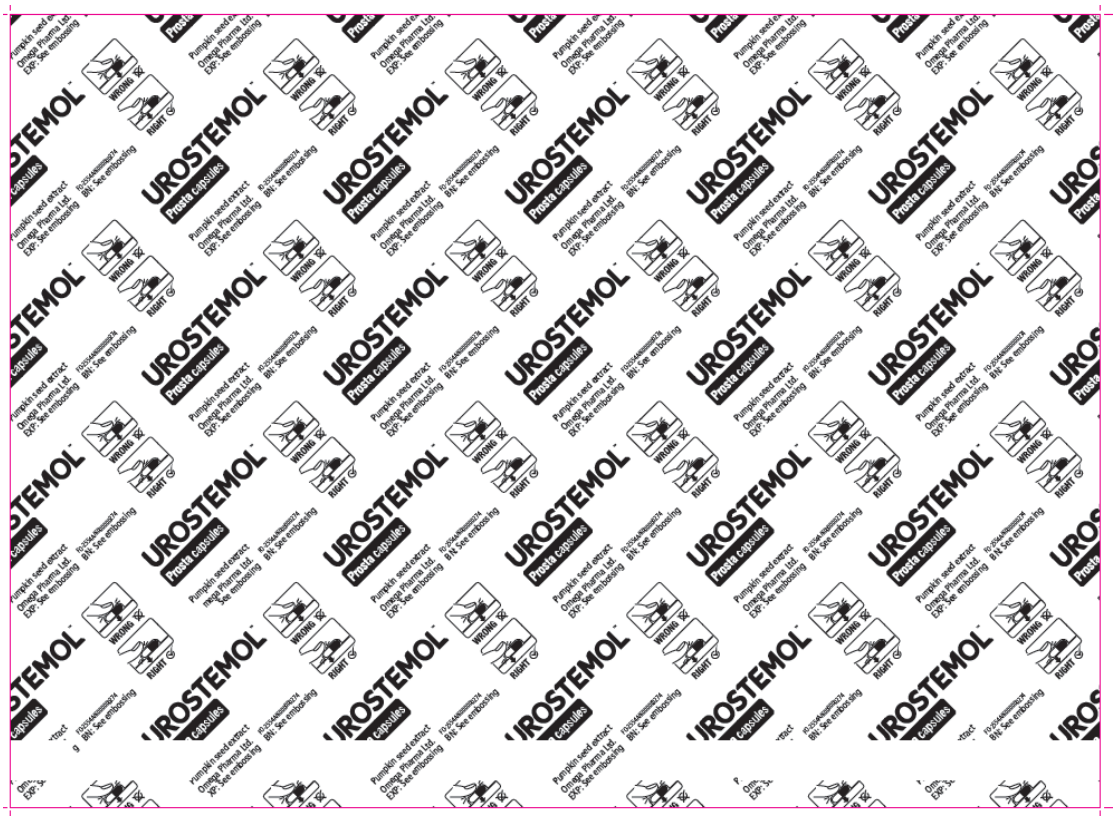
In accordance with Directive 2010/84/EU, the Summaries of Product Characteristics (SmPCs) for products authorised at a national level are available on the MHRA website.

PATIENT INFORMATION LEAFLET

In accordance with Directive 2010/84/EU, the Patient Information Leaflets (PILs) for products authorised at a national level are available on the MHRA website.

