SCHEDULING STATUS

S3

1. NAME OF MEDICINE

HYTRIN 1 mg tablets

HYTRIN 2 mg tablets

HYTRIN 5 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 1 mg, 2 mg or 5 mg terazosin respectively.

Excipients with known effect:

HYTRIN 1 mg	Each tablet contains 128,56 mg lactose monohydrate (sugar).
HYTRIN 2 mg	Each tablet contains 127,28 mg lactose monohydrate (sugar). Each tablet contains 0,1 mg Quinoline Yellow (E104) aluminium lake.
HYTRIN 5 mg	Each tablet contains 123,07 mg lactose monohydrate (sugar). Each tablet contains 0,75 mg iron oxide (E172) burnt sienna.

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets.

HYTRIN 1 mg	White, round, flat, bevelled-edge tablet, 7 mm in diameter and approximately 3 mm thick, with Abbott logo and triangular facets on one side, plain on reverse side.
HYTRIN 2 mg	Yellow, round, flat, bevelled-edge tablet, 7 mm in diameter and approximately 3 mm thick, with Abbott logo and triangular facets on one side, plain on reverse side.

HYTRIN 5 mg	Tan, round, flat, bevelled-edge tablet, 7 mm in diameter and approximately 3 mm thick, with Abbott logo and triangular facets on one side, plain on reverse side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

HYTRIN is indicated in the treatment of mild to moderate hypertension either as monotherapy or in combination with other antihypertensive medicines.

HYTRIN is also indicated as therapy for the symptomatic treatment of urinary obstruction caused by benign prostatic hyperplasia (BPH) in cases where conventional treatment cannot be implemented.

4.2 Posology and method of administration

The dose of HYTRIN should be adjusted according to the patient's individual response, within the prescribed dosage range. The following is a guide to its administration:

1. Initial dose

Hypertension and benign prostatic hyperplasia (BPH):

One mg at bedtime is the recommended dose and should not be exceeded, to minimise the potential of hypotensive episodes.

2. Maintenance dose

2.1 Hypertension

The single daily dose may be increased by approximately doubling the dose at weekly intervals, up to a daily dose of 20 mg, to achieve the desired blood pressure response. Doses over 20 mg do not appear to provide additional antihypertensive effect, while side effects are increased with higher dosages.

Blood pressure should be monitored at the end of the dosing interval to be sure control is maintained throughout the interval.

The usual maintenance dose is 1 to 5 mg administered once daily; however, up to 20 mg daily may

be used.

If HYTRIN administration is discontinued for several days or longer, therapy should be reinstituted using the initial dosing regimen.

2.2 Benign prostatic hyperplasia (BPH)

The usual recommended dose range is 5 to 10 mg administered once daily. The dose should be increased slowly to achieve the desired clinical response.

Blood pressure should be monitored at the end of the dosing interval to be sure control is maintained throughout the interval.

If terazosin administration is discontinued for several days or longer, therapy should be reinstituted using the initial dosing regimen.

Method of administration

For oral use.

4.3 Contraindications

HYTRIN is contraindicated in patients hypersensitive to terazosin hydrochloride or its analogues.

HYTRIN has been associated with sudden death when given to patients in congestive cardiac failure.

4.4 Special warnings and precautions for use

Syncope and "first-dose" effect

Terazosin can cause marked hypotension, especially postural hypotension, and syncope in association with the first dose or first few doses of therapy. A similar effect can be anticipated if therapy is interrupted for more than a few doses and then restarted. Syncope has also been reported with other alpha-adrenergic blocking medicines in association with rapid dosage increases or the introduction of another antihypertensive medicine. Syncope is believed to be due to an excessive postural hypotensive effect, although occasionally the syncopal episode has been preceded by a bout of severe supraventricular tachycardia with heart rates of 120 – 160 beats per minute.

To decrease the likelihood of syncope or excessive hypotension, treatment should always be initiated with a 1 mg dose of terazosin given at bedtime. The 2 mg, 5 mg and 10 mg tablets are not indicated as initial therapy. Dosage should then be increased slowly, according to recommendations under section 4.2 and additional antihypertensive medicines should be added with caution. The patient should be cautioned to avoid situations where injury could result should syncope occur during initiation of therapy.

If syncope occurs, the patient should be placed in a recumbent position and treated supportively as necessary. There is evidence that the orthostatic effect of terazosin is greater, even in chronic use, shortly after dosing.

Patients with a history of micturition syncope should not receive an alpha-blocker.

