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	Amiodarone Hydrochloride 50 mg/ mL Intravenous Injection (Solution, 18 mL)	FIN	F 008 641

SUGGESTED FORMULATION

Ingredient Listing	Qty.	Unit	NDC #	Supplier	Lot Number	Expiry Date
Amiodarone Hydrochloride, USP	0.900	g				
Benzyl Alcohol (Parenteral Application), NF	0.18	mL				
Polysorbate 80, NF	1.8	mL				
Sodium Chloride, USP	0.018	g				
Sterile Water for Injection, USP	10.0	mL				
Sterile Water for Injection, USP	q.s. to 18.0	mL				
Sodium Hydroxide 10% Solution	As required					
Hydrochloric Acid 10% Solution	As required					

SPECIAL PREPARATORY CONSIDERATIONS

Ingredient-Specific Information

Light Sensitive *(protect from light whenever possible):* *Amiodarone Hydrochloride, Benzyl Alcohol, Polysorbate 80*

Hygroscopic *(protect from moisture whenever possible):* *Polysorbate 80*

Oxygen sensitive *(protect from air whenever possible):* *Polysorbate 80*

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	Amiodarone Hydrochloride 50 mg/ mL Intravenous Injection (Solution, 18 mL)	FIN	F 008 641

SPECIAL PREPARATORY CONSIDERATIONS (CONTINUED)

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 **15 to 20%** of the required quantities of ingredients.

Special Instruction: This formula may contain one or more Active Pharmaceutical Ingredients (APIs) that may be classified as hazardous, please refer & verify the current NIOSH list of Antineoplastic and Other Hazardous Drugs in Healthcare Settings. At this time, **General Chapter <800> Hazardous Drugs – Handling in Healthcare Settings** is informational and not compendially applicable unless otherwise specified by regulators and enforcement bodies. For information on the scope, intended applicability, and implementation context for USP General Chapter <800>, see: https://www.usp.org/usp-800-context-for-implementation-fs.pdf.

This formula must be prepared within the appropriate facilities under adequate environmental conditions, following the necessary guidelines and procedures as stated within *USP 797* and *USP 800* when handling hazardous drugs. 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.

All required personal protective equipment (sterile and hazardous if applicable), such as but not limited to, gowns, aprons, sleeves, gloves both inner and outer if applicable, shoe covers, hairnet, head cap, beard cover, eyewear, appropriate face mask, respirator and face shield, etc., where applicable must be worn at all times. In addition, proper personnel cleansing must be done before entering the buffer or clean area.

If applicable, follow all required procedures for hazardous drug handling including but not limited to procurement, transport, storage, preparation, dispensing, administration, clean up (spills) & disposal.

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.

If you are a registered 503B facility, please refer to all relevant guidance documents including but not limited to the Code of Federal Regulations (CFR), Guidance for Industry (GFIs) and Compliance Policy Guides (CPGs).

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	Amiodarone Hydrochloride 50 mg/ mL Intravenous Injection (Solution, 18 mL)	FIN	F 008 641

SUGGESTED PREPARATION (for 18 mL)

Weigh and / or measure the following ingredients when appropriate:

Ingredient Listing	Qty.	Unit	Multiplication factor (*): ____	Processing Error	Qty. to measure
Amiodarone Hydrochloride, USP §	0.900	g			
Benzyl Alcohol (Parenteral Application), NF §	0.18	mL			
Polysorbate 80, NF	1.8	mL			
Sodium Chloride, USP	0.018	g			
Sterile Water for Injection, USP §	10.0	mL			
Sterile Water for Injection, USP §	q.s. to 18.0	mL			
Sodium Hydroxide 10% Solution §	As required				
Hydrochloric Acid 10% Solution §	As required				

* Takes into account increased batch size conversions and density conversions, if required.

§ Weigh / measure just prior to use.

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	Amiodarone Hydrochloride 50 mg/ mL Intravenous Injection (Solution, 18 mL)	FIN	F 008 641

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. By geometrical addition, combine and triturate the following ingredients together to form a fine, homogeneous powder blend:

   -Amiodarone Hydrochloride
   -Sodium Chloride

   B. Levigate the fine, homogeneous powder blend (Step 2A) with the Polysorbate 80.

   End result: Homogeneous liquid-like dispersion.

3. **Medium Integration:**

   A. In the given order, sequentially add the following ingredients to the Sterile Water for Injection (10.0 mL *plus* processing error adjustments):

   -Benzyl Alcohol (Parenteral Application)
   -Homogeneous liquid-like dispersion (Step 2B)

   Specifications: Continuously mix until all solid particles have completely dissolved.

   End result: Homogeneous liquid-like solution.

   Note: Add the next ingredient, once the previous one has been completely added and dissolved.

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	Amiodarone Hydrochloride 50 mg/ mL Intravenous Injection (Solution, 18 mL)	FIN	F 008 641

4. **pH testing:**

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

B. Test the pH of the sample. It should lie between 3.0 and 5.0.

C. If the pH < 3.0 carefully add in a dropwise manner the Sodium Hydroxide 10% Solution to the mixture:

1. Draw and transfer 1 or 2 drops of the Sodium Hydroxide 10% Solution to the mixture.
2. Stir for at least 5 minutes to evenly disperse the Sodium Hydroxide 10% Solution.
3. Re-test the pH.
4. Continue to add the Sodium Hydroxide 10% Solution until the pH of 3.0 to 5.0 is obtained.

