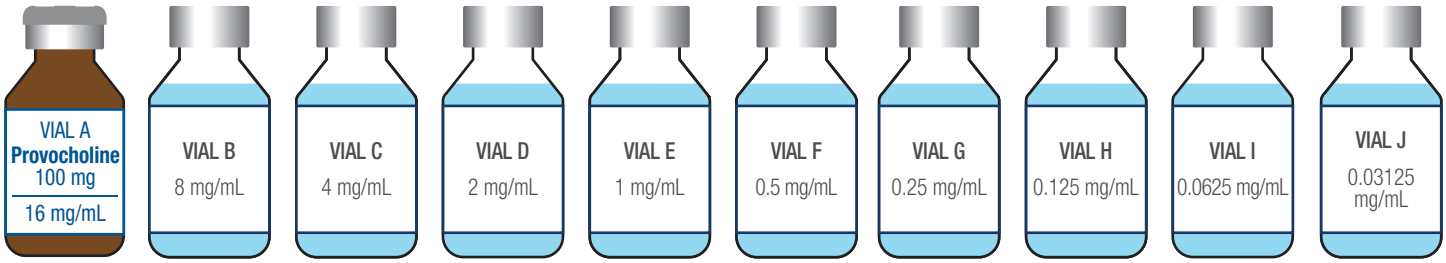
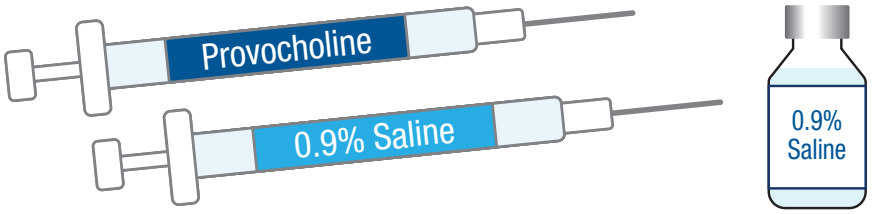
10 Steps to Diluting Provocholine®

Dilution Sequence Protocol for Provocholine 100 mg/vial

Getting Started

1. Attach labels to the vials.
2. Wipe down the stoppers of the Provocholine vial, diluent vial(s), and sterile empty vials with alcohol prep pads.
3. Label two (2) appropriately sized syringes (one for Provocholine, one for 0.9% Saline), and attach needles to each.

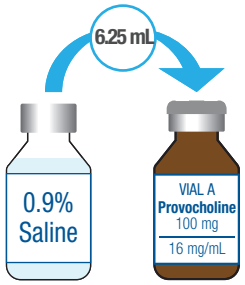




1 Preparing Vial A

16 mg/mL Solution

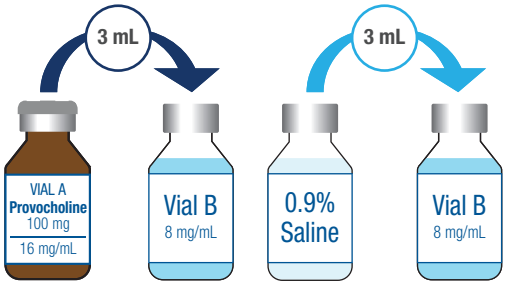
1. Using the diluent needle and syringe, draw 6.25 mL of the diluent and transfer to the Provocholine 100 mg vial.
2. Shake well.



2 Preparing Vial B

8 mg/mL Solution

1. Using the Provocholine needle and syringe, draw 3 mL from Vial A (16 mg/mL) and transfer to Vial B.
2. Using the diluent needle and syringe, draw 3 mL of diluent and transfer to Vial B.
3. Shake well.



Provocholine®
(methacholine chloride)

NOTE

1. Use a sterile hydrophilic Polyvinylidene Fluoride (PVDF) bacterial-retentive filter of pore size 0.22 µm when transferring the solution from each vial (at least 2 mL) to the nebuliser.
2. Be sure to follow your institutional policy for needle and sharps safety.

