



Provocholine[®]

[methacholine chloride USP]

powder for solution, for inhalation

Mixing Methacholine Dilutions for Bronchoprovocation Challenge Testing

®Provocholine is a registered trademark of Methapharm Inc. | Copyright © Methapharm Inc. 2016. All rights reserved. Healthcare professionals should consult the Provocholine package insert for the complete product safety information. A sterile 0.22 µm bacterial retentive filter (e.g., Millex GV®) should be used when transferring a solution to the nebulizer. **Warning:** Provocholine is a bronchoconstrictor agent for diagnostic purposes only and should not be used as a therapeutic agent. Provocholine inhalation challenge should be performed only under the supervision of a physician trained in and thoroughly familiar with all aspects of the technique of methacholine challenge, all contraindications, warnings and precautions, and the management of respiratory distress. Emergency equipment and medication should be immediately available to treat acute respiratory distress. For complete prescribing information, please consult the Product Insert which is available for download at www.provocholine.com or on request by calling Methapharm Medical Information at 1-800-287-7686 | +1-519-751-3602 ext 7804 or faxing us at +1-519-751-9149.

This information is provided as a professional courtesy, and it is intended to provide data available to us that may assist you in deriving your own conclusions and opinions. This information is not intended to advocate any indications, dosage, or other claim that is not described in the package insert.

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Overview

1. **Gathering Necessary Equipment**
2. **Special Precautions**
3. **Reconstituting Provocholine**

1 Supplies

- 100 mg vial of Provocholine



1 Supplies

- **Diluent options**
 - **0.9% Saline**
 - **0.9% Saline with 0.4% Phenol (pH 7.0)***
- **Sterile empty vials***
- **Syringes and needles**

* Available for purchase from Methapharm, Inc.

1 Supplies

- **0.22 µm sterile bacterial-retentive filter***
- **Alcohol preparation pads**
- **Green labels (included)**

* Available for purchase from Methapharm, Inc.

2 Reconstituting Precautions

- **Please refer to the Provocholine package insert for full instructions and safety precautions**

2 Reconstituting Precautions

- **Accurate sterile technique is essential to obtain appropriate test results while maintaining patient safety**

2 Precautions – Green Labels

- Fill in all information on the labels
- Include 14 day expiration on Vials A-D
- Vial E should be prepared the day of testing

Strength:		Provocholine [®]	www.methapharm.com
Diluent:		Mfr. Lot No.	
Prep. Date:	/ /	P-	
Exp. Date:	/ /	Initials	

2 Precautions – Green Labels

The diagram shows a green rectangular label for Provocholine. The label is divided into several sections. On the left side, there are four rows of text: 'Strength:', 'Diluent:', 'Prep. Date:', and 'Exp. Date:'. The 'Prep. Date:' and 'Exp. Date:' fields contain slashes indicating date format. On the right side, there are three rows: 'Provocholine[®]', 'Mfr. Lot No.', and 'Initials'. The 'Mfr. Lot No.' field contains a large 'P-' followed by a blank space. A vertical URL 'www.methapharm.com' is printed on the right edge of the label. Six callout boxes with lines pointing to specific fields are labeled: 'Dilution Strength' (points to the Strength field), 'Type of Diluent Used' (points to the Diluent field), 'Preparation Date' (points to the Prep. Date field), 'Expiration Date' (points to the Exp. Date field), 'Lot number' (points to the Mfr. Lot No. field), and 'Initials of person performing dilution' (points to the Initials field).

Strength:		Provocholine [®]	
Diluent:		Mfr. Lot No.	
Prep. Date:	/ /	P-	
Exp. Date:	/ /	Initials	

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Callouts:

- Dilution Strength
- Type of Diluent Used
- Preparation Date
- Expiration Date
- Lot number
- Initials of person performing dilution

3 Dosing Protocols

US Package Insert (mg/mL)	ATS Short (mg/mL)
25	16
10	4
2.5	1
0.25	0.25
0.025	0.0625
Diluent	Diluent

Step 1

Attach the completed green labels to the sterile empty vials.

