NOVARTIS

ONBREZ BREEZHALER® (indacaterol maleate)

150 µg (Dry Powder Inhalation Capsules)

Professional Information

Document status: Final

Release date: 23 August 2020

SCHEDULING STATUS

S3

1 NAME OF THE MEDICINAL PRODUCT

ONBREZ BREEZHALER® 150 µg (Dry Powder Inhalation Capsules)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

ONBREZ BREEZHALER® 150 µg: Each capsule contains indacaterol maleate equivalent to 150 µg indacaterol. The delivered dose leaving the mouthpiece of the ONBREZ Breezhaler inhaler is indacaterol maleate equivalent to 120 microgram indacaterol. Each capsule contains 24,8 mg lactose.

Excipients with known effect

Contains sugar: Lactose

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

ONBREZ BREEZHALER® 150 µg: Black product code "IDL 150" printed above and black company logo printed under black bar on yellowish transparent (uncoloured) capsule.

***Appearance of content*:** White to practically white powder.

Appearance of capsule shell: *Aspect* - Yellowish transparent (uncoloured) cap and body;

Imprint - *Cap*: black " " under black bar; *Body:* black "IDL 150" above black bar.

Size: Capsule size 3

ONBREZ BREEZHALER® inhaler: White plastic device protected by a white plastic cap. Colour of push buttons: translucent blue.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

ONBREZ BREEZHALER is a long-acting beta$_2$-agonist indicated for long-term, once-daily, maintenance bronchodilator treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD).

4.2 Posology and method of administration

Do not exceed the recommended dose.

Adults

The recommended dosage of ONBREZ BREEZHALER is the once-daily inhalation of the content of one 150 microgram ONBREZ capsule using the ONBREZ BREEZHALER inhaler.

Dosing in special populations

No dosage adjustment is required for geriatric patients, patients with mild and moderate hepatic impairment, or renally impaired patients. No data is available for subjects with severe hepatic impairment (see Pharmacokinetic properties).

ONBREZ BREEZHALER should not be used in patients under 18 years of age.

Method of administration

ONBREZ BREEZHALER capsules must be administered only by the oral inhalation route and only using the ONBREZ BREEZHALER inhaler. These capsules must not be swallowed. ONBREZ BREEZHALER should be administered at the same time of the day each day. If a dose is missed, the next dose should be taken at the usual time the next day.

ONBREZ BREEZHALER capsules must always be stored in the blister, and only removed IMMEDIATELY BEFORE USE.

4.3 Contraindications

Hypersensitivity to indacaterol, lactose or any of the ingredients of ONBREZ BREEZHALER.

4.4 Special warnings and precautions for use

Asthma

ONBREZ BREEZHALER should not be used in asthma due to the absence of long-term outcome data in asthma with ONBREZ BREEZHALER.

Long-acting beta$_2$-adrenergic agonists may increase the risk of asthma-related serious adverse events, including asthma-related deaths, when used for the treatment of asthma.

Hypersensitivity

Immediate hypersensitivity reactions have been reported after administration of ONBREZ BREEZHALER. If signs suggesting allergic reactions (in particular, difficulties in breathing or swallowing, swelling of tongue, lips and face, urticaria, skin rash) occur, ONBREZ BREEZHALER should be discontinued immediately and alternative therapy instituted.

Paradoxical bronchospasm

Administration of ONBREZ BREEZHALER may result in paradoxical bronchospasm that may be life-threatening. If paradoxical bronchospasm occurs, ONBREZ BREEZHALER should be discontinued immediately and alternative therapy instituted.

Deterioration of disease

ONBREZ BREEZHALER is not indicated for the initial treatment of acute episodes of bronchospasm, *i.e.,* as a rescue therapy. In case of deterioration of COPD whilst on treatment with ONBREZ BREEZHALER, a reevaluation of the patient and the COPD treatment regimen should be undertaken. An increase in the daily dose of ONBREZ BREEZHALER beyond the maximum dose is not appropriate.

