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Healthcare Professional Leaflet
The following information is intended for healthcare professionals only.

# Bronchitol (mannitol) 40 mg, inhalation powder, hard capsules

## 1. Things to be aware of before prescribing Bronchitol

Prescribers of Bronchitol need to be aware of the following risks:
- **Bronchospasm –** during Bronchitol initiation dose assessment (BIDA)
- **Bronchospasm –** during treatment
- **Haemoptysis**
- **Problems related to coughing.**

Please look at the full Summary of Product Characteristics (SPC) before prescribing Bronchitol – the SPC is provided as part of this educational package.

### Bronchospasm – during Bronchitol initiation dose assessment (BIDA)

The Bronchitol initiation dose assessment (BIDA) identifies patients with bronchial hyperresponsiveness in response to inhaled mannitol. The assessment measures the degree of bronchoconstriction following sequential administrations of mannitol.

- The BIDA must be passed before the patient starts treatment with Bronchitol.

The BIDA must be done under the supervision and monitoring of an experienced and appropriately trained healthcare professional who must be:

- able to monitor oxygen saturation ($SpO_2$), do spirometry and manage acute bronchospasm – including use of resuscitation equipment (see 'Equipment required for BIDA' in section 2 for the full list required)
- close enough to respond quickly to an emergency.

Patients must be pre-medicated with a bronchodilator 5 to 15 minutes before the initiation dose – but after the baseline $FEV_1$ and $SpO_2$ measurement.

- Do not leave patients unattended once the assessment has started.
- After the test, monitor patients until their $FEV_1$ has returned to baseline levels.

### Bronchospasm – during treatment

Bronchoconstriction may happen during long-term use – even if the patient is not hyperresponsive to the initiation dose.

To help reduce the risk of bronchospasm during use:

- Tell patients to use a bronchodilator 5 to 15 minutes before their dose of Bronchitol – you must check patients are able to self-medicate with a bronchodilator correctly and safely on their own.
- Tell patients to stop using Bronchitol immediately and see their physician if they have difficulty breathing or if their breathing becomes more difficult.

Review all patients for drug induced bronchospasm after approximately 6 weeks (see section 4.4 of the SPC).

- Always repeat the initiation dose assessment if you are unsure about patients reporting signs and symptoms of bronchoconstriction.

### Haemoptysis

Bronchitol has not been studied in patients with a history of significant haemoptysis (at least 60 ml) in the previous 3 months. This means such patients should be carefully monitored.

Do not use Bronchitol after massive or serious haemoptysis – this is:

- acute bleeding with a loss of at least 240 ml in a 24 hour period
- recurrent bleeding with a loss of at least 100 ml per day over several days.

Use clinical judgement to decide on continued use after smaller episodes of haemoptysis. See section 4.4 of the SPC for more detailed information on categorising episodes of haemoptysis and withholding and reinstitution of Bronchitol.

To help reduce the risk of haemoptysis:

- Tell patients to report any haemoptysis or any increase in haemoptysis if they have a recent history (previous three months) to their physician.
- Tell patients to stop using Bronchitol immediately and see their physician if they have a massive or serious haemoptysis.

### Problems related to coughing

Inhalation of Bronchitol may cause coughing (very common) or a dry throat (common). In particular, inhaling Bronchitol too quickly may cause coughing.

To help reduce the risk of problems related to coughing:

- Train patients in correct inhaler use during the BIDA. Make sure the patient is given a Patient Information Leaflet (PIL). This contains detailed instructions on how to use the inhaler. Refer to the PIL included as part of the educational package.
- Tell patients that coughing may be controlled by slowing the rate of inhalation of the medicine. However, they must still make sure that the flow rate is enough to empty the capsule.
- Tell patients that a sip of water after the dose helps to clear any powder left in the mouth and throat.

If the cough does not get better, tell patients to talk to their physician.

# 2. Bronchitol initiation dose assessment (BIDA)

## How to complete the BIDA

The patient should be seated for the test. Explain the procedure to the patient and include what is required for an FVC manoeuvre, an $FEV_1$ measurement and the type of flow needed when using the inhaler. The patient should use the inhaler following steps 1 to 10 in the "How to use the inhaler" section of the PIL. Demonstrate as required.

- All $FEV_1$ measurements and $SpO_2$ monitoring should be performed 60 seconds after dose inhalation.
- Follow your usual protocol for measuring $FEV_1$ and $SpO_2$.
- If the patient shows any signs of significant bronchoconstriction such as wheezing or shortness of breath during the test, measure $FEV_1$ and treat accordingly.
- There are three possible outcomes to the BIDA: pass, fail or incomplete. The criteria for assessing these outcomes are described below.

