DUOZAQ 0,5 mg/0,4 mg

SCHEDULING STATUS S4

1. NAME OF THE MEDICINE
DUOZAQ 0,5 mg/0,4 mg hard capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
The hard capsules contain: one dutasteride 0,5 mg soft capsule and tamsulosin hydrochloride (HCl) pellets in the equivalent weight of 0,4 mg of tamsulosin HCl.
DUOZAQ 0,5 mg/0,4 mg is sugar free.

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM
Hard capsules.
DUOZAQ 0,5 mg/0,4 mg is a hard capsule with brown body and orange cap. The hard capsules contain: one dutasteride 0,5 mg soft capsule (yellow) and tamsulosin HCl pellets (white to off-white) in the equivalent weight of 0,4 mg of tamsulosin HCl.

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
DUOZAQ 0,5 mg/0,4 mg is indicated for treatment of moderate to severe symptoms of benign prostatic hyperplasia (BHP).

4.2 Posology and method of administration
Posology
Adult males (including elderly)
The recommended dose of DUOZAQ 0,5 mg/0,4 mg is one capsule taken orally approximately 30 minutes after the same meal each day (see section 5.2 – Absorption).
The capsules should be swallowed whole and not chewed or opened.
Contact with the contents of the dutasteride capsule contained within the hard-shell capsule may result in irritation of the oropharyngeal mucosa.

Special populations
Renal impairment
The effects of renal impairment on DUOZAQ 0,5 mg/0,4 mg pharmacokinetics have not been studied. However, no adjustment in dose is anticipated for patients with renal impairment (see section 5.2 – Renal impairment).

Hepatic impairment
The effects of hepatic impairment on DUOZAQ 0,5 mg/0,4 mg pharmacokinetics have not been studied (see sections 4.4 and 5.2 – Hepatic impairment).

Method of administration
DUOZAQ 0,5 mg/0,4 mg is to be taken orally approximately 30 minutes after the same meal each day (see section 5.2).

4.3 Contraindications
- hypersensitivity to dutasteride, other 5α-reductase inhibitors, tamsulosin hydrochloride or to any of the excipients of DUOZAQ 0,5 mg/0,4 mg listed in section 6.1
- use in women and children (see section 4.6)
- patients with history or orthostatic hypotension
- severe hepatic impairment.

4.4 Special warnings and precautions for use
Leaking capsule
Dutasteride is absorbed through the skin; therefore, women and children must avoid contact with leaking capsules (see section 4.6). If contact is made with leaking capsules, the contact area should be washed immediately with soap and water.

Inhibitors of CYP3A4 and CYP2D6
Concomitant administration of tamsulosin hydrochloride with strong inhibitors of CYP3A4 (e.g. ketoconazole), or to a lesser extent, with strong inhibitors of CYP2D6 (e.g. paroxetine) can increase tamsulosin exposure (see section 4.5). DUOZAQ 0,5 mg/0,4 mg is therefore not recommended in patients taking a strong CYP3A4 inhibitor (e.g. erythromycin), a strong or moderate CYP2D6 inhibitor a combination of both CYP3A4 and CYP2D6 inhibitors, or in patients known to be poor metabolisers of CYP2D6.

Hepatic impairment
The effect of hepatic impairment on dutasteride pharmacokinetics has not been studied. Because dutasteride is extensively metabolised and has a half-life of 3 to 5 weeks, caution should be used in the administration of DUOZAQ 0,5 mg/0,4 mg to patients with liver disease (see sections 4.2, 4.3 and 5.2).

Combination therapy with tamsulosin and cardiac failure
In patients with other risk factors for cardiac failure, DUOZAQ 0,5 mg/0,4 mg may increase the risk to develop cardiac failure.
In two 4-year clinical studies, the incidence of cardiac failure (a composite term of reported events, primary cardiac failure, and congestive cardiac failure) was higher among subjects taking the combination of dutasteride and an alpha blocker, primarily tamsulosin, than it was among subjects not taking the combination. In these two trials, the incidence of cardiac failure was low (≤ 1%) and variable between the studies.

Effects on prostate specific antigen (PSA) and prostate cancer detection
Prior to initiating therapy with DUOZAQ 0,5 mg/0,4 mg, as well as periodically thereafter, a digital rectal examination, as well as other evaluations for prostate cancer, should be performed on patients with BHP.
DUOZAQ 0,5 mg/0,4 mg causes a decrease in mean PSA levels by approximately 50 % after six months of treatment.
Patients receiving DUOZAQ 0,5 mg/0,4 mg should have a new PSA baseline established before starting treatment with DUOZAQ 0,5 mg/0,4 mg and after 6 months of treatment. It is recommended to monitor PSA values regularly thereafter.
Any confirmed increase from PSA level during DUOZAQ 0,5 mg/0,4 mg therapy may signal the presence of prostate cancer (particularly high-grade cancer) or non-compliance to therapy with DUOZAQ 0,5 mg/0,4 mg and should be carefully evaluated, even if those values are still within the normal range for men not taking a 5α-reductase inhibitor. In the interpretation of a PSA value for a patient on DUOZAQ 0,5 mg/0,4 mg therapy, previous PSA values should be sought for comparison.
DUOZAQ 0,5 mg/0,4 mg therapy does not interfere with the use of PSA as a tool to assist in the diagnosis of prostate cancer after a new baseline has been established.
Total serum PSA levels return to baseline within 6 months of discontinuing treatment.
The ratio of free to total PSA remains constant even under the influence of DUOZAQ 0,5 mg/0,4 mg. If healthcare professionals elect to use percent free PSA as an acid in the detection of prostate cancer in men undergoing dutasteride therapy, no adjustment to its value is necessary.

Prostate cancer and high grade tumours
In a 4-year study of over 8 000 men aged 50 to 75, with a prior negative biopsy for prostate cancer and baseline PSA between 2,5 ng/mL and 10,0 ng/mL (the REDUCE study), 1 517 men were diagnosed with prostate cancer. There was a higher incidence of Gleason 8 - 10 prostate cancers in the dutasteride group compared to the placebo group . There was no increased incidence in Gleason 5 - 6 or 7 - 10 prostate cancer. Men taking DUOZAQ 0,5 mg/0,4 mg should be regularly evaluated for prostate cancer risk including PSA testing.

Breast cancer in men
In clinical trials and during the post-marketing period, breast cancer has been reported in men taking dutasteride, as in DUOZAQ 0,5 mg/0,4 mg. Medical practitioners should instruct their patients to promptly report any changes in their breast tissue such as lumps or nipple discharge.

Hypotension
Orthostatic hypotension can occur in patients treated with tamsulosin, as in DUOZAQ 0,5 mg/0,4 mg, which can result in syncope.
Patients beginning treatment with DUOZAQ 0,5 mg/0,4 mg should be cautioned to sit or lie down at the first signs of orthostatic hypotension (dizziness and vertigo) until the symptoms have resolved.
Caution is advised when alpha adrenergic blocking medicines including tamsulosin are co-administered with PDE5 inhibitors. Alpha adrenergic blockers and PDE5 inhibitors are both vasodilators that can lower blood pressure. Concomitant use of these two medicine classes may cause symptomatic hypotension (see section 4.5).

