

Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986

This medicine is to be supplied upon physician's prescription only

Spiolto[®] Respimat[®]

Inhalation solution

Each actuation releases:

2.5 microgram tiotropium (as bromide monohydrate)

2.5 microgram olodaterol (as hydrochloride)

2 puffs, comprising one medicinal dose, contain:

5 microgram tiotropium (as bromide monohydrate)

5 microgram olodaterol (as hydrochloride)

Inactive ingredients and allergens in the medicine: see section 'Important information about some of this medicine's ingredients' in section 2 and section 6 'Additional information'.

Read the entire leaflet carefully before using this medicine. This leaflet contains essential information about this medicine. If you have any further questions, refer to the physician or the pharmacist.

This medicine has been prescribed to treat your illness. Do not pass it on to others. It may harm them, even if it seems to you that their illness is similar.

1. What is this medicine intended for?

Spiolto Respimat is indicated as a maintenance bronchodilator treatment to relieve symptoms in patients with chronic obstructive pulmonary disease (COPD).

Therapeutic group: Long acting bronchodilators. Tiotropium belongs to the sub-group of anticholinergics. Olodaterol belongs to the sub-group of long acting β_2 receptor agonists.

More about the medicine

Spiolto Respimat helps adult patients who have chronic obstructive pulmonary disease (COPD) to breathe more easily. COPD is a long-term lung disease that causes shortness of breath and coughing. The medical term COPD describes the conditions chronic bronchitis and emphysema.

Spiolto Respimat helps to open your airways and make it easier to get air in and out of the lungs. Regular use of Spiolto Respimat may help you when you suffer from persistent shortness of breath resulting from your illness, and will also help to minimise the effects of the disease on your everyday life.

As COPD is a long-term disease you should take Spiolto Respimat every day and not only when you have breathing problems or other symptoms related to the disease.

2. Before using this medicine

Do not use this medicine if:

- You are sensitive (allergic) to the active ingredients tiotropium or olodaterol or to any of the other ingredients that this medicine contains (for the list of inactive ingredients, see section 6).
- You are sensitive (allergic) to atropine or substances related to it, e.g. ipratropium or oxitropium.

Special warnings regarding the use of this medicine**Before the treatment with Spiolto Respimat tell your physician if you:**

- have asthma (you should not use Spiolto Respimat for the treatment of asthma).
- have diseases of the heart.
- have high blood pressure.
- have epilepsy.
- have a specific thyroid gland problem called thyrotoxicosis.
- have an abnormal widening of an artery called aneurysm.
- have diabetes.
- have severe liver disease.
- have kidney disease.
- are about to have a planned surgery.
- have an eye problem called narrow-angle glaucoma.
- have prostate problems or have difficulty passing urine.

Special warnings

- **Stop using the medicine and contact your physician immediately** if you experience tightness of the chest, coughing, wheezing or breathlessness immediately after using the medicine. These may be signs of a condition called bronchospasm (see section 4 – 'Side effects').
- If your breathing has got worse or if you experience rash, swelling or itching directly after using your inhaler, stop using this medicine and consult your physician immediately (see section 4 - 'Side effects').
- If you experience any side effects affecting your heart (increase in pulse rate, increase in blood pressure and/or increase in symptoms like chest pain), tell your physician immediately (see section 4 - 'Side effects').
- If you experience muscle spasm, muscle weakness or abnormal heart rhythm, consult your physician as these may be related to low blood levels of potassium (see section 4 - 'Side effects').

Avoid contact of the medicine with your eyes. This may result in eye pain or discomfort, blurred vision, seeing halos around lights or colored images in association with red eyes (i.e. narrow angle glaucoma). The eye symptoms may be accompanied by headache, nausea or vomiting. Immediately wash your eyes in warm water, stop using Spiolto Respimat and immediately consult your physician for further advice.

Spiolto Respimat is indicated for maintenance treatment of your chronic obstructive pulmonary disease. **It should not be used to treat a sudden attack of breathlessness or wheezing.**

Do not use Spiolto Respimat together with medicines containing active ingredients of the group of long-acting beta-adrenergic agonists, like salmeterol or formoterol.

