APO-TERAZOSIN

1. PRODUCT NAME

APO-TERAZOSIN (1mg, 2mg and 5mg tablets)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Terazosin 1mg, 2mg & 5mg (as hydrochloride dihydrate)

Excipient(s) of known effect

Apo-Terazosin does not contain gluten.
Apo-Terazosin contains lactose.

If you have been told by your doctor that you have intolerance to some sugars contact your doctor before taking this medicinal product.

This should be taken into account in patients with diabetes mellitus.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

APO-TERAZOSIN 1mg tablets are white, round, flat-faced, beveled-edge tablet, engraved “APO” on one side and “T1” on the other side. Each tablet typically weighs approximately 150mg.

APO-TERAZOSIN 2mg tablets are orange, round, flat-faced, beveled edged tablet, engraved “APO” on one and “T2” on the other side. Each tablet weighs approximately 150mg.

APO-TERAZOSIN 5mg tablets are tan, round, flat-faced, beveled edged tablet, engraved “APO” on one and “T5” on the other side. Each tablet weighs approximately 150mg.

Please note: These tablets are not capable of providing a divided dose. Do not halve the tablets.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Terazosin is indicated for the symptomatic and pathophysiologic treatment of benign prostatic hyperplasia (BPH) when:
prostatectomy is not indicated
patient is not fit for surgery
elective surgery must be postponed (e.g., waiting list)
patient refuses surgical treatment.
(See section 4.5Interactions with other medicines and other forms of interactions)

Terazosin is also indicated in the treatment of hypertension. It can be used alone or in combination with other antihypertensive agents such as diuretics or beta-adrenergic blocking agents.

4.2 Dose and method of administration

Dose

The dose of Terazosin should be adjusted according to the patient’s responses. The following is a guide to its administration.

Adults

Initial dose

1mg at bedtime is the recommended starting dose for all patients, and this dose should not be exceeded. This initial dosing regimen should be strictly observed to minimise the potential for severe hypotensive

effects.

Subsequent Doses
Benign Prostatic Hyperplasia: The dose may be slowly increased to achieve the desired clinical response in BPH patients. The usual recommended dose range is 5 to 10 mg administered once a day. Urine flow rate measured approximately 24 hours after the last dose has shown that the beneficial effect in BPH persists for the recommended dosing interval. Symptom improvements have been detected as early as two weeks after starting treatment with terazosin. Improvements in flow rate may be seen somewhat later. If terazosin administration is discontinued for several days or longer, therapy should be reinstituted using the initial dosing regimen.

Hypertension: The dose may be slowly increased to achieve the desired blood pressure response. The usual recommended dose range is 1mg to 5mg administered once a day. However, some patients may benefit from doses as high as 20mg per day. Doses over 20mg do not appear to provide further blood pressure effect and doses over 40mg have not been studied.

Blood pressure should be monitored at the end of the dosing interval to be sure control is maintained throughout the interval. It may also be helpful to measure blood pressure 2-3 hours after dosing to see if the maximum and minimum responses are similar, and to evaluate symptoms such as dizziness or palpitations which can result from excessive hypotensive response. If response is substantially diminished at 24 hours, an increased dose or use of a twice daily regimen can be considered. If terazosin administration is discontinued for several days or longer, therapy should be reinstituted using the initial dosing regimen. In clinical trials, except for the initial dose, the dose was given in the morning.

These tablets are not capable of providing a divided dose. Do not halve the tablets.

Use with Other Medications
Caution should be observed when terazosin is administered concomitantly with other antihypertensive agents (e.g. calcium antagonists) to avoid the possibility of significant hypotension. When adding a diuretic or other antihypertensive agent, dosage reduction and retitration may be necessary, (see section 4.5 Interactions with other medicines and other forms of interaction)

Children
Not recommended for children.

Method of Administration

The tablets are to be administered orally. The tablets should be swallowed whole with water.

4.3 Contraindications
Terazosin is contraindicated in patients known to be sensitive to terazosin hydrochloride or its analogues.

4.4 Special warnings and precautions for use

Syncope and "First-dose" Effect
Terazosin, like other alpha-adrenergic blocking agents, can cause marked lowering of blood pressure, 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 agents 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 and 5 mg tablets are not indicated as initial therapy.