***Do not attach filter until AFTER solution has been drawn into syringe.**

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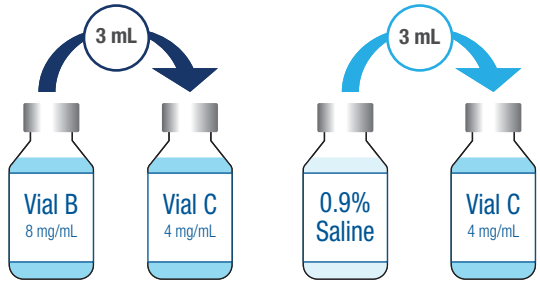
3 Preparing Vial C

4 mg/mL Solution

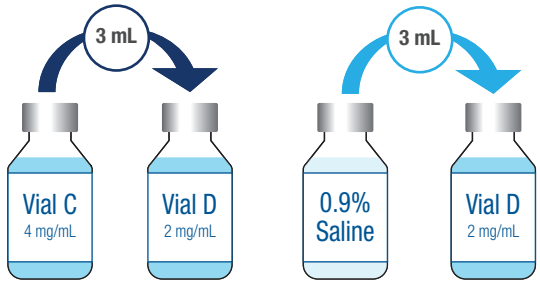
1. Using the Provocholine needle and syringe, draw 3 mL from Vial B (8 mg/mL) and transfer to Vial C.
2. Using the diluent needle and syringe, draw 3 mL of diluent and transfer to Vial C.
3. Shake well.



4 Preparing Vial D

2 mg/mL Solution

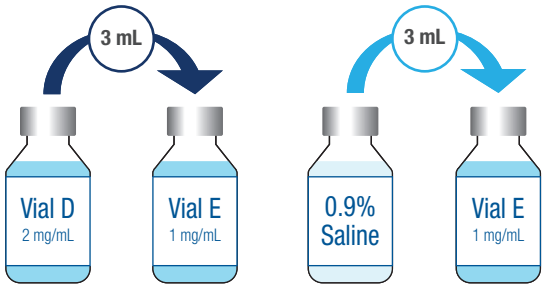
1. Using the Provocholine needle and syringe, draw 3 mL from Vial C (4 mg/mL) and transfer to Vial D.
2. Using the diluent needle and syringe, draw 3 mL of diluent and transfer to Vial D.
3. Shake well.



5 Preparing Vial E

1 mg/mL Solution

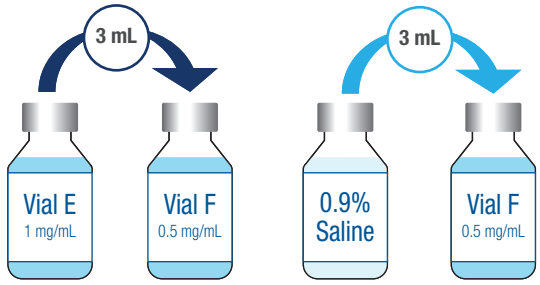
1. Using the Provocholine needle and syringe, draw 3 mL from Vial D (2 mg/mL) and transfer to Vial E.
2. Using the diluent needle and syringe, draw 3 mL of diluent and transfer to Vial E.
3. Shake well.



6 Preparing Vial F

0.5 mg/mL Solution

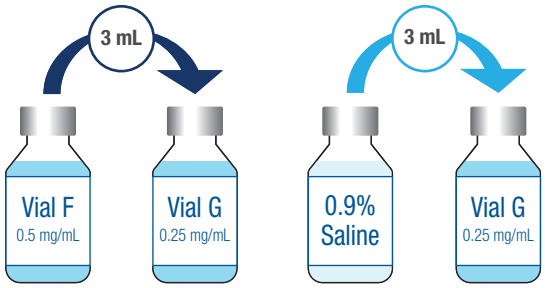
1. Using the Provocholine needle and syringe, draw 3 mL from Vial E (1 mg/mL) and transfer to Vial F.
2. Using the diluent needle and syringe, draw 3 mL of diluent and transfer to Vial F.
3. Shake well.



7 Preparing Vial G

0.25 mg/mL Solution

1. Using the Provocholine needle and syringe, draw 3 mL from Vial F (0.5 mg/mL) and transfer to Vial G.
2. Using the diluent needle and syringe, draw 3 mL of diluent and transfer to Vial G.
3. Shake well.



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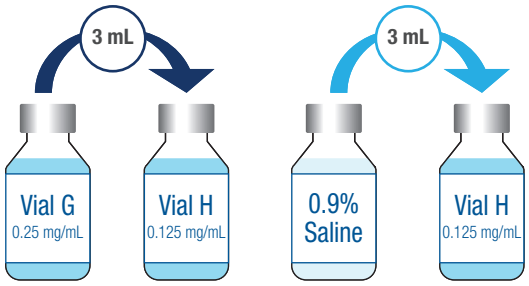
8 Preparing Vial H

0.125 mg/mL Solution

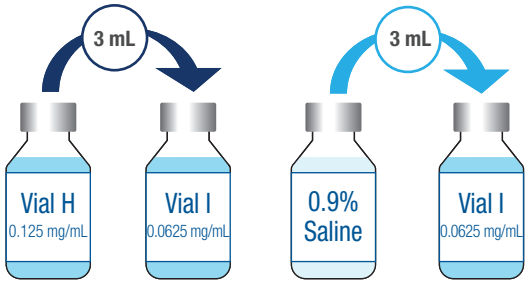
1. Using the Provocholine needle and syringe, draw 3 mL from Vial G (0.25 mg/mL) and transfer to Vial H.
2. Using the diluent needle and syringe, draw 3 mL of diluent and transfer to Vial H.
3. Shake well.