If you regularly take medicines containing active ingredients of the group of short-acting beta-adrenergic agents, like salbutamol, continue using these medicines only to relieve acute symptoms such as acute shortness of breath.

Dry mouth which has been observed with anti-cholinergic treatment may in the long term be associated with dental caries. Therefore, please remember to pay attention to oral hygiene.

Do not take this medicine more frequently than once daily.

Children and adolescents

Spiolto Respimat **is not intended** for use **in children and adolescents** (under 18 years old).

Other medicines and Spiolto Respimat

If you are taking or have recently taken other medicines, including non-prescription medications and nutritional supplements, inform your physician or pharmacist.

Particularly if you are taking:

- Other medicines that are similar to Spiolto Respimat (containing similar active ingredients, such as anticholinergic medicines or beta-adrenergic agents). Use of these medicines may increase the risk of side effects.
- Medicines of the beta blockers group used for reduction of blood pressure or treatment of other heart problems (such as propranolol), or for eye problem called glaucoma (such as timolol). This may result in loss of the effect of Spiolto Respimat.
- Medicines that lower the amount of potassium in your blood, including:
 - steroids (e.g. prednisolone),
 - diuretics,
 - medicines for breathing problems (such as theophylline).

If you use these medicines together with Spiolto Respimat, symptoms such as muscle spasm, muscle weakness or abnormal heart rhythm may occur.

- Medicines of the group of tricyclic antidepressants or monoamine oxidase (MAO) inhibitors (like selegiline or moclobemide) that are used to treat neurological or psychiatric disorders like Parkinson's disease or depression; the use of these drugs will increase the likelihood that you experience side effects affecting your heart.

Pregnancy, breastfeeding, and fertility

If you are pregnant, think you may be pregnant, planning to have a baby or are breastfeeding, you should consult a physician before starting to take this medicine.

Do not use the medicine unless it has been explicitly recommended by the physician.

Driving and using machines

No studies of the effects on the ability to drive and use machines have been performed.

If you feel dizzy while taking Spiolto Respimat, do not drive or use any machines.

Important information about some of this medicine's ingredients

This medicine contains 0.0011 mg banzalkonium chloride in each actuation.

Benzalkonium chloride may cause wheezing or difficulty breathing (bronchospasm), especially if you have asthma.

3. How should you use the medicine?

Always use according to the physician's instructions. You should check with the physician or the pharmacist if you are unsure about dosage and how to take the medicine.

The dosage and treatment will be determined only by the physician.

Spiolto Respimat is for inhalation use only.

The standard dose for adults is usually:

Spiolto Respimat is effective for 24 hours so you will need to use Spiolto Respimat only **ONCE A DAY**, if possible at the same time of the day. Each time you use it take **TWO PUFFS**.

As COPD is a long-term disease take Spiolto Respimat every day and not only when you experience breathing problems.

Do not exceed the recommended dose.

Dosage for children and adolescents

Spiolto Respimat is not intended for use in children and adolescent under 18 years old.

Make sure that you understand how to use the Spiolto Respimat inhaler properly. The instructions for use of the Spiolto Respimat inhaler are provided below.

If you have accidentally taken a higher dose

If you have taken an overdose, or if a child has accidentally swallowed some medicine, contact the physician immediately or go to a hospital emergency room and bring the medicine package with you. If you have taken a higher dose, you may be at a higher risk of experiencing side effects such as dry mouth, constipation, difficulties passing urine, blurred vision, chest pain, high or low blood pressure, faster or irregular heartbeat or feeling of heart beat, dizziness, nervousness, difficulty in sleeping, anxiety, headache, shaking, muscle cramps, nausea, fatigue, malaise, low blood levels of potassium (which may cause symptoms of muscle spasm, muscle weakness or abnormal heart rhythm), high blood sugar, or high acid level in your blood (which may cause symptoms such as nausea, vomiting, weakness, muscle cramps and more rapid breathing).

If you forget to take the medicine

If you forgot to take your daily dose, take the next dose at the usual time on the next day. Do not take a double dose to make up for a forgotten dose.

If you stop taking the medicine

Before you stop taking Spiolto Respimat, you should consult your physician or pharmacist. If you stop the treatment prematurely, your signs and symptoms of COPD may worsen.

