

Package leaflet: Information for the user

Provocholine® 100 mg powder for nebuliser solution Methacholine Chloride

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 nurse.
- 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 nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Provocholine is and what it is used for
2. What you need to know before you take Provocholine
3. How to take Provocholine
4. Possible side effects
5. How to store Provocholine
6. Contents of the pack and other information

1. What Provocholine is and what it is used for

What Provocholine is

Provocholine contains a medicine called 'methacholine chloride'. It works on the airways causing them to tighten and become narrower or retract. The product is for diagnostic use only.

What is Provocholine used for

Provocholine is used in adults and children (5 years or older). It is used as part of a breathing test called a 'methacholine challenge test'.

Your doctor or nurse will do this test to help:

- decide if you have asthma
- check how severe your asthma is
- decide if you have 'occupational asthma'.

2. What you need to know before you take Provocholine

Do not take Provocholine if:

- you are allergic to methacholine chloride or other cholinergic drugs, such as those used to treat conditions such as myasthenia gravis, glaucoma, and urinary retention
- you are a child under 5 years of age
- you have asthma or difficulty breathing
- you are taking medicines that are beta-blockers
- you have already done a 'methacholine challenge test' with Provocholine on the same day - you should not have more than one test on the same day.
- you have a slow heart rate called 'bradycardia'
- you have a specific condition in your aorta, the body's main artery called an 'aortic aneurysm'
- you have had a heart attack or stroke in the last 3 months
- you have uncontrolled high blood pressure
- you have an illness called 'myasthenia gravis' and are being treated with medicines that belong to a group called 'cholinesterase inhibitors'
- you have had recent eye surgery or are at risk of high intracranial pressure
- you have had a blood clot in the lung known as 'pulmonary embolism'
- you are pregnant
- you are breast-feeding

Do not take Provocholine if any of the above apply to you. If you are not sure, talk to your doctor or nurse before taking Provocholine.

Warnings and precautions

Talk to your doctor or nurse before taking Provocholine if:

- you have epilepsy
- you have problems with your heart and blood vessels
- you have an ulcer
- you have thyroid disease
- you have a blockage in your water-works (called 'obstructed urinary tract')
- you have problems with a nerve in your body called the 'vagus nerve'.

If any of the above apply to you (or you are not sure), talk to your doctor or nurse before taking Provocholine.

Children

The safety and efficacy of Provocholine in children under 5 years of age has not been established. No data are available.

Other medicines and Provocholine

Tell your doctor or nurse if you are taking, have recently taken or might take any other medicines. This includes medicines obtained without a prescription and herbal medicines.

- This is because some medicines may affect the safety of a breathing test with Provocholine.
- Also, some other medicines can affect the results of a breathing test with Provocholine.

Discuss with your doctor if you should stop taking these medicines before you have your test. Your doctor or nurse will tell you how long you need to stop the other medicines for.

In particular, do not take this medicine and tell your doctor or nurse if you are taking any of the following medicines:

- beta-blockers to lower your blood pressure
- cholinesterase inhibitors to treat a condition called 'myasthenia gravis'.

If any of the above apply to you, or you are not sure, talk to your doctor or nurse before taking Provocholine.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, or think you may be pregnant, ask your doctor or nurse for advice before taking this medicine.

Do not take Provocholine if you are pregnant or think you might be pregnant. This is because it may harm the unborn baby.

Do not take Provocholine if you are breast-feeding. It is not known whether this medicine may pass into the mother's milk.

Driving and using machines

Provocholine has no influence on the ability to drive and use machines.

3. How to take Provocholine

Provocholine has been specially supplied for administration only by healthcare professionals in an asthma clinic or lung function testing laboratory.

About the Methacholine Challenge Test

Provocholine is given by a doctor or nurse as part of a breathing test called a 'methacholine challenge test'.

