BLADEONZ
P1529823

BLADEONZ
P1529823

Professional Information for Medicines for Human Use

SCHEDULING STATUS: S3

1. NAME OF MEDICINE

BLADEONZ 5 mg (film-coated tablets)
BLADEONZ 10 mg (film-coated tablets)

2. QUALITATIVE AND QUANTITIVE COMPOSITION:

BLADEONZ 5 mg:
Each film-coated tablet contains solifenacin succinate 5 mg.
Contains sugar: 80,30 mg lactose.

BLADEONZ 10 mg:
Each film-coated tablet contains solifenacin succinate 10 mg.
Contains sugar: 80,30 mg lactose.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablets.

BLADEONZ 5 mg:
Light yellow coloured, round shaped, biconvex, film-coated tablets debossed with 'CC' on one side and '31' on the other side.

BLADEONZ 10 mg:
Light pink coloured, round shaped, biconvex, film-coated tablets debossed with 'CC' on one side and '32' on the other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

BLADEONZ is indicated for the symptomatic treatment of overactive bladder syndrome: symptoms of urinary urgency, frequent micturition and/or urge incontinence.

4.2 Posology and method of administration

Posology

Adults, including the elderly
The recommended dose is 5 mg once daily. If needed, the dose may be increased to 10 mg once daily.

Special populations

Patients with renal impairment
No dose adjustment is necessary for patients with mild to moderate renal impairment (creatinine clearance > 30 mL/min). Patients with severe renal impairment (creatinine clearance ≤ 30 mL/min) should be treated with caution and receive not more than 5 mg once daily.

Patients with hepatic impairment
No dose adjustment is necessary for patients with mild hepatic impairment. Patients with moderate hepatic impairment should be treated with caution and receive not more than 5 mg once daily.

Potent inhibitors of cytochrome P450 3A4
The maximum dose of **BLADEONZ** should be limited to 5 mg when treated simultaneously with ketoconazole or therapeutic doses of other potent CYP3A4-inhibitors e.g. ritonavir, nelfinavir, itraconazole.

Paediatric population
Safety and effectiveness of **BLADEONZ** in children have not yet been established. Therefore, **BLADEONZ** is not recommended for children.

Method of administration
BLADEONZ should be taken orally and should be swallowed whole with liquids. It can be taken with or without food, as is convenient.

4.3 Contraindications

- Hypersensitivity to the solifenacin or to any of the excipients of **BLADEONZ** (see section 6.1)
- Urinary retention.
- Uncontrolled narrow angle glaucoma.
- Myasthenia gravis.
- Toxic megacolon.
- Patients undergoing haemodialysis.
- Patients with severe hepatic impairment.
- Patients with severe renal impairment (Clcr < 30 mL/min) and on treatment with a strong CYP3A4 inhibitor e.g. ketoconazole (see section 4.5).
- Patients with moderate hepatic impairment and on treatment with a strong CYP3A4 inhibitor, e.g. ketoconazole (see section 4.5).
- Patients with a prolonged QT interval, either congenital or acquired.
- Pregnancy and lactation (see section 4.6).

4.4 Special warnings and precautions for use

Other causes of frequent urination (heart failure or renal disease) should be assessed before treatment with **BLADEONZ**. If urinary tract infection is present, an appropriate antibacterial therapy should be started.

BLADEONZ should be used with caution in patients with:
- Significant decompensated bladder outlet obstruction at risk of urinary retention.
- Gastrointestinal obstructive disorders.
- Risk of decreased gastrointestinal motility.
- Severe renal impairment (creatinine clearance ≤ 30 mL/min and doses should not exceed 5 mg for these patients.
- Moderate hepatic impairment (Child Pugh score of 7 to 9) and doses should not exceed 5 mg for these patients.
- Concomitant use of a potent CYP3A4 inhibitor, e.g. ketoconazole.
- Hiatus hernia/gastro-oesophageal reflux and/or who are concurrently taking medicinal products (such as bisphosphonates) that can cause or exacerbate oesophagitis.
- Autonomic neuropathy.

QT prolongation and Torsade de Pointes have been observed in patients with risk factors, such as pre-existing long QT syndrome and hypokalaemia (see section 4.3).

Safety and efficacy have not yet been established in patients with a neurogenic cause for detrusor over activity.

Angioedema with airway obstruction has been reported in some patients on solifenacin. If angioedema occurs, **BLADEONZ** should be discontinued and appropriate therapy and/or measures should be taken.

Anaphylactic reaction has been reported in some patients treated with solifenacin. In patients who develop anaphylactic reactions, **BLADEONZ** should be discontinued and appropriate therapy and/or measures should be taken.

The maximum effect of **BLADEONZ** can be determined after 4 weeks at the earliest.

BLADEONZ contains lactose
Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicines and other forms of interaction

Pharmacological interactions
Concomitant medication with other medicinal products with anticholinergic properties may result in more pronounced therapeutic effects and undesirable effects. An interval of approximately one week should be allowed after stopping treatment with **BLADEONZ**, before commencing other anticholinergic therapy. The therapeutic effect of **BLADEONZ** may be reduced by concomitant administration of cholinergic receptor agonists. **BLADEONZ** can reduce the effect of medicinal products that stimulate the motility of the gastrointestinal tract, such as metoclopramide and cisapride.