Systemic effects

Although no clinically relevant effect on the cardiovascular system is usually seen after the administration of ONBREZ BREEZHALER at the recommended doses, ONBREZ BREEZHALER, should be used with caution in patients with cardiovascular disorders, (coronary artery disease, acute myocardial infarction, cardiac dysrhythmias and hypertension), in patients with convulsive disorders or thyrotoxicosis, and in patients who are unusually responsive to beta$_2$-adrenergic agonists.

ONBREZ BREEZHALER should not be used more often or at higher doses than recommended.

ONBREZ BREEZHALER should not be used in conjunction with other long-acting beta$_2$-adrenergic agonists or medications containing long-acting beta$_2$-adrenergic agonists.

Cardiovascular effects

ONBREZ BREEZHALER may produce a clinically significant cardiovascular effect in some patients as measured by increases in pulse rate, blood pressure, and/or symptoms. In case such effects occur, ONBREZ BREEZHALER may need to be discontinued. In addition, beta-adrenergic agonists such as ONBREZ BREEZHALER have been reported to produce ECG changes, such as flattening of the T wave, prolongation of the QT interval, and ST segment depression. The clinical significance of these findings is unknown. Therefore, long-acting beta$_2$-adrenergic agonists (LABA) or LABA containing products such as ONBREZ BREEZHALER should be used with caution in patients with known or suspected prolongation of the QT interval or patients treated with medicinal products affecting the QT interval.

Hypokalaemia

Beta$_2$-adrenergic agonists such as ONBREZ BREEZHALER may produce significant hypokalaemia in some patients, which has the potential to produce adverse cardiovascular effects. The decrease in serum potassium is usually transient, not requiring supplementation. In patients with severe COPD, hypokalaemia may be potentiated by hypoxia and concomitant treatment (see Interactions) which may increase the susceptibility to cardiac

dysrhythmias.

Hyperglycaemia

Inhalation of high doses of beta$_2$-adrenergic agonists may produce increases in plasma glucose. Upon initiation of treatment with ONBREZ BREEZHALER plasma glucose should be monitored more closely in diabetic patients.

During clinical studies, clinically notable changes in blood glucose were generally more frequent by 1 - 2 % on ONBREZ BREEZHALER at the recommended doses than on placebo. ONBREZ BREEZHALER has not been investigated in patients with not well controlled diabetes mellitus.

ONBREZ BREEZHALER contains lactose, which may have an effect on the glycaemic control of patients with diabetes mellitus. Patients with rare hereditary problems of lactose intolerance or severe lactase deficiency should not use ONBREZ BREEZHALER.

4.5 Interaction with other medicines and other forms of interaction

Medicines known to prolong QTc interval

ONBREZ BREEZHALER, as other beta$_2$-adrenergic agonists, should be administered with caution to patients being treated with monoamine oxidase inhibitors, tricyclic antidepressants, or medicines known to prolong the QT interval, as any effect of these on the QT interval may be potentiated. Medicines known to prolong the QT-interval may increase the risk of ventricular dysrhythmia (see Warnings and Special Precautions).

Sympathomimetic medicines

Concomitant administration of other sympathomimetic medicines (alone or as part of combination therapy) may potentiate the undesirable effects of ONBREZ BREEZHALER (see Warnings and Special Precautions).

Hypokalaemia

Concomitant treatment with methylxanthine derivatives, steroids, or non-potassium-sparing diuretics may potentiate the possible hypokalaemic effect of $beta_2$-adrenergic agonists (see Warnings and Special Precautions).

Beta-adrenergic blockers

Beta-adrenergic blockers may weaken or antagonise the effect of $beta_2$-adrenergic agonists. Therefore ONBREZ BREEZHALER should not be given together with beta-adrenergic blockers (including eye drops) unless there are compelling reasons for their use.

