PACKAGE LEAFLET: INFORMATION FOR THE USER

Berodual Respimat, oplossing voor inhalatie 20 microgram/ 50 microgram
ipratropium bromide monohydrate/fenoterol hydrobromide

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Berodual Respimat 20/50 microgram/dose is and what it is used for

Berodual Respimat is a medicine that contains two active ingredients (the anticholinergic agent ipratropim bromide and the beta2-agonist fenoterol hydrobromide) in combination. Both active ingredients relax the airway muscles and thus cause the bronchi to widen.

Berodual Respimat is used to prevent and to treat Bronchial spasms (bronchospasms) in asthma and chronic obstructive pulmonary disease (COPD). COPD is a long-term lung disease that causes shortness of breath and coughing. A concomitant ant-inflammatory therapy should be considered.

2. What you need to know before you take Berodual Respimat

Please read the following questions carefully. If you can answer any of these questions with `**Yes**` please discuss this with your doctor **before** taking **Berodual Respimat**

- are you allergic to the active substances (ipratropium bromide monohydrate and fenoterol hydrobromide), to atropine or similar drugs or to the other ingredients of this medicine?
- are you taking any other medicinal products containing atropine-like substances?
- are you pregnant, do you think you are pregnant, or are you breastfeeding?
- are you suffering from fast heartbeat or irregular heartbeats (tachyarrhythmia) or from a disease of the heart muscle with muscular narrowing of the outflow tract of the left ventricle (hypertrophic obstructive cardiomyopathy)?
- do you have a history of heart disease, irregular heartbeat or chest pain (angina pectoris)?

Do not take Berodual Respimat
- if you are allergic to the active substances (ipratropium bromide monohydrate and fenoterol hydrobromide), to any of the other ingredients of this medicine (listed in section 6) or to other atropine-like substances

- if you suffer from fast heartbeat with irregular heartbeat (tachyarrhythmia) or from a disease of the heart muscle with muscular narrowing of the outflow tract of the left ventricle (hypertrophic obstructive cardiomyopathy).

Warnings and precautions

Talk to your doctor immediately in the event of acute, rapidly worsening breathlessness.

In rare cases, immediate hypersensitivity reactions may occur following the use of Berodual Respimat, such as nettle rash, swelling of the face, skin and mucous membranes involving the mucous membrane of the mouth and throat, rash, spasms of the airways and severe allergic reactions called anaphylaxis that may be life-threatening.

As with other inhaled medicines Berodual Respimat may result in a coughing spell similar to an asthma attack (called paradoxical bronchospasm) that may be life-threatening. If this event occurs Berodual Respimat should be discontinued immediately and alternative therapy substituted. Therefore, contact your doctor immediately.Berodual Respimat, like other drugs of the same class (anticholinergic agents), should be used with caution if you are predisposed to increased intra-ocular pressure (narrow-angle glaucoma).

When taking Berodual Respimat take care not to let any spray enter your eyes. If any spray does get into your eyes you may get widening of the pupils, increased intra-ocular pressure (narrow-angle glaucoma) and eye pain. Talk to your doctor for further advice.

NOTE
Your doctor must therefore instruct you in the correct use of Berodual Respimat. Care must be taken not to allow the product to enter the eyes.

Signs of acute narrow-angle glaucoma may be:
- eye pain or discomfort
- blurred vision
- coloured rings around sources of light
- unreal colour sensation
- red eyes due to the congestion of blood in the conjunctiva or cornea.

Should any combination of these symptoms develop, you should seek specialist advice immediately so that treatment with pupil-narrowing (miotic) eye drops can be initiated.

<u>Particular caution should also be taken with Berodual Respimat if you suffer from the following, particularly if the recommended dosage is exceeded:</u>
- insufficiently controlled diabetes mellitus
- recent heart attack
- severe organic heart or vascular disorders
- hyperfunctioning of the thyroid gland (hyperthyroidism)
- tumour of the adrenal marrow (phaeochromocytoma)
- urinary outflow tract obstruction (e.g. if you have an enlargement of the prostate gland (prostatic hyperplasia) or a bladder-neck obstruction)

The administration of high doses of beta2-agonists (as also contained in Berodual Respimat) can result in a marked fall in potassium levels in the blood (hypokalaemia).