Dosage should then be increased slowly, according to recommendations in the Dosage and Administration section and additional antihypertensive agents should be added with caution. The patient should be cautioned to avoid situations where injury could result should syncope occur during initiation of therapy. In multiple dose clinical trials involving nearly 2000 hypertensive patients, syncope was reported in about 1% of patients, in no case severe or prolonged, and not necessarily associated with early doses. In clinical studies involving treatment of approximately 1200 patients with BPH, the incidence of syncope was 0.7%. 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.

Orthostatic Hypotension

While syncope is the most severe orthostatic effect of terazosin other symptoms of lowered blood pressure, such as dizziness, lightheadedness, and palpitations, are more common. Patients with occupations in which such events represent potential problems should be treated with particular caution.

Weight Gain

There is a tendency for patients to gain weight during terazosin therapy. In placebo-controlled monotherapy trials, male and female patients receiving terazosin gained a mean of 0.8 and 1kg (1.7 and 2.2 pounds) respectively, compared to losses of 0.1 and 0.5kg (0.2 and 1.1 pounds) respectively, in the placebo group. Both differences were significant.

Laboratory Tests

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

Information for Patients

Patients should be made aware of the possibility of syncopal and orthostatic symptoms, especially at the initiation of therapy, and to avoid driving or hazardous tasks for 12 hours after the first dose, after dosage increase, and after resumption of therapy when treatment has been interrupted. They should be cautioned to avoid situations where injury could result should syncope occur during initiation of terazosin therapy. They should also be advised of the need to sit or lie down when symptoms of lowered blood pressure occur, although these symptoms are not always orthostatic, and to be careful when rising from a sitting or lying position. If dizziness, lightheadedness, or palpitations are bothersome they should be reported to the physician, so that dose adjustment can be considered.

PDE-5 Inhibitors

Hypotension has been reported when terazosin has been used with phosphodiesterase-5 (PDE-5), (see section 4.5 Interactions with other medicines and other forms of interaction)

Cataract Surgery

Intraoperative Floppy Iris Syndrome (IFIS) has been observed during cataract surgery in some patients on/or previously treated with alpha-1 blockers. This variant of small pupil syndrome is characterized by the combination of a flaccid iris that billows in response to intraoperative irrigation currents, progressive intraoperative miosis despite preoperative dilation with standard mydriatic drugs, and potential prolapse of the iris toward the phacoemulsification incisions. The patient's ophthalmologist should be prepared for possible modifications to their surgical technique, such as the utilization of iris hooks, iris dilator rings, or viscoelastic substances. There does not appear to be a benefit of stopping alpha-1 blocker therapy prior to cataract surgery.

Pediatric use

Safety and effectiveness in children have not been determined.

4.5 Interactions with other medicines and other forms of interactions

In clinical trials in BPH patients the number reporting dizziness or other dizziness-related adverse events appears to be greater in those patients receiving terazosin and ACE inhibitors or diuretics than in the total population of terazosin patients from double-blind, placebo-controlled studies. No interactions were observed in patients treated concurrently with theophylline, anti-anginal agents or oral hypoglycaemic agents. In controlled trials in hypertensive patients, terazosin has been added to diuretics, and several beta-adrenergic blockers; no unexpected interactions were observed. Terazosin has also been used in patients on a variety of concomitant therapies; while these were not formal interaction studies, no interactions were observed. Terazosin has been used concomitantly in at least 50 patients on the following medicines or types of medicine.

1. analgesic/anti-inflammatory (e.g. paracetamol, aspirin, codeine, ibuprofen, indomethacin)
2. antibiotics (e.g. erythromycin, trimethoprim, sulphamethoxazole)
3. anticholinergic/sympathomimetics (e.g. phenylephrine hydrochloride, phenylpropanolamine hydrochloride, pseudoephedrine hydrochloride)
4. antigout (e.g. allopurinol)
5. antihistamines (e.g. chlorpheniramine)
6. cardiovascular agents (e.g. atenolol, hydrochlorothiazide, methyclothiazide, propranolol)
7. corticosteroids
8. gastrointestinal agents (e.g. antacids)
9. hypoglycaemics
10. sedatives and tranquillizers (e.g. diazepam).

Hypotension has been reported when terazosin has been used with phosphodiesterase-5 (PDE-5) inhibitors, (see section 4.4 Special Warnings and Precautions for use)

Caution should be observed when terazosin is administered concomitantly with other antihypertensive agents to avoid the possibility of significant hypotension. When adding a diuretic or other antihypertensive agent dosage reduction and retitration may be necessary.

Concomitant use of phosphodiesterase-5-inhibitors (e.g. sildenafil, tadalafil, vardenafil) and terazosin may lead to symptomatic hypotension in some patients.

