APPROVED PROFESSIONAL INFORMATION

SCHEDULING STATUS

S3

PROPRIETARY NAME (and dosage form):

URODOXA 1 mg (Tablet)

URODOXA 2 mg (Tablet)

URODOXA 4 mg (Tablet)

URODOXA 8 mg (Tablet)

COMPOSITION:

URODOXA 1 mg:

Each uncoated tablet contains doxazosin mesilate equivalent to doxazosin 1 mg.

URODOXA 2 mg:

Each uncoated tablet contains doxazosin mesilate equivalent to doxazosin 2 mg.

URODOXA 4 mg:

Each uncoated tablet contains doxazosin mesilate equivalent to doxazosin 4 mg.

URODOXA 8 mg:

Each uncoated tablet contains doxazosin mesilate equivalent to doxazosin 8 mg.

The other ingredients of the formulations are cellulose microcrystalline, lactose anhydrous, sodium starch glycolate and magnesium stearate.

PHARMACOLOGICAL CLASSIFICATION:

A.7.1 Vasodilators, hypotensive medicines.

PHARMACOLOGICAL ACTION:

Pharmacodynamic properties:

Doxazosin exerts a vasodilator effect via selective and competitive blockade of post-junctional alpha-1-adrenoceptors. Doxazosin has been shown to block the 1A subtype of the alpha-1-adrenoceptor which accounts for over 70 % of the subtypes in the prostate.

Pharmacokinetic properties:

Doxazosin is well absorbed after oral administration, with peak blood levels occurring at about 2 hours. The plasma elimination is biphasic with the terminal elimination half-life being 19 to 22 hours, hence providing the basis for once daily dosing. Doxazosin is extensively metabolised with less than 5 % excreted unchanged.

Maximum reduction in blood pressure normally occurs about 6 hours after dosing.

Most (98 %) of plasma doxazosin is protein bound. *In vitro* data in human plasma indicates that doxazosin has no effect on protein binding of the medicines tested (digoxin, phenytoin, warfarin or indomethacin).

INDICATIONS:

Hypertension:

URODOXA is indicated for the treatment of mild to moderate hypertension.

Benign Prostatic Hyperplasia:

URODOXA is also indicated for the treatment of the urinary outflow obstruction and symptoms associated with benign prostatic hyperplasia (BPH). **URODOXA** may be used in BPH patients who are either hypertensive or normotensive.

CONTRAINDICATIONS:

URODOXA is contraindicated in patients with a known hypersensitivity to quinazolines or any of the ingredients of **URODOXA**.

URODOXA is contraindicated in

- Pregnancy and lactation (see **"PREGNANCY AND LACTATION"**).
- Patients with a history of orthostatic hypotension

- Patients with benign prostatic hyperplasia and concomitant congestion of upper urinary tract, chronic urinary tract infection of bladder stones
- As monotherapy in patients either overflow bladder or anuria or without progressive renal insufficiency

WARNINGS AND SPECIAL PRECAUTIONS:

URODOXA is not recommended for the treatment of heart failure caused by mechanical obstruction, for example aortic or mitral valve stenosis, pulmonary embolism, and restrictive pericardial disease. It should be used with caution is patients with angina pectoris.

Treatment with **URODOXA** should be introduced with caution due to the risk of sudden collapse after the initial dose.

Extra caution is necessary in patients with hepatic or renal impairment and in the elderly.

There is no experience with the use of **URODOXA** in children.

Patients undergoing cataract surgery: Intraoperative Floppy Iris Syndrome (IFIS) has been observed during cataract surgery in some patients on or previously treated with alpha1 blockers. This variant of small pupil syndrome is characterised by the combination of a flaccid iris that billows in response to intraoperative irrigation currents, progressive intraoperative miosis despite preoperative dilation with standard mydriatic medicines, and potential prolapse of the iris toward the phacoemulsification incisions. The patient's surgeon should be prepared for possible modifications to their surgical technique, such as the utilisation of iris hooks, iris dilator rings, or viscoelastic substances. This does not appear to be a benefit of stopping alpha1 blocker therapy prior to cataract surgery.

Patients taking PDE-5 Inhibitors: Concomitant administration of **URODOXA** with a PDE-5 inhibitor can result in additive blood pressure lowering effects and symptomatic hypotension.

