MEDISCA® NETWORK INC.
TECHNICAL SUPPORT SERVICES
FORMULATION CHEMISTRY DEPARTMENT
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| Suggested Formula | Epinephrine 1 mg/ mL Injection (Solution, 100 mL) | FIN | F 002 207v2 |
|---|---|---|---|

## SUGGESTED FORMULATION

| Ingredient Listing | Qty. | Unit | NDC # | Supplier | Lot Number | Expiry Date |
|---|---|---|---|---|---|---|
| Epinephrine, USP | 0.100 | g | | | | |
| Sodium Metabisulfite, NF | 0.17 | g | | | | |
| Sodium Chloride, USP | 0.58 | g | | | | |
| Benzyl Alcohol, NF | 1.0 | mL | | | | |
| Sterile Water for Injection, USP | 80.0 | mL | | | | |
| Sterile Water for Injection, USP | q.s. to 100.0 | mL | | | | |
| Hydrochloric Acid 5% solution | As required | | | | | |

## SPECIAL PREPARATORY CONSIDERATIONS

Ingredient-Specific Information

***Light sensitive*** *(protect from light whenever possible):* *Epinephrine, Sodium Metabisulfite, Benzyl Alcohol*

***Air sensitive*** *(protect from air whenever possible):* *Epinephrine, Sodium Metabisulfite*

***Moisture Sensitive*** *(protect from humidity whenever possible):* *Sodium Metabisulfite*

Suggested Preparatory Guidelines

☐ Non-Sterile Preparation ■ Sterile Preparation

Processing Error / Testing Considerations: To account for processing error, pH testing, 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 |
|---|---|---|---|---|---|
| Epinephrine, USP § | 0.100 | g | | | |
| Sodium Metabisulfite, NF § | 0.17 | g | | | |
| Sodium Chloride, USP § | 0.58 | g | | | |
| Benzyl Alcohol, NF § | 1.0 | mL | | | |
| Sterile Water for Injection, USP § | 80.0 | mL | | | |
| Sterile Water for Injection, USP§ | q.s. to 100.0 | mL | | | |
| Hydrochloric Acid 5% 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>Following the manufacturer's specifications, sterilize glass, and heat-resistant plastic and metal equipment, then return to ambient temperature and pressure. |
| 2. | **Powder preparation:**<br>A. Combine and triturate the following ingredients together to form a fine, homogeneous powder blend:<br>-Epinephrine<br>-Sodium Metabisulfite<br>-Sodium Chloride |
| 3. | **Powder preparation to medium incorporation:**<br>A. Sequentially add the following ingredients to the Sterile Water for Injection (80.0 mL *plus* processing error adjustments):<br>-Benzyl Alcohol<br>-Fine, homogeneous powder blend (Step 2A)<br>Specifications: Continuously mix until all solid particles have completely dissolved.<br>End result: Homogeneous liquid-like solution.<br>Note: Add the next ingredient, once the previous one has been completely added and dissolved. |

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4. **pH testing:**

   A. Draw an appropriate amount of the mixture (Step 3A).

   B. Test the pH of the sample. It should lie between 2.2 and 5.0.

   C. If the pH > 5.0, carefully add in a dropwise manner the Hydrochloric Acid 5% Solution to the mixture:

      1. Draw and transfer 1 or 2 drops of the Hydrochloric Acid 5% Solution to the mixture.
      2. Stir for at least 5 minutes to evenly disperse the Hydrochloric Acid 5% Solution.
      3. Re-test the pH.
      4. Continue to add the Hydrochloric Acid 5% Solution until the pH of 2.2 to 5.0 is obtained.

         IMPORTANT: Do not allow the pH to fall below 2.2.

5. **Filling to volume:**

   A. Add additional Sterile Water to the above mixture to fill to the required batch size (100.0 mL *plus* processing error adjustments).

      Specifications: Continuously mix.

      End result: Homogeneous liquid-like solution.

6. **Filtering and transferring:**

   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.

7. **Filter integrity test:**

   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.

8. **Sterility testing:**

   Validate the Test sample for sterility in accordance to current USP 797 regulatory guidelines.

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## SUGGESTED PRESENTATION

| | | | | | |
|---|---|---|---|---|---|
| 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 unit dose injection vials. |
| Auxiliary Labels | 1 | Use as directed. Do not exceed prescribed dose. | | 6 | Discard container after use. |
| | 2 | Keep out of reach of children. | | 7 | Equilibrate to room temperature before use. |
| | 3 | Do not use if discolored. | | 8 | Do not use if a precipitate forms. |
| | 4 | Keep in a dry place. | | 9 | Protect from light. |
| | 5 | Consult your health care practitioner if any prescription or over-the-counter medications are currently being used or are prescribed for future use. | | 10 | Keep refrigerated. Do not freeze. |
| Pharmacist Instructions | Add any auxiliary labels specific to the API to the dispensing container as deemed necessary. | | | | |
| Patient Instructions | Contact your pharmacist in the event of adverse reactions. | | | | |

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## REFERENCES


1. USP <797> Pharmaceutical Compounding – Sterile Preparations. US Pharmacopeial Convention, Inc. *United States Pharmacopeia XXVIII / National Formulary 23.* Rockville, MD. 2004: 2461.
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10. Epinephrine Injection. *United States Pharmacopeia XXVIII / National Formulary 23.* Rockville, MD. US Pharmacopeial Convention, Inc. 2004: 740.