Intra-operative Floppy Iris Syndrome
Intra-operative Floppy Iris Syndrome (IFIS, a variant of small pupil syndrome) has been observed during cataract surgery in some patients treated with alpha-1 adrenergic blockers, including tamsulosin, as in DUOZAQ 0,5 mg/0,4 mg. IFIS may increase the risk of eye complications during and after the operation.
During pre-operative assessment, contract surgeons and ophthalmic teams should consider whether patients scheduled for cataract surgery are being or have been treated with DUOZAQ 0,5 mg/0,4 mg in order to ensure that appropriate measures will be in place to manage IFIS should it occur during surgery.
Discontinuing tamsulosin 1 - 2 weeks prior to cataract surgery is anecdotally considered helpful, but the benefit and duration of stopping of therapy prior to cataract surgery has not yet been established.

Renal impairment
The treatment of patients with severe renal impairment (creatinine clearance of less than 10 mL/min) should be approached with caution as these patients have not been studied.

Non-alcoholic fatty liver disease and other liver diseases
It has been observed that patients may experience metabolic changes (e.g. glucose intolerance) and non-alcoholic fatty liver disease (NAFLD), during the use of dutasteride as contained in DUOZAQ. This includes the possibility of other liver diseases e.g. cirrhosis and liver necrosis. Patients at high risk for metabolic diseases should be carefully assessed before commencing treatment and during therapy.

4.5 Interaction with other medicines and other forms of interaction
Although no interaction studies have been conducted for DUOZAQ 0,5 mg/0,4 mg, the following statements reflect the information available on the individual active ingredients:

Dutasteride
In vitro metabolism studies show that dutasteride is metabolised by human cytochrome P450 isoenzyme CYP3A4. Therefore, blood concentrations of dutasteride may increase in the presence of inhibitors of CYP3A4.
Phase II data showed a decrease in clearance of dutasteride when co-administered with CYP3A4 inhibitors verapamil and diltiazem. In contrast, no decrease in clearance was seen when amlodipine, another calcium channel antagonist, was co-administered with dutasteride.
A decrease in clearance and subsequent increase in exposure to dutasteride, in the presence of CYP3A4 inhibitors, is unlikely to be clinically significant due to the wide margin of safety (up to 10 times the recommended dose has been given to patients for up to six months), therefore no dose adjustment is necessary.

In vitro, dutasteride is not metabolised by human cytochrome P450 isoenzymes CYP1A2. CYP2A6, CYP2E1, CYP2C8, CYP2C9, CYP2C19, CYP2B6, and CYP2D6. Dutasteride neither inhibits human cytochrome P450 drug-metabolising enzymes *in vitro* nor induces cytochrome P450 isoenzymes CYP1A, CYP2B, and CYP3A in rats and dogs *in vivo*.
In vitro studies demonstrate that dutasteride does not displace warfarin, diazepam, or phenytoin form plasma protein, nor do these medicines displace dutasteride.
Medicines that have been tested for interaction in man include tamsulosin, terazosin, warfarin, digoxin and cholestyramine and no clinically significant interactions have been observed.
Although specific interaction studies were not performed with other medicines, approximately 90 % of the subjects in large Phase III studies receiving dutasteride were taking other medications concomitantly. No clinically significant adverse interactions were observed in clinical trials when dutasteride was co-administered with anti-hyperlipidemics, angiotensin-converting enzyme (ACE) inhibitors, beta-adrenergic blocking agents, calcium channel blockers, corticosteroids, diuretics, nonsteroidal anti-inflammatory medicines (NSAIDs), phosphodiesterase Type V inhibitors, and quinolone antibiotics.

Tamsulosin
There is a risk of enhanced hypotensive effects when tamsulosin hydrochloride is co-administered with medicines which can reduce blood pressure, including anaesthetic medicine, PDE5 inhibitors and other alpha-1 adrenergic blockers. DUOZAQ 0,5 mg/0,4 mg should not be used in combination with other alpha-1 adrenergic blockers.
Concomitant administration of tamsulosin hydrochloride and ketoconazole (a strong CYP3A4 inhibitor) resulted in an increase of the C_{max} and AUC of tamsulosin hydrochloride by a factor of 2,2 and 2,8 respectively. Concomitant administration of tamsulosin hydrochloride and paroxetine (a strong CYP2D6 inhibitor) resulted in an increase of the C_{max} and AUC of tamsulosin hydrochloride by a factor of 1,3 and 1,6 respectively. A similar increase in exposure is expected in CYP2D6 poor metabolisers as compared to extensive metabolisers when co-administered with a CYP3A4 inhibitor.

The effects of co-administration of both CYP3A4 and CYP2D inhibitors with tamsulosin hydrochloride have not been evaluated clinically, however there is a potential for significant increase in tamsulosin exposure (see section 4.4).

Concomitant administration of tamsulosin hydrochloride (0,4 mg) and cimetidine (400 mg every six hours for six days) resulted in a decrease in the clearance and increase in the AUC of tamsulosin hydrochloride. Caution should be used when DUOZAQ 0,5 mg/0,4 mg is used in combination with cimetidine.

A definitive interaction study between tamsulosin hydrochloride and warfarin has not been conducted. Results from limited *in vitro* and *in vivo* studies are inconclusive. Caution should be exercised with concomitant administration of warfarin and tamsulosin hydrochloride.

No interactions have been seen when tamsulosin hydrochloride was given concomitantly with either atenolol, enalapril, nifedipine or theophylline. Concomitant furosemide brings about a fall in plasma levels of tamsulosin, but as levels remain within the normal range posology need not be adjusted.

In vitro neither diazepam nor propranolol, trichlormethiazide, chlormadinone, amitriptyline, diclofenac, glibenclamide and simvastatin change the free fraction of tamsulosin in human plasma. Neither does tamsulosin change the free fractions of diazepam, propranolol, trichlormethiazide, and chlormadinone.

4.6 Fertility, pregnancy, and lactation
Pregnancy
DUOZAQ 0,5 mg/0,4 mg is contraindicated for use in women.

Dutasteride: DUOZAQ 0,5 mg/0,4 mg has not been studied in women, because pre-clinical data suggests that the suppression of circulating levels of dihydrotestosterone may inhibit the development of the external organs in a male foetus carried by a woman exposed to dutasteride.

Tamsulosin: Administration of tamsulosin hydrochloride to pregnant female rats and rabbits at higher than the therapeutic dose showed no evidence of foetal harm.

Breastfeeding
DUOZAQ 0,5 mg/0,4 mg is contraindicated for use in women.
It is not known whether dutasteride or tamsulosin are excreted in breast milk.

Fertility
Male patients on treatment with DUOZAQ 0,5 mg/0,4 mg are advised to use condoms.

Dutasteride: Dutasteride reduces sperm count and sperm motility which may be irreversible after discontinuation. Discontinuation on sperm counts or sperm function have not been evaluated.