Pharmacokinetic interactions
In vitro studies have demonstrated that at therapeutic concentrations, solifenacin does not inhibit CYP1A1/2, 2C9, 2C19, 2D6, or 3A4 derived from human liver microsomes. Therefore, **BLADEONZ** is unlikely to alter the clearance of drugs metabolised by these CYP enzymes.

Effect of other medicinal products on the pharmacokinetics of solifenacin
Since solifenacin is metabolised by CYP3A4, pharmacokinetics interactions are possible with other CYP3A4 substrates, inhibitors and inducers.

Ketoconazole and other CYP3A4 inhibitors:
Simultaneous administration of ketoconazole (200 mg/day), a potent CYP3A4 inhibitor, resulted in a two-fold increase of the AUC of solifenacin, while ketoconazole at a dose of 400 mg/day resulted in a three-fold increase of the AUC of solifenacin.

Therefore, the maximum dose of solifenacin should be restricted to 5 mg, when used simultaneously with ketoconazole or therapeutic doses of other potent CYP3A4 inhibitors (e.g. ritonavir, nelfinavir, itraconazole).

Simultaneous treatment of **BLADEONZ** and a strong CYP3A4 inhibitor is contra indicated in patients with severe renal impairment or moderate hepatic impairment. (see section 4.3).

The effects of enzyme induction on the pharmacokinetics of solifenacin and its metabolites have not been studied as well as the effect of higher affinity CYP3A4 substrates on solifenacin exposure. Since solifenacin is metabolised by CYP3A4, pharmacokinetic interactions are possible with other CYP3A4 substrates with higher affinity (e.g. verapamil, diltiazem) and CYP3A4 inducers (e.g. rifampicin, phenytoin, carbamazepine).

Effect of solifenacin on the pharmacokinetics of other medicinal products

Oral Contraceptives
Intake of solifenacin showed no pharmacokinetic interaction of solifenacin on combined oral contraceptives (ethinyl estradiol/levonorgestrel), as both are CYP3A4 substrates.

Warfarin:
Intake of solifenacin did not alter the pharmacokinetics of R-warfarin (substrate for CYP3A4) or S-warfarin (substrate for CYP2C9) or their effect on the INR.

Digoxin:
Intake of solifenacin showed no effect on the pharmacokinetics of digoxin.

4.6 Fertility, pregnancy and lactation

Pregnancy
BLADEONZ is contraindicated during pregnancy (see section 4.3). Foetal toxicity has been shown in rodents.

Breastfeeding
Solifenacin, as in **BLADEONZ** is excreted into breast milk. It is contraindicated during lactation (see section 4.3), therefore women taking **BLADEONZ** should not breastfeed their infants.

Fertility
Animal studies do not indicate direct harmful effects on fertility, embryonal/foetal development or parturition. The potential risk for humans is unknown.

4.7 Effects on ability to drive and use machines

Since **BLADEONZ**, may cause blurred vision, somnolence and fatigue (see section 4.8), the ability to drive and use machines may be negatively affected.

4.8 Undesirable Effects

Due to the pharmacological effect of solifenacin**, BLADEONZ** may cause anticholinergic side effects of mild or moderate severity in general.

The most frequently reported adverse reaction **BLADEONZ** was dry mouth. The severity of dry mouth was generally mild.

Infectious and infestations:
Less frequent: Urinary tract infection, cystitis.

Nervous system disorders:
Less frequent: Somnolence, dysgeusia.

Eye disorders:
Frequent: Blurred vision.
Less frequent: Dry eyes.

Respiratory, thoracic and mediastinal disorders:
Less frequent: Nasal dryness.

Gastrointestinal disorders:
Frequent: Dry mouth, constipation, nausea, dyspepsia, abdominal pain.
Less frequent: Gastro-oesophageal reflux diseases, dry throat, colonic obstruction, faecal impaction.

Skin and subcutaneous tissue disorders:
Less frequent: Dry skin.

Renal and urinary disorders:
Less frequent: Difficulty in micturition, urinary retention.

General disorders and administration site conditions:
Less frequent: Fatigue, peripheral oedema.

Post-marketing data:
Immune system disorders:
Frequency unknown: Anaphylactic reaction.

Metabolism and nutrition disorders:
Frequency unknown: Decreased, appetite, hyperkalaemia.

DETACH BEFORE DISPENSING

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS:

S3

BLADEONZ 5 mg (film-coated tablet)
BLADEONZ 10 mg (film-coated tablet)
Solifenacin succinate
Contains sugar: 80,30 mg lactose monohydrate per tablet

Read all of this leaflet carefully before you start taking BLADEONZ.
- Keep this leaflet. You may need to read it again.
- **BLADEONZ** 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.
- If you have further questions, please ask your doctor or your pharmacist.

What is in this leaflet

1. What **BLADEONZ** is and what it is used for
2. What you need to know before you take **BLADEONZ**
3. How to take **BLADEONZ**
4. Possible side effects
5. How to store **BLADEONZ**
6. Contents of the pack and other information

1. WHAT BLADEONZ IS AND WHAT IT IS USED FOR

BLADEONZ contains a medicine called solifenacin succinate.
The active substance of **BLADEONZ** belongs to a group of medicines called anticholinergic.
BLADEONZ is used to reduce the activity of an overactive bladder. This enables you to wait longer before having to go to the bathroom and increases the amount of urine that can be held by your bladder.