Metabolic and transporter based medicine interaction

Inhibition of the key contributors of indacaterol clearance, CYP3A4 and P-gp (P-glycoprotein), has no impact on safety of therapeutic doses of ONBREZ BREEZHALER.

Medicine interaction studies were carried out using potent and specific inhibitors of CYP3A4 and P-gp (*i.e.*, ketoconazole, erythromycin, verapamil and ritonavir). Verapamil was used as the prototypic inhibitor of P-gp and resulted in 1,4- to two-fold increase in AUC and 1,5-fold increase in C_{max}. Co-administration of erythromycin with ONBREZ BREEZHALER resulted in an increase of 1,4- to 1,6-fold for AUC and 1,2 fold for C_{max}. Combined inhibition of P-gp and CYP3A4 by the very strong dual inhibitor ketoconazole caused a 2-fold and 1,4-fold increase in AUC and C_{max}, respectively. Concomitant treatment with ritonavir, another dual inhibitor of CYP3A4 and P-gp, resulted in a 1,6- to 1,8-fold increase in AUC whereas C_{max} was unaffected. Taken together, the data suggest that systemic clearance is influenced by modulation of both P-gp and CYP3A4 activities and that the 2-fold AUC increase caused by the strong dual inhibitor ketoconazole reflects the impact of maximal combined inhibition. The magnitude of exposure increases due to medicine interactions does not raise any safety concerns given the safety experience of treatment with ONBREZ BREEZHALER in clinical trials of up to one year at doses two- to four-fold the recommended therapeutic doses.

ONBREZ BREEZHALER has not been shown to cause medicine interactions with co-medications. *In vitro* investigations have indicated that indacaterol has negligible potential to cause metabolic interactions with medicines at the systemic exposure levels achieved in clinical practice.

4.6 Fertility, pregnancy and lactation

Pregnancy:

Safety in pregnancy and breastfeeding has not been demonstrated.

Labour and delivery

ONBREZ BREEZHALER may inhibit labour due to a relaxant effect on uterine smooth muscle.

4.7 Effect on the ability to drive and use machines

ONBREZ BREEZHALER will have no or negligible influence on the ability to drive and use machines.
If you experience headaches or neck pain after treatment with ONBREZ BREEZHALER, do not drive or use machines until you have confirmed that ONBREZ BREEZHALER does not affect your performance.

4.8 Undesirable effects

The safety experience with ONBREZ BREEZHALER comprises exposure of up to one year at doses two- to four-fold the recommended therapeutic doses. The most common adverse medicine reactions at the recommended doses were nasopharyngitis, upper respiratory tract infection, cough headache and muscle spasms.

The ONBREZ BREEZHALER Phase III clinical development program consisted of 16 key studies and enrolled over 9 000 patients with a clinical diagnosis of moderate to severe COPD. Safety data from 11 of these studies with treatment durations of 12 weeks or longer were pooled from 4 764 patients exposed to indacaterol up to 600 microgram once-daily, of which 2 611 were on treatment with 150 microgram once-daily and 1 157 on treatment with 300 microgram once-daily. Approximately 41 % of patients had severe COPD. The mean age of patients was 64 years, with 48 % of patients aged 65 years or older, and the majority (80 %) was Caucasian.

Adverse medicine reactions are from this pooled COPD safety database, listed according to MedDRA system organ class and sorted in descending order of frequency on ONBREZ BREEZHALER 150 µg once -daily. Within each system organ class, the adverse reactions are ranked by frequency, with the most frequent reactions first. In addition, the corresponding frequency category using the following convention (CIOMS III) is also provided for each adverse reaction: Very common (≥1/10); common (≥1/100, <1/10); uncommon (≥1/1 000, <1/100); rare (≥1/10 000, <1/1 000); very rare (<1/10 000).