Step 2

Wipe the top of the Provocholine vial, the diluent vial and the sterile empty vials with alcohol preparation pads.

Step 3

Label two syringes, one for the Provocholine and one for the diluent.

Step 4 – Package Insert Dilutions

Using the Diluent syringe, withdraw 4 mL of diluent and inject it into the Provocholine vial creating a stock solution. Shake well.

This solution contains 25 mg/mL of methacholine chloride.

Step 5 – Package Insert Dilutions

Using the Provocholine vial as your stock solution, withdraw 1 mL of the 25 mg/mL solution with the Provocholine syringe and add it to the vial labeled Vial B.

Step 5 – Package Insert Dilutions

Using the Diluent syringe, add 1.5 mL of diluent to the same vial. Shake well.

Vial B will contain a 10 mg/mL solution of methacholine chloride.

Step 6 – Package Insert Dilutions

Using the Provocholine vial as your stock solution, withdraw 1 mL of the 25 mg/mL solution with the Provocholine syringe and add it to the vial labeled Vial C.

Step 6 – Package Insert Dilutions

Using the Diluent syringe, add 9 mL of diluent to the same vial. Shake well.

Vial C will contain a 2.5 mg/mL solution of methacholine chloride.

Step 7 – Package Insert Dilutions

From here, we will perform a serial dilution to make the remaining two concentrations.

Using the Provocholine syringe, withdraw 1 mL from Vial C (2.5 mg/mL) and add it to the vial labeled Vial D.

Step 7 – Package Insert Dilutions

Using the Diluent syringe, add 9 mL of diluent to the same vial. Shake well.

Vial D will contain a 0.25 mg/mL solution of methacholine chloride.

Step 8 – Package Insert Dilutions

Repeat the same process for Vial E the day of the test, withdrawing 1 mL from Vial D (0.25 mg/mL) and adding 9 mL of diluent.

Vial E will contain a 0.025 mg/mL solution of methacholine chloride.

Step 4 – ATS Short Dilutions

Using the Diluent syringe, withdraw 6.25 mL of diluent and inject it into the Provocholine vial. Shake well.

This solution contains 16 mg/mL of methacholine chloride.

Step 5 – ATS Short Dilutions

For the ATS Short Dilutions you will perform a serial dilution using the previous dilution as the stock solution at each step.

Using the Provocholine vial, withdraw 3 mL of the 16 mg/mL solution using the Provocholine syringe and add it to the vial labeled Vial B.

Step 5 – ATS Short Dilutions

Using the Diluent syringe, add 9 mL of diluent to the same vial. Shake well.

Vial B will contain a 4 mg/mL solution of methacholine chloride.

Step 6 – ATS Short Dilutions

Using the previous vial (Vial B), withdraw 3 mL of the 4 mg/mL solution using the Provocholine syringe and add it to the vial labeled Vial C.

Step 6 – ATS Short Dilutions

Using the Diluent syringe, add 9 mL of diluent to the same vial. Shake well.

Vial C will contain a 1 mg/mL solution of methacholine chloride.

Step 7 – ATS Short Dilutions

Using the Provocholine syringe, withdraw 3 mL from Vial C (1 mg/mL) and add it to the vial labeled Vial D. Add 9 mL of diluent to the same vial. Shake well.

Vial D will contain a 0.25 mg/mL solution of methacholine chloride.

Step 8 – ATS Short Dilutions

Repeat the same process for vial E the day of the test, withdrawing 3 mL from Vial D (0.25 mg/mL) and adding 9 mL of diluent.

Vial E will contain a 0.0625 mg/mL solution of methacholine chloride.

3 Storage of Dilutions

- **Refrigerate reconstituted solutions at 36° to 46°F (2° to 8°C) for up to 2 weeks for vials A-D**
- **Vial E must be prepared on the day of testing**
- **Freezing does not affect stability of the dilutions**

Summary

US Package Insert (mg/mL)	ATS Short (mg/mL)
25	16
10	4
2.5	1
0.25	0.25
0.025	0.0625
Diluent	Diluent

Questions or Concerns

Contact Methapharm at 1-800-287-7686