LABELLING

Blister:



Cartons:


NEW
UROSTEMOL™
Prosta capsules
BN
EXP
NEW
UROSTEMOL™
Prosta capsules
Pumpkin seed extract
Traditional herbal medicinal product used for the relief of lower urinary tract symptoms in men related to an
✓ overactive bladder
✓ confirmed diagnosis of benign prostatic hyperplasia (BPH)
Based on traditional use only.
FOR MEN
TRADITIONALLY USED TO RELIEVE
frequent & urgent urination
feeling of incomplete bladder emptying
weak urinary flow
40 capsules
OMEGA PHARMA
ZER 60000136ZBP 70006311
ZAZ 10003973_000_01
8/14
RIGHT
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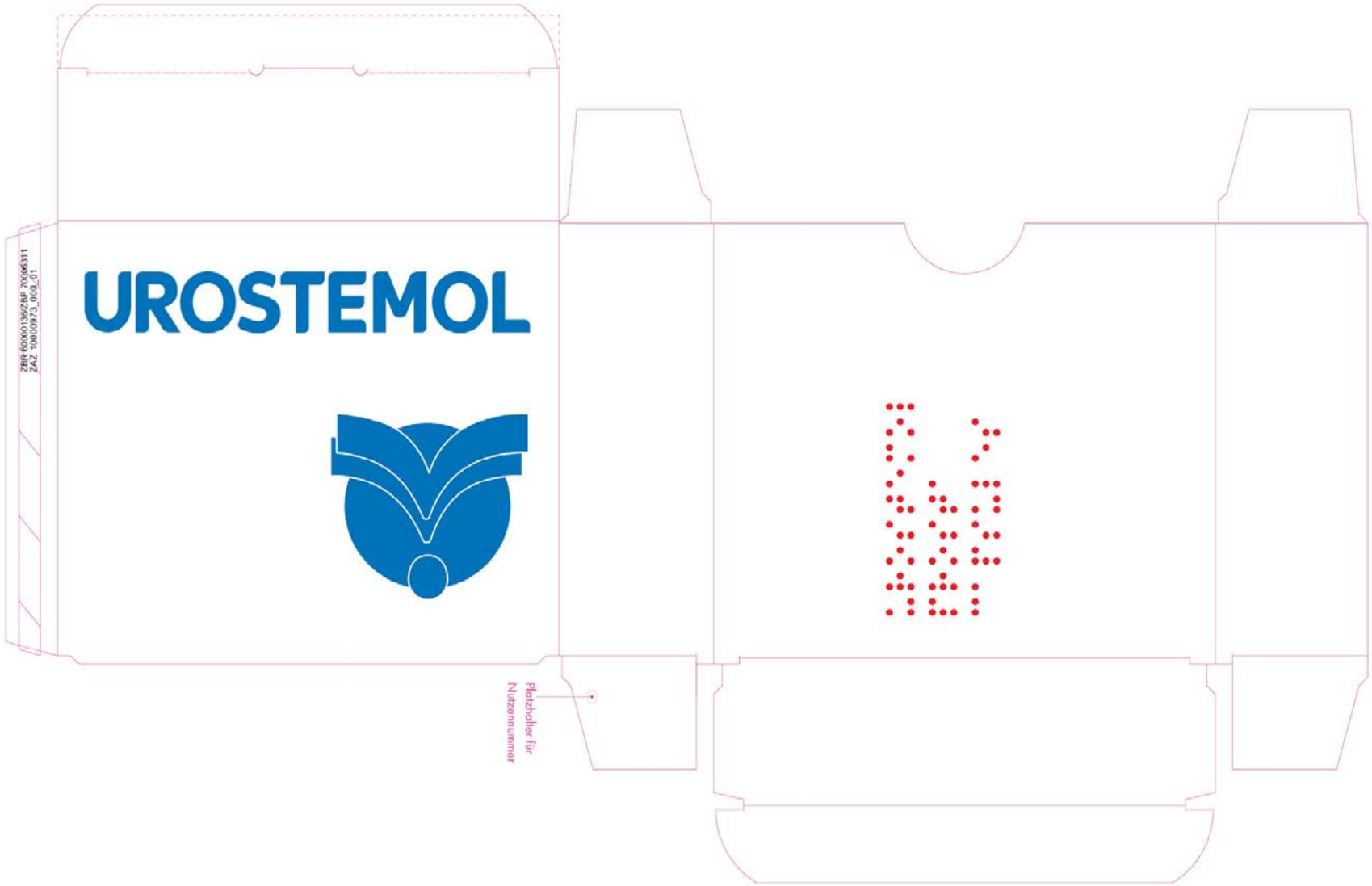
100000541 2
UROSTEMOL
Prosta capsules
Ingredients:
Each hard capsule contains the active ingredient:
500 mg Pumpkin seed soft extract (Cucurbita pepo L. convar. citrullina l. Greb. var. styriaca l. Greb) (15-25 : 1), extraction solvent ethanol 92% (m/v).
See leaflet for further information.
Platzhalter für Nutzennummer
RIGHT
UROSTEMOL™
Prosta capsules
Urostemol Prosta is a traditional herbal medicinal product used for the relief of lower urinary tract symptoms in men related to an overactive bladder, or who have a confirmed diagnosis of enlarged prostate (benign prostatic hyperplasia; BPH). This is based on traditional use only.
Used to relieve symptoms such as: • urgency to urinate • frequent urination day and night • incomplete emptying of the bladder • weak or interrupted urinary flow.
Prior to treatment other serious conditions should have been ruled out by a doctor.
FOR ORAL USE.
How to take: Adults and the elderly: Take 1 capsule twice a day with water, ideally before meals.
DO NOT EXCEED THE STATED DOSE
THR
Certification Mark
5 012616 262722
THR 02855/0241
THR Holder: Omega Pharma Ltd.,
32 Vauxhall Bridge Road,
London, SW1V 2SA, UK.
WRONG
UROSTEMOL
Prosta capsules
READ THE PACKAGE LEAFLET BEFORE USE.
Warnings:
Not recommended for children and adolescents under 18.
This product is for men only and therefore must not be used by women.
Do not use if you are allergic to any of the ingredients or other pumpkin-like plants (such as watermelon, courgettes, etc.).
Storage:
Store in the original package.
Keep out of the sight and reach of children.
WRONG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Platzhalter für
Nutzennummer