Urinary symptoms

Before treating the symptoms of benign prostatic hyperplasia (BPH) with alpha-blockers, other causes of impaired urinary flow or urinary symptoms should be excluded. Also, where the diagnosis of BPH has been established, it should be confirmed that there is no concomitant obstruction of the upper urinary tract or any signs of infection before treating with HYTRIN. Patients with benign prostatic hyperplasia, who simultaneously suffer from congestion of the upper urinary tract, chronic urinary tract infection or bladder stones, should not be treated with HYTRIN.

HYTRIN should not be given to patients with bladder overflow, anuria or advanced renal failure.

Concomitant use with other antihypertensive medicines

Due to the risk of an excessive decrease in blood pressure, caution is advised for the concomitant administration of HYTRIN and thiazides or other antihypertensive medicines. If a thiazide diuretic or another antihypertensive medicine is added during treatment with HYTRIN, the HYTRIN dose must be reduced or the medicine discontinued. A new dose-titration is essential. When administering HYTRIN in addition to other antihypertensives, the dose of the other antihypertensives should be reduced before commencement of therapy and adjusted after discontinuation of HYTRIN (see section 4.5).

Cardiac conditions

Due to the vasodilatory effect of HYTRIN, it should be administered with caution if the following cardiac conditions are present:

- pulmonary oedema due to aortic or mitral valve stenosis
- high output cardiac insufficiency
- right-sided cardiac insufficiency due to pulmonary embolism or pericardial effusion
- left-sided cardiac insufficiency with low filling pressure.

In patients with severe coronary heart disease, a very rapid or excessive decrease in blood pressure can lead to an exacerbation of angina pectoris.

Laboratory tests

Small but statistically significant decreases in haematocrit, haemoglobin, white blood cells, total protein and albumin were observed in controlled clinical trials. These laboratory findings suggest the possibility of haemodilution. Treatment with HYTRIN for up to 24 months had no significant effect on prostate specific antigen (PSA) levels.

Medicines influencing hepatic metabolism

Caution is also recommended, when HYTRIN is administered concomitantly with medicines, which may influence hepatic metabolism.

Phosphodiesterase type 5 (PDE5) inhibitors

Hypotension has been reported when HYTRIN has been used with PDE5 inhibitors (see section 4.5).

Cataract surgery

The 'Intraoperative Floppy Iris Syndrome' (IFIS, a variant of small pupil syndrome) has been observed during cataract surgery in some patients on or previously treated with tamsulosin. Isolated reports

have also been received with other alpha-adrenoceptor blockers and the possibility of a class effect cannot be excluded. As IFIS may lead to increased procedural complications during cataract operation current or past use of alpha-adrenoceptor blockers should be made known to the ophthalmic surgeon in advance of surgery.

Paediatric population

HYTRIN is not recommended for the treatment of children under the age of 12 years, since safety and effectiveness in children have not been established.

HYTRIN tablets contain lactose

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take HYTRIN tablets.

4.5 Interaction with other medicines and other forms of interaction

Hypertension

In patients receiving terazosin plus ACE inhibitors or diuretics the proportion reporting dizziness or related side effects was greater than in the total population of terazosin treated patients from clinical trials.

Hypotensive effects is enhanced when Terazosin is taken along with adrenergic neurone blockers, alcohol, aldesleukin, alprostadil, anaesthetic (general), angiotensin – II receptor antagonists, antipsychotics, anxiolytics and hypnotics, baclofen, beta-blockers, calcium-channel blockers, clonidine, diazoxide, diuretics, hydralazine, levodopa, monoamine oxidase inhibitors (MAOIs), Methyldopa, Minoxidil, Moxisylyte, Moxonidine, nitrates, sodium nitroprusside, Tizanidine. Caution should be observed when terazosin is administered with thiazide diuretic or other antihypertensive agents, to avoid the possibility of significant hypotension. When adding terazosin to a diuretic or other antihypertensive agent, dosage reduction and retitration may be necessary.

In in-vitro experiments, terazosin has been shown to antagonise phenylephrine-induced contractions of human pro static tissue. In clinical trials terazosin has been shown to improve the urodynamics and

symptomatology in patients with BPH.

Terazosin has been given without interaction with analgesics/antiinflammatories, cardiac glycosides, hypoglycemics, antiarrhythmics, anxiolytics/sedatives, antibacterials, hormones/steroids and drugs used for gout. Hypotensive effects of terazosin are antagonised by the following: corticosteroids, non-steroidal anti-inflammatory drugs (NSAIDs) and oestrogens.
The hypotensive effect is enhanced when terazocin is given with Phosphodiesterase-5-inhibitors (e.g. sildenafil, tadalafil, vardenafil) (see section 4.4). Avoid giving terazocin for 4 hours after Phosphodiesterase-5-inhibitor administration.