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE BLADEONZ

Do not take BLADEONZ:
- If you are hypersensitive (allergic) to solifenacin succinate or any of the ingredients of **BLADEONZ** listed in section 6.
- If you have the inability to pass water or to empty the bladder completely (urinary retention).
- If you suffer from increased pressure in the eyes, with gradual loss of eyesight (glaucoma).
- If you suffer from the muscle disease called myasthenia gravis, which can cause an extreme weakness of certain muscles.
- If you have a severe stomach or bowel condition (toxic megacolon).
- If you are undergoing kidney dialyses.
- If you have a severe liver disease.
- If you have a severe kidney or moderate liver disease and at the same time being treated with medicines that may decrease the removal of **BLADEONZ** from the body (for example, ketoconazole).
- If you have disorder of the heart known as prolonged QT interval, whether it is inherited or acquired.
- If you are pregnant or breastfeeding.

Warnings and precautions
Tell your doctor before taking BLADEONZ:
Take special care with BLADEONZ:
- If you have other underlying diseases (for example: heart failure or kidney disease) which may also lead to the urge to frequently urinate. Your doctor should address these conditions first before treatment with **BLADEONZ**.
- If you have trouble emptying your bladder (bladder obstruction) or have difficulty in passing urine. Risk of accumulation of urine in the bladder (urinary retention) is much higher.
- If you have some obstruction of the digestive system (constipation).
- If you are at risk of your digestive system slowing down (stomach constipation).
- If you suffer from severe kidney disease.
- If you have moderate liver disease.
- If you are taking medicines which decreases the rate of breakdown of **BLADEONZ** by the body for example ketoconazole.
- If you have a stomach tear (hiatus hernia) or heartburn.
- If you have a nervous system disorder (autonomic neuropathy).
- If you have a condition called QT syndrome or Torsades De Pointes, which are conditions associated with changes in the electrical activity of the heart (ECG), irregular heartbeat, faster heartbeat
- Skin allergy that results in swelling of the tissue just below the skin (angioedema) with obstruction of the airway has been reported. If this occurs, you should stop taking **BLADEONZ** and inform your doctor immediately.
- Potentially life-threatening allergic reactions (anaphylactic reactions) have been reported. If you experience any allergic reaction, you should stop taking **BLADEONZ** and inform your doctor immediately.

BLADEONZ will only reach its complete effect after 4 weeks at the earliest

Children and adolescents
Safety in children has not been established, therefore **BLADEONZ** is not recommended for children under 18 years.

Other medicines with BLADEONZ:
Always tell your health care provider if you are taking any other medicine. (This includes complementary or traditional medicines).
- Amantadine (used as an anti-viral or Parkinson's disease), some antihistamines, phenothiazine (for psychiatric disorders), and tricyclic antidepressants as they can reduce the effect of **BLADEONZ**.
- Metoclopramide, domperidone and cisapride, which make the digestive system work faster, as **BLADEONZ** can reduce their effect.
- Ketoconazole, ritonavir, nelfinavir, itraconazole, verapamil and diltiazem, which decrease the rate at which **BLADEONZ** is broken down by the body. If you have severe kidney disease you should not take these medicines with **BLADEONZ** (see section 2).
- Rifampicin, phenytoin and carbamazepine, as they increase the rate at which **BLADEONZ** is broken down by the body.

Taking BLADEONZ with food, drink and alcohol:
BLADEONZ can be taken with or without food.

Pregnancy, breastfeeding and fertility:
If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other health care provider for advice before taking this medicine.
BLADEONZ is contraindicated in pregnancy and during breastfeeding.

Driving and using machines
BLADEONZ may cause blurred vision, sleepiness and a general feeling of tiredness (somnolence and fatigue). If you suffer from these side effects, do not drive or operate machinery as it may affect these activities.

BLADEONZ contains lactose:
BLADEONZ contains lactose, which is a type of sugar. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

3. HOW TO TAKE BLADEONZ

Do not share medicines prescribed for you with any other person.
Always take exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure.
The usual dose for **BLADEONZ** is 5 mg per day, unless your doctor told you to take 10 mg per day if needed.
Try to take **BLADEONZ** at the same time each day. You should swallow the whole tablet with some liquid.
It can be taken with or without food.

If you take more BLADEONZ 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.
The most frequent side effects side effects associated with overdose of **BLADEONZ** are headache, dry mouth, dizziness, drowsiness and blurred vision with overdose.

If you forget to take BLADEONZ:
It is important that you do not miss any doses. If you miss a dose of **BLADEONZ**, take it as soon as you remember. If it is almost time for your next dose, skip the missed dose and go back to your regular dosing schedule once daily.
Do not take a double dose to make up for the forgotten individual doses.

If you stop taking BLADEONZ
Do not stop taking **BLADEONZ** unless your doctor tells you to do so. If you have further questions on the use of **BLADEONZ**, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

BLADEONZ can have side effects.
If any of the following happens, stop taking **BLADEONZ** 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,
- yellowing of the skin and eyes, also called jaundice.

These are all very serious side effects. If you have them, you may have had a serious allergic reaction to **BLADEONZ**. 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:
- Chest pain,
- angina,
- changes in the way your heart beats e.g. if you notice it beating faster,
- difficulty in breathing,
- less urine than is normal for you.

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

Tell your doctor if you notice any of the following:
The following side effects have frequently been reported:
- Blurred vision,
- dry mouth, constipation, nausea, heartburn (dyspepsia), stomach pain.

