PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986

The medicine is dispensed with a doctor's prescription only.

BRAMITOB

Solution for Inhalation.

Intended for inhalation with a nebuliser. See "*Instructions for Use*" section.

Composition

Each 4 ml ampoule contains the active ingredient:

- Tobramycin 300 mg

Inactive ingredients: see section 6 in the leaflet.

Read this leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.

This medicine has been prescribed for the treatment of your ailment. Do not pass it on to others. It may harm them, even if it seems to you that their ailment is similar.

The medicine is not intended for children below the age of 6.

Bramitob contains an aminoglycoside antibiotic called tobramycin, that acts against infections caused by the *Pseudomonas aeruginosa* bacterium.

1. WHAT IS THE MEDICINE INTENDED FOR?

Bramitob is used to treat chronic lung infection caused by the *Pseudomonas aeruginosa* bacterium, in patients with cystic fibrosis above the age of 6. The medicine kills the bacteria and helps to improve breathing. Pseudomonas is a very common bacterium and infects the lungs of nearly all patients with cystic fibrosis at some time during their lives. Some people get the bacterium at a later stage in life, while others get it at a very young age. If the infection is not properly treated, it will continue to cause damage to the lungs as well as additional problems. As Bramitob is administered by inhalation, the tobramycin antibiotic directly reaches the lungs to act against the infecting bacteria. To achieve the best treatment results, please use the medicine in accordance with the recommended instructions.

Therapeutic group: Aminoglycoside class antibiotic.

2. BEFORE USING THE MEDICINE

☒ Do not use the medicine if:

- you are sensitive (allergic) to the active ingredient tobramycin, to any of the other ingredients contained in the medicine (see section 6 in the leaflet), or to any type of aminoglycoside antibiotic.
- you are taking potent diuretics, such as furosemide or ethacrynic acid, for fear of toxicity to the auditory system.
- you are taking urea or intravenous or oral mannitol (preparations used to treat severe conditions in hospitalized patients).

Special warnings regarding use of this medicine

Tobramycin, the active ingredient of Bramitob, belongs to a group of medicines that may sometimes cause hearing loss, dizziness or kidney damage (also see section 4 "Side effects").

❗ Before use or during treatment with Bramitob, tell the doctor if:

- You experience chest tightness after using Bramitob. The doctor will supervise the administration of the first dose and check your lung functions before and after Bramitob administration. If you do not use a bronchodilator (e.g. salbutamol), the doctor may ask you to do so before using Bramitob.
- You are suffering/have suffered in the past from any neuromuscular disorder such as Parkinson's or other conditions characterized by muscle weakness, including myasthenia gravis.
- You are suffering/have suffered in the past from a kidney function disorder. Before starting treatment, the doctor may perform kidney functions tests, including blood and urine tests. The doctor may perform the tests regularly during the course of treatment.
- You are suffering/have suffered in the past from ringing in the ears, any other hearing problem or dizziness. The doctor may test your hearing before and during the course of treatment with the medicine.
- You cough or spit up blood. Inhaling medicines may cause you to cough and the doctor may ask you to stop treatment with Bramitob until you stop spitting up blood.
- You are concerned that the medicine is not as effective as it should be. Bacteria can sometimes develop resistance to antibiotic treatment.
- You are suffering from an allergic reaction, including rash, itching, difficulty breathing and swallowing.

❗ If you are taking, or have recently taken, other medicines, including non-prescription medicines or nutritional supplements, tell the doctor or pharmacist. Do not use Bramitob without first consulting with the doctor, if you are taking:

- diuretics containing furosemide or ethacrynic acid.
- urea or intravenous or oral mannitol (preparations used to treat serious conditions in hospitalized patients) – avoid using together with Bramitob.
- Other medicines that may cause harm to the kidneys or hearing. Treatment with Bramitob may worsen the effect.
- It is possible that, in addition to treatment with Bramitob, you are also being/will also be treated with injections of tobramycin or other aminoglycosides. Such injections may increase the very low body levels of aminoglycosides caused by inhaling Bramitob; avoid using the following medicines concomitantly with Bramitob:
  - Amphotericin B, cefalotin, ciclosporin, tacrolimus, polymyxins.
  - Platinum compounds (e.g., carboplatin and cisplatin)
  - Cholinesterase inhibitors (e.g., neostigmine and pyridostigmine), botulinum toxin

If these medicines were prescribed to you while using Bramitob, inform the doctor.