9 Preparing Vial I

0.0625 mg/mL Solution

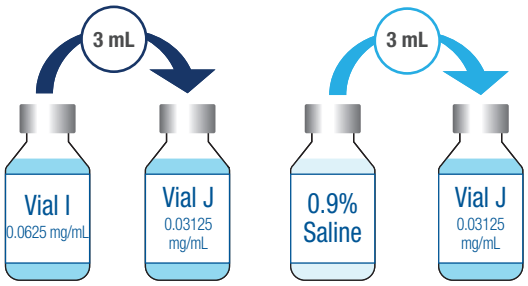
1. Using the Provocholine needle and syringe, draw 3 mL from Vial H (0.125 mg/mL) and transfer to Vial I.
2. Using the diluent needle and syringe, draw 3 mL of diluent and transfer to Vial I.
3. Shake well.



10 Preparing Vial J

0.031 mg/mL Solution

1. Using the Provocholine needle and syringe, draw 3 mL from Vial I (0.0625 mg/mL) and transfer to Vial J.
2. Using the diluent needle and syringe, draw 3 mL of diluent and transfer to Vial J.
3. Shake well.



Vial	Concentration	Final Volume
A	16 mg/mL	3.25 mL
B	8 mg/mL	3 mL
C	4 mg/mL	3 mL
D	2 mg/mL	3 mL
E	1 mg/mL	3 mL
F	0.5 mg/mL	3 mL
G	0.25 mg/mL	3 mL
H	0.125 mg/mL	3 mL
I	0.0625 mg/mL	3 mL
J	0.03125 mg/mL	6 mL

General Instructions

- Provocholine powder should not be stored above 30ºC
- Once reconstituted, the prepared solutions should be used immediately
- All dilutions must be made with 0.9% sodium chloride solution for injection, using empty sterile borosilicate Type I glass vials.

For additional mixing support please visit

www.provocholine.co.uk/educational-resources/mixing-visuals/

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Dilution Check Sheet and Control Record 100 mg - Provocholine

PROVOCHOLINE DILUTIONS FOR CHALLENGE TESTING

Date _____ Prepared by _____ Checked by _____

Provocholine (see vial on label) Lot Number _____ Expiration Date _____

Diluent _____ Lot Number _____ Expiration Date _____

Take Provocholine	Add diluent (Shake well!)	Obtain dilution	Vial name	Initial / Date
Provocholine 100 mg	6.25 mL	16 mg/mL	Vial A - 16 mg/mL	
3 mL from Vial A	3 mL	8 mg/mL	Vial B - 8 mg/mL	
3 mL from Vial B	3 mL	4 mg/mL	Vial C - 4 mg/mL	
3 mL from Vial C	3 mL	2 mg/mL	Vial D - 2 mg/mL	
3 mL from Vial D	3 mL	1 mg/mL	Vial E - 1 mg/mL	
3 mL from Vial E	3 mL	0.5 mg/mL	Vial F - 0.5 mg/mL	
3 mL from Vial F	3 mL	0.25 mg/mL	Vial G - 0.25 mg/mL	
3 mL from Vial G	3 mL	0.125 mg/mL	Vial H - 0.125 mg/mL	
3 mL from Vial H	3 mL	0.0625 mg/mL	Vial I - 0.0625 mg/mL	
3 mL from Vial I	3 mL	0.03125 mg/mL	Vial J - 0.03125 mg/mL	

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PLEASE REFER TO THE SUMMARY OF PRODUCT CHARACTERISTICS FOR FULL PRODUCT INFORMATION.

Presentation: Provocholine® (methacholine chloride) 100mg Powder for nebuliser solution.

Indications: Provocholine is for diagnostic use in a methacholine challenge test only. Provocholine is indicated in adults (aged 17 and over) to detect bronchial airway hyperreactivity, to assist in the diagnosis of asthma when the clinical history is suggestive of asthma but there is normal spirometry and the diagnosis remains uncertain after additional evaluation.

