Fifth Edition

Extended Stability *for Parenteral Drugs*

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Dedication

To the ever-growing network of colleagues who continue to inspire and encourage us:

It is impossible to recognize and thank you all appropriately for your continued support of this ongoing drug information project.

Acknowledgments

As with the prior editions, the preparation of this updated reference was a team effort that would not have been possible without the exceptional group of capable writers and reviewers. They spent many hours on what some might consider minutia but this team considers essential. The editors appreciate the dedication and focus that these extremely talented and very busy professionals applied to this edition.

Contents

Contents

Contents

Preface

The scarcity of published and/or labeled stability data beyond 24 hours at any temperature has been a historically complicating factor in the care of patients in the alternate care site. When home infusion practice emerged and grew in the 1980–90s, accurate information on extended parenteral stability was very limited. Independent and hospital-based home care pharmacists were challenged to find drug stability data that supported realistic and cost-effective compounding and patient delivery schedules. Some national infusion companies put considerable resources to the task of compiling drug stability information to support their operational and patient care processes and maintained full-time drug-information specialists supporting clinicians at their many national locations. The highly competitive nature of the home infusion industry also led to the development of unpublished, proprietary drug stability data based on independent studies contracted by large home infusion companies and drug product manufacturers.

The home infusion industry experienced tremendous change in the later part of the 1990s. Many formerly competing industry leaders merged or were acquired, resulting in fewer but larger national companies. A new trend includes acquisitions of home and specialty infusion providers by chain pharmacy corporations, pharmacy benefit managers, and pharmacy-by-mail companies. Hospital and health-system infusion programs expanded in number, scope, and size in many areas. Growth in the subacute care component of long-term care pharmacy continues to contribute to the increased use of infusion products outside the hospital setting. Free-standing, hospital-based, and physician-office-based ambulatory infusion programs have also increased in number and scope of services. Reduced reimbursement, increased case management, and changes in technology have reduced the typical length of service for alternate site infusion services from primarily long-term (months to years) parenteral nutrition therapy to include much more short-term (days to weeks) drug therapies such as anti-infectives. Inpatient pharmacy services increasingly rely on extended beyond-use dating to minimize the wastage of high cost parenteral medication via appropriate recycling of unused compounded sterile parenterals. Implementation of sterile compounding practices under USP <797> and other strict standards help to support extending beyond-use dating for many medications past the more traditional 24-hour post-admixture expiration date.

The extended stability monographs and parenteral nutrition monographs in this edition represent a continuing drug information project focused on identifying, reviewing, and compiling relevant available information in a concise format. Monographs selected include most of the anti-infective medications and other parenterals with useful extended stability dating. They cite the majority of extended stability data available at the time of the edition. Many of the monographs reference well-known sources, such as the *Handbook on Injectable Drugs* (a "must-have" reference for every pharmacy that compounds sterile preparations). Additional references and sources include previously unpublished data for specific types of infusion devices and containers, direct communications from drug and device manufacturers, and a focused review of previously published data from the perspective of practitioners who use this information in home and specialty infusion. The third edition included a comprehensive chapter on total parenteral nutrition; this chapter was reformatted for the fourth edition with stability and compatibility data summarized in parenteral nutrition monographs for some of the most common additives to parenteral nutrition preparations.

The practices and integrity of pharmacists and others who compound sterile preparations have been under great scrutiny in recent years. Increased awareness in the lay public, boards of pharmacy, and Federal regulators further presses us to employ the diligence and professionalism with which we are entrusted to protect the public. We strongly emphasize the importance of using the extended stability data in this compilation responsibly and as part of the overall quality and standards-focused process of preparing sterile compounds.

Preface

One objective of ASHP and the Section of Ambulatory Care Practitioners is to support the professional needs of its membership, including pharmacists practicing in alternate care sites. The monographs and chapters are compiled as an easy-to-use reference on extended stability of the parenteral drugs and biologicals most common to alternate site infusion practice, including data in container types commonly used outside the acute care setting. Opportunities to obtain, review, and share unpublished or proprietary data will continue. Future editions will incorporate these data as they become available. We welcome your suggestions and pledge to review all resource material made available for future editions of this compendium.