Tamsulosin: Effects of tamsulosin hydrochloride on sperm counts or sperm function have not been evaluated.

4.7 Effects on ability to drive and use machines
DUOZAQ 0,5 mg/0,4 mg may cause orthostatic hypotension which may interfere with driving and operating machinery. Patients should be informed about the occurrence of symptoms related to orthostatic hypotension, such as dizziness when taking DUOZAQ 0,5 mg/0,4 mg.

4.8 Undesirable effects
a). Summary of the safety profile
There have been no clinical trials conducted with DUOZAQ 0,5 mg/0,4 mg, however co-administration information is available from the CombAT (Combination of dutasteride and Tamsulosin) study, a comparison of dutasteride 0,5 mg and tamsulosin 0,4 mg once daily for four years as co-administration or monotherapy.

b). Tabulated summary of adverse reactions

System Organ Class	Frequency	Side effects
Nervous system disorders	*Frequent*	Dizziness
Cardiac disorders	*Less frequent*	Cardiac failure, comprised of cardiac failure congestive, cardiac failure, left ventricular failure, cardiac failure acute, cardiogenic shock, left ventricular failure acute, right ventricular failure, right ventricular failure acute, ventricular failure, cardiopulmonary failure, congestive cardiomyopathy
Reproductive system and breast disorders	*Frequent*	Impotence, altered (decreased) libido, ejaculation disorders, breast disorders (breast tenderness and breast enlargement)

c) Dutasteride monotherapy

System Organ Class	Frequency	Side effects
Immune system disorders	*Frequency unknown*	Allergic reactions including rash, pruritus, urticarial, localised oedema, and angioedema
Psychiatric disorders	*Frequency unknown*	Depressed mood
Cardiac disorders	*Less frequent*	Cardiac failure, comprised of cardiac failure congestive, cardiac failure, left ventricular failure, cardiac failure acute, cardiogenic shock, left ventricular failure acute, right ventricular failure, right ventricular failure acute, ventricular failure, cardiopulmonary failure, congestive cardiomyopathy
Skin and subcutaneous tissue disorders	*Frequency unknown*	Alopecia (primarily body hair loss), hypertrichosis
Reproductive system and breast disorders	*Frequent*	Testicular pain and testicular swelling, impotence, altered (decreased) libido, ejaculation disorders, breast disorders (breast tenderness and breast enlargement)

d) Tamsulosin monotherapy

System Organ Class	Frequency	Side effects
Immune system disorders	*Less frequent*	Rash, pruritus, urticaria, angioedema, Stevens-Johnson syndrome
Nervous system disorders	*Frequent* *Less frequent*	Dizziness Headache, syncope
Eye disorders	*Frequency unknown*	Intra-operative Floppy Iris Syndrome (IFIS), blurred vision, visual impairment
Cardiac disorders	*Less frequent* *Frequency unknown*	Palpitations Atrial fibrillation*, dysrhythmia, tachycardia, dyspnoea
Skin and subcutaneous tissue disorders	*Frequency unknown*	Erythema multiforme, dermatitis exfoliative
Vascular disorders	*Less frequent*	Postural hypotension
Respiratory, thoracic, and mediastinal disorders	*Less frequent* *Frequency unknown*	Rhinitis Epistaxis
Hepato-biliary disorders	*Frequency unknown*	Non-alcoholic fatty liver disease (NAFLD), cirrhosis, liver necrosis and other liver diseases
Gastrointestinal disorders	*Less frequent*	Constipation, diarrhoea, vomiting, nausea
Reproductive system and breast disorders	*Frequent* *Less frequent*	Abnormal ejaculation Priapism
General disorders and administrative site conditions	*Less frequent*	Asthenia

* Post-marketing adverse effects

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 online service for adverse drug reaction reporting, by following the link: https://www.sahpra.org.za/Publications/Index/8.

An email can be sent directly to the company, pharmacovigilance@pharmadynamics.co.za to ensure safety of the product.

4.9 OVERDOSE
Management of overdose
Dutasteride
There is no specific antidote for dutasteride therefore, in cases of suspected overdosage symptomatic and supportive treatment should be given as appropriate.

Tamsulosin
In case of acute hypotension occurring after overdosage with tamsulosin hydrochloride cardiovascular support should be given. Restoration of blood pressure and normalisation of heart rate may be accomplished by lying the patient down. If this is inadequate, administration of volume expanders and if necessary, vasopressors should be used and renal function should be monitored and supported as needed. Laboratory data indicate that tamsulosin hydrochloride is 94 % to 99 % protein bound: therefore, dialysis is unlikely to be of benefit in removing tamsulosin from the body.

5. PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Alpha adrenoreceptor antagonists
ATC code: G04CA52
Pharmacological classification: A21.12 Hormone inhibitors

Mechanism of action
Dutasteride-tamsulosin is a combination of two medicines, dutasteride, a dual 5α-reductase inhibitor (5 ARI) and tamsulosin hydrochloride an antagonist of α_{1a}-adrenoreceptors.
Dutasteride inhibits both type 1 and type 2, 5α-reductase isoenzymes, which are responsible for the conversion of testosterone to 5-alpha dihydrotestosterone (DHT). DHT is the androgen primarily responsible for hyperplasia of glandular prostatic tissue.
Tamsulosin inhibits α_{1a}-adrenergic receptors in the stromal prostatic smooth muscle and bladder neck. Approximately 75 % of the α_1-receptors in the prostate are of the α_{1a}-subtype.
The pharmacodynamics effects of dutasteride-tamsulosin have not been studied.

Dutasteride: Dutasteride lowers DHT levels, reduces prostate volume, improves lower urinary tract symptoms.
The maximum effects of daily doses of dutasteride on the reduction on DHT is dose-dependent and is observed within one to two weeks.

Tamsulosin: Tamsulosin increases maximum urinary flow rate by reducing smooth muscle tension in the prostrate and urethra, thereby relieving obstruction.

5.2 Pharmacokinetic properties
The single dose bioequivalence study was performed in both the fasted and fed states. A 30 % reduction in C_{max} was observed for the tamsulosin component of dutasteride-tamsulosin in the fed state compared to the fasted state. Food had no effect on AUC of tamsulosin.

Absorption
Dutasteride: Following administration of a single 0,5 mg dose, peak serum concentration of dutasteride occur within 1 to 3 hours.
Absolute bioavailability in man is approximately 60 %. The bioavailability of dutasteride is not affected by food.

Tamsulosin: Tamsulosin hydrochloride is absorbed from the intestine and is almost completely bioavailable. Tamsulosin hydrochloride exhibits linear kinetics, following single and multiple dosing, with achievement of steady state concentration by the fifth day of once-a-day dosing.
The rate of absorption of tamsulosin hydrochloride is reduced by a recent meal.
Uniformity of absorption can be prompted by the patient always taking tamsulosin hydrochloride approximately 30 minutes after the same meal each day.