Dosage and administration: Methacholine challenge, may occasionally induce severe bronchospasm and should only be conducted in specialist respiratory centres with appropriate resuscitation facilities. The product is intended for single use only. Once reconstituted the prepared solutions should be used immediately and administered in solution for inhalation. Before starting a methacholine challenge test, pulmonary function must be tested and confirmed to be within the normal range. For the challenge test to proceed, the patient's forced expiratory volume in 1 second/forced vital capacity (FEV_1/FVC) ratio (without exposure to nebulised diluent or Provocholine), must be >70% (considered normal). Prior to nebulisation with Provocholine, the FEV_1 should be measured after exposure to the nebulised diluent (post-diluent FEV_1). The test should not proceed to Provocholine if there is a 20% or greater decline in post-diluent FEV_1 compared to baseline (without nebulised diluent). Post-diluent FEV_1 should be used to calculate any subsequent decline in FEV_1 following exposure to increasing concentrations of Provocholine. The test should be terminated if there is a 20% or greater decline in FEV_1 compared to the post-diluent FEV_1. For preparation of the Provocholine solutions and administration instructions, please refer to the training materials on the product website : www.provocholine.co.uk.

NOTE: To ensure the safe and effective use of Provocholine, patients should be informed about the symptoms that may occur as a result of the test and how to manage them. A

Contraindications: Hypersensitivity to the active substance or other parasympathetic agents; clinically apparent asthma, wheezing or abnormal baseline spirometry (FEV_1/FVC ratio less than 70%); patients on beta blockers or those with bradycardia; known aortic aneurysm, heart attack or stroke (in the previous 3 months), uncontrolled hypertension, myasthenia gravis (treated with cholinesterase inhibitors); recent eye surgery or those at risk of elevated intracranial pressure (cerebral aneurysm). Repeated administration of Provocholine through inhalation of doses higher than the dose administered on the day of the diagnostic test.

Warnings and precautions: Provocholine is a bronchoconstrictor agent for diagnostic purposes and should be administered by inhalation only. When administered orally or by injection, methacholine chloride may induce nausea, vomiting, substernal pain or pressure, hypertension, fainting and transient heart block. A full clinical respiratory history should be taken prior to the test, due to the potential for false positives in other respiratory conditions such as influenza, allergic rhinitis, upper respiratory tract infections or immunisations, elderly patients or patients with chronic pulmonary disease, patients exposed to aerial contaminants and smokers. The challenge test must only be carried out under specialist medical supervision by a doctor familiar with all aspects of the methacholine inhalation challenge testing technique and the management of respiratory failure. The patient should never be left unattended. Emergency equipment and medication must be available to treat acute respiratory failure. Severe bronchoconstriction and reduced respiratory function may occur following administration and if severe, should be reversed immediately by a rapid-acting inhaled bronchodilator (beta agonist). Administration to patients with epilepsy, cardiovascular disease (with bradycardia), vagotonia, peptic ulcer, thyroid disease, urinary tract obstruction or other conditions adversely affected by cholinergic agents should only be carried out only if the benefits outweigh the risks. Asthma sufferers are more sensitive to bronchoconstriction induced by methacholine than healthy subjects. Laboratory staff with asthma or allergies should be mindful of the risks associated with possible occupational exposure. Please consult the SmPC for

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for the UK. Provocholine is a registered trademark of Methapharm Inc.

MWK Healthcare
mwkhealthcare.co.uk

For more information please contact MWK Heathcare at +44 (0) 1691 664243 or visit provocholine.co.uk

Interactions: Use of beta blockers is contraindicated. Medications for the treatment of asthma or medications that may decrease airway hyperresponsiveness should be interrupted before the test, these include, ß agonists (short, long or ultra-long acting), long acting antimuscarinic agents, oral theophylline and ipratropium. Withholding times vary depending on the medication (See section 4.5 of the SmPC for full details).

Fertility, Pregnancy and Lactation: There have been no animal reproduction studies. It is unknown whether methacholine chloride causes foetal harm or whether methacholine chloride is excreted in breast milk. Provocholine should not be used during pregnancy or breastfeeding, unless the benefits clearly outweigh the risks.

Undesirable effects: A positive reaction to methacholine challenge may produce symptoms of bronchospasm, such as chest tightness, cough or wheezing that may be relieved with a bronchodilator. Adverse reactions are rare, and include headache, throat irritation, light-headedness and itching.

Handling and Disposal: Please consult the SmPC for further instructions.

MA Holder: MWK Healthcare Ltd

License number: PL 40565/0001

Legal category: POM

NHS price: £420.00

Date of revision of the API text: November 2020

Adverse events should be reported.
Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or MHRA Yellow Card in the Google Play or Apple App Store.

Adverse events should also be reported to MWK Healthcare Limited at +44(0)1691 664243 or via email: medinfo@mwkhealthcare.co.uk

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