Patients with cystic fibrosis may be more prone to disturbances of the capacity for movement in the gastro-intestinal region (gastro-intestinal motility disorders) when treated with inhaled anticholinergics (as also contained in Berodual Respimat).

Information about prolonged use of Berodual Respimat:
If you suffer from bronchial asthma Berodual Respimat should be used only on an as-needed basis. If you suffer from mild chronic obstructive pulmonary disease (COPD), on demand treatment (symptom-oriented) may be preferable to regular use.

If you suffer from asthma or steroid-responsive COPD you should discuss with your doctor whether the addition or increase of anti-inflammatory therapy should be considered to control airway inflammation and to prevent your condition from worsening.

In asthma patients, the use of increasing amounts of $beta_2$-agonist containing products, such as Berodual Respimat, to treat bronchial obstruction may suggest that the condition is worsening.

If bronchial obstruction deteriorates, it is inappropriate and possibly hazardous to simply increase the use of medicines containing $beta_2$-agonists (such as Berodual Respimat) beyond the recommended dose over extended periods of time.

In these circumstances, your doctor should review the treatment plan and, in particular, the adequacy of anti-inflammatory therapy with inhaled corticosteroids to prevent a potentially life-threatening worsening of your symptoms.

Other bronchodilating products with $beta_2$-agonists should only be used in combination with Berodual Respimat under medical supervision.

Children and adolescents

Berodual Respimat is not recommended for use in children below 18 years due to insufficient data on safety and efficacy.

Other medicines and Berodual Respimat

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.
The long-term use of Berodual Respimat together with other medicines in the same class (anticholinergic drugs) has not been studied. Therefore, the long-term use of Berodual Respimat together with other anticholinergic drugs is not recommended.

The effect of Berodual Respimat can be affected by the following drugs or drug groups if administered simultaneously.

Potentiation of the effect to the extent even of an increased risk of side effects:
- other beta-adrenergics (such as salbutamol or salmeterol used e.g. for treatment of symptoms in COPD or in asthma),
- other anticholinergics (such as tiotropium used e.g. for treatment of symptoms in COPD),
- xanthine derivatives (such as theophylline used e.g. for treatment of symptoms in COPD or in asthma),
- certain psychotropic agents (monoamine oxidase inhibitors used e.g. in major depression),
- certain medicines for depression (tricyclic antidepressants used e.g. for treatment of depressive and anxiety disorders),

- anaesthesia with halogenated hydrocarbons (e.g. halothane, trichlorethylene and enflurane used for inhalation anaesthesia).
  The effects on the cardiovascular system in particular may be increased.

Attenuation of the effect:
- certain blood pressure-lowering medicines (beta-receptor blockers used e.g. for therapy of high blood pressure)

Other possible interactions:
- A fall in potassium levels in the blood caused by beta2-agonists (as also contained in Berodual Respimat) can be increased by simultaneous treatment with xanthine derivatives (such as theophylline), certain anti-inflammatory medicines (corticosteroids) and water-eliminating medicines (diuretics).
  This should be borne in mind by your doctor, particularly if you have severe airway obstruction.
  - If you are taking medicines with the active ingredient digoxin (a medicine for treating heart failure) at the same time, the fall in potassium levels in the blood can increase the tendency to heart rhythm disorders. If a lack of oxygen (hypoxia) occurs in the body in addition to the deficiency of potassium, this can affect the heart rate. In these cases it is recommended that your doctor should monitor your serum potassium levels regularly.
  - The risk of an acute increase in intra-ocular pressure (attack of glaucoma, see also section "Warnings and precautions") is increased if aerosolised ipratropium bromide, either alone or in combination with a $beta_2$-agonists (as also contained in Berodual Respimat), comes into contact with the eyes.

Pregnancy and breastfeeding

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine. Your doctor will only prescribe Berodual Respimat for you after carefully assessing the risks and benefits.

Pregnancy
There are no sufficient data from the use of Berodual Respimat in pregnant women. Animal studies do not indicate a direct or indirect harmful effect. The potential risk for humans is unknown.

