



Suggested Formula	Acyclovir 500 mg/10 mL Intravenous Injection (Solution, 10 mL)	FIN	F 002 333v3
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SUGGESTED FORMULATION

Ingredient Listing	Qty.	Unit	NDC #	Supplier	Lot Number	Expiry Date
Acyclovir, USP	TBD					
Sodium Chloride, USP	0.02	g				
Sterile Water for Injection, USP	7.5	mL				
Sterile Water for Injection, USP	q.s. to 10.0	mL				
Sodium Hydroxide 20% Solution	As required					

SPECIAL PREPARATORY CONSIDERATIONS

Ingredient-Specific Information

Light Sensitive (protect from light whenever possible): Acyclovir

Moisture Sensitive (protect from humidity whenever possible): Acyclovir





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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 **20 to 25%** 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/compounding/general-chapter-hazardous-drugs-handling-healthcare>.

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.

Compounder needs to verify as per USP, if 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 (GFI) 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.



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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
Acyclovir, USP §	TBD				
Sodium Chloride, USP §	0.02	g			
Sterile Water for Injection, USP §	7.5	mL			
Sterile Water for Injection, USP §	q.s. to 10.0	mL			
Sodium Hydroxide 20% 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.



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2. **Ingredient quantification:**

A. Determine the potency of Acyclovir based on the certificate of analysis:

	100%
MINUS	
Water Content (from certificate of analysis)	_____ %
DIVIDED BY	100
EQUALS	
Quantity of water free Acyclovir, in decimal	_____
MULTIPLIED BY	
Assay on anhydrous basis result (from certificate of analysis)	_____ %
DIVIDED BY	100
EQUALS	
i. Potency of Acyclovir, in decimal	_____



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3.	<u>Ingredient quantification:</u>	<p>A. Determine the quantity (in g) of Acyclovir to make an Acyclovir 500 mg/10 mL Intravenous Injection, batch size (10 mL):</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="padding: 5px;">Quantity of Acyclovir required for a 10 mL Injection</td> <td style="text-align: right; padding: 5px;">0.500 g</td> </tr> <tr> <td colspan="2" style="padding: 5px;">DIVIDED BY</td> </tr> <tr> <td style="padding: 5px;">Potency of Acyclovir, in decimal (Step 2Ai)</td> <td style="text-align: right; padding: 5px;">_____</td> </tr> <tr> <td colspan="2" style="padding: 5px;">EQUALS</td> </tr> <tr> <td style="padding: 5px;">i. Quantity of Acyclovir needed for a 10 mL Injection</td> <td style="text-align: right; padding: 5px;">_____ g</td> </tr> <tr> <td colspan="2" style="padding: 5px;">MULTIPLIED BY</td> </tr> <tr> <td style="padding: 5px;">Processing error adjustments (20 to 25%)</td> <td style="text-align: right; padding: 5px;">1.20 to 1.25</td> </tr> <tr> <td colspan="2" style="padding: 5px;">EQUALS</td> </tr> <tr> <td style="padding: 5px;">ii. Quantity of Acyclovir needed <i>plus</i> processing error adjustments</td> <td style="text-align: right; padding: 5px;">_____ g</td> </tr> </table>	Quantity of Acyclovir required for a 10 mL Injection	0.500 g	DIVIDED BY		Potency of Acyclovir, in decimal (Step 2Ai)	_____	EQUALS		i. Quantity of Acyclovir needed for a 10 mL Injection	_____ g	MULTIPLIED BY		Processing error adjustments (20 to 25%)	1.20 to 1.25	EQUALS		ii. Quantity of Acyclovir needed <i>plus</i> processing error adjustments	_____ g
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4.	<u>Powder preparation:</u>	<p>A. Triturate the Acyclovir (amount determine from Step 3Aii) to form a fine, homogeneous powder.</p>																		
5.	<u>Medium preparation:</u>	<p>A. Combine and mix the following ingredients together:</p> <ul style="list-style-type: none"> -Sodium Chloride -Sterile Water for Injection (7.5 mL <i>plus</i> processing error adjustments) <p><u>Specifications:</u> Continuously mix until all solid particles have completely dissolved.</p> <p><u>End result:</u> Homogeneous liquid-like solution.</p>																		
6.	<u>Powder to medium integration:</u>	<p>A. Incrementally add the fine homogeneous powder (Step 4A) to the homogeneous liquid-like solution (Step 5A).</p> <p><u>Specifications:</u> Continuously mix.</p> <p><u>End result:</u> Homogeneous liquid-like dispersion.</p>																		