Distribution
Dutasteride: Pharmacokinetic data following single and repeat oral doses show that dutasteride has a large volume of distribution (300 to 500 L). Dutasteride is highly bound to plasma proteins (greater than 99,5 %).
Following daily dosing, dutasteride serum concentrate achieve 65 % of steady state concentration after one month and approximately 90 % after three months. Steady state serum concentration (Css) of approximately 40 ng/mL are achieved after six months of dosing 0,5 mg once a day. Similarly, to serum, dutasteride concentrations in semen achieve steady state at six months. After 52 weeks of therapy, semen dutasteride concentration averaged 3,4 ng/mL (range 0,4 to 14 ng/mL). Dutasteride partitioning from serum into semen averaged 11,5 %.

Tamsulosin: The mean steady-state apparent volume of distribution of tamsulosin hydrochloride after intravenous administration to ten healthy male adults was 16 L, which is suggestive of distribution into extracellular fluids in the body.
Tamsulosin hydrochloride is extensively bound to human plasma proteins (94 % to 99 %), primary alpha-1 acid glycoprotein (AAG), with linear binding over a wide concentration range (20 to 600 ng/mL).

Biotransformation
Dutasteride: *In vitro*, dutasteride is metabolised by human cytochrome P450 isoenzyme CYP3A4 to two minor monohydroxylated metabolites, but it is not metabolised by CYP1A2, CYP2C9, CYP2C19 or CYP2D6.
In human serum, the following dosing to steady state, unchanged dutasteride, three major metabolites (4'-hydroxydutasteride, 1,2-dihydrodutasteride and 6-hydroxydutasteride) and 2 minor metabolites (6,4'-dihydroxydutasteride and 15-hydroxydutasteride), have been detected.

Tamsulosin: There is no enantiomeric bioconversion from tamsulosin hydrochloride (R(-) isomer) to the S(+) isomer in humans. Tamsulosin hydrochloride is extensively metabolised by cytochrome P450 enzymes in the liver and less than 10 % of the dose is excreted in urine unchanged. However, the pharmacokinetic profile of the metabolites in humans has not been established. *In vitro* results indicate that CYP3A4 and CYP2D6 are involved in metabolism of tamsulosin as well as some minor participation of other CYP isoenzymes. Inhibition of hepatic medicine metabolising enzymes may lead to increased exposure to tamsulosin.
The metabolites of tamsulosin hydrochloride undergo extensive conjugation to glucuronide or sulphate prior to renal excretion.

Elimination
Dutasteride: Dutasteride is extensively metabolised. Following oral dosing of dutasteride 0,5 mg/day to steady state in humans, 1,0 % to 15,4 % (mean of 5,4 %) of the administrated dose is excreted as dutasteride in the faeces as four major metabolites comprising 39 %, 21 %, 7 %, and 7 % each of medicine-related material and six minor metabolites (less than 5 % each). Only trace amounts of unchanged dutasteride (less than 0,1 % of the dose) are detected in human urine.
At low serum concentration (less than 3 ng/mL), dutasteride is cleared by both the concentration-dependant and concentration-independent elimination pathways. Single doses of 5 mg or less showed evidence of clearance and half-life of 3 - 9 days.
At serum concentrations greater than 3 mg/mL, dutasteride is cleared slowly (0,35 to 0,58 L/h) primarily by linear, non-saturable elimination with terminal half-life of 3 - 5 weeks. At therapeutic concentrations, the terminal half-life of dutasteride is three to five weeks and following repeat dosing of 0,5 mg/day, the slower clearance dominates and the total clearance is linear and concentration-independent. Serum concentration remain detectable (greater then 0,1 ng/mL) for up to 4 - 6 months after discontinuation of treatment.

Tamsulosin: Tamsulosin half-life is 5 - 7 hours. Approximately 10 % is excreted unchanged in urine.

Pharmacokinetics in special patient groups
No pharmacokinetic studies have been conducted on special patient populations for dutasteride-tamsulosin. The following statements reflect the information available on the individual active ingredients.

Elderly
Dutasteride: Exposure of dutasteride, represented by AUC and C_{max} values, was not statistically different when comparing age groups. No differences in medicine effect as measured by DHT reduction were observed between age groups. Results indicated that no dutasteride dose-adjustment based on age is necessary.

Tamsulosin: The pharmacokinetic disposition of tamsulosin hydrochloride may be slightly prolonged in elderly males compared to young healthy male volunteers. Intrinsic clearance is independent of tamsulosin hydrochloride binding to AAG, but diminishes with age, resulting in 40 % overall higher exposure (AUC) in subjects of age 55 - 75 years compare to subjects of age 20 - 32 years.

Renal impairment
Dutasteride: The effect of renal impairment on dutasteride pharmacokinetics has not been studied. However, less than 0,1 % of a steady-state 0,5 mg dose of dutasteride is recovered in human urine, therefore no adjustment in dosage is anticipated for patients with renal impairment.

Tamsulosin: The pharmacokinetics of tamsulosin hydrochloride have been compared in 6 subjects with mild-moderate ($30 \leq CL_{cr} < 70$ mL/min/1,73 m²) or moderate-severe ($10 \leq CL_{cr} < 30$ mL/min/1,173 m²) renal impairment and 6 normal subjects ($CL_{cr} > 90$ mL/min/1,73 m²). While a change in overall plasma concentration of tamsulosin hydrochloride was observed as a result of altered binding to alpha-1 acid glycoprotein (AAG), the unbound (active) concentration of tamsulosin hydrochloride, as well as the intrinsic clearance, remained relatively constant. Therefore, patients with renal impairment do not require an adjustment in tamsulosin hydrochloride capsules dosing. However, patients with end-stage renal disease ($CL_{cr} < 10$ mL/min/1,73 m²) have not been studied.

Hepatic impairment
Dutasteride: The effect of hepatic impairment on dutasteride pharmacokinetics has not been studied (see section 4.4).

Tamsulosin: The pharmacokinetics of tamsulosin hydrochloride have been compared in subjects with moderate hepatic dysfunction (Child-Pugh's classification: Grade A and B) and normal subjects. While a change in the overall plasma concentration of tamsulosin hydrochloride was observed as the result of altered binding to AAG, the unbound (active) concentration of tamsulosin hydrochloride does not change significantly with only modest (32 %) change in intrinsic clearance of unbound tamsulosin hydrochloride. Therefore, patients with moderate hepatic dysfunction do not require an adjustment in tamsulosin hydrochloride dosage. Tamsulosin hydrochloride has not been studied in patients with severe hepatic dysfunction.

6. PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Dutasteride soft capsules
Butylhydroxytoluene (BHT)
Gelatin
Glycerol
Glycerol monocaprylocaprate
Lecithin (soya)
Titanium dioxide (E171)
Triglycerides, medium chain
Yellow iron oxide (E172)

Tamsulosin pellets
Magnesium stearate
Methacrylic acid-ethyl acrylate copolymer (1:1)
Methacrylic acid-ethyl acrylate copolymer (1:1) dispersion (30%)
Microcrystalline cellulose
Purified talc
Sodium hydroxide
Titanium dioxide (E171)
Triacetin
Talc

Hard capsules
Carrageenan
Hypromellose
Potassium chloride
Red iron oxide (E172)
Sunset yellow (E110)
Titanium dioxide (E171)

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
36 months

6.4 Special precautions for storage
Store at or below 30 °C.
Keep blisters in outer carton until required for use.
Keep bottle closed until required for use.