However, there is the possibility that the beta-adrenergic fraction in Berodual Respimat may inhibit labour. Your doctor should bear this in mind where appropriate.

Use of $beta_2$-agonist like fenoterol hydrobromide in the end of the pregnancy or in high doses may cause negative effects in the newborn baby (tremor, tachycardia, blood glucose fluctuations, hypokalaemia).

Breastfeeding
Studies in animals have shown that fenoterol hydrobromide passes into breast milk. It is not known whether ipratropium is excreted into breast milk. It is however unlikely, particularly after inhalational use, that significant quantities of ipratropium will reach the infant. Caution should be exercised when Berodual Respimat is administered to nursing mothers.

Driving and using machines

No studies on the effects on the ability to drive and use machines have been performed.
However, you may experience undesirable effects such as dizziness, shivering and difficulties viewing clearly during treatment with Berodual Respimat. Therefore, you should be careful when driving a car

or operating machinery. If you experience the above mentioned side effects you should avoid potentially hazardous tasks such as driving or operating machinery.

Berodual Respimat contains benzalkonium chloride

This medicine contains 1.12 microgram benzalkonium chloride in each actuation.
Benzalkonium chloride may cause wheezing and breathing difficulties (bronchospasm), especially if you have asthma.

3. How to take Berodual Respimat

Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

The recommended dose is:
The dosage depends on the nature and severity of the illness.
The following dosages are recommended for adults:

For acute asthma attacks:
One puff of Berodual Respimat is sufficient for prompt relief in many cases. If there has been no noticeable improvement 5 minutes after the first inhalation, a further puff can be taken. If a severe attack cannot be relieved by a second puff, either further puff may be necessary. In these cases, you must see your doctor or go to the nearest hospital immediately.

Intermittent and long-term treatment (in asthma Berodual Respimat should be used only as-needed)

Adults:
1 puff of Berodual Respimat up to 4 times daily.

The total daily dose should not exceed 6 puffs, because generally a higher dose is not likely to provide increased efficacy. However, the risk of potentially serious adverse reaction may be increased.

Berodual Respimat is intended for inhalation use only. The cartridge can only be inserted and used in the Respimat inhaler.
Make sure that you know how to use your Respimat inhaler properly. Read the instructions on how to use the Respimat inhaler device which are provided at the end of this leaflet.

If you take more Berodual Respimat than you should

If you take Berodual Respimat more than as recommended in one day talk to your doctor immediately.

You may be at a higher risk of experiencing a side effect such as
racing heart, palpitation, tremor, high blood pressure, low blood pressure, widening of the pulse pressure, chest pain (anginal pain), abnormal heart rhythm (arrhythmias), low potassium level in blood, flushing due to an overdose with fenoterol hydrobromide. Too much acid in the blood has also been observed with fenoterol when taken in doses higher than recommended for the approved indications of Berodual.

The following symptoms of an overdose with ipratropium bromide may occur:
dry mouth, visual accommodation disorder and increase of heart rate.

If you forget to take Berodual Respimat

Do not take a double dose to make up for a forgotten dose. Inhale the next dose as usual.

If you stop taking Berodual Respimat

You should talk to your doctor or pharmacist before you stop taking Berodual Respimat
If you stop taking Berodual Respimat the signs and symptoms of your condition may worsen.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

As with all inhalation therapy, Berodual Respimat may show symptoms of local irritation.
The most frequent side effects reported in clinical trials were cough, dry mouth, headache, shivering, sore throat, sickness, dizziness, voice disturbance, irregular heart beat, palpitations, vomiting, increased blood pressure and nervousness.

The side effects described in the table below have been experienced by patients taking Berodual Respimat. Evaluation of the side effects is based on the following frequencies:

Common: may affect up to 1 in 10 people
Uncommon: may affect up to 1 in 100 people
Rare: may affect up to 1 in 1,000 people
Very rare: may affect up to 1 in 10,000 people
Not known: frequency cannot be estimated from the available data

You may experience the following side effects:

System Organ Class	**Frequency**
Immune System Disorders	
Anaphylactic reaction	Rare
Hypersensitivity	Rare
Metabolism and nutricional disorders	
Hypokalemia	Rare
Psychiatric Disorders	
Nervousness	Uncommon
Agitation	Rare
Mental disorder	Rare
Nervous System Disorders	
Headache	Uncommon
Tremor	Uncommon
Dizziness	Uncommon
Hyperactivity	Not known
Eye Disorders	

Glaucoma	Rare
Intraocular pressure increased	Rare
Accommodation disorder	Rare
Pupil widening (Mydriasis)	Rare
Vision blurred	Rare
Eye pain	Rare
Corneal oedema	Rare
Red eyes due to the congestion of blood in the conjunctiva (conjunctival hyperaemia)	Rare
Coloured rings around sources of light (Halo vision)	Rare
Cardiac disorders	
Tachycardia, heart rate increased	Uncommon
Palpitations	Uncommon
Irregular heart beat (Arrhythmia)	Rare
Atrial fibrillation	Rare
Supraventricular tachycardia	Rare
Myocardial ischaemia	Rare
Respiratory, Thoracic and Mediastinal Disorders	
Cough	Common
Pharyngitis	Uncommon
Voice disturbance (Dysphonia)	Uncommon
Bronchospasm	Rare
Throat irritation	Rare
Pharyngeal oedema	Rare
Laryngospasm	Rare
Bronchospasm paradoxical	Rare
Dry throat	Rare
Gastro-intestinal Disorders	
Vomiting	Uncommon
Sickness (Nausea)	Uncommon
Dry mouth	Uncommon
Sore oral mucosa (Stomatitis)	Rare
Sore tongue (Glossitis)	Rare
Gastrointestinal motility disorder	Rare
Diarrhoeia	Rare
Constipation	Rare
Oedema mouth	Rare
Skin and Subcutaneous Disorders	
Urticaria	Rare
Rash	Rare
Pruritus	Rare
Angioedema	Rare
Hyperhidrosis	Rare

Musculoskeletal and connective Tissue Disorders	
Muscle pain (Myalgia)	Rare
Muscle spasms	Rare
Muscular weakness	Rare
Renal and Urinary Disorders	
Urinary retention	Rare
Investigations	
Blood pressure systolic increased	Uncommon
Blood pressure diastolic decreased	Rare

The following side effects were not observed in clinical trials with Berodual Respimat but are known to be associated with products in the same pharmacological class as the components of Berodual Respimat.

Beta$_2$-agonists (such as fenoterol hydrobromide)

Sweating and muscle weakness may occur. In rare cases, particularly after the intake of high doses, a decrease in diastolic blood pressure and an increase in systolic blood pressure were observed. Treatment with beta$_2$-agonists may cause a sharp reduction in the levels of potassium in the blood.

Although it is not known exactly how often this happens, some people may occasionally experience chest pain (due to heart problems such as angina pectoris). Tell your doctor if you develop these symptoms whilst receiving treatment with Berodual Respimat, but do not stop using this medicine unless told to do so.

Anticholinergic agents (such as ipratropium bromide)

Specific disturbances in the heart rhythm (supraventricular tachycardia), disorders of the capacity for movement in the gastro-intestinal region, and urinary retention may occur. Side effects in the eye such as disturbances of accommodation, widening of the pupils, raised intra-ocular pressure and eye pain were reported (see also section “Warnings and precautions”). Hypersensitivity reactions such as swelling of the tongue, lips and face (angiooedema of the tongue, lips and face) may occur.

As with other inhalation therapy, application-induced bronchial spasms (bronchospasm) may occur immediately after dosing.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Berodual Respimat

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the cartridge, Respimat inhaler and the carton. The expiry date refers to the last day of the month.
The cartridge can be used for three months after insertion into the Respimat inhaler.

Do not freeze.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. Contents of the pack and other information

What Berodual Respimat contains

The active substances are ipratropium bromide monohydrate and fenoterol hydrobromide. The delivered dose (the dose that leaves the mouthpiece of the Berodual Respimat) is 20 microgram ipratropium bromide monohydrate (equivalent to 19 microgram ipratropium bromide anhydrous) and 50 microgram fenoterol hydrobromide per puff.