❗ Pregnancy and breastfeeding: If you are pregnant, think you may be pregnant, are planning to have a baby or breastfeeding, consult a doctor before using this medicine.

❗ Driving and operating machinery: Bramitob has little effect on driving or ability to use machinery. Bramitob may cause dizziness. Therefore, it is possible that Bramitob will affect your ability to drive or to use machines.

3. HOW SHOULD YOU USE THE MEDICINE?

- Always use according to the doctor's instructions.
- Check with the doctor or pharmacist if you are uncertain.
- See "*Instructions for use*" of Bramitob, after the "*Dosage*" section.
- **Do not mix or dilute** Bramitob with any other medicine in the nebuliser.
- Open the single-dose Bramitob ampoule immediately before use. Any unused solution that is not immediately used, should be discarded.
- If you are receiving additional treatments for cystic fibrosis disease, take them in the following order:
- Bronchodilator (e.g., salbutamol), followed by chest physiotherapy, followed by other inhaled medicines, and at the end, Bramitob.

  Confirm the order with the doctor.

Dosage:

The dosage and treatment regimen will be determined by the doctor only. The usual dosage is generally:

- The dose is identical for all patients above the age of 6.
- Use the single-dose ampoule (an ampoule contains 4 ml), twice a day (one in the morning and one in the evening), for 28 days. To be inhaled via a PARI LC PLUS nebuliser and an appropriate compressor. Maintain a 12-hour gap between the doses.
- After taking the medicine for 28 days, take a 28-day break during which you will not inhale Bramitob at all; afterwards, a new treatment cycle will begin.
- It is important to maintain a treatment regimen of twice-daily dosing during your 28 days on treatment, and to maintain **the 28-day on/28-day off** cycle. Continue with this treatment regimen until you receive other instructions from the doctor.
- **Do not exceed the recommended dose.**
- **Tests and Follow-up:** During the course of treatment, the doctor will refer you for kidney function tests that include blood and urine tests, as well as a hearing test.
- **If you accidentally took a higher dosage,** you may become hoarse. Tell the doctor as soon as possible. If a child has accidentally swallowed the medicine, refer immediately to a doctor or proceed to a hospital emergency room, and bring the package of the medicine with you.
- **If you forget to take the medicine:**
  - if more than 6 hours remain until taking the next dose (ampoule), take a dose now. If less than 6 hours remain until the next dose, skip the forgotten dose. Never take two doses together.
- Adhere to the treatment regimen recommended by the doctor.
- Even if there is an improvement in your health, do not stop treatment with the medicine without consulting the doctor or pharmacist.

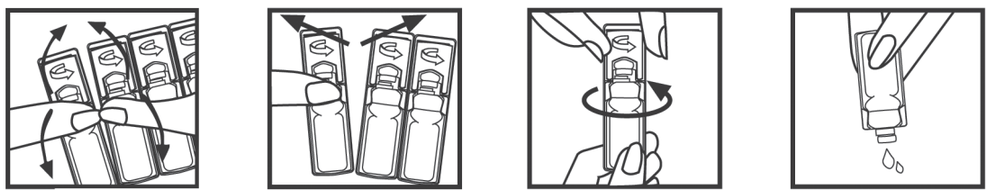
Instructions for use:

Bramitob is intended for inhalation through a properly working, multi-use, clean and dry PARI LC PLUS nebuliser (for your own personal use only) and appropriate compressor. Consult with the doctor or physiotherapist regarding the type of compressor. Do not use the medicine in any other way.

1. Wash your hands thoroughly with soap and water before opening the single-dose ampoule, according to the following instructions
2. Each foil envelope contains 4 attached ampoules.

   Do the following to separate between the attached ampoules:

a. Bend the ampoule backwards and forwards (Figure A).
b. Carefully separate the ampoule from the strip of ampoules, starting from the top, and progressing to the middle (Figure B), and place the remaining ampoules in the foil envelope.
3. Open the ampoule by holding it at the bottom with one hand and rotating the top part of the ampoule with the other hand, as indicated by the arrow (Figure C).
4. Gently squeeze the contents of the ampoule into the nebuliser (Figure D).
5. Turn on the compressor.