The following side effects have been reported less frequently:
- Bladder infection, inflammation of the bladder due to infection (cystitis),
- sleepiness, impaired sense of taste (dysgeusia),
- dry eyes,
- dry nasal passages,
- reflux disease (gastro-oesophageal reflux), dry throat, obstruction of the colon, lodging, of a large amount of hardened stool in the large intestine (faecal impaction),
- dry skin,
- difficulty in passing urine,
- tiredness, accumulation of fluid in the lower legs (oedema),
- hallucinations, confusion,
- dizziness and headache,
- vomiting
- allergic rash, itching of the skin (pruritus), rash, reddening of patches of the skin (erythema multiforme) or hives (urticaria).

The following side effects have been reported with unknown frequency:
- Dilation of the pupils (mydriasis), difficulty in adjusting focus (cycloplegia), painful eyes with bright light (photophobia),
- reduced secretion of the mucus of the chest,
- flushing of the skin,
- decreased appetite, high levels of blood potassium which can cause abnormal heart rhythm,
- disturbed state of mind characterised by restlessness, illusions and confusion (delirium),
- increased pressure in the eyes (glaucoma),
- voice disorder (dysphonia),
- a painful obstruction of the ileum or other part of the intestine, stomach discomfort,
- liver disorder,
- muscular weakness,
- kidney disorder.

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

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects to SAHPRA via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications: http://www.sahpra.org.za/Publications/Index/8.
By reporting side effects, you can help provide more information on the safety of **BLADEONZ**.

5. HOW TO STORE BLADEONZ

Store at or below 25 °C.
Keep the blisters in the carton until required for use.
STORE ALL MEDICINES OUT OF REACH OF CHILDREN.
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 BLADEONZ contains
The active substance is solifenacin.
The other ingredients of **BLADEONZ** are the other ingredients of **BLADEONZ** are hypromellose, lactose monohydrate, magnesium stearate, maize starch, silica colloidal anhydrous. In addition 5 mg contains Aquarius™ BP14332 yellow and 10 mg contains Aquarius™ BP10212 pink.
BLADEONZ 5 mg:
Aquarius™ BP14332 yellow contains hypromellose, polyethylene glycol, talc, titanium dioxide (C.I. NO: 77891) and yellow iron oxide (C.I. NO: 77492).
BLADEONZ 10 mg:
Aquarius™ BP10212 pink contains hypromellose, polyethylene glycol, talc, titanium dioxide (C.I. NO: 77891) and red iron oxide (C.I. NO: 77491).

What BLADEONZ looks like and contents of the pack
BLADEONZ 5 mg:
Light yellow coloured, round shaped, biconvex, film coated tablets debossed with 'CC' on one side and '31' on the other side.
BLADEONZ 10 mg:
Light pink coloured, round shaped, biconvex, film coated tablets debossed with 'CC' on one side and '32' on the other side.
Blister pack:
Tablets are packed in clear 250 micron PVC film as the forming material and 25 micron aluminum foil with 7 g/m² heat seal lacquer as the lidding material.
Pack size: 30's - Each carton contains 3 blisters of 10 tablets each.
HDPE container:
Tablets are packed in white opaque round 40 mL HDPE container with 33 mm neck finish closed with 33 mm white opaque polypropylene continuous thread closure with vad having induction sealing liner.
Pack size: 30's – Each HDPE container contains 30 tablets.

Holder of Certificate of Registration
AUROGEN SA (Pty) Ltd
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53 Phillip Engelbrecht Avenue
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Johannesburg
South Africa

Registration number
BLADEONZ 5 mg: 50/5.4/0625
BLADEONZ 10 mg: 50/5.4/0626

This leaflet was revised
09 November 2021

Psychiatric disorders:
Less frequent: Hallucinations, confusional state.
Frequency unknown: Delirium.

Nervous system disorders:
Less frequent: Dizziness, headache

Eye disorders:
Frequency unknown: Glaucoma.

Cardiac disorders:
Frequency unknown: Torsade de Pointes, electrocardiogram QT prolonged, atrial fibrillation, palpitations, tachycardia.

Respiratory, thoracic and mediastinal disorders:
Frequency unknown: Dysphonia.

Gastrointestinal disorders:
Less frequent: Vomiting.
Frequency unknown: Ileus, abdominal discomfort.

Hepatobiliary disorders:
Frequency unknown: Liver disorder, abnormal liver function test.

Skin and subcutaneous tissue disorder:
Less frequent: Pruritus, rash, erythema multiforme, urticaria, angioedema.
Frequency unknown: Exfoliative dermatitis.

Musculoskeletal, connective tissue and bone disorders:
Frequency unknown: Muscular weakness.

Renal and urinary disorders:
Frequency unknown: Renal impairment.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the '**6.04 Adverse Drug Reactions Reporting Form**'. Found online under SAHPRA's publications: https://www/sahpra.org.za/Publications/Index/8.

4.9 Overdosage

Symptoms

Overdosage with solifenacin succinate can potentially result in severe anticholinergic effects. In the event of overdose with **BLADEONZ,** the patient should be treated with activated charcoal.

Standard supportive treatment should be applied, as necessary.

Symptoms can be treated as follows:

- Severe central anticholinergic effects such as hallucinations or pronounced excitation: treat with physostigmine or carbachol.
- Convulsions or pronounced excitation: treat with benzodiazepines.
- Respiratory insufficiency: treat with artificial respiration.
- Tachycardia: treat with beta-blockers.
- Urinary retention: treat with catheterisation.
- Mydriasis: treat with pilocarpine eye drops and/or place patient in dark room.