6.5 Nature and contents of container
30 capsules: Alu-Alu blisters are packed in a printed outer carton.
HDPE bottles containing 30 capsules are packed in a printed outer carton.

*Not all pack presentations may be marketed.

6.6 Special precautions for disposal
Dutasteride is absorbed through the skin, therefore contact with leaking capsules must be avoided. If contact is made with leaking capsules, the contact area should be washed immediately with soap and water (see section 4.4).

7. HOLDER OF THE CERTIFICATE OF REGISTRATION
Pharma Dynamics (Pty) Ltd
1st Floor Grapevine House, Steenberg Office Park
Silverwood Close
Westlake, Cape Town
7945, South Africa

8. REGISTRATION NUMBER
A56/21.12/0796

9. DATE OF FIRST AUTHORISATION
July 2023

pharma dynamics
416045/00

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS S4

DUOZAQ 0,5 mg/0,4 mg hard capsules
Dutasteride and Tamsulosin hydrochloride
DUOZAQ 0,5 mg/0,4 mg is sugar free

Read all of this leaflet carefully before you start taking DUOZAQ 0,5 mg/0,4 mg
- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other healthcare provider.
- DUOZAQ 0,5 mg/0,4 mg has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What DUOZAQ 0,5 mg/0,4 mg is and what it is used for
DUOZAQ 0,5 mg/0,4 mg is a combination of two different medicines called dutasteride and tamsulosin. Dutasteride belongs to a group of medicines called 5-alpha reductase inhibitors and tamsulosin belongs to a group of medicines called alpha blockers.

DUOZAQ 0,5 mg/0,4 mg is used to treat men with an enlarged prostate (benign prostatic hyperplasia) – a noncancerous growth of the prostate gland.

2. What you need to know before you take DUOZAQ 0,5 mg/0,4 mg
Do not take DUOZAQ 0,5 mg/0,4 mg:
- if you are hypersensitive (allergic) to dutasteride, other 5-alpha reductase inhibitors, tamsulosin, or to any of the ingredients of DUOZAQ 0,5 mg/0,4 mg (see section 6)
- if you are female or under the age of 18 years as DUOZAQ 0,5 mg/0,4 mg is for use in adult men only
- if you have low blood pressure which makes you feel dizzy, lightheaded or faint (orthostatic hypotension)
- if you have severe liver disease.

Warnings and precautions
Take special care with DUOZAQ 0,5 mg/0,4 mg:
- women, children and adolescents must not handle leaking DUOZAQ 0,5 mg/0,4 mg capsules, because the active ingredient can be absorbed through the skin. Wash the affected area immediately with soap and water if there is any contact with the skin
- if you have liver disease, ask your doctor if DUOZAQ 0,5 mg/0,4 mg is suitable for you. Your doctor may want to perform regular medical check-ups whilst you are taking DUOZAQ 0,5 mg/0,4 mg
- if you have heart failure (your heart does not pump blood as well as it should), inform your doctor about this, as your heart condition may worsen
- DUOZAQ 0,5 mg/0,4 mg affects a blood test for PSA (prostate-specific antigen), which is sometimes used to detect prostate cancer.
  Men taking DUOZAQ 0,5 mg/0,4 mg should have their PSA measured 6 months after starting therapy and regularly thereafter. Although DUOZAQ 0,5 mg/0,4 mg will reduce the amount of PSA in your blood, you could still be at risk for prostate cancer. In spite of the effect DUOZAQ 0,5 mg/0,4 mg has on PSA count, your doctor can still use PSA level to detect prostate cancer by comparing your test result each time you have a PSA test
- if you notice breast lumps or nipple discharge you should talk to your doctor about these changes as these may be signs of a serious condition, such as breast cancer
- DUOZAQ 0,5 mg/0,4 mg can lower your blood pressure, causing dizziness, light-headedness and fainting. Talk to your doctor should you experience any of these symptoms
- if you are going to have cataract (cloudy lens) surgery, your doctor may ask you to stop taking DUOZAQ 0,5 mg/0,4 mg for a while before your operation
- make sure your doctor knows if you have severe kidney disease.

Other medicines and DUOZAQ 0,5 mg/0,4 mg
Always tell your healthcare provider if you are taking any other medicine (this includes complementary or traditional medicines).

Do not take DUOZAQ 0,5 mg/0,4 mg with these medicines:
- other alpha blockers e.g. doxazosin and prazosin (to treat high blood pressure), terazosin (to treat high blood pressure and benign prostatic hyperplasia), silodosin (to treat benign prostatic hyperplasia).

DUOZAQ 0,5 mg/0,4 mg is not recommended with these medicines:
- ketoconazole (to treat fungal infections), paroxetine (used to treat depression), erythromycin (an antibiotic to treat infections).

Some medicines can react with DUOZAQ 0,5 mg/0,4 mg and may make it more likely that you'll have side effects. These medicines include:
- PDE5 inhibitors (used to help achieve or maintain an erection) such as vardenafil, sildenafil citrate and tadalafil, as it can cause high blood pressure
- cimetidine (for stomach ulcers)
- warfarin (used in the treatment of blood clotting).

DUOZAQ 0,5 mg/0,4 mg with food and drink
DUOZAQ 0,5 mg/0,4 mg should be taken 30 minutes after the same meal everyday.

Pregnancy, breastfeeding and fertility
DUOZAQ 0,5 mg/0,4 mg is contraindicated for use in women.
Women who are pregnant (or may be) must not handle leaking capsules. Dutasteride, one of the active ingredients in DUOZAQ 0,5 mg/0,4 mg is absorbed through the skin and can affect the normal development of a male baby. This is a particular risk in the first 16 weeks of pregnancy.

If you are a man using DUOZAQ 0,5 mg/0,4 mg, it is advised that you use condoms.

Driving and using machines
DUOZAQ 0,5 mg/0,4 mg makes some people feel dizzy, especially when standing up, so it may affect your ability to drive or operate machinery safely.
It is not always possible to predict to what extent DUOZAQ 0,5 mg/0,4 mg may interfere with your daily activities. You should ensure that you do not engage in the above activities until you are aware of the measure to which DUOZAQ 0,5 mg/0,4 mg affects you.

3. How to take DUOZAQ 0,5 mg/0,4 mg
Do not share medicines prescribed for you with any other person. Always use DUOZAQ 0,5 mg/0,4 mg exactly as your doctor has instructed. You should check with your doctor or pharmacist if you are unsure.

The recommended dose is one capsule taken once a day, 30 minutes after the same meal each day.

The capsules should be swallowed whole and not chewed or opened.
Contact with the contents of the dutasteride yellow capsule (containing oily yellowish liquid) contained within the hard-shell capsule may make your mouth or throat sore.
Your doctor will tell you how long your treatment with DUOZAQ 0,5 mg/0,4 mg will last. If you have the impression that the effect of DUOZAQ 0,5 mg/0,4 mg is too strong or too weak, tell your doctor or pharmacist.