Infections and infestations

Very common: Nasopharyngitis, upper respiratory tract infection

Common: sinusitis

Immune system disorders

Uncommon: Hypersensitivity[1]

Respiratory, thoracic and mediastinal disorders

Common: Cough, oropharyngeal pain (including throat irritation), rhinorrhoea

Uncommon: Paradoxical bronchospasm

Nervous system disorders

Common: Headache, dizziness

Uncommon: Paraesthesia

Skin and subcutaneous tissue disorders

Common: Pruritus/rash

Musculoskeletal and connective tissue disorders

Common: Muscle spasm, musculoskeletal pain

Uncommon: Myalgia

Cardiac disorders

Common: Palpitations, ischaemic heart disease

Uncommon: Atrial fibrillation, tachycardia

General disorders and administration site conditions

Common: Chest pain, peripheral oedema

Metabolism and nutrition disorders

Common: Diabetes mellitus and hyperglycaemia

Adverse medicine reactions selected based on pooled COPD safety database frequencies based on percentage of patients with respective

adverse medicine reactions in the COPD safety population; frequency category based on 150 microgram or 300 microgram dose, whichever had higher rate. [1] Reports of hypersensitivity have been received from post-approval marketing experience in association with the use of ONBREZ BREEZHALER, Because these were reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate the frequency or establish a causal relationship to medicine exposure. Therefore the frequency was calculated from clinical trial experience.

Selected adverse medicine reactions

In Phase III clinical studies, health care providers observed that at clinic visits on average 17- 20 % of patients experienced sporadic cough that occurred usually within 15 seconds following inhalation and typically lasted for 5 seconds. This cough experienced post inhalation was generally well tolerated and did not lead to any patient discontinuing from the studies at the recommended doses (cough is a symptom of COPD and up to 8,2 % of patients reported cough as an adverse event). There is no evidence that cough experienced post inhalation is associated with bronchospasm, exacerbations, and deteriorations of disease or loss of efficacy.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions allows continued monitoring of the benefit/risk balance of ONBREZ BREEZHALER. Healthcare professionals are asked to report any suspected adverse reactions via patientsafety.sacg@novartis.com and via the "6.04 Adverse Drug Reaction Reporting Form" found online under SAHPRA`s publications: https://www.sahpra.org.za/Publications/Index/8.

4.9 Overdose

In COPD patients, single doses of 10 times the maximum recommended therapeutic dose were associated with a moderate increase in pulse rate, systolic blood pressure increase and QTc interval.

An overdose of ONBREZ BREEZHALER is likely to lead to exaggerated effects typical of beta$_2$-adrenergic stimulants *i.e.*, tachycardia, tremor, palpitations, headache, nausea, vomiting, drowsiness, ventricular dysrhythmias, metabolic acidosis, hypokalaemia and hyperglycaemia.

Supportive and symptomatic treatment is indicated. In serious cases, patients should be hospitalised. Use of cardio selective beta-blockers may be considered, but only under the supervision of a medical practitioner and with extreme caution since the use of beta-adrenergic blockers may provoke bronchospasm.

5 PHARMACOLOGICAL PROPERTIES

PHARMACOLOGICAL CLASSIFICATION

A 10.2.1 Medicines acting on respiratory system. Bronchodilators (inhalants).

5.1 Pharmacodynamic properties:

Indacaterol is a long-acting beta2-adrenergic agonist. The pharmacological effects of indacaterol, are at least in part attributable to stimulation of intracellular adenyl cyclase, the enzyme that catalyzes the conversion of adenosine tri-phosphate (ATP) to cyclic-3', 5'-adenosine monophosphate (cyclic mono-phosphate). Increased cyclic AMP levels cause relaxation of bronchial smooth muscle. In vitro studies have shown that indacaterol has more than 24-fold greater agonist activity at beta2-receptors compared to beta1-receptors and 20-fold greater agonist activity compared to beta3-receptors.

When inhaled, indacaterol acts locally in the lung as a bronchodilator. In isolated human bronchus, indacaterol has a rapid onset of action and a long duration of action.