- You inhale the medicine - your doctor or nurse will show you how to do this before the test begins.
- You will normally be given a number of doses during the test. You start with a low dose and the dose is then gradually increased. The doses are given in this order:
 - 0.0312 mg/mL → 0.0625 mg/mL → 0.125 mg/mL → 0.25 mg/mL → 0.5 mg/mL → 1 mg/mL → 2 mg/mL → 4 mg/mL → 8 mg/mL → 16 mg/mL.
 - Once your lung function (how your lungs are working) has reached the target level, (the level at which you show response of bronchoconstriction or the maximum concentration of the test), the test will be stopped at that dose.

When will the test be stopped?

The test will be stopped if:

- your lung function reaches to the level determined by the healthcare professional.
- you have reached the highest dose of Provocholine
- your doctor or nurse decides you are not able to carry on with the test because of side effects.
- At the end of the test, you may be given a medicine called a 'reversal agent'. The reversal agent will cause the airways to expand and dilate (i.e.) it will reverse the airways constriction effect of Provocholine. Your doctor or nurse will measure how your lungs are working to make sure your breathing is back to normal before you are sent home.

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

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. The following side effects may happen with this medicine. Frequency is not known for all side effects because it cannot be estimated from the available data.

- Headache, dizziness
- Throat irritation
- Bronchospasm, chest tightness, cough, wheezing
- Bronchoconstriction
- Itching

Tell your doctor or nurse if you notice any of the side effects listed above during or after the test. If any of the side effects become serious, tell your doctor or nurse straight away.

Reporting of side effects

If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the [\[To be completed nationally\]](#). By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Provocholine

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 vial label or carton after "Exp.". The expiry date refers to the last day of that month.

The un-reconstituted medicinal product does not require any special storage conditions.

Once the medicine has been mixed with solvent, the solution should be used straight away. Any unused liquid should be disposed of safely.

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

NOTE: Provocholine is a diagnostic drug. It should never be removed from the asthma clinic or lung function testing laboratory.

6. Contents of the pack and other information

What Provocholine contains

- Methacholine chloride as the active substance at 100 mg per vial
- There are no other ingredients in Provocholine®.

What Provocholine looks like and contents of the pack

- Provocholine is a white or off-white powder for nebuliser solution.
- Provocholine is supplied in an amber coloured glass vial. Each carton contains 6 vials.

Marketing Authorisation Holder and Manufacturer

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This medicinal product is authorised in the Member States of the EEA under the following names:

Denmark, France, Netherlands, Norway, Sweden
Product Name: Provocholine®

This medicinal product is authorised in the Member States of the EEA under the following names:

Ireland
Product Name: Methacholine Chloride 100 mg

This leaflet was last revised in 04/2020

The following information is intended for healthcare professionals only

Provocholine® is supplied in powder and must be reconstituted and diluted before use. Provocholine® is administered only in solution for inhalation using a nebuliser.

Do not inhale the powder. Do not handle this product if you suffer from asthma or allergies. All dilutions must be made with 0.9% sodium chloride solution for injection, using empty, sterile borosilicate Type I glass vials. After adding the sodium chloride solution, shake each vial until you obtain a clear solution. A low resistance filter should be applied to an expiratory port of any dosing apparatus, as necessary, to prevent Provocholine® aerosol from being released into the air of the room.

Before starting a Provocholine® challenge test, baseline pulmonary function tests must be performed with the recommended diluent. For a patient to be able to undergo the test, he must present with an FEV₁ (Forced Expiratory Volume in 1 second) greater than 60% of the predicted value (in adults and children) and an FEV₁ greater than 1.5 L (in adults) following exposure to nebulised diluent that can be considered normal baseline spirometry. The methacholine challenge test is considered positive if there is a reduction in FEV₁ of 20% or more from baseline FEV₁ with the recommended diluent. The test should be stopped at this point. The reduction value must be calculated and recorded before starting the test with Provocholine®.

This medicinal product does not require any special storage conditions. Reconstituted and diluted solutions of the medicinal product should be used immediately, discard any remainder.

From a microbiological point of view, unless the method of opening/reconstitution/dilution precludes the risk of microbial contamination, the product should be used immediately.