4.6 Fertility, pregnancy and lactation

Pregnancy

Category B2

There are no adequate and well controlled studies in pregnant women and the safety of terazosin in pregnancy has not been established. Terazosin is not recommended during pregnancy unless the potential benefit justifies the potential risk to the mother and fetus. For further information for teratogenic effects, see section 5.3 Preclinical safety data.

Lactation

Use in nursing mothers

It is not known whether terazosin is excreted in breast milk. Because many medicines are excreted in breast milk, caution should be exercised when terazosin is administered to a nursing woman.

Fertility

See section 5.3 Preclinical safety data.

4.7 Effects on ability to drive and use machines

Patients should be told that drowsiness or somnolence can occur with Terazosin, requiring caution in people who must drive or operate heavy machinery.

4.8 Undesirable effects

Benign Prostatic Hyperplasia (BPH)

Each selected adverse event in Table 1 was chosen on the basis of meeting one or more of the following criteria: 1) prevalence of ≥5% or clinical relevance in previous terazosin hypertension clinical studies; 2) prevalence ≥5% in terazosin BPH clinical studies; 3) it was a component of the dizziness-related adverse event complex, which includes dizziness, hypotension, postural hypotension, syncope and vertigo; or 4) it was related to sexual function.

Table 1 Summary of Selected Adverse Events from Six double-Blind, Placebo-Controlled Studies In Benign Prostatic Hyperplasia (BPH)

	TERAZOSIN (N=636)	PLACEBO (N=360)
*P ≤0.05 compared to placebo group		
CARDIOVASCULAR SYSTEM		
Hypotension	0.6%	0.6%
Palpitation	0.9%	1.1%
Postural Hypotension	3.9%*	0.8%
Syncope	0.6%	0.0%
Tachycardia	0.3%	0.0%
SPECIAL SENSES		
Blurred Vision/Amblyopia	1.3%	0.6%
DIGESTIVE SYSTEM		
Nausea	1.7%	1.1%
METABOLIC/NUTRITIONAL DISORDERS		
Peripheral Oedema	0.9%	0.3%
Weight Gain	0.5%	0.0%
NERVOUS SYSTEM		
Dizziness	9.1%*	4.2%
Libido Decreased	0.9%	0.3%
Somnolence	3.6%*	1.9%
Vertigo	1.4%	0.3%
UROGENITAL SYSTEM		
Impotence	1.6%*	0.6%
RESPIRATORY SYSTEM		
Dyspnoea	1.7%	0.8%
Nasal Congestion/Rhinitis	1.9%*	0.0%
BODY AS WHOLE		
Asthenia	7.4%*	3.3%
Headache	4.9%	5.8%

The most common adverse events with terazosin were dizziness, asthenia, headache, postural hypotension, somnolence, nasal congestion and impotence. All but headache were significantly (P ≤0.05) more frequent than with placebo.

Hypertension

The prevalence rate presented below are based on adverse experiences (events) from14 placebo controlled studies involving once a day administration of terazosin as monotherapy or in combination with other antihypertensive agents, at doses ranging from 1 to 40mg. Table 2 summarises those adverse experiences reported for hypertensive patients in these studies where the prevalence rate for the terazosin group was at least 5% where the prevalence rate for the terazosin group was at least 2% and was greater than the prevalence rate for the placebo group, or where the reaction is of particular interest.

Asthenia, blurred vision, dizziness, nasal congestion, nausea, peripheral oedema, palpitations, and somnolence were the only symptoms that were significantly (p less than or equal to 0.05) more common in patients receiving terazosin than in patients receiving placebo. Similar adverse reaction rates were observed in placebo-controlled monotherapy trials as in combination therapy trials (see Table 2).