4.6 Fertility, pregnancy and lactation

Pregnancy

The safety of terazosin in pregnancy has not been established.

Terazosin, as in HYTRIN, was not teratogenic in either rats or rabbits when administered at oral doses up to 1 330 and 165 times, respectively, the maximum recommended human dose.

Foetal resorptions occurred in rats dosed with 480 mg/kg/day, approximately 1 330 times the maximum recommended human dose. Increased foetal resorptions, decreased foetal weight and an increased number of supernumerary ribs were observed in offspring of rabbits dosed with 165 times the maximum recommended human dose. These findings (in both species) were most likely secondary to maternal toxicity. There are no adequate and well-controlled studies in pregnant women and the safety of terazosin in pregnancy has not been established.
HYTRIN is not recommended during pregnancy.

Lactation

It is not known whether terazosin is excreted in breast milk.

Safety in breastfeeding has not been established.

4.7 Effects on ability to drive and use machines

Syncopal and orthostatic symptoms are possible, especially at the initiation of therapy, and driving or hazardous tasks should be avoided for 12 hours after the first dose, after a dosage increase, and after interruption of therapy when treatment is resumed. Drowsiness or somnolence can also occur with HYTRIN therapy, requiring caution in people who must drive a vehicle or operate heavy machinery.

4.8 Undesirable effects

The most common side effects occurring after the administration of HYTRIN include dizziness, asthenia, headache, nasal congestion, nausea and peripheral oedema. Blurred vision, tachycardia, palpitations, somnolence, dyspnoea, hypotension, postural hypotension and impotence may also occur. These side effects may disappear with continued therapy.

Syncopal episodes may occur within 30 to 90 minutes of the initial dose of HYTRIN, but this adverse effect is self-limiting and does not normally recur after initial treatment (see section 4.4).

When standing up from a lying or sitting position, dizziness, light-headedness or faintness may occur. These symptoms may occur in association with missed doses and subsequent re-initiation of HYTRIN therapy. Patients should be advised of this possibility and instructed to lie down if these symptoms appear and then sit for a few minutes before standing to prevent their recurrence.

Adverse drug effects reported with HYTRIN from multiple sources including clinical trials and spontaneous reports:

System Organ Class	Frequency	Adverse reaction
Blood and lymphatic system disorder	Not known	Thrombocytopenia
Immune system disorders	Not known	Anaphylactoid reaction

Psychiatric disorders	Not known	Depression, nervousness, anxiety, insomnia
Nervous system disorders	Not known	Dizziness, somnolence, headache, paraesthesia, vertigo
Eye disorders	Not known	Blurred vision, amblyopia, visual impairment, conjunctivitis
Ear and labyrinth disorders	Not known	Tinnitus
Cardiac disorders	Not known	Palpitations, tachycardia, dysrhythmia, atrial fibrillation
Vascular disorders	Not known	Postural hypotension, syncope, vasodilatation
Respiratory, thoracic and mediastinal disorders	Not known	Nasal congestion, rhinitis, dyspnoea, sinusitis, bronchitis, epistaxis, flu symptoms, pharyngitis, cold symptoms, cough
Gastrointestinal disorders	Not known	Nausea, abdominal pain, constipation, diarrhoea, dry mouth, dyspepsia, flatulence, vomiting
Skin and subcutaneous tissue disorders	Not known	Pruritus, rash, hyperhidrosis, angioedema
Musculoskeletal and connective tissue disorders	Not known	Back pain, pain in extremity, neck pain, shoulder pain, gout, arthralgia, arthritis, joint disorders, myalgia
Renal and urinary disorders	Not known	Pollakiuria, urinary tract infection and urinary incontinence (primarily reported in postmenopausal women)
Reproductive system and breast disorders	Not known	Libido decreased, erectile dysfunction, priapism
General disorders and administration site conditions	Not known	Asthenia, peripheral oedema, oedema, chest pain, face oedema, pyrexia
Investigations	Not known	Increased weight, decreased haematocrit, haemoglobin,

		white blood cell count, total protein and blood albumin (suggestive of haemodilution). Treatment with terazosin for up to 24 months had no significant effect on prostate specific antigen (PSA) levels.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of HYTRIN is important. It allows continued monitoring of the benefit/risk balance of HYTRIN. Health care providers are asked to report any suspected adverse reactions 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

Overdosage of HYTRIN may lead to severe hypotension; support of the cardiovascular system is of first importance.