Specific attention should be paid to patients with known risk for QT-prolongation (i.e. hypokalaemia, bradycardia and concurrent administration of medicines known to prolong QT-interval) and relevant pre-existing cardiac diseases (i.e. myocardial ischaemia, dysrhythmia, congestive heart failure).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Urinary antispasmodics, ATC code: G04B D08.
Pharmacological classification: A 5.4 Cholinolytics (anticholinergics).

Solifenacin is a competitive, specific cholinergic-receptor antagonist. *In vitro* studies demonstrated that solifenacin binds to muscarinic receptors, with high affinity.

5.2 Pharmacokinetics

Pharmacokinetic properties:

Absorption

Following the oral administration of solifenacin succinate tablets, maximum solifenacin plasma concentrations (C_{max}) are reached after 3 to 8 hours. The T_{max} is independent of the dose. The C_{max} and area under the curve (AUC) increase in proportion to the dose between 5 to 40 mg. Absolute bioavailability is approximately 90 %. Food intake does not affect the C_{max} and AUC of solifenacin.

Distribution

The apparent volume of distribution of solifenacin following intravenous administration is about 600 L. Solifenacin is largely (approximately 98 %) bound to plasma proteins, primarily α 1-acid glycoprotein.

Biotransformation

Solifenacin is extensively metabolised by the liver, primarily by cytochrome P450 3A4 (CYP3A4). However, alternative metabolic pathways exist, that can contribute to the metabolism of solifenacin. The systemic clearance of solifenacin is about 9,5 L/h and the terminal half-life of solifenacin is 45 to 68 hours. After oral dosing, one pharmacologically active (4*R*-hydroxy solifenacin) and three inactive metabolites (*N*-glucuronide, *N*-oxide and 4*R*-hydroxy-N-oxide of solifenacin) have been identified in plasma in addition to solifenacin.

Elimination

After a single administration of 10 mg [^{14}C-labelled]-solifenacin, about 70 % of the radioactivity was detected in urine and 23 % in faeces over 26 days.

In urine, approximately 11 % of the radioactivity is recovered as unchanged drug; about 18 % as the *N*- oxide metabolite, 9 % as the 4*R*-hydroxy-*N*-oxide metabolite and 8 % as the 4*R*-hydroxy metabolite (active metabolite).

Linearity/Non-linearity

Pharmacokinetics is linear in the therapeutic dose range.

Special populations:

Age

No dosage adjustment based on patient age is required. Studies in elderly have shown that the exposure to solifenacin, expressed as the AUC, after administration of solifenacin succinate (5 mg and 10 mg once daily) was similar in healthy elderly subjects (aged 65 through 80 years) and healthy young subjects (aged less than 55 years). The mean rate of absorption expressed as T_{max} was slightly slower in the elderly and the terminal half-life was approximately 20 % longer in elderly subjects. These modest differences were considered not clinically significant.

The pharmacokinetics of solifenacin has not been established in children.

Gender

The pharmacokinetics of solifenacin is not influenced by gender.

Renal impairment

The AUC and C_{max} of solifenacin in mild and moderate renal impaired patients, was not significantly different from that found in healthy volunteers. In patients with severe renal impairment (creatinine clearance ≤ 30 ml L/min) exposure to solifenacin was significantly greater than in the controls with increases in C_{max} of about 30 %, AUC of more than 100 % and $t_{½}$ of more than 60 %. A statistically significant relationship was observed between creatinine clearance and solifenacin clearance.

Pharmacokinetics in patients undergoing haemodialysis has not been studied.

Hepatic impairment

In patients with moderate hepatic impairment the C_{max} is not affected, AUC increase with 60 % and $t_{½}$ doubled. Pharmacokinetics of solifenacin in patients with severe hepatic impairment has not been studied.

6 Pharmaceutical particulars

6.1 List of excipients

The other ingredients of **BLADEONZ** are the other ingredients of **BLADEONZ** are hypromellose, lactose monohydrate, magnesium stearate, maize starch, silica colloidal anhydrous. In addition, 5 mg contains Aquarius™ BP14332 yellow and 10 mg contains Aquarius™ BP10212 pink.

BLADEONZ 5 mg:

Aquarius™ BP14332 yellow contains hypromellose, polyethylene glycol, talc, titanium dioxide (C.I. NO: 77891) and yellow iron oxide (C.I. NO: 77492).

BLADEONZ 10 mg:

Aquarius™ BP10212 pink contains hypromellose, polyethylene glycol, talc, titanium dioxide (C.I. NO: 77891) and red iron oxide (C.I. NO: 77491).

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store at or below 25 °C.

Do not remove blister from carton until required for use.

6.5 Nature and contents of container

Blister pack:

Tablets are packed in clear 250 micron PVC film as the forming material and 25 micron aluminum foil with 7 g/m^2 heat seal lacquer as the lidding material.
Pack size: 30's - Each carton contains 3 blisters of 10 tablets each.

HDPE container:
Tablets are packed in white opaque round 40 mL HDPE container with 33 mm neck finish closed with 33 mm white opaque polypropylene continuous thread closure with wad having induction sealing liner.

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

7.6 Special precautions for disposal and other handling

Procedures for safe handling of cytotoxic drugs should be followed.