Primary Pharmacodynamic Effects

Indacaterol provided consistently significant improvement in lung function (FEV1) over 24 hours in a number of clinical pharmacodynamic and efficacy trials. There was a rapid onset of action within 5 minutes after inhalation of indacaterol and a peak effect occurring between 2-4 hours following the dose. There was no evidence for tachyphylaxis to the bronchodilator effect after repeated dosing for up to 52 weeks. The bronchodilator effect did not depend on the time of dosing (morning or evening).

Secondary Pharmacodynamic Effects

The characteristic adverse effects of inhaled indacaterol occur as a result of activation of systemic beta-adrenergic receptors. The most common adverse effects include skeletal muscle tremor and cramps, insomnia, tachycardia, decreases in serum potassium and increases in plasma glucose.

Effects on cardiac electrophysiology

The effect of indacaterol on the QT interval was evaluated in a double-blind, placebo- and active (moxifloxacin)-controlled study following multiple doses of indacaterol 150 microgram, 300 microgram or 600 microgram once-daily for 2 weeks in 404 healthy volunteers. Fridericia's method for heart rate correction was employed to derive the corrected QT interval (QTcF). Maximum mean prolongation of QTcF intervals were <5 ms, and the upper limit of the 90 % confidence interval was below 10 ms for all time-matched comparisons versus placebo. There was no evidence of a concentration-delta QTc relationship in the range of doses evaluated.

Electrocardiographic monitoring in patients with COPD

The effect of indacaterol on heart rate and rhythm was assessed using continuous 24-hour ECG recording (Holter monitoring) in a subset of 605 patients with COPD from a 26-week, double-blind, placebo-controlled Phase III

study. Holter monitoring occurred once at baseline and up to 3 times during the 26-week treatment period (at weeks 2, 12 and 26).

A comparison of the mean heart rate over 24 hours showed no increase from baseline for doses evaluated, 150 microgram once-daily and 300 microgram once-daily. The hourly heart rate analysis was similar for both doses compared to placebo and tiotropium. The pattern of diurnal variation over 24 hours was maintained and was similar to placebo.

No difference from placebo was seen in the rates of atrial fibrillation, time spent in atrial fibrillation and also the maximum ventricular rate of atrial fibrillation. No clear patterns in the rates of single ectopic beats, couplets or runs were seen across visits.

Because the summary data on rates of ventricular ectopic beats can be difficult to interpret, specific pro-dysrhythmic criteria were analysed. In this analysis, baseline occurrence of ventricular ectopic beats was compared to change from baseline, setting certain parameters for the change to describe the pro-dysrhythmic response. The number of patients with a documented pro-dysrhythmic response was very similar across both indacaterol doses compared to placebo.
Overall, there was no clinically relevant difference in the development of dysrhythmic events in patients receiving indacaterol treatment over those patients who received placebo.

Effects on serum potassium and plasma glucose

Changes in serum potassium and plasma glucose were evaluated in a 26-week, double-blind, placebo-controlled Phase III study. At 1 hour post-dose at week 12, mean changes compared to placebo in serum potassium ranging from 0,03 to 0,05 mmol/L and in mean plasma glucose ranging from 0,25 to 0,31 mmol/L were observed.

5.2 Pharmacokinetic properties

Absorption

The median time to reach peak serum concentrations of indacaterol was approximately 15 min after single or repeated inhaled doses. Systemic exposure to indacaterol increased with increasing dose (150 microgram to 600 microgram) in a dose proportional manner. Absolute bioavailability of indacaterol after an inhaled dose was on average 43 - 45 %. Systemic exposure results from a composite of pulmonary and intestinal absorption.

Indacaterol serum concentrations increased with repeated once-daily administration. Steady state was achieved within 12 to15 days. The mean accumulation ratio of indacaterol, i.e., AUC over the 24-h dosing interval on Day 14 or Day 15 compared to Day 1, was in the range of 2,9 to 3,5 for once-daily inhaled doses between 75 microgram and 600 microgram.