NEW
UROSTEMOL™
Prosta capsules
BN
EXP
NEW
UROSTEMOL™
Prosta capsules
Pumpkin seed extract
Traditional herbal medicinal product used for the relief of lower urinary tract symptoms in men related to an
✓ overactive bladder
✓ confirmed diagnosis of benign prostatic hyperplasia (BPH)
Based on traditional use only.
FOR MEN
TRADITIONALLY USED TO RELIEVE
frequent & urgent urination
feeling of incomplete bladder emptying
weak urinary flow
80 capsules
OMEGA PHARMA
RIGHT
CT08208A
100000541 3
UROSTEMOL
Prosta capsules
Ingredients:
Each hard capsule contains the active ingredient:
500 mg Pumpkin seed soft extract (Cucurbita pepo L. convar. citrullina I. Greb. var. styriaca I. Greb) (15-25 : 1), extraction solvent ethanol 92% (m/v).
See leaflet for further information.
RIGHT
UROSTEMOL™
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Used to relieve symptoms such as: • urgency to urinate • frequent urination day and night • incomplete emptying of the bladder • weak or interrupted urinary flow.
Prior to treatment other serious conditions should have been ruled out by a doctor.
FOR ORAL USE.
How to take: Adults and the elderly: Take 1 capsule twice a day with water, ideally before meals.
DO NOT EXCEED THE STATED DOSE
THR
Certification Mark
5 012616 262746
THR 02855/0241
THR Holder: Omega Pharma Ltd., 32 Vauxhall Bridge Road, London, SW1V 2SA, UK.
WRONG
UROSTEMOL
Prosta capsules
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Warnings:
Not recommended for children and adolescents under 18.
This product is for men only and therefore must not be used by women.
Do not use if you are allergic to any of the ingredients or other pumpkin-like plants (such as watermelon, courgettes, etc.).
Storage:
Store in the original package.
Keep out of the sight and reach of children.
WRONG
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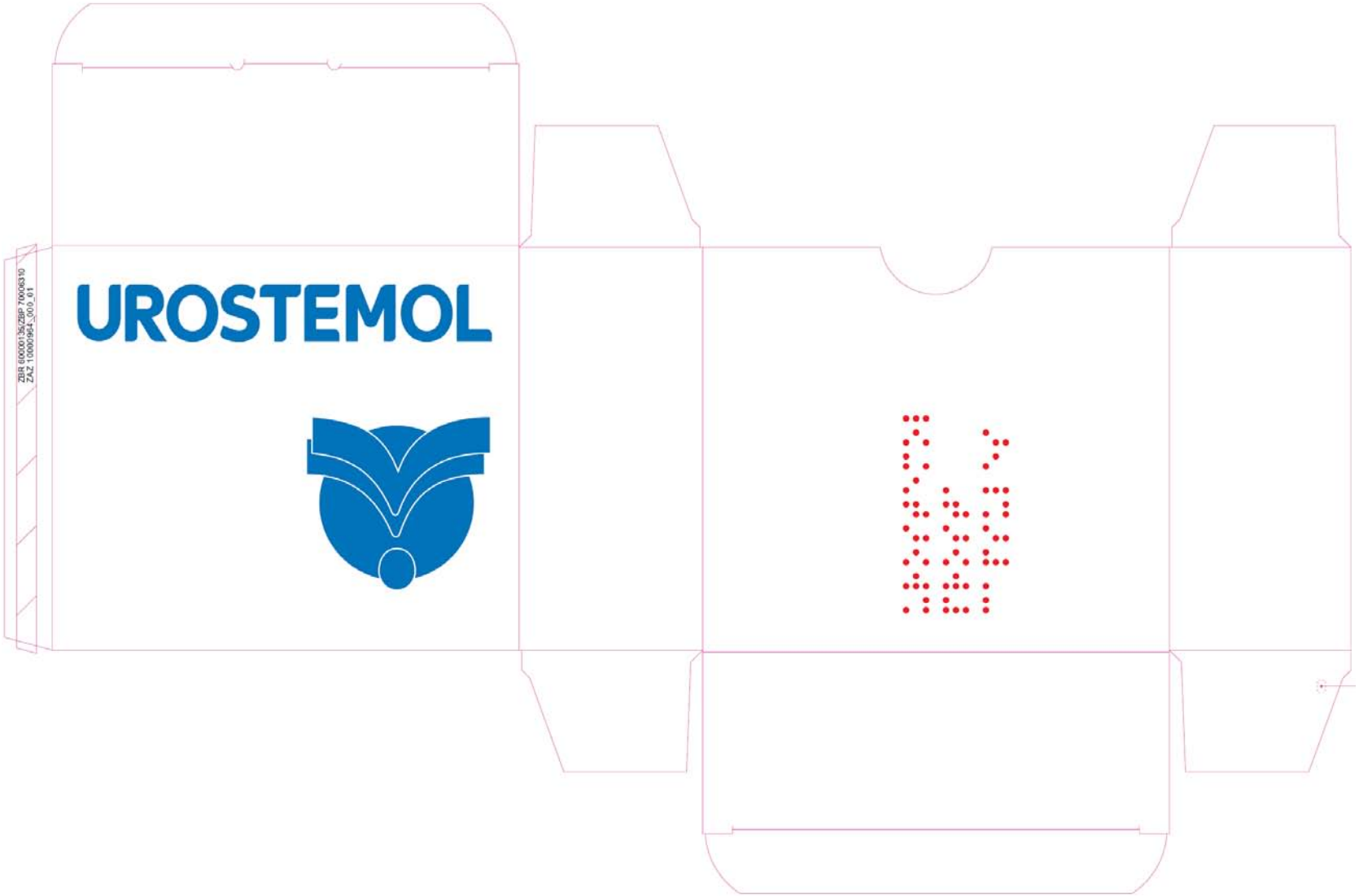
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