National Home Infusion Association

# Guidance for Addressing Shortages of Sterile Water for Injection and Sodium Chloride 0.9% for Injection for Compounding Sterile Preparations

Sterile water for injection (SWFI) and sodium chloride 0.9% for injection (NS) for use in compounding sterile preparations in the United States are in limited supply. This shortage can directly impact patient care, and NHIA is continually addressing the ongoing shortage by working with manufacturers and suppliers, other professional health care organizations, and clinicians. Through these efforts, the association is staying up to date on the status of the shortages, collaborating to resolve them, and providing resources for managing the limited supply.

NHIA has developed product shortage recommendations to help clinicians manage patients during this time when diluents, and small and large volume parenteral solutions may not be readily available.

During a shortage period, the following measures may apply:

- Consider ways to conserve SWFI for reconstitution of compounded medications.
    - Batching the preparation of medications that require reconstitution with SWFI and scheduling compounding activities to minimize waste of SWFI available in bags.
    - Identify medications suitable for reconstitution with an alternative to SWFI (e.g. NS, D5W, LR).
        - See Table 1: Medications Reconstituted with SWFI Alternatives
    - Withdraw reconstitution volume from the final infusion container (e.g. mini-bag) used for compounding the dose when diluent is also appropriate for reconstitution.
- Consider ways to conserve NS small volume parenteral bags.
    - Identify medications stable and compatible in alternative diluents (e.g. D5W, D5NS, LR).
    - Identify medications suitable for IV push administration or other option for medication delivery.
        - Medication lists for IV push administration are available online and may be used to develop internal lists specific to a pharmacy's inventory.
        - (Example: https://www.elsevier.com/__data/assets/pdf_file/0010/1008955/IVP-Drug-Administration_27April2020.pdf)
            - Reference: O'Horo, John C (2020) *IV Push Administration of Drugs.* Elsevier.
- Consideration for compounding from large volume bags of SWFI or NS and repackaging small volumes into empty sterile vials, syringes, or smaller containers:
    - Consult stability references for storage conditions (e.g. container, temperature) and USP <797> for assigning beyond use dates for repackaged solutions.
- Changes to procedures and workflows may increase risk of compounding errors. NHIA encourages the reporting of any medication errors related to drug shortages to the Institute for Safe Medication Practices (ISMP).
- Changes to procedures and workflows increase risk of additional drug shortages as supply of larger containers are used to compound smaller volumes.

