MEDISCA® NETWORK INC.
TECHNICAL SUPPORT SERVICES
FORMULATION CHEMISTRY DEPARTMENT
TOLL-FREE: 866-333-7811
TELEPHONE: 514-905-5096
FAX: 514-905-5097
technicalservices@medisca.net

Suggested Formula	Diphenhydramine Hydrochloride 50 mg/mL Injection (Solution, 10 mL)	FIN	F 002 232v2

SUGGESTED FORMULATION

Ingredient Listing	Qty.	Unit	NDC #	Supplier	Lot Number	Expiry Date
Diphenhydramine Hydrochloride, USP	0.500	g				
Benzyl Alcohol, NF	0.2	mL				
Sterile Water for Injection, USP	8.0	mL				
Sterile Water for Injection, USP	q.s. to 10.0	mL				
Sodium Hydroxide 5% Solution	As required					
Hydrochloric Acid 5% Solution	As required					

SPECIAL PREPARATORY CONSIDERATIONS

Ingredient-Specific Information

Light sensitive *(protect from light whenever possible):* *Diphenhydramine Hydrochloride*, *Benzyl Alcohol*

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 **20 to 25%** 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.

MEDISCA® NETWORK INC.
TECHNICAL SUPPORT SERVICES
FORMULATION CHEMISTRY DEPARTMENT
TOLL-FREE: 866-333-7811
TELEPHONE: 514-905-5096
FAX: 514-905-5097
technicalservices@medisca.net

Suggested Formula	Diphenhydramine Hydrochloride 50 mg/mL Injection (Solution, 10 mL)	FIN	F 002 232v2

SUGGESTED PREPARATION (for 10 mL)

Weigh and / or measure the following ingredients when appropriate:

Ingredient Listing	Qty.	Unit	Multiplication factor (*): ____	Processing Error	Qty. to measure
Diphenhydramine Hydrochloride, USP §	0.500	g			
Benzyl Alcohol, NF §	0.2	mL			
Sterile Water for Injection, USP §	8.0	mL			
Sterile Water for Injection, USP §	q.s. to 10.0	mL			
Sodium Hydroxide 5% Solution §	As required				
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 **IMPORTANT: All preparatory procedures must be performed using proper Aseptic Technique**	
1.	**Equipment sterilization:** Following the manufacturer's specifications, sterilize and depyrogenate all heat stable, reusable materials and equipment, then return to ambient temperature.
2.	**Powder-Liquid preparation:** A. Triturate the Diphenhydramine Hydrochloride to form a fine, homogeneous powder. B. Levigate the fine, homogeneous powder (Step 2A) with the following ingredient: -Benzyl Alcohol End result: Homogeneous paste-like dispersion.
3.	**Powder-Liquid preparation to medium incorporation:** A. Incrementally add the homogeneous paste-like dispersion (Step 2B) to the following ingredient: -Sterile Water for Injection (8.0 mL *plus* processing error adjustments) Specifications: Continuously mix until all solid particles have completely dissolved. End result: Homogeneous liquid-like solution.

MEDISCA® NETWORK INC.
TECHNICAL SUPPORT SERVICES
FORMULATION CHEMISTRY DEPARTMENT
TOLL-FREE: 866-333-7811
TELEPHONE: 514-905-5096
FAX: 514-905-5097
technicalservices@medisca.net

Suggested Formula	Diphenhydramine Hydrochloride 50 mg/mL Injection (Solution, 10 mL)	FIN	F 002 232v2

4.	**pH testing:** A. Draw an appropriate amount of the mixture. B. Test the pH of the sample. It should lie between 4.0 and 6.5. C. If the pH < 4.0, carefully add in a dropwise manner the Sodium Hydroxide 5% Solution to the mixture: 1. Draw and transfer 1 or 2 drops of the Sodium Hydroxide 5% Solution to the mixture. 2. Stir for at least 5 minutes to evenly disperse the Sodium Hydroxide 5% Solution. 3. Re-test the pH. 4. Continue to add the Sodium Hydroxide 5% Solution until the pH of 4.0 to 6.5 is obtained. IMPORTANT: Do not allow the pH to rise above 6.5. D. If the pH > 6.5, 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 4.0 to 6.5 is obtained. IMPORTANT: Do not allow the pH to fall below 4.0.
5.	**Filling to volume:** A. Add additional Sterile Water for Injection to the above mixture to fill to the required batch size (10.0 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 and endotoxins, in accordance to current USP 797 regulatory guidelines.