Table 2 Adverse Reactions During Placebo-Controlled Studies In Hypertension

	TERAZOSIN (N=859)	PLACEBO (N=506)
CARDIOVASCULAR SYSTEM		
Palpitations	4.3%*	1.2%
Postural hypotension	1.3%	0.4%
Syncope	1.0%	0.2%
Tachycardia	1.9%	1.2%
SPECIAL SENSES		
Blurred Vision	1.6%*	0.0%
DIGESTIVE SYSTEM		
Nausea	4.4%*	1.4%
METABOLIC / NUTRITIONAL DISORDERS		
Oedema	0.9%	0.6%
Periphera Oedema	5.5%*	2.4%
Weight Gain	0.5%	0.2%
MUSCULOSKELETAL SYSTEM		
Pain Extremities	3.5%	3.0%
NERVOUS SYSTEM		
Depression	0.3%	0.2%
Dizziness	19.3%*	7.5%
Libido Decreased	0.6%	0.2%
Nervousness	2.3%	1.8%
Paraesthesia	2.9%	1.4%
Somnolence	5.4%*	2.6%
UROGENITAL SYSTEM		
Impotence	1.2%	1.4%
RESPIRATORY SYSTEM		
Dyspnoea	3.1%	2.4%
Nasal congestion	5.9%*	3.4%
Sinusitis	2.6%	1.4%
BODY AS A WHOLE		
+Asthenia	11.3%*	4.3%
Back pain	2.4%	1.2%
Headache	16.2%	15.8%

\+ Includes weakness, tiredness, lassitude and fatigue

* Statistically significant at $p \leq 0.05$ level

The adverse reactions were usually mild or moderate in intensity, but sometimes were serious enough to interrupt treatment. The adverse reactions that were most bothersome, as judged by their being reported as reasons for discontinuation of therapy by at least 0.5% of the terazosin group and being reported more often than in the placebo group are shown in the Table 3. Overall, 9.9% of the 859 patients taking

terazosin discontinued therapy because of adverse effects, as compared with 4.2% of 506 patients taking placebo.

Table 3 Discontinuations During Placebo Controlled Studies In Hypertension

	TERAZOSIN (N=859)	PLACEBO (N=506)
CARDIOVASCULAR SYSTEM		
Palpitations	1.4%	0.2%
Postural hypotension	0.5%	0.0%
Syncope	0.5%	0.2%
Tachycardia	0.6%	0.0%
SPECIAL SENSES		
Blurred Vision	0.6%	0.0%
DIGESTIVE SYSTEM		
Nausea	0.8%	0.0%
METABOLIC / NUTRITIONAL DISORDERS		
Peripheral Oedema	0.6%	0.0%
NERVOUS SYSTEM		
Dizziness	3.1%	0.4%
Paraesthesia	0.8%	0.2%
Somnolence	0.6%	0.2%
RESPIRATORY SYSTEM		
Dyspnoea	0.9%	0.6%
Nasal congestion	0.6%	0.0%
BODY AS WHOLE		
Asthenia	1.6%	0.0%
Headache	1.3%	1.0%

Additional adverse reactions have been reported, but these are, in general, not distinguishable from symptoms that might have occurred in the absence of exposure to terazosin. The following additional adverse reactions were reported by at least 1% of 1987 patients who received terazosin in controlled or open, short- or long-term clinical studies or have been reported during marketing experience.

Cardiovascular System – arrhythmia, vasodilation
Special Senses – abnormal vision, conjunctivitis, tinnitus
Digestive System – constipation, diarrhea, dry mouth, dyspepsia, flatulence, vomiting.
Metabolic / Nutritional Disorders – gout.
Musculoskeletal System – arthralgia, arthritis, joint disorder, myalgia
Nervous System - anxiety, insomnia.
Urogenital System – urinary frequency, urinary tract infection, and urinary incontinence primarily reported in postmenopausal women.
Respiratory System – bronchitis, cold symptoms, epistaxis, flu symptoms, increased cough, pharyngitis, rhinitis.
Skin and Appendages – pruritus, rash, sweating
Body as a whole – chest pain, facial oedema, fever, abdominal pain, neck pain, shoulder pain.

Post-marketing Experience

Priapism has been reported. Thrombocytopenia has been reported. Atrial fibrillation has been reported; however, a cause and effect relationship has not been established. Anaphylaxis has rarely been reported. Angioedema has been reported.

During cataract surgery, a variant of small pupil syndrome known as Intraoperative Floppy Iris Syndrome (IFIS) has been reported in association with alpha-1 blocker therapy, (see section 4.4Special warnings and precautions).

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 professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/

4.9 Overdose

Should overdosage of terazosin lead to 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, shock should first 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 terazosin is highly protein bound and therefore, dialysis may not be of benefit.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764 766).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Urologicals
ATC code: G04CA03, Drugs used in benign prostatic hypertrophy, Alpha-adrenoreceptor antagonists

Actions

Terazosin for benign prostatic hyperplasia, is an alpha-1-selective adrenoceptor blocking agent.

Studies suggest that alpha-1-adrenoceptor blockade is useful in improving the urodynamics in patients with chronic bladder outlet obstruction, such as in Benign Prostatic Hyperplasia (BPH).