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7.	<p><u>pH testing:</u></p> <p>A. Draw an appropriate amount of the mixture (Step 6A).</p> <p>B. Test the pH of the sample. It should lie between 11.2 and 11.5.</p> <p>C. <u>If the pH < 11.2, carefully add in a dropwise manner the Sodium Hydroxide 20 % Solution to the mixture:</u></p> <ol style="list-style-type: none">1. Draw and transfer 1 or 2 drops of the Sodium Hydroxide 20% Solution to the mixture.2. Stir for at least 5 minutes to evenly disperse the Sodium Hydroxide 20% Solution.3. Re-test the pH.4. Continue to add the Sodium Hydroxide 20% Solution until the pH of 11.2 to 11.5 is obtained <u>and all solid particles are completely dissolved.</u> <p><u>Specifications:</u> Continuously mix.</p> <p><u>End result:</u> Homogeneous liquid-like solution.</p> <p>IMPORTANT: Do not allow the pH to rise above 11.5.</p>		
8.	<p><u>Filling to volume:</u></p> <p>A. Add additional Sterile Water for Injection to the above mixture to fill to the required batch size (10.0 mL <i>plus</i> processing error adjustments).</p> <p><u>Specifications:</u> Continuously mix.</p> <p><u>End result:</u> Homogeneous liquid-like solution.</p>		
9.	<p><u>Filtering and transferring:</u></p> <p>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.</p>		
10.	<p><u>Filter integrity test:</u></p> <p>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.</p>		
11.	<p><u>Terminal Sterilization:</u></p> <p>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 specification.</p>		



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12.	<p><u>Sterility and Endotoxin testing:</u></p> <p>Validate the Test sample for sterility and endotoxins, in accordance to current USP 797 regulatory guidelines.</p>
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SUGGESTED PRESENTATION

Estimated Beyond-Use Date	24 hours controlled room temperature, 3 days refrigerated, or 45 days frozen, as per USP 797. BUD based on successful endotoxin test result.	Packaging Requirements	Sterile, tightly closed, light-resistant injection vials.	
Auxiliary Labels	1	Use as directed. Do not exceed prescribed dose.	7	For veterinary use only.
	2	Keep out of reach of children.	8	Protect from light.
	3	Keep at controlled room temperature, (20°C – 25°C), refrigerated (2°C – 8°C) or frozen (-25°C to -10°C).	9	Discard container after use.
	4	Discard in the presence of particulate matter.	10	Do not use if discolored.
	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	May impair mental and/or physical ability
	6	Do not take with alcohol, sleep aids, tranquilizers or other CNS depressants.	12	Precipitation occurs upon storage. Reheat the solution until clear
Pharmacist Instructions	<p>Add any auxiliary labels specific to the API to the dispensing container as deemed necessary.</p> <p>IMPORTANT: Using proper aseptic techniques, one must dilute the Acyclovir 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.</p>			
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. <i>United States Pharmacopeia XXVIII / National Formulary 23</i> . Rockville, MD. 2004: 2461.
2.	Parenteral Preparations. In: Allen, LV, Jr. <i>The Art, Science and Technology of Pharmaceutical Compounding</i> . American Pharmaceutical Association; 1998: 251.
3.	Acyclovir Sodium Injection. In: Canadian Pharmacists Association. <i>Compendium of Pharmacists and Specialties, 2006</i> . 37.
4.	Sodium Chloride. In: Rowe RC. <i>Handbook of Pharmaceutical Excipients, 4th Edition</i> . American Pharmaceutical Association; 2003: 556.
5.	Aciclovir. In: Sweetman SC, ed. <i>Martindale: The Complete Drug Reference, 34th Edition</i> . London, England: The Pharmaceutical Press; 2005: 626.
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8.	Acyclovir Systemic. Thomson Micromedex. <i>USP DI – Drug Information for the Health Care Professional, 26th Edition</i> . Taunton, MA: US Pharmacopeial Convention, Inc; 2006: 29.

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