Postural hypotension with or without symptoms (e.g. dizziness) may develop within a few hours following administration of **URODOXA**. However, infrequently, symptomatic postural hypotension has also been reported later than a few hours after dosing. As with other alpha-blockers, there is a potential for syncope, especially after the initial dose or after an increase in dosage strength. Patients

should be warned of the possible occurrence of such events and should avoid situations where injury could result should syncope occur. Care should be taken when **URODOXA** is administered to patients with symptomatic hypotension or patients who have had a hypotensive response to other medications.

URODOXA contains lactose and should not be given to patients with rare hereditary problems or a history of galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption.

Effect on the ability to drive and use machinery:

The ability to engage in activities such as driving a motor vehicle or operating machinery may be impaired, especially when initiating therapy. **URODOXA** may cause drowsiness or dizziness therefore patients affected should not drive or operate machinery.

INTERACTIONS:

No adverse medicine interaction has been noted in clinical experience with thiazide diuretics, furosemide, beta-blocking agents, oral hypoglycaemic medicines, antibiotics, uricosuric agents or anticoagulants.

However the hypotensive effects of **URODOXA** may be enhanced by use with diuretics and other anti-hypertensives, and by alcohol and other medicines that cause hypotension.

The risk of first-dose hypotension may be particularly increased in patients receiving beta-blockers or calcium channel blockers.

Concomitant administration of **URODOXA** with a PDE-5 inhibitor can result in additive blood pressure lowering effects and symptomatic hypotension; therefore, PDE-5 inhibitor therapy should be initiated at the lowest dose in patients taking **URODOXA**.

PREGNANCY AND LACTATION:

The safety of **URODOXA** in pregnancy or lactation has not yet been established (see **"CONTRA-INDICATIONS"**).

DOSAGE AND DIRECTIONS FOR USE:

Benign Prostatic Hyperplasia:

The initial dosage of **URODOXA** is 1 mg given once daily. Depending on the individual patient's urodynamics and BPH symptomatology, dosage may then be increased to 2 mg and thereafter to 4 mg and up to the maximum recommended dose of 8 mg. The recommended titration interval is 1 - 2 weeks. The usual recommended dose is 2 - 4 mg once daily. Blood pressure should be evaluated routinely in these patients.

SIDE EFFECTS:

Blood and the lymphatic system disorders:

The following side effects have been reported and frequencies are unknown:

Thrombocytopenia, leukopenia.

Immune system disorders:

The following side effects have been reported and frequencies are unknown:

Allergic medicine reactions

Psychiatric disorders:

Less frequent:

Nervousness

The following side effects have been reported and frequencies are unknown:

Depression, insomnia, agitation

Nervous system disorders:

Frequent:

Dizziness, vertigo, headache

Less frequent:

Somnolence.

The following side effects have been reported and frequencies are unknown:

Tremor, paraesthesia, postural dizziness

Eye disorders:

The following side effects have been reported and frequencies are unknown:

Blurred vision, abnormal vision

Cardiac disorders:

Less frequent:

Cardiac dysrhythmias, palpitations, tachycardia

The following side effects have been reported and frequencies are unknown:

Myocardial infarction, angina pectoris

Vascular disorders:

Less frequent:

Hypotension

The following side effects have been reported and frequencies are unknown:

Cerebrovascular accidents

Respiratory, thoracic and mediastinal disorders:

Less frequent:

Dyspnoea, rhinitis

The following side effects have been reported and frequencies are unknown:

Epistaxis

Gastrointestinal disorders:

Less frequent:

Nausea, abdominal pain

The following side effects have been reported and frequencies are unknown:

Diarrhoea, dry mouth, vomiting

Hepato-biliary disorders:

The following side effects have been reported and frequencies are unknown:

Jaundice, hepatitis, cholestasis

Skin and subcutaneous tissue disorders:

The following side effects have been reported and frequencies are unknown:

Skin rashes, pruritus, purpura

Renal and urinary disorders:

The following side effects have been reported and frequencies are unknown:

Haematuria. Cases of urinary incontinence were reported; this effect may be related to the pharmacological action of **URODOXA**.