Do not take medicines in the dark! Check the label and the dose each time you take the medicine. Wear glasses if you need them.

If you have any further questions regarding the use of this medicine, consult the physician or the pharmacist.

4. Side effects

As with any medicine, Spiolto Respimat may cause side effects in some users. Do not be alarmed by reading the list of side effects. You may not experience any of them.

Stop the treatment with this medicine and contact the physician immediately if:

- Immediate allergic reactions to this medicine are rare (they affect up to 1 user in 1,000). These reactions may occur individually or as part of a severe allergic reaction (anaphylactic reaction) after administration of Spiolto Respimat. These include rash, nettle rash (urticaria), swelling of the mouth and face, sudden difficulties in breathing (angioedema) or other hypersensitivity reactions (such as sudden reduction of your blood pressure or dizziness).
- As with all medicines for inhaling, you may experience tightness in your chest together with coughing, wheezing, or shortness of breath immediately after inhaling the medicine (paradoxical bronchospasm). The frequency of this cannot be estimated from the available data.
- Seeing halos around lights or colored images in association with red eyes (glaucoma). The frequency of this side effect is not known.
- Blocked intestine or absence of bowel movement (including ileus paralytic). The frequency of this side effect is not known.

Uncommon side effects: may affect up to 1 in 100 users

- Rapid heart rate (tachycardia)
- Dizziness
- Headache
- Cough
- Hoarseness
- Dry mouth

Rare side effects: may affect up to 1 in 1,000 users

- Irregular heartbeat (atrial fibrillation)
- Rapid heartbeat (supraventricular tachycardia)
- feeling your heartbeats (palpitations)
- High blood pressure (hypertension)
- Difficulty passing urine (urinary retention)
- Urinary tract infection
- Painful urination
- Sore throat
- Inflammation of the throat
- Inflammation of the gums
- Inflammation of the mouth (stomatitis)
- Fungal infections of the oral cavity and throat
- Nosebleed
- Difficulty sleeping (insomnia)
- Blurred vision
- Tightness of the chest associated with coughing, wheezing or breathlessness immediately after inhalation (bronchospasm)
- Constipation
- Feeling sick (nausea)
- Itching
- Joint pain
- Swelling of joints
- Back pain

Unknown frequency side effects (cannot be estimated from the available data)

- Increase in intraocular pressure
- Inflammation of the nose and throat (nasopharyngitis)
- Inflammation of the sinuses (sinusitis)
- Difficulty swallowing
- Inflammation of the tongue
- Heartburn
- Dental caries
- Infections or ulcerations of the skin
- Dryness of the skin
- Dehydration

You may also experience side effects which are known to occur during treatment with other medicines for breathing problems with mechanism of action similar to that of Spiolto Respimat (active ingredients of the group of beta-adrenergic agents):

Irregular heartbeat, chest pain, low blood pressure, shaking, nervousness, muscle cramps, fatigue, malaise, low blood levels of potassium (which may cause symptoms such as: muscle spasm, muscle weakness or abnormal heart rhythm), high blood sugar, or too much acid in your blood (which may cause symptoms such as: nausea, vomiting, weakness, muscle cramps and more rapid breathing).

If any side effect appears, if any side effect gets worse, or if you suffer from a side effect not mentioned in the leaflet, you should consult the physician.

Reporting side effects

You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Medication' on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects. You can also use this link:

<https://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.gov.il>

5. How to store the medicine?

- Avoid poisoning! This medicine and any other medicine should be kept in a closed place out of sight and reach of children and/or infants in order to avoid poisoning. Do not induce vomiting without an explicit instruction from the physician.
- Do not use the medicine after the expiry date (exp. date) appearing on the carton and label. The expiry date refers to the last day of that month.
- Do not use Spiolto Respimat for more than 3 months after the first use (see instructions for use below in the leaflet).
- Store the medicine at a temperature below 25°C.
- Do not freeze.
- Do not discard the medicine to the wastewater or household waste. Consult the pharmacist about how to dispose of the medicine. These measures will help in environmental protection.

6. Additional information

The active substances are tiotropium and olodaterol. The delivered dose is 2.5 microgram tiotropium (as bromide monohydrate) and 2.5 microgram olodaterol (as hydrochloride) per

puff.