Distribution

After intravenous infusion the volume of distribution (VD) of indacaterol was 2 361 l to 2 557 l indicating an extensive distribution. The in vitro human serum and plasma protein binding was 94,1 to 95,3 % and 95,1 to 96,2 %, respectively.

Biotransformation/Metabolism

After oral administration of radiolabelled indacaterol in a human ADME (absorption, distribution, metabolism, excretion) study, unchanged indacaterol was the main component in serum, accounting for about one third of total indacaterol-related AUC over 24 h. A hydroxylated derivative was the most prominent metabolite in serum. Phenolic O-glucuronides of indacaterol and hydroxylated indacaterol were further prominent metabolites. A diastereomer of the hydroxylated derivative, a N-glucuronide of indacaterol, and C- and N-dealkylated products were further metabolites identified.

In vitro investigations indicated that UGT1A1 is the only UGT isoform that metabolised indacaterol to the phenolic O-glucuronide. The oxidative metabolites were found in incubations with recombinant CYP1A1, CYP2D6, and CYP3A4. CYP3A4 is concluded to be the predominant isoenzyme responsible for hydroxylation of indacaterol. In vitro investigations further indicated that indacaterol is a low affinity substrate for the efflux pump.

Elimination

In clinical studies, which included urine collection, the amount of indacaterol excreted unchanged via urine was generally lower than 2 % of the dose. Renal clearance of indacaterol was, on average, between 0,46 and 1,20 L/h. When compared with the serum clearance of indacaterol of 18,8 to 23,3 L/h, it is evident that renal clearance plays a minor role (about 2 to 6 % of systemic clearance) in the elimination of systemically available indacaterol.

In a human ADME study where indacaterol was given orally, the faecal route of excretion was dominant over the urinary route. Indacaterol was excreted into human faeces primarily as unchanged parent substance (54 % of the dose) and, to a lesser extent, hydroxylated indacaterol metabolites (23 % of the dose). Mass balance was complete with ≥90 % of the dose recovered in the excreta.

Indacaterol serum concentrations declined in a multi-phasic manner with an average terminal half-life ranging from 45,5 to 126 hours. The effective half-life, calculated from the accumulation of indacaterol after repeated dosing ranged from 40 to 56 hours, which is consistent with the observed time-to-steady state of approximately 12 to 15 days.

Special Populations

A population analysis of the effect of age, gender and weight on systemic exposure in COPD patients after inhalation indicated no significant differences. It did not suggest any difference between ethnic subgroups in this population. Limited treatment experience is available for the black population.

The pharmacokinetics of indacaterol was investigated in two different UGT1A1 genotypes – the fully functional [(TA) 6, (TA) 6] genotype and the low activity [(TA) 7, (TA)7] genotype (Gilbert's syndrome genotype). The study demonstrated that steady-state AUC and Cmax of indacaterol were 1,2-fold higher in the [(TA)7, (TA)7] genotype, indicating that systemic exposure to indacaterol is only insignificantly affected by this UGT1A1 genotypic variation.

Patients with mild and moderate hepatic impairment showed no relevant changes in Cmax or AUC of indacaterol, nor did protein binding differ between mild and moderate hepatic impaired subjects and their healthy controls. Studies in subjects with severe hepatic impairment were not performed.

Due to the very low contribution of the urinary pathway to total body elimination, a study in renally impaired subjects was not performed.

6 PHARMACEUTICAL PARTICULARS

6.1 EXCIPIENTS:

List of excipients: Lactose monohydrate and gelatin.

6.2 Incompatibilities

Not applicable.

6.3 Shelf-life

24 Months

6.4 Special precautions for storage

Store at or below 30 °C.

ONBREZ BREEZHALER capsules must always be stored in the blister to protect from moisture and only removed immediately before use.

KEEP ALL MEDICINES OUT OF THE REACH OF CHILDREN.