If you take more DUOZAQ 0,5 mg/0,4 mg than you should
In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison control centre.

If you forget to take DUOZAQ 0,5 mg/0,4 mg
If you forget to take DUOZAQ 0,5 mg/0,4 mg, take as soon as you remember on the same day. If you do not take a tablet that same day, take your normal dose the next day. Do not take a double dose to make up for forgotten individual doses.

If you stop taking DUOZAQ 0,5 mg/0,4 mg
Don't stop taking DUOZAQ 0,5 mg/0,4 mg without talking to your doctor first.

4. Possible side effects
DUOZAQ 0,5 mg/0,4 mg can have side effects.
Not all side effects reported for DUOZAQ 0,5 mg/0,4 mg are included in this leaflet. Should your general health worsen, or if you experience any untoward effects while using DUOZAQ 0,5 mg/0,4 mg, please consult your healthcare provider for advice.

If any of the following happens, stop using DUOZAQ 0,5 mg/0,4 mg and tell your doctor immediately or go to the casualty department at your nearest hospital:
- swelling of the hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing
- rash or itching
- fainting.

These are all very serious side effects. If you have them, you may have had a serious allergic reaction to DUOZAQ 0,5 mg/0,4 mg. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:
- a widespread rash with blisters and peeling skin, particularly around the mouth, nose, eyes, and genitals (Stevens-Johnson syndrome)
- irregular heartbeats and/or rapid heartbeats
- heart failure (heart becomes less efficient at pumping blood around the body. You may have symptoms such as shortness of breath, extreme tiredness and swelling in your ankles and legs)
- your heart suddenly stops circulating blood throughout your body (cardiogenic shock).

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:
Frequent side effects:
- dizziness
- impotence (not able to achieve or maintain an erection)
- decreased sex drive (libido)
- difficulty with ejaculation, such as a decrease in the amount of semen released during sex
- breast enlargement or tenderness (gynecomastia)
- pain or swelling of the testicles.

Less frequent side effects:
- skin rash, hives, itching, swelling of hands and feet
- headache
- fast heartbeat (palpitations)
- fall in blood pressure on standing up which makes you feel dizzy or faint
- itchy, blocked, or runny nose (rhinitis)
- constipation, diarrhoea, vomiting, nausea
- persistent and painful erection of the penis (priapism)
- weakness or loss of strength.

The following side effects have been reported but the frequency for them to occur is not known:
- swelling in a specific area
- depressed mood
- hair loss (usually from the body) or hair growth, excessive sweating
- changes in vision (blurred vision or visual impairment), an eye condition called Floppy Iris Syndrome (a complication during cataract surgery)
- shortness of breath
- nosebleeds
- liver problems (if you experience a sudden onset of nausea, weakness, fatigue, abdominal pain and sleepiness contact your doctor to do blood tests).

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects
If you get side effects, talk to your doctor, pharmacist or nurse. You can also report side effects to SAHPRA via the online service for adverse drug reaction reporting by following the link: https://www.sahpra.org.za/Publications/Index/8.
An email can be sent directly to the company, pharmacovigilance@pharmadynamics.co.za to ensure safety of the product.
By reporting side effects, you can help provide more information on the safety of DUOZAQ 0,5 mg/0,4 mg.

5. How to store DUOZAQ 0,5 mg/0,4 mg
Store all medicines out of reach of children.
Store at or below 30 °C.
Keep blisters in carton until required for use.
Keep bottle closed until required for use.
Do not use after the expiry date stated on the carton. Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information
What DUOZAQ 0,5 mg/0,4 mg contains:
The hard capsules contain: one dutasteride 0,5 mg soft capsule (yellow) and tamsulosin HCl pellets (white to off-white) in the equivalent weight of 0,4 mg of tamsulosin HCl.

The other ingredients are:
Dutasteride soft capsules
Butylhydroxytoluene (BHT), gelatin, glycerol, glycerol monocaprylocaprate, lecithin (soya), titanium dioxide, triglycerides – medium chain, yellow iron oxide.

Tamsulosin pellets
Magnesium stearate, methacrylic acid-ethyl acrylate copolymer (1:1), methacrylic acid-ethyl acrylate copolymer (1:1) dispersion (30%), microcrystalline cellulose, purified talc, sodium hydroxide, titanium dioxide, triacetin, talc.

Hard capsules
Carrageenan, hypromellose, potassium chloride, red iron oxide, sunset yellow, titanium dioxide.

What DUOZAQ 0,5 mg/0,4 mg looks like and contents of the pack
DUOZAQ 0,5 mg/0,4 mg is a hard capsule with brown body and orange cap.
30 capsules: Alu-Alu blisters are packed in a printed outer carton.
HDPE bottles containing 30 capsules are packed in a printed outer carton.
* Not all pack presentations may be marketed.

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PASIËNTINLIGTINGSBLAD

SKEDULERINGSTATUS S4

DUOZAQ 0,5 mg/0,4 mg harde kapsules
Dutasteried en Tamsulosienhidrochloried
DUOZAQ 0,5 mg/0,4 mg is suikervry

Lees hierdie hele inligtigsblad deeglik deur, voordat u begin om DUOZAQ 0,5 mg/0,4 mg te gebruik
- Hou hierdie inligtingsblad. Dit mag nodig wees vir u om dit weer te lees.
- Indien u verdere vrae het, vra asseblief u dokter, apteker, verpleegkundige, of ander gesondheidsorgverskaffer.
- DUOZAQ 0,5 mg/0,4 mg is vir u persoonlik voorgeskryf en u moet nie u medisyne met ander mense deel nie. Dit mag skadelik wees vir hulle, selfs al is hulle simptome dieselfde as u eie.

Inhoud van hierdie inligtingsblad

1. Wat DUOZAQ 0,5 mg/0,4 mg is en waarvoor dit gebruik word
DUOZAQ 0,5 mg/0,4 mg is 'n kombinasie van twee afsonderlike medisyne, wat dutasteried en tamsulosien genoem word. Dutasteried behoort aan 'n groep medisyne wat 5-alfa-reduktaseremmers genoem word en tamsulosien behoort aan 'n groep medisyne wat alfa-blokkers genoem word.

DUOZAQ 0,5 mg/0,4 mg word gebruik om mans met 'n vergrote prostaat (benigne prostatiese hiperplasie) te behandel – 'n nie-kwaadaardige gewas van die prostaatklier.

2. Wat u nodig het om te weet, voordat u DUOZAQ 0,5 mg/0,4 mg gebruik
Moet nie DUOZAQ 0,5 mg/0,4 mg neem:
- indien u hipersensitief (allergies) is vir dutasteried, ander 5-alfa-reduktaseremmers, tamsulosien, of vir enige van die ander bestanddele van DUOZAQ 0,5 mg/0,4 mg nie (kyk afdeling 6)
- indien u vroulik of jonger as 18 jaar oud is nie, aangesien DUOZAQ 0,5 mg/0,4 mg slegs gebruik word deur volwasse mans
- indien u aan lae bloeddruk, wat u duiselig, lighoofdig of flouerig laat voel, ly nie (ortostatiese hipotensie)
- indien u erge lewersiekte het nie.