What's New in This Edition

The 160 stability monographs in this fifth edition include updates to all but five of the monographs from the fourth edition, and 10 new stability monographs: Acetaminophen, Ceftaroline fosamil, Coagulation Factor XIII, Doripenem, Ethanol lock, Ibuprofen, Pantoprazole, Telavancin, Toclizumab, and Ziconotide acetate. The monograph updates include data revisions for a number of container types, and new information for elastomeric infusion device brands. The Parenteral Nutrition chapter includes updates to five nutrition monographs and additional considerations for calcium and phosphate solubility. The Applying Stability Data in Patient Care now includes a nursing perspective, with a primer on the types of vascular access devices used in medication administration and important considerations for pH, osmolality, concentration, and administration device. Something else is new . . . a co-editor! My long time friend and colleague Anna Nowobilski-Vasilios has been a monograph writer/reviewer since the first edition of this book over a decade ago. Her contribution as a writer and now co-editor to this edition has been invaluable. As with prior editions, the publisher, editors, and writers welcome your feedback and suggestions for continued improvement.

Caryn Dellamorte Bing, April 2013
Las Vegas, NV

About the Editors

Caryn Dellamorte Bing, RPh, MS, FASHP

Caryn is Senior Manager Clinical Services and PGY1 Residency Program Director for Critical Care Systems (CCS), Inc., a national home and specialty infusion provider. Her corporate responsibilities at CCS have included development of clinical standards of practice, clinician training and professional development, and leadership and management of CCS PGY1 Pharmacy Residency program at five locations. Caryn's 30-year career includes corporate leadership, general management, operations, clinical management, accreditation surveyor, consulting, training, and pharmacy practice roles in home/specialty infusion and other alternate site and acute care practice settings. Caryn holds a BS from University of Illinois College of Pharmacy and MS in Health Systems Management from Rush University. She completed her pharmacy residency at Rush-Presbyterian-St. Luke's Medical Center. She is a Rho Chi Scholar and Fellow of the American Society of Health-System Pharmacists. Caryn has been active in professional association leadership throughout her career, including terms as a presidential officer for the Illinois and Nevada ASHP state affiliates, and as an ASHP Delegate and Alternate Delegate numerous times. She served on the ASHP Home Care Section Executive Committee and was Chairperson for the ASHP Continuity of Care Task Force. Caryn received the first Distinguished Service Award from the ASHP Home Care Section. She served on editorial boards for *AJHP*, the *Journal of Pharmacy Practice*, and *Perspectives in Pharmacy*; has published a number of articles and book chapters; and has presented at many state and national meetings. Caryn has been Editor of *Extended Stability for Parenteral Drugs* since its inception.

Anna Nowobilski-Vasilios, PharmD, MBA, FASHP, CNSC, BCNSP

Anna is Principal at Anovation, Inc.; a Surveyor for the Accreditation Commission for Health Care; and Adjunct Assistant Professor at Midwestern University. Her experience includes over 30 years in pharmacy and over 25 years in home infusion and specialty pharmacy services. She served Option Care for 14 years as Senior Vice President for Care Management Services, Residency Director, Continuing Education Administrator, Vice President of Clinical Services, Senior Director of Program Development, National Director of Pharmacy, and Director of Franchise Implementation. She also held management and clinical positions with other regional and national home infusion providers and in hospital pharmacy practice. Anna holds a BS in Pharmacy from the University of Illinois, a MBA from Keller Graduate School of Management, and a PharmD from Midwestern University. She is a Rho Chi Scholar, board certified in nutrition support as well as nutrition support pharmacy, and a Fellow of the American Society of Health-System Pharmacists; she has served as Director-At-Large for ASHP's Section of Ambulatory Care Practitioners. She is an active member in the National Home Infusion Association, American Society of Health-System Pharmacists, American Society for Parenteral and Enteral Nutrition, Infusion Nurses Society, the Illinois Council of Health-System Pharmacists, and the Polish American Pharmacists' Association. Anna has delivered numerous presentations and has published articles on the subjects of home infusion therapy, specialty pharmacy, nutrition support, new drug approvals, and interdisciplinary collaboration. She is the author of the Home Infusion Chapter in the 22nd edition of *Remington: The Science and Practice of Pharmacy* and has been a contributing writer to each edition of *Extended Stability for Parenteral Drugs*.

