MEDISCA® NETWORK INC.
TECHNICAL SUPPORT SERVICES
FORMULATION CHEMISTRY DEPARTMENT
TOLL-FREE: 866-333-7811
TELEPHONE: 514-905-5096
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technicalservices@medisca.net



| Suggested Formula | Acetylcysteine 20% Inhalation Liquid (Solution, 100 mL) | FIN | F 004 873v2 |
|---|---|---|---|

## SUGGESTED FORMULATION

| Ingredient Listing | Qty. | Unit | NDC # | Supplier | Lot Number | Expiry Date |
|---|---|---|---|---|---|---|
| Acetylcysteine (N-Acetyl-L-Cysteine), USP | 20.000 | g | | | | |
| Benzalkonium Chloride 50% Solution | 0.02 | mL | | | | |
| Edetate Disodium, USP | 0.10 | g | | | | |
| Sterile Water For Injection, USP | 50.0 | mL | | | | |
| Sterile Water For Injection, USP | q.s. to 100.0 | mL | | | | |
| Sodium Hydroxide 20% Solution | As required | | | | | |

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## SPECIAL PREPARATORY CONSIDERATIONS

Ingredient-Specific Information

| | |
|---|---|
| ***Light sensitive*** *(protect from light whenever possible):* | *Acetylcysteine (N-Acetyl-L-Cysteine), Benzalkonium Chloride 50% Solution* |
| ***Air sensitive*** *(protect from air whenever possible):* | *Benzalkonium Chloride 50% Solution* |
| ***Metal reactive*** *(do not allow to come into contact):* | *Benzalkonium Chloride 50% Solution, Acetylcysteine (N-Acetyl-L-Cysteine)* |
| ***Hygroscopic*** *(protect from moisture whenever possible):* | *Benzalkonium Chloride 50% Solution,\ Edetate Disodium* |
| ***Oxygen sensitive*** *(protect from oxygen whenever possible):* | *Acetylcysteine (N-Acetyl-L-Cysteine)* |
| ***Rubber reactive*** *(do not allow to come into contact):* | *Acetylcysteine (N-Acetyl-L-Cysteine)* |

Suggested Preparatory Guidelines

☐ Non-Sterile Preparation ■ Sterile Preparation

Processing Error / Testing Considerations: To account for processing error, sterility and endotoxin testing considerations during preparation, it is suggested to measure an additional **5 to 9%** of the required quantities of ingredients.

Special Instruction: This formula must be prepared within the appropriate facilities under adequate environmental conditions, following the necessary guidelines and procedures as stated within *USP 797*. Only trained and qualified personnel must prepare this formula.

All heat stable, reusable materials and equipment must be sterilized and depyrogenated by dry heat sterilization at 250°C for 2 hours prior to use.

Every batch of final product compounded using this procedure must be sterility and endotoxin tested before being dispensed.

Protective apparel, such as a sterile gown, sterile gloves, shoe covers, head cap, eyewear and face-masks should always be worn. In addition, proper personnel cleansing must be done before entering the buffer or clean area.

Filter integrity must be validated by performing a filter stress test. If the test demonstrates that the filter might be defective, the solution must be discarded and remade.

This procedure requires the use of very small quantities of ingredients. All calculations and preparation techniques must be verified before dispensing the final product.

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## SUGGESTED PREPARATION (for 100 mL)

Weigh and / or measure the following ingredients when appropriate:

| Ingredient Listing | Qty. | Unit | Multiplication factor (*): ____ | Processing Error | Qty. to measure |
|---|---|---|---|---|---|
| Acetylcysteine (N-Acetyl-L-Cysteine), USP § | 20.000 | g | | | |
| Benzalkonium Chloride 50% Solution § | 0.02 | mL | | | |
| Edetate Disodium, USP § | 0.10 | g | | | |
| Sterile Water For Injection, USP § | 50.0 | mL | | | |
| Sterile Water For Injection, USP § | q.s. to 100.0 | mL | | | |
| Sodium Hydroxide 10% Solution § | As required | | | | |

* Takes into account increased batch size conversions and density conversions, if required.
§ Weigh / measure just prior to use.