Waarskuwings en voorsorgmaatreëls
Neem spesiale sorg met DUOZAQ 0,5 mg/0,4 mg:
- vroue, kinders en adolessente, moet nie lekkende DUOZAQ 0,5 mg/0,4 mg kapsules hanteer nie, aangesien die aktiewe bestanddeel deur die vel geabsorbeer mag word. Was die blootgestelde oppervlakte onmiddellik met seep en water af, indien daar enige kontak met die vel was
- indien u lewersiekte het, vra u dokter of DUOZAQ 0,5 mg/0,4 mg gepas is vir u. U dokter mag dalk gereelde mediese opvolgondersoeke aanvra, terwyl u DUOZAQ 0,5 mg/0,4 mg gebruik
- u moet u dokter inlig indien u hartversaking het (u hart pomp nie bloed so doeltreffend as wat dit behoort nie), aangesien u harttoestand mag versleg
- DUOZAQ 0,5 mg/0,4 mg beïnvloed 'n bloedtoets vir PSA (prostaatspesifieke antigeen), wat somtyds gebruik word om prostaatkanker op te spoor.
  Mans wie DUOZAQ 0,5 mg/0,4 mg neem, moet hulle PSA vasstel, 6 maande nadat behandeling begin is en gereeld, daarna. Alhoewel DUOZAQ 0,5 mg/0,4 mg die hoeveelheid PSA in u bloed verminder, kan u nog steeds 'n risiko toon vir prostaatkanker. Ten spyte van die invloed wat DUOZAQ 0,5 mg/0,4 mg op die PSA-telling het, mag u dokter steeds die PSA-vlak gebruik om prostaatkanker op te spoor, deur u toetsresultate te vergelyk elke keer wanneer u 'n PSA-toets ondergaan
- indien u knoppe in u borste, of 'n afskeiding vanuit die tepels opmerk, moet u die dokter raadpleeg omtrent hierdie veranderinge, aangesien dit tekens van 'n ernstige toestand, soos borskanker, mag wees
- DUOZAQ 0,5 mg/0,4 mg kan u bloeddruk verlaag en duiseligheid, lighoofdigheid en floute veroorsaak. Praat met u dokter, sou u enige van hierdie simptome ervaar
- indien u 'n katarak- (wasige lens) operasie beplan, mag u dokter versoek dat u die gebruik van DUOZAQ 0,5 mg/0,4 mg vir 'n wyle voor u operasie, staak
- maak seker dat u dokter weet, indien u aan 'n ernstige niersiekte ly.

Ander medisyne en DUOZAQ 0,5 mg/0,4 mg
Vertel altyd u gesondheidsorgverskaffer, indien u enige ander medisyne neem (dit sluit aanvullende, of tradisionele medisyne in).

Moet nie DUOZAQ 0,5 mg/0,4 mg saam met hierdie medisyne neem nie:
- ander alfa-blokkers bv. doksasosien en prasosien (om hoë bloeddruk te behandel), terasosien (om hoë bloeddruk en benigne prostatiese hiperplasie te behandel), silodosien (om benigne prostatiese hiperplasie te behandel).

DUOZAQ 0,5 mg/0,4 mg word nie aanbeveel saam met hierdie medisyne nie:
- ketokonasool (om swaminfeksies te behandel), paroksetien (gebruik vir depressie), eritromisien ('n antibiotikum wat gebruik word om infeksies te behandel).

Sommige medisyne kan met DUOZAQ 0,5 mg/0,4 mg reageer en mag die moontlikheid vir u om newe-effekte te ervaar, verhoog. Hierdie medisyne sluit die volgende in:
- PDE5-remmers (gebruik om 'n ereksie te bekom, of te behou) soos vardenafil, sildenafilsitraat en tadalafil, aangesien dit hoë bloeddruk mag veroorsaak
- simetidien (vir maagulkusse)
- warfarien (gebruik vir die behandeling van bloedklontvorming).

DUOZAQ 0,5 mg/0,4 mg saam met kos en drinkgoed
DUOZAQ 0,5 mg/0,4 mg moet 30 minute na dieselfde maaltyd, elke dag geneem word.

Swangerskap, borsvoeding en fertiliteit
DUOZAQ 0,5 mg/0,4 mg word teenaangedui vir gebruik deur vroue.
Vroue wie swanger is (of mag wees), moet nie lekkende kapsules hanteer nie. Dutasteried, een van die aktiewe bestanddele van DUOZAQ 0,5 mg/0,4 mg, word deur die vel geabsorbeer en kan die normale ontwikkeling van 'n manlike baba beïnvloed. Hierdie is veral 'n risiko tydens die eerste 16 weke van swangerskap.

Indien u 'n man is wie DUOZAQ 0,5 mg/0,4 mg neem, word daar aanbeveel dat u kondome gebruik.

Bestuur en die hantering van masjiene
DUOZAQ 0,5 mg/0,4 mg mag sommige mense duiselig laat voel, veral wanneer hulle opstaan. Dit mag dus u vermoë om te bestuur, of masjinerie veilig te hanteer, beïnvloed.
Dit is nie altyd moontlik om te voorspel tot watter mate DUOZAQ 0,5 mg/0,4 mg met u daaglikse aktiwiteite sal inmeng nie. U moet verseker dat u nie betrokke raak by bogenoemde aktiwiteite, totdat u bewus is tot watter mate DUOZAQ 0,5 mg/0,4 mg u aantas nie.

3. Hoe om DUOZAQ 0,5 mg/0,4 mg te neem
Moet nie medisyne wat vir u voorgeskryf is, met enige ander persoon deel nie. Gebruik DUOZAQ 0,5 mg/0,4 mg altyd presies soos deur u dokter aanbeveel word. U moet u dokter, of apteker raadpleeg indien u onseker is.

Die aanbevole dosis is een kapsule, een keer per dag geneem, 30 minute na dieselfde maaltyd elke dag.

Die kapsules moet heel gesluk word en nie gekou, of oopgemaak word nie.
Aanraking met die inhoud van die dutasteried geel kapsule (bevat olierige, geel vloeistof), wat binne-in die harde kapsuledop voorkom, mag u mond of keel beseer.
U dokter sal u vertel vir hoe lank u behandeling met DUOZAQ 0,5 mg/0,4 sal duur. Indien u onder die indruk is dat die uitwerking van DUOZAQ 0,5 /0,4 mg té sterk, of té swak is, vertel u dokter of apteker.

Indien u meer DUOZAQ 0,5 mg/0,4 mg neem as wat u behoort
In die geval van oordosering, raadpleeg u dokter of apteker. Indien beide nie beskikbaar is nie, kontak die naaste hospitaal, of gifbeheersentrum.