7 Holder of certificate of registration

AUROGEN SA (Pty) Ltd
Woodhill Office Park, Building 1, First Floor
53 Phillip Engelbrecht Avenue
Meyersdal, Ext. 12, 1448
Johannesburg
South Africa

8 Registration number

BLADEONZ 5 mg: 50/5.4/0625
BLADEONZ 10 mg: 50/5.4/0626

9 Date of first authorisation:

09 November 2021

P1529823

DETACH BEFORE DISPENSING

PASIËNTINLIGTINGSBLAD

SKEDULERINGSTATUS:

S3

BLADEONZ 5 mg (filmbedekte tablet)
BLADEONZ 10 mg (filmbedekte tablet)
Solifenasiensuksinaat
Bevat suiker: 80,30 mg laktosemonohidraat per tablet

Lees hierdie hele pamflet sorgvuldig deur voordat u begin om BLADEONZ te neem.

- Hou hierdie pamflet. U moet dit dalk weer lees.
- **BLADEONZ** is vir u persoonlik voorgeskryf en u moet nie u medisyne met ander mense deel nie. Dit kan skadelik vir hulle wees, al het hulle dieselfde simptome as u.
- Indien u verdere vrae het, vra asseblief u dokter of apteker.

Wat is in hierdie pamflet

1. Wat **BLADEONZ** is en waarvoor dit gebruik word
2. Wat u moet weet voordat u **BLADEONZ** neem
3. Hoe om **BLADEONZ** te neem
4. Moontlike newe-effekte
5. Hoe om **BLADEONZ** te berg
6. Inhoud van die verpakking en ander inligting

1. WAT BLADEONZ IS EN WAARVOOR DIT GEBRUIK WORD

BLADEONZ bevat 'n medisyne wat solifenasiensuksinaat genoem word. Dit behoort aan 'n groep medisyne wat anticholinergiese medisyne genoem word.

Die aktieve bestanddeel van **BLADEONZ** behoort aan 'n groep medisyne wat anticholinergiese medisyne genoem word.

BLADEONZ word gebruik om die aktiwiteit van 'n ooraktiewe blaas te verminder. Dit stel u in staat om langer te wag voor u na die badkamer moet gaan en verhoog die hoeveelheid urine wat deur u blaas gehou kan word.

2. WAT U MOET WEET VOORDAT U BLADEONZ NEEM

Moenie BLADEONZ neem nie:

- Indien u hipersensitief (allergies) is vir solifenasiensuksinaat of enige van die bestanddele van **BLADEONZ** gelys in afdeling 6.
- Indien u 'n onvermoë het om water uit te skei of om u blaas heeltemal leeg te maak (urienretensie).
- Indien u ly aan verhoogde druk in die oë, met geleidelike verlies van sig (gloukoom).
- Indien u lyk aan 'n spiersiekte wat myasthenia gravis genoem word (toksiese megakolon).
- Indien u 'n ernstige maag- of dermtoestand het (toksiese megakolon).
- Indien u nierdialise ondergaan.
- Indien u 'n ernstige lewersiekte het.
- Indien u 'n ernstige nier- of matige lewersiekte het en terselfdertyd behandel word met medisyne wat die verwydering van **BLADEONZ** uit die liggaam kan verminder (byvoorbeeld ketokonasool).
- Indien u 'n hartafwyking het wat bekend staan as verlengde QT-interval, of dit nou oorgeërf of verworwe is.
- Indien u swanger is of borsvoed.

Waarskuwings en voorsorgmaatreëls

Vertel u dokter voordat u BLADEONZ neem:

Neem spesiale sorg met BLADEONZ:

- Indien u ander onderliggende siektes het (byvoorbeeld: hartversaking of niersiekte) wat ook kan lei tot 'n dringende behoefte om gereeld te urineer. U dokter moet hierdie toestande eers aanspreek voor behandeling met **BLADEONZ**.
- Indien u sukkel om u blaas leeg te maak (blaasobstruksie) of swak urinestraal het (hardlywigheid, naarheid, sooibrand (dispepsie), maagpyn, ophoping van urine in die blaas (urienretensie) is baie hoër.
- Indien u 'n matige tot ernstige obstruksie in u spysverteringstelsel het (hardlywigheid).
- Indien u 'n risiko het dat u spysverteringstelsel stadiger word (maag- en dermbewegings).
- Indien u aan ernstige niersiekte ly.
- Indien u matige lewersiekte het.
- Indien u medisyne neem wat die tempo waarteen **BLADEONZ** deur die liggaam afgebreek word, verlaag, byvoorbeeld ketokonasool.
- Indien u 'n maagskeur (hiatus hernia) of sooibrand het.
- Indien u 'n senuweestelselafwyking het (outonome neuropatie).
- Indien u 'n toestand het wat QT-sindroom of Torsades De Pointes genoem word. Dié toestande hou verband met veranderinge in die elektriese aktiviteit van die hart (EKG), onreëlmatige hartklop, voel u hartklop, vinniger hartklop.
- Vélallergie, wat lei tot swelling van die weefsel net onder die vel (angioedeem) met obstruksie van die lugweg, is aangemeld. Indien dit gebeur, moet u ophou om **BLADEONZ** te neem en u dokter onmiddellik in kennis stel.
- Potensieel lewensgevaarlike allergiese reaksies (anafilaktiese reaksies) is aangemeld. Indien u enige allergiese reaksie ervaar, moet u ophou om **BLADEONZ** te neem en u dokter onmiddellik in kennis stel.