| Preparatory Instruction<br>**IMPORTANT: All preparatory procedures must be performed using proper Aseptic Technique** | |
|---|---|
| 1. | **Equipment sterilization:**<br><br>Following the manufacturer's specifications, sterilize and depyrogenate all heat stable, reusable materials and equipment, then return to ambient temperature. |
| 2. | **Medium incorporation:**<br><br>A. In the given order, sequentially add the following ingredients to the Sterile Water For Injection (50.0 mL *plus* processing error adjustments)<br><br>-Acetylcysteine (N-Acetyl-L-Cysteine)<br>-Benzalkonium Chloride 50% Solution<br>-Edetate Disodium<br><br>Specifications: Continuously mix.<br><br>End result: Homogeneous liquid-like dispersion.<br><br>Note: Add the next ingredient, once the previous one has been completely added and dispersed. |

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| 3. | **pH testing:**<br>A. Draw an appropriate amount of the mixture (Step 2A).<br>B. Test the pH of the sample. It should lie between 6.0 and 7.5.<br>C. If the pH < 6.0, carefully add in a dropwise manner the Sodium Hydroxide 10% solution to the mixture:<br>1. Draw and transfer 1 or 2 drops of the Sodium Hydroxide 10% solution to the mixture.<br>2. Stir for at least 5 minutes to evenly disperse the Sodium Hydroxide 10% solution.<br>3. Re-test the pH.<br>4. Continue to add the Sodium Hydroxide 10% solution until the pH of 6.0 to 7.5 is obtained.<br>IMPORTANT: Do not allow the pH to rise above 7.5<br>**Note: Continuously mix until all solid particles have completely dissolved.** |
| 4. | **Filling to volume:**<br>A. Add additional Sterile Water for Injection to the above mixture to fill to the required batch size (100.0 mL *plus* processing error adjustments).<br>Specifications: Continuously mix.<br>End result: Homogenous liquid-like solution. |
| 5. | **Filtering and transferring:**<br>Aseptically filter the solution through a 0.22-µm sterile filter into the recommended dispensing container (see Packaging requirements). Transfer the remainder into a separate dispensing container. This is to be used as the Test sample for sterility and endotoxin testing. |
| 6. | **Filter integrity test:**<br>Validate filter integrity by performing a filter stress test. If the test demonstrates that the filter might be defective, the solution must be discarded and remade. |
| 7. | **Sterility testing:**<br>Validate the Test sample for sterility, in accordance to current USP 797 regulatory guidelines. |

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## SUGGESTED PRESENTATION

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|---|---|---|---|---|
| Estimated Beyond-Use Date | 14 days, refrigerated as per USP 797.<br>BUD based on a successful sterility and endotoxin test result. | | Packaging Requirements | Sterile, tightly closed, light-resistant inhalation bottle. |
| Auxiliary Labels | 1 | Use as directed. Do not exceed prescribed dose. | 7 | May impair mental and/or physical ability. Use care when operating a car or machinery. |
| | 2 | Keep out of reach of children. | 8 | **Not for use in infants.** |
| | 3 | Keep refrigerated. Do not freeze. | 9 | Discard container after use. |
| | 4 | Consult your health care practitioner if any other prescription or over-the-counter medications are currently being used or are prescribed for future use. | 10 | Do not use if product changes color. |
| | 5 | Discard in the presence of particulate matter. | 11 | Do not take with alcohol, sleep aids, tranquilizers or other CNS depressants. |
| | 6 | For nebulizer use only. | 12 | **Hypertonic solution; it may cause irritation.** |
| Pharmacist Instructions | Add any auxiliary labels specific to the active ingredient to the dispensing container as deemed necessary. | | | |
| Patient Instructions | Contact your pharmacist in the event of adverse reactions. | | | |

## REFERENCES


1. Parenteral Preparations. In: Allen, LV, Jr. *The Art, Science and Technology of Pharmaceutical Compounding Third Edition*. American Pharmaceutical Association; 2008: 313.
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3. Acetylcysteine (Monograph). In: O'Neil MJ. *The Merck Index 14th Edition*. Whitehouse Station, NJ: Merck & Co, Inc.; 2006: Monograph #88.
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