Indien u vergeet om DUOZAQ 0,5 mg/0,4 mg te neem
Indien u vergeet om DUOZAQ 0,5 mg/0,4 mg te neem, neem dit so gou as wat u onthou op die dieselfde dag. Indien u nie 'n kapsule, op dieselfde dag neem nie, neem die gewone dosis, die volgende dag. Moet nie 'n dubbeldosis neem om op te maak vir die vergete, individuele doserings nie.

Indien u die gebruik van DUOZAQ 0,5 mg/0,4 mg staak
Moet nie die gebruik van DUOZAQ 0,5 mg/0,4 mg staak, sonder om u dokter eers te raadpleeg nie.

4. Moontlike newe-effekte
DUOZAQ 0,5 mg/0,4 mg kan newe-effekte hê.
Nie alle newe-effekte wat vir DUOZAQ 0,5 mg/0,4 mg aangemeld is, word in hierdie inligtingsblad ingesluit nie. Sou u algemene gesondheid versleg, of indien u enige ongewenste effekte ervaar terwyl u DUOZAQ 0,5 mg/0,4 mg gebruik, raadpleeg asseblief u gesondheidsorgverskaffer vir advies.

Indien enige van die volgende gebeur, staak die gebruik van DUOZAQ 0,5 mg/0,4 mg en vertel u dokter onmiddellik, of gaan na die ongevalleafdeling by u naaste hospitaal:
- swelling van die hande, voete, enkels, gesig, lippe, mond of keel, wat sluk en asemhaling mag bemoeilik
- uitslag of gejeuk
- floute.

Hierdie is alles ernstige newe-effekte. Indien u dit ervaar, kon u 'n ernstige allergiese reaksie teenoor DUOZAQ 0,5 mg/0,4 mg gehad het. U mag dringende mediese aandag of hospitalisasie benodig.

Vertel u dokter onmiddellik, of gaan na die ongevalleafdeling by u naaste hospitaal, indien u enige van die volgende opmerk:
- 'n wydverpreide uitslag met blase en velafskilfering, veral rondom die mond, neus, oë en geslagsdele (Stevens-Johnson-sindroom)
- onreëlmatige hartklop en of 'n vinnige hartklop
- hartversaking (die hart word minder doeltrffend om bloed deur die liggaam te pomp. U mag simtome soos, asemnood, uiterste moegheid en swelling in u enkels en bene ervaar)
- u hart versuim skielik om bloed deur u liggaam te sirkuleer (kardiogene skok).

Hierdie is alles ernstige newe-effekte. U mag dringende mediese aandag benodig.

Vertel u dokter indien u enige van die volgende benodig:
Newe-effekte wat dikwels voorkom:
- duiseligheid
- impotensie (onvermoë om 'n ereksie te verkry of te behou)
- afname in seksdrang (libido)
- probleme met ejakulasie, soos 'n vermindering in die volume semen wat vrygestel word, tydens seks
- vergroting of gevoeligheid van borste (ginekomastie)
- pyn of swelling van die testikels.

Minder algemene newe-effekte:
- veluitslag, galbulte, gejeuk, swelling van die hande en voete
- hoofpyn
- vinnige hartklop (palpitasies)
- skielike bloeddrukverlaging wanneer u opstaan, wat u duiselig of lighoofdig laat voel
- jeukende, toe neus, of lopende neus (rinitis)
- hardlywigheid, diarree, braking, naarheid
- volhardende en pynlike ereksie van die penis (priapisme)
- swakheid, of kragverlies.

Die volgende newe-effekte is aangemeld, maar die frekwensie van voorkoms is onbekend:
- swelling in 'n bepaalde area
- depressiewe bui
- haarverlies (gewoonlik vanaf die liggaam), of haargroei, uitermatige gesweet
- verandering in sig (wasige visie of sigbelemmering), 'n oogtoestand wat Slap-irissindroom genoem word ('n komplikasie tydens 'n katarakoperasie)
- asemnood
- neusbloeding
- lewerprobleme (indien u 'n skielike intrede van naarheid, swakheid, moegheid, pyn in die buikarea en lomerigheid ervaar, kontak u dokter om bloedtoetse te doen).

Indien u enige newe-effekte opmerk, wat nie in hierdie inligtingsblad genoem word nie, raadpleeg asseblief u dokter of apteker.

Aanmelding van newe-effekte
Indien u enige newe-effekte ervaar, praat met u dokter, apteker, of verpleegkundige. U kan ook newe-effekte by SAHPRA via die aanlyndiens vir ongewenste geneesmiddelreaksie aanmeld by die volgende webskakel: https://www.sahpra.org.za/Publications/Index/8.
'n E-pos kan direk aan die maatskappy gestuur word by:
pharmacovigilance@pharmadynamics.co.za om die veiligheid van die medisyne te verseker.
U kan help om meer inligting aangaande die veiligheid van DUOZAQ 0,5 mg/0,4 mg te bekom, deur newe-effekte aan te meld.

5. Hoe om DUOZAQ 0,5 mg/0,4 mg te bewaar
Bewaar alle medisyne buite die bereik van kinders.
Bewaar teen of benede 30 °C.
Hou stulpstroke in die kartonhouer, totdat dit benodig word vir gebruik.
Hou die bottel dig geseël, totdat dit benodig word vir gebruik.
Moet nie gebruik na die vervaldatum wat op die kartonhouer aangedui word nie.
Neem alle ongebruikte medisyne terug na u apteker.
Moet nie ongebruikte medisyne in dreine of rioolstelsels (bv. toilette), weggooi nie.

6. Verpakkingsinhoud en ander inligting
Wat DUOZAQ 0,5 mg/0,4 mg bevat:
Die harde kapsule bevat: een dutasteried 0,5 mg sagte kapsule (geel) en tamsulosien HCl-korrels (wit tot naaswit), gelykstaande aan 'n gewig van 0,4 mg tamsulosien HCl.

Die ander bestanddele is:
Dutasteried sagte kapsules
Butielhidroksitolueen (BHT), geel ysteroksied, gelatien, gliserol, gliserolmonokaprielkapraat, lesitien (soja), titaandioksied, trigliseriede – mediumketting.

Tamsulosienkorrels
Gesuiwerde talkum, magnesiumstearaat, metakrielsuur-etielakrilaatkopolimeer (1:1), metakrielsuur-etielakrilaatkopolimeer (1:1) dispersie (30%), mikrokristallyne sellulose, natriumhidroksied, titaandioksied, triasetien, talkum.

Harde kapsules
Hipromellose, kaliumchloried, karrageenan, rooi ysteroksied, sunset geel, titaandioksied.

Hoe DUOZAQ 0,5 mg/0,4 mg lyk en die verpakkingsinhoud
DUOZAQ 0,5 mg/0,4 mg is 'n harde kapsule, met 'n bruin liggaam en oranje doppie.
30 kapsules: Alu-Alu stulpstroke word verpak in 'n gedrukte buitenste kartonhouer.
HDPE bottels wat 30 kapsules bevat, word verpak in 'n gedrukte buitenste kartonhouer.
* Nie alle verpakkingsvoorstelle mag bemark word nie.

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