**Table 1: Reconstitution Alternatives for Infusion Medications**

| Medication | Reconstitution Alternatives[a] | Special Considerations | Reference |
|---|---|---|---|
| Acyclovir | SWFI, NS | Manufacturer PI recommends reconstitution in SWFI. Referenced study supports Acyclovir reconstituted with NS. | 1, 2 |
| Alglucosidase Alfa (LUMIZYME®) | SWFI, NS | Manufacturer PI recommends reconstitution in SWFI. Referenced manufacturer letter supports Alglucosidase alfa reconstituted with NS if SWFI is unavailable. | 3 |
| Ampicillin Sodium/Sulbactam Sodium | SWFI, NS | Manufacturer PI supports both SWFI or NS for reconstitution | 4, 5 |
| Caspofungin Acetate | SWFI, NS | Manufacturer PI supports both SWFI or NS for reconstitution | 6 |
| ceFAZolin Sodium | SWFI, NS | Cefazolin reconstitution information from the PI varies by vial size and concentration. The 10 gm bulk vial may be reconstituted with both SWFI and NS at concentrations of 100-200 mg/mL (PI Sagent 2018) The smaller vials and reconstitution of higher concentrations (225-330 mg/mL) SWFI is recommended to minimize risk of crystallization. Referenced study supports 1 gm vials reconsituted with NS. | 7, 8, 9 |
| Cefepime HCL | SWFI, NS, D5W | Manufacturer PI supports SWFI, NS, or D5W for reconstitution | 10 |
| Cefotaxime | SWFI, NS | Manufacturer PI recommends reconstitution in SWFI. Referenced study supports Cefotaxime reconstituted with NS. | 11 |
| cefOXitin Sodium | SWFI, NS, D5W | Manufacturer PI supports SWFI, NS, or D5W for reconstitution | 12, 13 |
| Ceftaroline Fosamil | SWFI, NS, D5W, LR | Manufacturer PI supports SWFI, NS, D5W, or LR for reconstitution | 14 |
| cefTAZidime | SWFI, NS | Manufacturer PI recommends reconstitution in SWFI. Referenced study supports Ceftazidime reconstituted with NS. | 15 |
| cefTAZidime/Avibactam Sodium | SWFI, NS, D5W, LR | Manufacturer PI supports SWFI, NS, D5W, or LR for reconstitution | 16 |
| Ceftolozane/Tazobactam Sodium | SWFI, NS | Manufacturer PI supports both SWFI or NS for reconstitution | 17 |
| cefTRIAXone Sodium | SWFI, NS, D5W | Manufacturer PI supports SWFI, NS, or D5W for reconstitution | 18 |
| Cefuroxime | SWFI, NS | Manufacturer PI recommends reconstitution in SWFI. Referenced study supports Cefuroxime reconstituted with NS. | 19 |
| DAPTOmycin (original formulation) | NS, SWFI | Manufacturer PI recommends reconstitution in NS. Referenced manufacturer letter supports DAPTOmycin reconstituted with SWFI. | 20 |
| Doxycycline Hyclate | SWFI, NS, D5W, LR | Manufacturer PI supports SWFI, NS, D5W, or LR for reconstitution | 21 |
| Ertapenem Sodium | SWFI, NS | Manufacturer PI supports both SWFI or NS for reconstitution | 22 |
| Imipenem/Cilastatin Sodium | NS, D5W, D5NS | Manufacturer PI supports NS, D5W, or D5NS for reconstitution | 23 |
| InFLIXimab (Remicade®) | SWFI, NS | Manufacturer PI recommends reconstitution in SWFI. Referenced manufacturer letter supports InFLIXimab reconstituted with NS if SWFI is unavailable. | 24 |
| Meropenem | SWFI, NS | Manufacturer PI recommends reconstitution in SWFI. Referenced study supports meropenem reconstituted with NS. | 15 |
| MethylPREDNIsolone sodium succinate | SWFI, NS | Manufacturer PI recommends reconstitution in SWFI. Referenced study supports reconstitution with NS. | 25 |
| Micafungin Sodium | NS, D5W | Manufacturer PI supports both NS or D5W for reconstitution | 26 |
| Nafcillin Sodium | SWFI, NS | Manufacturer PI supports both SWFI or NS for reconstitution | 27 |
| Oxacillin Sodium | SWFI, NS | Manufacturer PI supports both SWFI or NS for reconstitution | 28 |
| Penicillin G Potassium | SWFI, NS | Manufacturer PI supports both SWFI or NS for reconstitution | 29 |
| Penicillin G Sodium | SWFI, NS, D5W | Manufacturer PI supports SWFI, NS, or D5W for reconstitution | 30 |
| Pentamidine Isethionate | SWFI, D5W | Manufacturer PI supports both SWFI or D5W for reconstitution | 31 |
| Piperacillin Sodium/Tazobactam Sodium | SWFI, NS, D5W | Manufacturer PI supports SWFI, NS, or D5W for reconstitution | 32 |
| Remdesivir | SWFI, NS | Manufacturer PI recommends reconstitution in SWFI. Referenced manufacturer letter supports Remdesivir reconstituted with NS if SWFI is unavailable. | 36, 37 |
| Telavancin HCL | SWFI, NS, D5W | Manufacturer PI supports SWFI, NS, or D5W for reconstitution | 33 |
| Tigecycline | NS, D5W, LR | Manufacturer PI supports NS, D5W, or LR for reconstitution | 34 |
| Vancomycin | SWFI, NS | Manufacturer PI recommends reconstitution in SWFI. Referenced study supports reconstitution with NS. | 35 |

[a] Abbreviations: SWFI: Sterile Water for Injection, NS: Sodium Chloride 0.9%, D5W: Dextrose 5% in Water, D5NS: Dextrose 5% in Sodium Chloride 0.9%, LR: Lactated Ringers

Notes:

1. Neither the FDA nor pharmaceutical manufacturers can make recommendations outside of product labeling. Primary literature or tertiary sources may have information about the suitability of alternatives to SW for injection.
2. Normal saline reconstitution of medications for IV push administration may produce solutions at or near the solution's saturation point.
3. Do not dilute or reconstitute IV push medications by drawing up the contents into a commercially available, prefilled flush syringe of 0.9% sodium chloride.[38]

References:


1. Acyclovir Sodium [Package Insert]. Eatontown, NJ: Westward Pharmaceuticals; December 2018.
2. Ling J, Gupta VD. Stability of acyclovir sodium after reconstitution in 0.9% sodium chloride injection and storage in polypropylene syringes for pediatric use. Int J Pharm Compd. 2001;5(1):75-7. PubMed PMID: 23981803.
3. Lumizyme (Alglocosidase Alfa) [Personal Communication] MIS 1-1277662768. Gaithersburg, MD: Genzyme; August 2018.
4. Ampicillin Sodium and Sulbactam Sodium Injection Powder [Package Insert]. New York, NY: Pfizer Injectables; April 2018.
5. Ampicillin Sodium and Sulbactam Sodium Injection Powder [Package Insert]. Lake Forest, IL: Sandoz, Inc. March 2017.
6. Cancidas (caspofungin acetate) [Package Insert]. Whitehouse Station, NJ: Merck and Co, Inc; August 2021.
7. Cefazolin Sodium [Package Insert] 1 gm vial. Schaumburg, IL: Sagent Pharmaceuticals; December 2020.
8. Cefazolin Sodium [Package Insert] 10 gm Bulk Vial. Schaumburg, IL: Sagent Pharmaceuticals; September 2018.
9. Gupta VD. Chemical stability of cefazolin sodium after reconstituting in 0.9% sodium chloride injection and storage in polypropylene syringes for pediatric use. Int J Pharm Compd. 2003;7(2):152-4. PubMed PMID: 23979546.
10. Cefepime HCL [Package Insert]. Lake Forest, IL: Hospira Inc.; August 2021.
11. Gupta VD. Stability of cefotaxime sodium after reconstitution in 0.9% sodium chloride injection and storage in polypropylene syringes for pediatric use. Int J Pharm Compd. 2002;6(3):234-6. PubMed PMID: 23979191.
12. Cefoxitin [Package Insert] Bulk Vial. Schaumburg, IL: Sagent Pharmaceticals; September 2018.
13. Cefoxitin [Package Insert] SDV. Schaumburg, IL: Sagent Pharmaceuticals; September 2018.
14. Teflaro (cetaroline fosamil) [Package Insert]. Madison, NJ: Allergan USA, Inc.; September 2021.
15. Gandhi RG, Steiger SN, Elshaboury RH, Lund JT. I.V. push administration of medications reconstituted with 0.9% sodium chloride injection. Am J Health Syst Pharm. 2018;75(12):851-2. doi: 10.2146/ajhp180132. PubMed PMID: 29880520.
16. Avycaz (ceftazidime avibactam) [Package Insert]. Madison, NJ: Allergan USA, Inc.; October 2019.
17. Zerbaxa (ceftolozane sodium tazobactam) [Package Insert]. Whitehouse Station, NJ: Merck & Co., Inc.; September 2020.
18. Ceftriaxone Sodium [Package Insert]. Weston, FL: Apotex Corp.; November 2019.
19. Gupta VD. Chemical stability of cefuroxime sodium after reconstitution in 0.9% sodium chloride injection and storage in polypropylene syringes for pediatric use. Int J Pharm Compd. 2003;7(4):310-2. PubMed PMID: 23979702.
20. Cubicin® (daptomycin) [Personal Communication] 008298. Lexington, MA. Cubist Pharmaceuticals. February 2015.
21. Doxycycline [Package Insert]. New York, NY: Pfizer Inc.; September 2013.
22. Ertapenem [Package Insert]. Weston, FL: Apotex Corp.; January 2019.
23. Imipenem Cilastatin [Package Insert]. Lake Forest, IL: Fresenius Kabi; August 2018.
24. Remicade® (infliximab) [Personal Communication] 02835133. Horsham, PA. Jansen Biotech. June 2021.
25. Gupta VD. Chemical stability of methylprednisolone sodium succinate after reconstitution in 0.9% sodium chloride injection and storage in polypropylene syringes. Int J Pharm Compd. 2001;5(2):148-50. PubMed PMID: 23981837.
26. Mycamine (micafungin sodium) [Package Insert]. Northbrook, IL: Astellas Pharma US, Inc.; July 2020.
27. Nafcillin Sodium [Package Insert]. Schaumburg, IL: Sagent Pharmaceuticals; September 2020.
28. Oxacillin Sodium [Package Insert]. Schaumburg, IL: Sagent Pharmaceuticals Inc; April 2020.
29. Penicillin G Potassium [Package Insert]. New York, NY: Pfizer Injectables; November 2019.
30. Penicillin G Sodium [Package Insert]. Toronto, ON: Fresenius Kabi; July 2016.
31. Pentamidine [Package Insert]. Schaumburg, IL: APP Pharmaceuticals LLC.; March 2008.
32. Piperacillin Tazobactam [Package Insert]. Philadelphia, PA: Pfizer Injectables, Inc.; May 2012.
33. Telavancin [Package Insert]. Nashville, TN: Cumberland Pharmaceuticals;July 2020.
34. Tygacil (tigecycline) [Package Insert]. Philadelphia, PA: Pfizer Injectables; June 2021.
35. Masse M, Genay S, Martin Mena A, Carta N, Lannoy D, Barthelemy C, et al. Evaluation of the stability of vancomycin solutions at concentrations used in clinical services. Eur J Hosp Pharm. 2020;27(e1):e87-e92. Epub 20200205. doi: 10.1136/ejhpharm-2019-002076. PubMed PMID: 32296513; PubMed Central PMCID: PMC7147549.
36. Velkury (remdesivir) [Package Insert]. Foster City, CA: Gilead Sciences, Inc. February 2021.
37. Velkury (remdesivir) [Manufacturer Letter]. Foster City, CA. Gilead Sciences, Inc; December 2021.
38. Safe Practice Guidelines for Adult IV Push Medications. Horsham, PA: Institute for Safe Medication Practices (ISMP); 2015.