The other ingredients are:
Benzalkonium chloride, disodium edetate, purified water and hydrochloric acid 3.6% for pH adjustment

What Berodual Respimat looks like and contents of the pack

Berodual Respimat is composed of one cartridge with inhalation solution and one Respimat inhaler. The cartridge has to be inserted into the inhaler before the first use.

Single pack:	1 Respimat inhaler and 1 cartridge, providing 120 puffs
Double pack:	2 single packs, each containing 1 Respimat inhaler and 1 cartridge providing 120 puffs
Hospital pack:	8 single packs, each containing 1 Respimat inhaler and 1 cartridge providing 120 puffs

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

The Marketing Authorisation Holder for Berodual Respimat is:

Boehringer Ingelheim International GmbH
Binger Straße 173
D-55216 Ingelheim am Rhein
Germany

The manufacturer for Berodual Respimat is:

Boehringer Ingelheim Pharma GmbH & Co. KG
Binger Straße 173
D-55216 Ingelheim am Rhein
Germany

For any information about this medicinal product, please contact the local representative of the Marketing Authorisation Holder.

This medicine is authorised in the Member States of the European Economic Area under the following names:

Germany and the Netherlands: Berodual Respimat

Dit geneesmiddel staat in het register ingeschreven onder RVG 26896

Deze bijsluiter is voor het laatst goedgekeurd in juli 2022

How to use the Respimat inhaler device

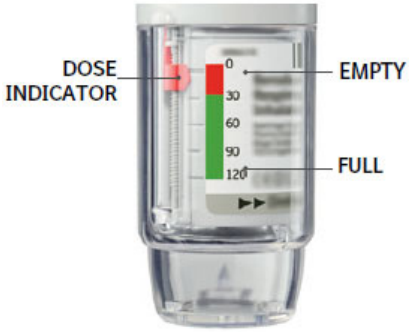
Respimat is an inhaler device that generates a spray for inhalation. Respimat is for you only and intended for multiple uses.

Read these instructions before you start using Berodual Respimat.

- If Berodual Respimat has not been used for more than 7 days release one puff towards the ground.
- If Berodual Respimat has not been used for more than 21 days repeat steps 4 to 6 under 'Prepare for first Use' until a cloud is visible. Then repeat steps 4 to 6 three more times.
- Do not touch the piercing element inside the clear base.

How to care for your Berodual Respimat

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



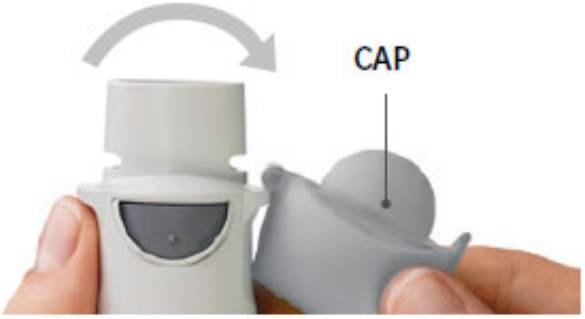
Any minor discoloration in the mouthpiece does not affect your Berodual Respimat inhaler performance.
If necessary, wipe the outside of your Berodual Respimat with a damp cloth.

When to get a new Berodual Respimat

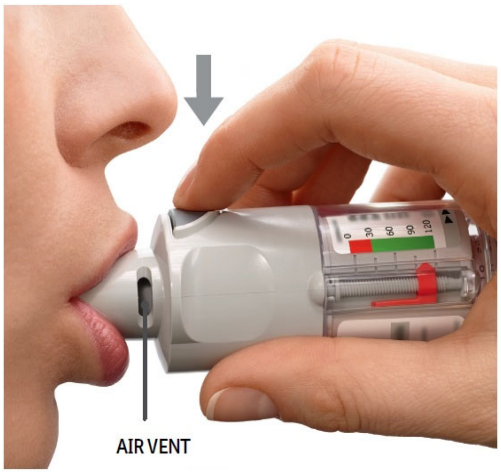
- Your Berodual Respimat inhaler contains 120 puffs (120 doses) if used as indicated.
- The dose indicator shows approximately how much medication is left.
- When the dose indicator enters the red area of the scale you need to get a new prescription; there is approximately medication for 7 days left (28 puffs).
- Once the dose indicator reaches the end of the red scale, your Berodual Respimat locks automatically – no more doses can be released. At this point, the clear base cannot be turned any further.
- Berodual Respimat should be discarded three months after you have prepared it for first use, even if it has not been fully used or used at all.