Restoration of blood pressure and normalisation of heart rate may be accomplished by keeping the patient in the supine position. If this measure is inadequate, hypotension should be treated with volume expanders. If necessary, vasopressors should then be used and renal function should be monitored and supported as needed. Laboratory data indicate that HYTRIN is highly protein-bound; therefore dialysis may not be of benefit.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 7.1 Vasodilators, hypotensive medicines

Pharmacotherapeutic group: alpha-adrenoreceptor antagonists

ATC code: G04CA03.

HYTRIN (terazosin hydrochloride) is a competitive alpha-one-adrenergic-receptor-blocking medicine. The resultant blood pressure decrease may be accompanied by reflex tachycardia.

Studies suggest that alpha-1-adrenoceptor-blockade is also useful in improving the uro-dynamics in patients with chronic bladder outlet obstruction, such as in benign prostatic hyperplasia (BPH).

A small statistically significant decrease in total cholesterol and the combination low-density and very low density lipoprotein fraction may occur. No significant changes were observed in high density lipoproteins or triglycerides.

5.2 Pharmacokinetic properties

Terazosin hydrochloride is completely absorbed in man. The plasma concentration of the parent drug reaches a maximum at about 1 hour after oral administration, then declines with a half-life of approximately 12 hours. Food has little or no effect on the plasma levels. The medicine is highly bound to plasma proteins.

The pharmacokinetics of terazosin appears to be independent of renal function.

5.3 Preclinical safety data

Preclinical data reveal no special hazards for humans based on conventional studies of safety pharmacology.

No evidence of a genotoxic effect of terazosin has been reported from *in vitro* and *in vivo* investigations of the mutagenic potential of the substance.

Decreased fertility and testicular atrophy were seen in rats at repeated administration of doses ≥ 20 – 30 times higher than the maximum recommended human dose. Foetal resorptions, decreased foetal weights, increased number of supernumerary ribs and decreased post-natal survival were noted in

reproductive toxicity studies in rats and rabbits at maternally toxic doses (60 – 280 times the maximum recommended human dose).

In male rats, terazosin induced benign adrenal medullary tumours at the highest administered dose corresponding to 175 times the maximum human dose.

Carcinogenicity: In male rats, terazosin induced benign adrenal medullary tumours at the highest administered dose corresponding to 175 times the maximum human dose. No such occurrences were seen in female rats or in a similar study in mice. The relevance of these findings with respect to the clinical use of the medicine in man is unknown.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

HYTRIN 1 mg:

Lactose monohydrate

Maize starch

Pregelatinised starch

Talc

Magnesium stearate.

HYTRIN 2 mg:

Lactose monohydrate

Maize starch

Pregelatinised starch

Talc

Magnesium stearate

Quinoline Yellow (E104) aluminium lake.

HYTRIN 5 mg:

Lactose monohydrate

Maize starch

Pregelatinised starch

Talc

Magnesium stearate

Iron oxide (E172) burnt sienna.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

60 months.

Store below 25 °C and protect from moisture.

Keep out of reach of children.

6.4 Special precautions for storage

This medicine does not require any special storage conditions.

6.5 Nature and contents of container

PVC/PVDC aluminium foil blister strip, packed in outer carton.

HYTRIN 1 mg is supplied in packs containing 10 tablets.

HYTRIN 2 mg and 5 mg are supplied in packs containing 28 tablets.

6.6 Special precautions for disposal

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Abbott Laboratories S.A. (Pty) Limited

Abbott Place

219 Golf Club Terrace

Constantia Kloof 1709

8. REGISTRATION NUMBER(S)

HYTRIN 1 mg	A27/7.1/0519
HYTRIN 2 mg	A 27/7.1/0520
HYTRIN 5 mg	A 27/7.1/0521

9. DATE OF FIRST AUTHORISATION/RENEAL OF THE AUTHORISATION

9 November 1993.

10. DATE OF REVISION OF THE TEXT

HYTRIN 1 mg	30 January 2023
HYTRIN 2 mg	30 January 2023
HYTRIN 5 mg	30 January 2023

NAME AND ADDRESS OF MANUFACTURER

Aesica Queensborough Limited

North Road

Queenborough

Kent ME11 5EL, United Kingdom

Country	Product	Registration number	Scheduling status
Zimbabwe	HYTRIN 1 mg	2001/12.3.1/3987	PP
	HYTRIN 2 mg	2001/12.3.1/3988	PP
	HYTRIN 5 mg	2001/12.3.1/3989	PP
Namibia	HYTRIN 1 mg	04/7.1/1259	NS2
	HYTRIN 2 mg	04/7.1/1260	NS2
	HYTRIN 5 mg	04/7.1/1261	NS2
	HYTRIN 10 mg	04/7.1/1262	NS2