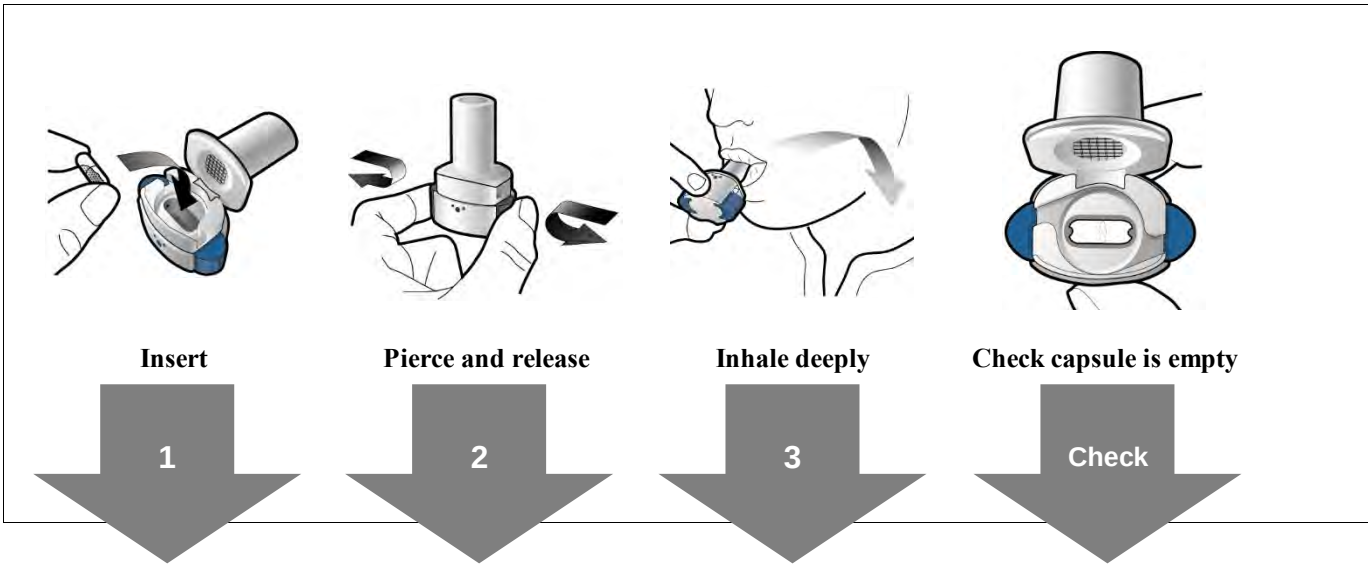
6.5 Nature and contents of container

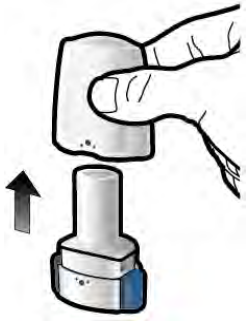
ONBREZ BREEZHALER® 150 µg: 30 or 60 capsules in aluminium blister strips and 1 inhaler. Each blister contains 10 capsules.

6.6 Special precautions for disposal and other handling

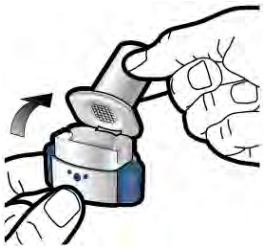
When prescribing ONBREZ BREEZHALER patients should be instructed on correct use of the inhaler.

Instructions for use





Step 1a:
Pull off cap



Step 1b:
Open inhaler



Step 2a:
Pierce capsule once

Hold the inhaler upright.

Pierce capsule by firmly pressing both side buttons at the same time.
You should hear a noise as the capsule is pierced.

Only pierce the capsule once.



Step 2b:
Release side buttons



Step 3a:
Breathe out fully
Do not blow into the inhaler.



Step 3b:
Inhale medicine deeply

Hold the inhaler as shown in the picture.