Prepare for first use

1. Remove clear base • Keep the cap closed. • Press the safety catch while firmly pulling off the clear base with your other hand.	
2. Insert cartridge • Insert the narrow end of the cartridge into the inhaler. • Place the inhaler on a firm surface and push down firmly until it clicks into place.	

3. Replace clear base • Put the clear base back into place until it clicks.	
4. Turn • Keep the cap closed. • Turn the clear base in the direction of the arrows on the label until it clicks (half a turn).	
5. Open • Open the cap until it snaps fully open	
6. Press • Point the inhaler toward the ground • Press the dose-release button. • Close the cap. • Repeat steps 4-6 until a cloud is visible. • **After a cloud is visible**, repeat steps 4-6 three more times. Your inhaler is now ready to use. These steps will not affect the number of doses available. After preparation your inhaler will be able to deliver 120 puffs (120 doses).	

Daily use

TURN • Keep the cap closed. • **TURN** the clear base in the direction of the arrows on the label until it clicks (half a turn).	
OPEN • **OPEN** the cap until it snaps fully open.	
PRESS • Breathe out slowly and fully. • Close your lips around the mouthpiece without covering the air vents. Point your Inhaler to the back of your throat. • While taking a slow, deep breath through your mouth, **PRESS** the dose-release button and continue to breathe in slowly for as long as comfortable. • Hold your breath for 10 seconds or for as long as comfortable. • Close the cap until you use your inhaler again.	

Answers to Common Questions

It is difficult to insert the cartridge deep enough.

Did you accidentally turn the clear base before inserting the cartridge? Open the cap, press the dose-release button, then insert the cartridge.
Did you insert the cartridge with the wide end first? Insert the cartridge with the narrow end first.

I cannot press the dose-release button.

Did you turn the clear base? If not, turn the clear base in a continuous movement until it clicks (half a turn).
Is the dose indicator on the Berodual Respimat pointing to zero? The Berodual Respimat inhaler is locked after 120 puffs (120 medicinal doses). Prepare and use your new Berodual Respimat inhaler.

I cannot turn the clear base.

Did you turn the clear base already?
If the clear base has already been turned, follow steps "OPEN" and "PRESS" under "Daily Use" to get your medicine.
Is the dose indicator on the Berodual Respimat pointing to zero?. The Berodual Respimat inhaler is locked after 120 puffs (120 medicinal doses). Prepare and use your new Berodual Respimat inhaler.

The dose indicator on the Berodual Respimat reaches zero too soon.

Did you use Berodual Respimat as indicated (one puff/1-4 times daily for intermittent and long-term treatment)? Berodual Respimat will last for at least 30 days.
Did you turn the clear base before you inserted the cartridge? The dose indicator counts each turn of the clear base regardless whether a cartridge has been inserted or not.
Did you spray in the air often to check whether the Berodual Respimat is working? Once you have prepared Berodual Respimat, no test-spraying is required if used daily.
Did you insert the cartridge into a used Berodual Respimat? Always insert a new cartridge into a **NEW** Berodual Respimat.

My Berodual Respimat sprays automatically.

Was the cap open when you turned the clear base? Close the cap, then turn the clear base.
Did you press the dose-release button when turning the clear base? Close the cap, so the dose-release button is covered, then turn the clear base.
Did you stop when turning the clear base before it clicked? Turn the clear base in a continuous movement until it clicks (half a turn).

My Berodual Respimat doesn't spray.

Did you insert a cartridge? If not, insert a cartridge.
Did you repeat Turn, Open, Press less than three times after inserting the cartridge? Repeat Turn, Open, Press three times after inserting the cartridge as shown in the.steps 4 to 6 under "Prepare for first Use".
Is the dose indicator on the Berodual Respimat pointing to 0? If the dose indicator points to 0, you have used up all your medication and the inhaler is locked.
Once your Berodual Respimat is assembled, do not remove the clear base or the cartridge. Always insert a new cartridge into a **NEW** Berodual Respimat.