MEDISCA® NETWORK INC.
TECHNICAL SUPPORT SERVICES
FORMULATION CHEMISTRY DEPARTMENT
TOLL-FREE: 866-333-7811
TELEPHONE: 514-905-5096
FAX: 514-905-5097
technicalservices@medisca.net

Suggested Formula	Diphenhydramine Hydrochloride 50 mg/mL Injection (Solution, 10 mL)	FIN	F 002 232v2

SUGGESTED PRESENTATION

Estimated Beyond-Use Date		14 days, as per USP 797. BUD based on a successful sterility and endotoxin test result.	Packaging Requirements		Sterile, light-resistant unit dose injection vials.
Auxiliary Labels	1	Use as directed. Do not exceed prescribed dose.		7	Discard container after use.
	2	Keep out of reach of children.		8	Equilibrate to room temperature before use.
	3	Keep refrigerated. Do not freeze.		9	Protect from light.
	4	**Do not take with alcohol, sleep aids, tranquilizers or other CNS depressants.**		10	**May impair mental and/or physical ability. Use care when operating a car or machinery.**
	5	**Consult your health care practitioner if any prescription or over-the-counter medications are currently being used or are prescribed for future use.**		11	Discard in the presence of particulate matter.
	6	Hypertonic solution, inject slowly.		12	Do not use if discolored.
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.				

Suggested Formula	Diphenhydramine Hydrochloride 50 mg/mL Injection (Solution, 10 mL)	FIN	F 002 232v2

REFERENCES

1. USP <797> Pharmaceutical Compounding – Sterile Preparations. US Pharmacopeial Convention, Inc. *United States Pharmacopeia XXVIII / National Formulary 23.* Rockville, MD. 2004: 2461.
2. Parenteral Preparations. In: Allen, LV, Jr. *The Art, Science and Technology of Pharmaceutical Compounding.* American Pharmaceutical Association; 1998: 251.
3. Benadryl Preparations. In: Canadian Pharmacists Association. *Compendium of Pharmacists and Specialties, 2006.* 288.
4. Benzyl Alcohol. In: Rowe RC. *Handbook of Pharmaceutical Excipients, 4th Edition*. American Pharmaceutical Association; 2003: 53.
5. Diphenhydramine Hydrochloride. In: Sweetman SC, ed. *Martindale: The Complete Drug Reference, 34th Edition.* London, England: The Pharmaceutical Press; 2005: 431.
6. Diphenhydramine Hydrochloride (Monograph). In: O'Neil MJ. *The Merck Index 13th Edition*. Whitehouse Station, NJ: Merck & Co, Inc.; 2001: 583.
7. Chapter 8: Buffered and Isotonic Solutions. In: Martin, A. *Physical Pharmacy, Fourth Edition.* Philadelphia, PA: Lipponcott Williams & Wilkins; 1993: 169~189.
8. Chapter 18: Tonicity, Osmoticity, Osmolaltiy and Osmolarity. In: Gennaro AR. *Remington: The Science and Practice of Pharmacy, 20th Edition.* Baltimore, MD: Lippincott Williams & Wilkins; 2000: 246~262.
9. Diphenhydramine Hydrochloride. In: Trissel LA. *Trissel's Stability of Compounded Formulations, 3rd Edition.* American Pharmaceutical Association; 2005: 148.
10. Diphenhydramine Hydrochloride (Monograph). *United States Pharmacopeia XXVIII / National Formulary 23.* Rockville, MD. US Pharmacopeial Convention, Inc. 2004: 667.
11. Diphenhydramine Hydrochloride Injection. *United States Pharmacopeia XXVIII / National Formulary 23.* Rockville, MD. US Pharmacopeial Convention, Inc. 2004: 668.