Place the mouthpiece in your mouth and close your lips firmly around it.

Do not press the side buttons.

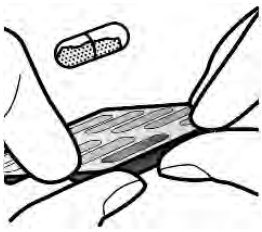


Check capsule is empty
Open the inhaler to see if any powder is left in the capsule.

If there is powder left in the capsule:
- Close the inhaler.
- Repeat steps 3a to 3c.



Powder Remaining **Empty**



Step 1c:
Remove capsule

Remove one capsule from the blister.

Do not swallow the capsule.



Step 1d:
Insert capsule
Never place a capsule directly into the mouthpiece.

Breathe in quickly and as deeply as you can.

During inhalation you will hear a whirring noise.

You may taste the medicine as you inhale.



Step 3c:
Hold breath

Hold your breath for up to 5 seconds.



Remove empty capsule

Put the empty capsule in your household waste.

Close the inhaler and replace the cap.

Important Information

- Onbrez Breezhaler capsules must always be stored in the blister card and only removed immediately before use.
- Do not swallow the capsule.
- Do not use the Onbrez Breezhaler capsules with any other inhaler.



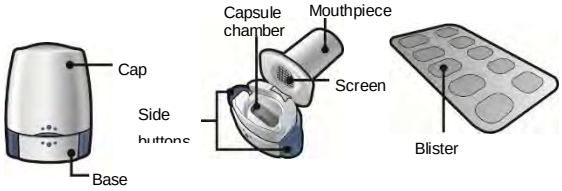
Step 1e:

Close inhaler

- Do not use the Onbrez Breezhaler inhaler to take any other capsule medicine.
- Never place the capsule into your mouth or the mouthpiece of the inhaler.
- Do not press the side buttons more than once.
- Do not blow into the mouthpiece.
- Do not press the side buttons while inhaling through the mouthpiece.
- Do not handle capsules with wet hands.
- Never wash your inhaler with water.

Your Onbrez Breezhaler Inhaler pack contains:

- One Onbrez Breezhaler inhaler
- One or more blister cards, each containing either 6 or 10 Onbrez Breezhaler capsules to be used in the inhaler



Inhaler **Inhaler base** **Blister Card**

Frequently Asked Questions

Why didn't the inhaler make a noise when I inhaled?

The capsule may be stuck in the capsule chamber. If this happens, carefully loosen the capsule by tapping the base of the inhaler. Inhale the medicine again by repeating steps 3a to 3c.

What should I do if there is powder left inside the capsule?

You have not received enough of your medicine. Close the inhaler and repeat steps 3a to 3c.

I coughed after inhaling – does this matter?

This may happen. As long as the capsule is empty you have received enough of

Cleaning the inhaler

Wipe the mouthpiece inside and outside with a clean, dry, lint-free cloth to remove any powder residue.

Keep the inhaler dry. Never wash your inhaler with water.

	your medicine. **I felt small pieces of the capsule on my tongue – does this matter?** This can happen. It is not harmful. The chances of the capsule breaking into small pieces will be increased if the capsule is pierced more than once.	**Disposing of the inhaler after use** Each inhaler should be disposed of after all capsules have been used. Ask your pharmacist how to dispose of medicines and inhalers that are no longer required.

7 MARKETING AUTHORISATION HOLDER

Novartis South Africa (Pty) Ltd

Magwa Crescent West

Waterfall City

Jukskei View

Johannesburg

2090

8 MARKETING AUTHORISATION NUMBER(S)

ONBREZ BREEZHALER® 150 µg: 44/10.2.1/0544

9 DATE OF FIRST AUTHORISATION

Date of registration: 07 June 2012

10 DATE OF REVISION OF THE TEXT

23 August 2020

Namibia: 13/10/2/1/0150	(NS2)
Botswana: BOT1302284	(S2)