The symptoms of BPH are caused mainly by the presence of an enlarged prostate and by the increased smooth muscle tone of the bladder outlet and the prostate, which is regulated by alpha-1-adrenergic receptors.

In *in vitro* experiments, terazosin has been shown to antagonize phenylephrine-induced contractions in human prostatic tissue. In clinical trials terazosin has been shown to improve the urodynamics and symptomatology in patients with BPH.

Terazosin also decreases blood pressure gradually within 15 minutes following oral administration.

The systolic and diastolic blood pressures are lowered in both the supine and standing positions. The effect is most pronounced on the diastolic blood pressure. These changes are usually not accompanied by reflex tachycardia. A greater blood pressure effect associated with peak plasma concentrations (first few hours after dosing) appears somewhat more position-dependent (greater in the erect position) than the effect of terazosin at 24 hours, and in the erect position there is also a 6-10 beat per minute increase in heart rate in the first few hours after dosing.

In animals, terazosin causes a decrease in blood pressure by decreasing total peripheral vascular resistance. The vasodilatory hypotensive action of terazosin appears to be produced mainly by blockade of alpha-1-adrenoceptors.

During controlled clinical studies, patients receiving terazosin had an improved lipid profile. Patients receiving terazosin monotherapy had a small but statistically significant decrease compared to placebo in total cholesterol and the combined low-density and very-low-density lipoprotein fractions. These patients

had increases from baseline in high-density lipoproteins, the HDL/LDL cholesterol ratio, and decreases from baseline in triglycerides. However, these changes were not significant when compared to placebo.

Long-term (6 months or longer) administration of terazosin has produced no pattern of clinically significant changes attributable to terazosin in the following clinical laboratory measurements: glucose, uric acid, creatinine, BUN, liver function tests, and electrolytes. Analysis of clinical laboratory data following administration of terazosin suggested the possibility of haemodilution based on decreases in haematocrit, haemoglobin, white blood cells, total protein, and albumin. Decreases in haematocrit and total protein have been observed with alpha-blockade and are attributed to haemodilution.

Treatment with terazosin for up to 24 months had no significant effect on prostate specific antigen (PSA) levels.

5.2 Pharmacokinetic properties

Relative to solution, terazosin hydrochloride administered as Terazosin tablets is essentially completely absorbed in man. Food has little or no effect on the bioavailability of terazosin administered in a capsule formulation. Terazosin has been shown to undergo minimal hepatic first-pass metabolism and nearly all of the circulating dose is in the form of parent compound. The plasma levels peak about one hour after dosing, and then decline with a half-life of approximately 12 hours. Terazosin is highly bound to plasma proteins and binding is constant over the clinically observed concentration range. Approximately 10% of an orally administered dose is excreted as parent medicine in the urine and approximately 20% is excreted in the faeces. The remainder is eliminated as metabolites. Overall, approximately 40% of the administered dose is excreted in the urine and approximately 60% in the faeces. The disposition of the compound in animals is qualitatively similar to that in man.

The pharmacokinetics of terazosin appears to be independent of renal function. This would obviate the need to adjust dosing regimens for patients with impaired renal function.

No special dosage recommendations are required for elderly patients. Studies have shown that there were no significant correlations between the age of the subjects and terazosin pharmacokinetics.

5.3 Preclinical safety data

Carcinogenesis

Terazosin administrated in the feed to rates at dosage of 8,40 and 250 mg/kg/day for two years, was associated with a statistically significant increase in benign adrenal medullary tumors in male rats exposed to the 250mg/kg/dose. This dose is 695 times the maximum recommended human dose of 20mg/55kg patient. Female rats were unaffected. Terazosin was not oncogenic in mice when administrated in feed for 2 years at a maximum tolerated dose of 32mg/kg/day.

The absence of mutagenicity in a battery of tests, of tumourigenicity of any cell type in the mouse carcinogenicity assay, of increased total tumor incidence in either species, and of proliferative adrenal lesions in female rats suggests a male rat species specific event. Numerous other diverse pharmaceutical and chemical compounds have also been associated with benign adrenal medullary tumors in male rates without supporting evidence for carcinogenicity for man.

Mutagenesis

Terazosin was devoid of mutagenic potential when evaluated in vivo and in vitro (the Ames test, in vivo cytogenetics, the dominant lethal test in mice, in vivo Chinese hamster chromosome aberration test and V79 forward mutation assay.