### Step 1: Baseline measurements and pre-medication

**A** Assess baseline $FEV_1$ and $SpO_2$ before starting test. Leave pulse oximeter on throughout test.

**B** Ask patient to pre-medicate with bronchodilator 5 to 15 minutes before 1st Bronchitol inhalation.

### Step 2: 1st Bronchitol inhalation

**A** Patient inhales Bronchitol 40 mg – 1 capsule

**B** Start stopwatch – record $SpO_2$ after 60 seconds

→ $SpO_2$ OK – continue test

→ $SpO_2$ falls by ≥10% – patient has failed the BIDA, stop test, go to Step 6 and treat as required

### Step 3: 2nd Bronchitol inhalation

**A** Patient inhales Bronchitol 80 mg – 2 capsules

**B** Start stopwatch – record $SpO_2$ after 60 seconds

→ $SpO_2$ OK – continue test

→ $SpO_2$ falls by ≥10% – patient has failed the BIDA, stop test, go to Step 6 and treat as required

### Step 4: 3rd Bronchitol inhalation

**A** Patient inhales Bronchitol 120 mg – 3 capsules

**B** Start stopwatch – record $SpO_2$ and measure $FEV_1$ after 60 seconds

→ $SpO_2$ and $FEV_1$ OK – continue test

→ $SpO_2$ falls by ≥10% or $FEV_1$ falls by ≥20% (from baseline) – patient has failed the BIDA, stop test, go to Step 6 and treat as required

### Step 5: 4th Bronchitol inhalation

**A** Patient inhales Bronchitol 160 mg – 4 capsules

**B** Start stopwatch – record $SpO_2$ and measure $FEV_1$ after 60 seconds

→ $SpO_2$ and $FEV_1$ OK – go to Step 6

→ $SpO_2$ falls by ≥10% or $FEV_1$ falls by ≥50% (from baseline) – patient has failed the BIDA, go to Step 6 and treat as required

→ $FEV_1$ falls by 20% to <50% (from baseline) – test inconclusive, go to Step 6

### Step 6: Post-assessment monitoring

**A** Measure $FEV_1$ after 15 minutes

**B** Monitor until $FEV_1$ has returned to baseline levels

### Only if inconclusive at Step 5:

- $FEV_1$ recovers to within <20% (from baseline) – patient has passed the BIDA and is suitable for Bronchitol
- $FEV_1$ does not recover to within <20% (from baseline) – patient has failed the BIDA, treat as required

**Incomplete tests:** If the patient experiences a distressing cough, vomiting or any other signs that they are not tolerating the BIDA, stop the test before completion. Report as an adverse event (see section 3 for contact details).

## 3. Further information

**Further information can be obtained by contacting the marketing authorisation holder:**
Pharmaxis Europe Limited, 108 Q House, Furze Road, Sandyford, Dublin 18, D18AY29, Ireland.
Tel: + 353 (0) 1431 9816 Email: medical.information@arnapharma.com

**Contact Details for Adverse Event Reporting:**
Email: adverse.events@arnapharma.com

Healthcare professionals are also asked to report any suspected adverse reactions via the Yellow Card Scheme in the UK, Website: www.mhra.gov.uk/yellowcard

### Equipment required for BIDA

Make sure the following equipment is available before performing the BIDA:

- Bronchitol initiation dose (containing 10 Bronchitol capsules, one inhaler device and a PIL).

You will also need:

- spirometry system that meets ERS/ATS requirements
- stopwatch (which can be set to 60 seconds)
- calculator
- bronchodilator
- stethoscope
- sphygmomanometer
- pulse oximeter.

The following emergency equipment should also be available:

- epinephrine (adrenaline) and atropine
- long or short acting $beta_2$ agonists (such as salbutamol) – in metered-dose inhalers
- oxygen
- a small-volume nebuliser for giving bronchodilators
- other relevant emergency equipment.

### Hints and tips for BIDA

- Do not clean the inhaler device during the BIDA. Discard the inhaler after the BIDA.
- Do not sterilise or re-use the inhaler – this may compromise the validity of subsequent assessments.
- When patients exhale during the BIDA, make sure they do so away from the inhaler. This will minimise humidity within the device.
- Pierce the capsule once only. Do this by pressing both buttons fully and at the same time. Re-piercing may cause the capsule to split or fragment.
- Patients should inhale from the device in a deep controlled manner. This should be at a rate fast enough to make the capsule spin and empty.
  - A second inhalation may be required if the capsule appears not to have emptied.
  - Patients should hold their breath for 5 seconds after each capsule inhalation.
- To help with the development of an osmotic gradient within the airway, sequential doses should be taken straight after one another – there should be minimal delay between doses.
- Do not use rubber gloves when administering the BIDA and handling Bronchitol capsules. This may increase static and stop capsule movement within the inhaler.
  - If you suspect that static is an issue or notice that the sound of the capsule 'rattling' cannot be heard during inhalation of Bronchitol, firmly tap the base of the inhaler (with the mouthpiece facing downwards at a 45° angle). This should ensure that the capsule has been 'dislodged' from the piercing chamber into the spinning chamber.