A B C D

6. Check if there is a steady mist coming out of the mouthpiece of the device.
7. Sit or stand in an upright position so that you can breathe normally.
8. Place the mouthpiece between your teeth on top of your tongue and breathe normally, only through your mouth. Nose clips may be helpful for breathing through the mouth only (if your doctor agrees to it). Be sure not to block the air passage with the tongue.
9. Continue with the treatment until all the Bramitob is used up; the process takes about 15 minutes.
10. If the treatment is interrupted by an external factor or if you need to cough or rest during the inhalation, turn off the compressor so as not to waste the medicine. Turn the compressor on again when you are ready to restart the treatment.
11. Treatment with a nebuliser – follow the manufacturer's instructions regarding the maintenance and use of the device and compressor. Remember to clean and disinfect the nebuliser after use, as per the manufacturer's instructions.

- **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 further questions regarding use of the medicine, consult the doctor or pharmacist.**

4. SIDE EFFECTS

Also see the "*Special warnings regarding use of this medicine"* section.

As with any medicine, use of Bramitob may cause side effects in some users. Do not be alarmed by the list of side effects. You may not suffer from any of them.

If you are uncertain about the meaning of any of the side effects listed below, ask the doctor to explain it to you.

Common side effects (occur in 1-10 in 100 patients): cough and hoarseness.

Uncommon side effects (occur in 1-10 in 1000 patients): thrush in the mouth, vertigo (spinning feeling), loss of hearing, increased production of saliva, inflammation of the tongue, rash, sore throat or chest pain, increased blood levels of hepatic enzymes, noisy breathing, nausea, dry nose, coughing up blood, decreased hearing, headache, shortness of breath, weakness, increased quantities of sputum, abdominal pain and fungal infection.

Rare side effects (occur in 1-10 in 10000 patients): loss of appetite, ringing in the ears, chest tightness or difficulty breathing, loss of voice, nose bleed, runny nose, mouth ulcers, vomiting, taste disturbances, asthma, dizziness, fever, pain, laryngitis.

Very rare side effects (occur in less than one in 10000 patients): fungal infections, swelling of lymph glands, drowsiness, ear problems, ear pains, hyperventilation, sinusitis, diarrhea, allergic reactions including urticaria and pruritus, deficiency of available oxygen in the blood and bodily tissues (hypoxia), back pain, abdominal pain, generally feeling unwell.

If a side effect occurs, if one of the side effects worsens or if you suffer from a side effect not mentioned in this leaflet, consult with the doctor.

Side effects can be reported to the Ministry of Health by clicking on the "Reporting of Side Effects due to Drug Treatment" link on the Ministry of Health website's homepage (www.health.gov.il) which links to the online side effect reporting form, or by logging on to the link:
https://sideeffects.health.gov.il

Additionally, you may also report to Kamada LTD to email address:
pharmacovigilance@kamada.com

5. HOW SHOULD THE MEDICINE BE STORED?

- Avoid poisoning! This medicine, and any other medicine, should be kept in a safe place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.
- For single-use only. Use the contents of the ampoule immediately after opening; discard the remaining solution.
- Do not use the medicine after the expiry date (exp. date) that appears on the outer package and label. The expiry date refers to the last day of that month.
- Store refrigerated (2-8°C: this is the temperature range in most household refrigerators).
- The ampoules can be stored in the foil envelope for up to three months at room temperature (below 25°C).
- Store the ampoules in their original packaging in order to protect from light.
- Do not dispose of medicines in waste water or in the household waste bin. Ask the pharmacist how to dispose of medicines no longer in use. These measures will help protect the environment.

6. FURTHER INFORMATION

- In addition to the active ingredient, the medicine also contains:
  Sodium chloride, Sulphuric acid, Sodium Hydroxide, water for injections.
- What the medicine looks like and the contents of the package:
  Bramitob is a clear, yellowish solution. There can be changes in the color of the preparation that do not indicate that its action is reduced, if stored according to recommended conditions.
  Bramitob comes in single-dose ampoules that contain 4 mL solution. Each opaque sachet contains 4 ampoules in pack sizes of 16, 28 or 56. Not all sizes may be marketed.
- **Manufacturer:** Chiesi Farmaceutici S.p.A., Italy.
- **License holder and Importer:** Kamada Ltd., Beit Kama.
- This leaflet was checked and approved by the Ministry of Health in 02/2015 and updated according to the guidelines of the Ministry of Health in 12/2019.
- Registration number of the medicine in the National Drug Registry of the Ministry of Health: 144-24-32986.