Reproductive studies

The effect of Terazosin on fertility was assessed in a standard fertility/reproductive performance study in which male and female rats were administered oral doses of 8, 30, and 120 mg/kg/day. Four of 20 male rats given 30 mg/kg and five of 19 male rats given 120 mg/kg failed to sire a litter. Testicular weights and morphology were unaffected by treatment. Vaginal smears at 30 and 120 mg/kg/day, however, appeared to contain less sperm than smears from control matings and good correlation was reported between sperm count and subsequent pregnancy.

Oral administration of terazosin for one or two years elicited a statistically significant increase in the incidence of testicular atrophy in rats exposed to 40 and 250 mg/kg/ day, but not in rats exposed to 8 mg/kg/day (greater than 20 times the maximum recommended human dose). Testicular atrophy was also observed in dogs dosed with 300 mg/kg/day (greater than 800 times the maximum recommended human dose) for three months but not after one year when dosed with 20 mg/kg/day. This lesion has also been seen with other selective-alpha-1 blocking agent.

Teratogenic effects

Terazosin was not teratogenic in either rats or rabbits when administrated in oral doses up to 1330 and 165 times, respectively, the maximum recommended human dose. Foetal resorptions occurred in rats dosed with 480 mg/kg/day, approximately 1330 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.

Nonteratogenic effects

In a peri and post-natal development study in rates, significantly more pups died in the group dosed with 120mg/kg/day (greater than 300 times the maximum recommended human dose) than in the control group during the three-week post-partum period.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Apo-Terazosin tablets contain the following excipients:

- Corn Starch
- Magnesium Stearate
- Anhydrous Lactose
- Microcrystalline Cellulose

2mg Colourant:

- D & C yellow #10 Aluminum Lake
- Sunset Yellow Aluminum Lake

5mg Colourant:

- Red Ferric Oxide – Orange Shade
- Ferric-Ferrous Oxide

6.2 Incompatibilities

Not applicable

6.3 Shelf life

APO-TERAZOSIN 1mg tablets – 24 months from date of manufacture
APO-TERAZOSIN 2mg and 5mg tablets – 36 months from date of manufacture.

6.4 Special precautions for storage

Store at or below 25°C
Protect from heat, light and moisture.

6.5 Nature and contents of container

Apo-Terazosin 1mg tablets are available in HDPE plastic bottles with PE cap of 28 and 100 tablets.

Apo-Terazosin 2mg and 5mg tablets are available in HDPE plastic bottles with PE cap of 100 and 500 tablets.

Not all pack types or pack sizes may be marketed

6.6 Special precautions for disposal

No special requirements for disposal.

Any unused medicine or waste material should be disposed of in accordance with local requirements.

7. MEDICINE SCHEDULE

Prescription Medicine

8. SPONSOR

Apotex NZ Ltd
32 Hillside Road
Glenfield
Private Bag 102-995
North Shore Mail Centre
Auckland
Telephone: (09) 444 2073
Fax: (09) 444 2951

9. DATE OF FIRST APPROVAL

02 November 2006

10. DATE OF REVISION OF THE TEXT

28 November 2018

Summary Table of Changes

Section changed	Summary of new information
Whole data sheet	Reformatted as per Medsafe new guideline for data sheet.
4.1	Indications – minor editorial changes to harmonise with innovator's data sheet.
4.2	Dosage and Administration – minor editorial changes to harmonise with innovator's data sheet.
4.4	Warnings and Precautions – minor editorial changes to harmonise with innovator's data sheet. Additional information to harmonise with innovator's data sheet: "**Peadiatric use** Safety and effectiveness in children have not been determined.**"**
4.8	Adverse Effects – Additional information to harmonise with innovator's data sheet: "Table 2 summarises those adverse experiences reported for hypertensive patients in these studies where the prevalence rate for the terazosin group was at least 5% where the prevalence rate for the terazosin group was at

Section changed	Summary of new information
	least 2% and was greater than the prevalence rate for the placebo group, or where the reaction is of particular interest."
4.8	Post-Marketing Experience - Additional information to harmonise with innovator's data sheet: "Angioedema has been reported. During cataract surgery, a variant of small pupil syndrome known as Intraoperative Floppy Iris Syndrome (IFIS) has been reported in association with alpha-1 blocker therapy (see Precautions)."
5.2	Pharmacokinetics – minor editorial changes to harmonise with innovator's data sheet.
6.1	Correction to typographical
1, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.1, 5.3	Minor editorial change.