IMPORTANT: Do not allow the pH to rise above 5.0.

D. If the pH > 5.0, carefully add in a dropwise manner the Hydrochloric Acid 10% Solution to the mixture:

1. Draw and transfer 1 or 2 drops of the Hydrochloric Acid 10% Solution to the mixture.
2. Stir for at least 5 minutes to evenly disperse the Hydrochloric Acid 10% Solution.
3. Re-test the pH.
4. Continue to add the Hydrochloric Acid 10% Solution until the pH of 3.0 to 5.0 is obtained.

IMPORTANT: Do not allow the pH to fall below 3.0.

5. **Filling to volume:**

A. Add additional Sterile Water for Injection to the mixture (Step 3A) to fill to the required batch size (18.0 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.

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	Amiodarone Hydrochloride 50 mg/ mL Intravenous Injection (Solution, 18 mL)	FIN	F 008 641

8.	**Terminal Sterilization:** In relation to the chemical composition of the formulation, final packaging, etc., select and validate an end-stage sterilization method and follow the manufacturer's specifications.
9.	**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	Amiodarone Hydrochloride 50 mg/ mL Intravenous Injection (Solution, 18 mL)	FIN	F 008 641

SUGGESTED PRESENTATION

Estimated Beyond-Use Date		14 days, refrigerated, as per USP. 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.		7	Discard in the presence of particulate matter.
	2	Keep out of reach of children.		8	Discard container after use.
	3	Keep refrigerated (2°C – 8°C). Do not freeze.		9	Do not use if product changes color.
	4	Protect from light.		10	Do not take with alcohol, sleep aids, tranquilizers or other CNS depressants.
	5	Equilibrate to room temperature before use.		11	May impair mental and/or physical ability. Use care when operating a car or machinery.
	6	Consult your health care practitioner if any other prescription or over-the-counter medications are currently being used or are prescribed for future use.			
Pharmacist Instructions	Add any auxiliary labels specific to the API to the dispensing container as deemed necessary. **IMPORTANT: Using proper aseptic techniques, one must dilute the Amiodarone Hydrochloride injection to the appropriate concentration with the appropriate sterile diluent prior to intravenous injection. Also it must be administered accordingly as determined by the prescribing physician.** **<u>NOTE</u>: Once diluted it must be used immediately and any unused portion must be discarded.**				
Patient Instructions	Contact your pharmacist in the event of adverse reactions.				

Suggested Formula	Amiodarone Hydrochloride 50 mg/ mL Intravenous Injection (Solution, 18 mL)	FIN	F 008 641

REFERENCES

1.	Parenteral Preparations. In: Allen, LV, Jr. *The Art, Science, and Technology of Pharmaceutical Compounding Fifth Edition.* American Pharmacists Association; 2016: 399.
2.	Sodium Chloride. In: Rowe RC. *Handbook of Pharmaceutical Excipients, 8th Edition*. American Pharmaceutical Association; 2017: 854.
3.	Amiodarone Hydrochloride for Injection Sandoz Standard. In: Canadian Pharmacists Association. *Compendium of Pharmacists and Specialties, 2008.* 139.
4.	Amiodarone Hydrochloride. In: Sweetman SC, ed. *Martindale: The Complete Drug Reference, 38th Edition.* London, England: The Pharmaceutical Press; 2014: 1300.
5.	Amiodarone (Monograph). In: O'Neil MJ. *The Merck Index 15th Edition*. Whitehouse Station, NJ: Merck & Co, Inc.; 2013: Monograph #478.
6.	Amiodarone Hydrochloride. In: Trissel LA. *Trissel's Stability of Compounded Formulations, 5rd Edition.* American Pharmaceutical Association; 2012: 32.
7.	Amiodarone Systemic. Thomson Micromedex. *USP DI – Drug Information for the Health Care Professional, 26th Edition.* Taunton, MA: US Pharmacopeial Convention, Inc; 2006: 106.
8.	Benzyl Alcohol. In: Rowe RC. *Handbook of Pharmaceutical Excipients, 8th Edition*. American Pharmaceutical Association; 2017: 105.
9.	Chapter 8: Buffered and Isotonic Solutions. In: Sinko, D. J. and Singh, Y. *Martin's Physical Pharmacy and Pharmaceutical Sciences, Sixth Edition.* Philadelphia, PA: Lipponcott Williams & Wilkins; 2011: 163-181.
10.	Chapter 18: Tonicity, Osmoticity, Osmolality and Osmolarity. In: D.B Troy. *Remington: The Science and Practice of Pharmacy, 21st Edition.* Baltimore, MD: Lippincott Williams & Wilkins; 2006: 250~265.
11.	USP <797>. *United States Pharmacopeia XLII / National Formulary 37.* Rockville, MD. US Pharmacopeial Convention, Inc. 2019: 6959.