Reproductive system and breast disorders:

Less frequent:

Priapism

The following side effects have been reported and frequencies are unknown:

Sexual dysfunction, and impotence.

General disorders and administrative site conditions:

Frequent:

Asthenia

The following side effects have been reported and frequencies are unknown:

Fatigue, malaise, chest pain, oedema

Investigations:

The following side effects have been reported and frequencies are unknown:

Abnormal liver function tests

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

See **"SIDE EFFECTS"**.

Dialysis is not indicated, since **URODOXA** is highly protein bound. Treatment is symptomatic and supportive.

IDENTIFICATION:

URODOXA 1 mg:

White to off-white, coloured, circular, biconvex shaped uncoated tablets debossed with 'H' on one side and '01' on other side.

URODOXA 2 mg:

White to off-white, coloured, caplet shaped uncoated tablets debossed with 'H02' on one side and breakline on other side.

URODOXA 4 mg:

White to off-white, coloured, diamond shaped uncoated tablets debossed with 'H03' on one side and breakline on other side.

URODOXA 8 mg:

White to off-white, coloured, caplet shaped uncoated tablets debossed with 'H04' on one side and breakline on other side.

PRESENTATION:

URODOXA 1 mg:

1) Tablets are packed in white opaque 250 micron PVC film coated with 60 gsm PVdC and printed 25 micron aluminium foil with 7 gsm heat seal lacquer. Each blister contains 10 tablets.

Pack size: 30's – Each carton contains 3 blister strips of 10 tablets each.

2) Tablets are packed in 40 ml HDPE container of 33 mm neck finish (OFC 51 ml) with 33 mm - 400 RS closure with TEKNIPLEX HS-123 induction sealing wad with rayon coil. The HDPE container is stored in a carton. Each container contains 30 tablets.

Pack size: 30's – One HDPE container contains 30 tablets.

URODOXA 2 mg:

1) Tablets are packed in white opaque 250 micron PVC film coated with 60 gsm PVdC and printed 25 micron aluminium foil with 7 gsm heat seal lacquer. Each blister contains 10 tablets.

Pack size: 30's – Each carton contains 3 blister strips of 10 tablets each.

2) Tablets are packed in 40 ml HDPE container of 33 mm neck finish (OFC 51 ml) with 33 mm – 400 RS closure with TEKNIPLEX HS-123 induction sealing wad with rayon coil. The HDPE container is stored in a carton. Each container contains 30 tablets.

Pack size: 30's - One HDPE container contains 30 tablets.

URODOXA 4 mg:

1) Tablets are packed in white opaque 250 micron PVC film coated with 60 gsm PVdC and printed 25 micron aluminium foil with 7 gsm heat seal lacquer. Each blister contains 10 tablets.

Pack size: 30's – Each carton contains 3 blister strips of 10 tablets each.

2) Tablets are packed in 40 ml HDPE container of 33 mm neck finish (OFC 51 ml) with 33 mm – 400 RS closure with TEKNIPLEX HS-123 induction sealing wad with rayon coil. The HDPE container is stored in a carton. Each container contains 30 tablets.

Pack size: 30's **-** One HDPE container contains 30 tablets.

URODOXA 8 mg:

1) Tablets are packed in white opaque 250 micron PVC film coated with 60 gsm PVdC and printed 25 micron aluminium foil with 7 gsm heat seal lacquer. Each blister contains 10 tablets.

Pack size: 30's – Each carton contains 3 blister strips of 10 tablets each.

2) Tablets are packed in 40 ml HDPE container of 33 mm neck finish (OFC 51 ml) with 33 mm - 400 RS closure with TEKNIPLEX HS-123 induction sealing wad with rayon coil. The HDPE container is stored in a carton. Each container contains 30 tablets.

Pack size: 30's - One HDPE container contains 30 tablets.

STORAGE INSTRUCTIONS:

Store at or below 25 °C. Protect from light. Keep original containers well closed. Do not remove blisters from carton until required for use.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER

URODOXA 1 **mg:** 45/7.1/0150

URODOXA 2 mg: 45/7.1/0151

URODOXA 4 mg: 45/7.1/0152

URODOXA 8 mg: 45/7.1/0153

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

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