The delivered dose is the dose which is available for the patient after passing the mouthpiece.

- In addition to the active ingredients the medicine also contains:
Benzalkonium chloride, disodium edetate, purified water and hydrochloric acid for pH adjustment.
- What does the medicine look like and what are the contents of the package:
The package of Spiolto Respimat contains one cartridge of inhalation solution and one Respimat inhaler. Attach the cartridge to the inhaler before the first use.
The cartridge content is sufficient for 60 puffs (30 medicinal doses). See instructions for use below in the leaflet.
- Registration holder: Boehringer Ingelheim Israel Ltd., 89 Medinat Ha-Yehudim, P.O.B. 4124, Hertzliya-Pituach 4676672.
- Manufacturer: Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim am Rhein, Germany.
- This leaflet was checked and approved by the Ministry of Health in August 2018 and revised in May 2019 in accordance with Ministry of Health guidelines.
- Registration number of the medicine in the National Drug Registry of the Ministry of Health: 155-58-34508-00

Instructions for Use

Introduction

Spiolto Respimat (tiotropium bromide and olodaterol). Please read the instructions before you start using Spiolto Respimat. Use this inhaler **only ONCE A DAY**. Each time you use it take **TWO PUFFS**.



- If you have not used Spiolto Respimat for more than 7 days, start by releasing one puff toward the ground.
- If you have not used Spiolto Respimat for more than 21 days, repeat steps 4-6 until you see a visible cloud. Then repeat steps 4-6 three more times.

How to care for your inhaler

Clean the mouthpiece including the metal part inside the mouthpiece with a damp cloth or tissue, at least once a week.

Any minor discoloration in the mouthpiece does not affect the performance of your Spiolto Respimat inhaler.

If necessary, wipe the outside of your Spiolto Respimat inhaler with a damp cloth.

When to get a new Spiolto Respimat inhaler:









- The Spiolto Respimat inhaler contains 60 puffs (30 doses) when used according to the instructions (two puffs/once a day). The dose counter on the inhaler shows the number of remaining puffs.
- When the counter points to the red area on the scale, you have enough doses for about 7 days (14 puffs).
- When the counter reaches the end of the red area on the scale, the Spiolto Respimat

locks automatically – you will not be able to release any more doses. At this point, you will not be able to turn the clear base any more.

- Discard the Spiolto Respimat inhaler three months after first preparing it for use, even if you have not used it up or you have not used it at all.

Preparing Spiolto Respimat for first use:

<p>1. Remove the clear base</p> <ul style="list-style-type: none"> • Make sure the cap is closed. • Press the safety catch while pulling off the clear base with your other hand. 	
<p>2. Inserting the cartridge</p> <ul style="list-style-type: none"> • Insert the narrow end of the cartridge into the inhaler. • Place the inhaler on a firm surface and press down until the cartridge is all the way in. 	
<p>3. Putting the clear base back</p> <ul style="list-style-type: none"> • Push the clear base back into place until you hear a click 	
<p>4. Turn</p> <ul style="list-style-type: none"> • Make sure the cap is closed. • Turn the clear base in the direction of the arrows on the label until you hear a click (half a turn). 	
<p>5. Open</p> <ul style="list-style-type: none"> • Open the cap until it is fully open. 	
<p>6. Press</p> <ul style="list-style-type: none"> • Point the inhaler at the ground. • Press the dose release button. • Close the cap. • Repeat steps 4-6 until you have a visible cloud. • After you created a visible cloud, repeat steps 4-6 three more times. <p>Your inhaler is ready to use and will be able to deliver 60 puffs (30 doses).</p>	

Daily use

Turn

- Make sure the cap is closed.
- **Turn** the clear base in the direction of the arrows on the label until you hear a click (half a turn).



Open

- Open the cap until it is fully open.



Press

- Breathe out fully and slowly.
- Close your lips around the mouthpiece without covering the air vents.
- While breathing in deeply and slowly through your mouth, **press** the dose release button and continue to breathe in.
- Hold your breath for 10 seconds or for as long as comfortable.
- Repeat the steps **Turn-Open-Press** one more time so that you get a total of two puffs.