BLADEONZ sal op die vroegste eers na 4 weke volledige effek bereik.

Kinders en adolessente

Veiligheid by kinders is nie vasgestel nie, daarom word **BLADEONZ** nie aanbeveel vir kinders onder 18 jaar nie.

Ander medisyne met BLADEONZ:

Vertel altyd u gesondheidsorgverskaffer indien u enige ander medisyne gebruik (Dit sluit komplementêre of tradisionele medisyne in).

- Amantadien (gebruik as 'n anti-viraal of vir Parkinson-siekte), sommige antihistamiene, fenotiasien (gebruik vir psigiatriese afwykings) en trisikliese antidepressante, aangesien dit die effek van **BLADEONZ** kan verminder.
- Metoklopramied, domperidoon en sisapried, wat die spysverteringstelsel vinniger laat werk, aangesien dit **BLADEONZ** hul effek kan verminder.
- Ketokonasool, ritinovir, nelfinavir, itrakonasool, verapamil en diltiasem, wat die tempo waarteen **BLADEONZ** in die liggaam afgebreek word, verlaag. Indien u 'n mediese toestand het wat erger kan word indien u 'n ernstige niersiekte het, moet u nie hierdie medisyne saam met **BLADEONZ** neem nie (sien afdeling 2).
- Rifampisien, fenitoïen en karbamasepien, aangesien hulle die tempo waarteen **BLADEONZ** afgebreek word, verhoog.

BLADEONZ saam met voedsel, drank en alkohol:

BLADEONZ kan met of sonder kos geneem word.

Swangerskap, borsvoeding en fertiliteit:

Indien u swanger is of borsvoed, dink u is dalk swanger of beplan om 'n baba te hê, raadpleeg asseblief u dokter, apteker of ander gesondheidsorgverskaffer vir advies voordat u hierdie medisyne neem.

BLADEONZ is teenaangedui tydens swangerskap en borsvoeding.

Bestuur en die gebruik van masjinerie:

BLADEONZ kan dowwe visie, slaperigheid en 'n algemene gevoel van moegheid (slaperigheid en uitputting) veroorsaak. Indien u aan hierdie newe-effekte ly, moenie bestuur of masjinerie gebruik nie, aangesien dit hierdie aktiwiteite kan beïnvloed.

BLADEONZ bevat laktose:

BLADEONZ bevat laktose, wat 'n soort suiker is. Indien u dokter u meegedeel het dat u 'n intoleransie teenoor sommige suikers het, kontak u dokter voordat u hierdie medisyne neem.

3. HOE OM BLADEONZ TE NEEM

Moenie medisyne wat vir u voorgeskryf is met enige ander persoon deel nie.

Neem altyd presies soos u dokter voorgeskryf het. U moet u dokter of apteker raadpleeg indien u onseker is.

Die gewone dosis vir **BLADEONZ** is 5 mg per dag, tensy u dokter u aanvanklik 'n laer dosis voorskryf het indien nodig.

Probeer om **BLADEONZ** elke dag op dieselfde tyd te neem. U moet die hele tablet met 'n bietjie vloeistof sluk.

Dit kan met of sonder voedsel geneem word.

Indien u meer BLADEONZ neem as wat u moet:

In die geval van oordosis, raadpleeg u dokter of apteker. Indien geen van hulle beskikbaar is nie, kontak die naaste hospitaal of gifbeheersentrum.

Die mees algemene newe-effekte wat met **BLADEONZ** oordosis geassosieer word, is hoofpyn, droë mond, duiseligheid, lomerigheid en dowwe visie.

Indien u vergeet om BLADEONZ te neem:

Dit is belangrik dat u geen dosisse mis nie. Indien u 'n dosis **BLADEONZ** mis, neem dit so gou as wat u onthou. Indien dit amper tyd is vir u volgende dosis, slaan die gemiste dosis oor en gaan voort met u gewone dosisskedule van eenkeer per dag.

Moenie 'n dubbeldosis neem om op te maak vir vergete individuele dosisse nie.

Indien u ophou om BLADEONZ te neem:

Moenie ophou om **BLADEONZ** te neem nie, tensy u dokter u beveel om dit te doen. Indien u verdere vrae het oor die gebruik van **BLADEONZ**, vra u dokter of apteker.

4. MOONTLIKE NEWE-EFFEKTE

BLADEONZ kan newe-effekte hê.

Indien enige van die volgende gebeur, hou op om **BLADEONZ** te neem en vertel u dokter onmiddellik of gaan na die ongevalle-afdeling van u naaste hospitaal.

- Swelling van u hande, voete, enkels, gesig, lippe, mond of keel, wat moeilike sluk of asemhaling kan veroorsaak,
- uitslag of jeuk,
- floute,
- vergeeling van die vel en oë, ook genoem geelsug.

Hierdie is almal baie ernstige newe-effekte. Indien u dit ervaar, het u moontlik 'n ernstige allergiese reaksie vir **BLADEONZ**. U benodig moontlik dringende mediese behandeling of hospitalisasie.

Vertel u dokter onmiddellik of gaan na die ongevalle-afdeling van u naaste hospitaal indien u enige van die volgende opmerk:

- Borspyn,
- angina,
- veranderinge in die manier hoe u hart klop bv. indien u agterkom u hart klop vinniger,
- moeilike asemhaling,
- minder urine wat normaal is vir u.

Hierdie is almal ernstige newe-effekte. U benodig moontlik mediese behandeling.

Vertel u dokter indien u enige van die volgende opmerk:

Die volgende neve-effekte is dikwels aangemeld:

- Dowwe visie,
- droë mond, hardlywigheid, naarheid, sooibrand (dispepsie), maagpyn.

Die volgende newe-effekte is minder dikwels aangemeld:

- Blaasinfeksie, inflammasie van die blaas as gevolg van infeksie (sistitis),
- slaperigheid, verswakte smaaksintuig (disgeusie),
- droë oë,
- droë neusgange,
- refluksiekte (gastro-esofageale refluks), droë keel, obstruksie van die kolon, vassit van 'n groot hoeveelheid verharde stoelgang in die dikderm (fekale impaksie),
- droë vel,
- moeilike urinering,
- moegheid, opeenhoping van vloeistof in die onderbene (edeem),
- hallusinasies, verwarring,
- duiseligheid en hoofpyn,
- braking,
- allergiese uitslag, jeuk van die vel (pruritus), uitslag, rooiheid van kolle op die vel (eriteem multiforme) of neteliroos (urikarië).

Die volgende neve-effekte is met onbekende frekwensie aangemeld:

- Verwyding van die pupille (mydriasis), moeilike aanpassing van fokus (sikloplegie), pynlike oë met helder lig (fotofobie),
- verminderde sekresie van die slym van die bors,
- rooi word van die vel,
- verminderde eetlus, hoë vlakke van bloedkalium wat abnormale hartritme kan veroorsaak,
- versteurde gemoedstoestand gekenmerk deur rusteloosheid, illusies en verwarring (delirium),
- verhoogde druk in die oë (gloukoom),
- stemafwyking (disfonie),
- 'n pynlike obstruksie in die ileum of ander deel van die ingewande, maagongemak,
- leweraftwyking,
- spierswakheid,
- nierafwyking.

Indien u enige newe-effekte opmerk wat nie in hierdie pamflet genoem word nie, stel asseblief u dokter of apteker in kennis.

Aanmelding van newe-effekte

Indien u enige newe-effekte ervaar, praat met u dokter, apteker of verpleegster. Dit sluit in enige newe-effekte wat nie in hierdie pamflet gelys is nie. U kan newe-effekte ook aan SAHPRA rapporteer via die "**6.04 Adverse Drug Reaction Reporting Form**", wat aanlyn onder SAHPRA se publikasies verskyn: https://www.sahpra.org.za/Publications/Index/8. Deur newe-effekte aan te meld, kan u meer inligting verskaf oor die veiligheid van **BLADEONZ**.

5. HOE OM BLADEONZ TE BERG

Berg teen of benede 25 °C.

Hou die stulpstroke in die karton, todat dit benodig word vir gebruik.

BERG ALLE MEDISYNE BUITE BEREIK VAN KINDERS.

Neem alle ongebruikte medisyne terug na u apteker.

Moenie ongebruikte medisyne in dreine of rioolstelsels (bv.toilette) weggooi nie.

6. INHOUD VAN DIE VERPAKKING EN ANDER INLIGTING

Wat BLADEONZ bevat

Die aktieve bestanddeel is solifenasien.

Die ander bestanddele van **BLADEONZ** is hipromellose, laktosemonohidraat, magnesiumstearaat, mieliestysel, watervrye kolloïdale silika. Daarbenewens bevat 5 mg Aquarius™ BP14332 geel en 10 mg bevat Aquarius™ BP10212 pienk.

BLADEONZ 5 mg:

Aquarius™ BP14332 geel bevat hipromellose, poliëtileenglikol, talk, titaandioksied (C.I. NO 77891) en geel ysteroksied (C.I. NO 77492).

BLADEONZ 10 mg:

Aquarius™ BP10212 pienk bevat hipromellose, poliëtileenglikol, talk, titaandioksied (C.I. NO 77891) en rooi ysteroksied (C.I. NO 77491).

Hoe BLADEONZ lyk en inhoud van die verpakking:

BLADEONZ 5 mg:

Liggeel gekleurde, ronde, bikonvekse, filmbedekte tablette gegraveer met 'CC' aan die een kant en '31' aan die ander kant.

BLADEONZ 10 mg:

Ligpienk gekleurde, ronde, bikonvekse, filmbedekte tablette gegraveer met 'CC' aan die een kant en '32' aan die ander kant.

Stulpverpakking:

Tablette word verpak in helder 250 mikron PVC-film as die vormingmateriaal en 25 mikron aluminiumfoelie met 7 g/m^2 hitte seëllak as dekselmateriaal.

Verpakkingsgroottes: 30's – Elke karton bevat 3 stulpstroke van 10 tablette elk.

HDPE-houer:

Tablette word verpak in wit, ondeursigtige, ronde 40 mL HDPE-houers met 33 mm nekafwerking toegemaak met 33 mm wit, ondeursigtige, polipropileen-deurlopende skroefdraad sluiting met watte en induksie seëlvoering.

Verpakkingsgrootte: 30's – Elke HDPE-houer bevat 30 tablette.

Houer van registrasiesertifikaat

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Woodhill Office Park, Gebou 1, Eerste Vloer
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Meyersdal. Uitbr. 12, 1448
Johannesburg
Suid-Afrika

Registrasienommer:

BLADEONZ 5 mg: 50/5.4/0625
BLADEONZ 10 mg: 50/5.4/0626

Hierdie pamflet is laas hersien in:
09 November 2021