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How to Use This Reference

Each monograph in this reference represents a drug for which some extended parenteral stability information is available from peer reviewed publications and/or drug and/or device/container manufacturers. Practitioners who are unfamiliar with this reference and the principles of extended stability should review the "Applying Stability Data in Patient Care" chapter. Selected monographs include shorter stability data that may be useful in alternate site practice. Stability monographs are alphabetical by generic drug name. Each monograph includes a compilation of drug stability data for various container systems, solutions, concentrations, and temperature storage and administration conditions. The parenteral nutrition additive monographs are only applicable to parenteral nutrition formulations.

The following temperature ranges were adapted from the USP to evaluate reported stability study conditions[1]:

Refrigerated	2°C to 8°C
Frozen	−25°C to −10°C
Room Temperature*	15°C to 30°C
Body Temperature	37°C

*See the USP definition of Controlled Room Temperature in Appendix B, Glossary of Terms.

When studied storage conditions fall outside these ranges, a monograph note will indicate the variation.

To use a stability monograph, find the desired container or material type in the first column. When a container type is not listed, then clinically useful or extended stability data were not available for the drug in that container type. Next, check the concentration, diluent, and manufacturer of the drug studied in that container type. The next column indicates the osmolality of the sample studied if it was assayed or calculated by the authors of the cited study. The pH column either includes the actual or range of pH for the specific concentration, or a note that ties to more general pH data for the drug product. Additional columns list the extended stability data that have been documented for the drug in the container and specified conditions. If frozen stability information is available, check the post-thaw stability data; this may differ from the room temperature and refrigerated stability data for the same drug in a never-frozen state. The final column indicates the reference or references used for the particular line in the monograph. When "n/a" is noted in any field, no information is available for that item.

Within the stability monograph, footnotes highlight important information. Each footnote corresponds to information in the Notes section of the monograph that is crucial to interpretation of the data. These include comments on variations from USP temperature ranges, detailed descriptions of storage conditions, and more. A Special Considerations section includes special information on drug storage, preparation, and administration.

Flush compatibility refers to the chemical compatibility of the drug with common solutions used to flush vascular access devices. Practitioners should be aware of nursing practice guidelines (such as those of the Intravenous Nurses Society), access device specifications, and drug-solution compatibility when determining the type and volume of solution(s) used for line maintenance. When a drug is incompatible with heparinized saline (i.e., heparin lock flush), it may be necessary to flush with saline before and after administration. (Commonly referred to as SASH, this stands for Saline-Administration-Saline-Heparin.) A few drugs are not compatible with saline or heparinized saline; in these cases, flushing with an alternative compatible solution, such as D5W, may be necessary. If the line flush procedures for a specific therapy vary from the organization's standard approach, the pharmacist should provide written directions to clarify the flush method used. Heparinization may not always be required to maintain line patency for some access devices (e.g., Groshong catheters) or when positive displacement catheter caps are used.

Use of Additional Resources

The information contained in these monographs is a compilation of extended stability data from multiple sources. This information is not a substitute for the official product literature. Practitioners should consult the primary literature and the product manufacturer to determine the applicability of stability data to a particular patient and practice scenario. Practitioners should maintain current drug reference resources as well as the most current edition of a comprehensive reference on drug stability and compatibility. Every pharmacy that compounds or provides sterile preparations should maintain resource files, including the phone numbers and all correspondence with the medical or clinical affairs departments of pharmaceutical manufacturers. The pharmacy should also have access to a drug information center or the expertise and ability to conduct a literature search for the most up-to-date clinical and pharmaceutical information on parenteral drugs.

General Abbreviations

d	day(s)
h	hour(s)
iso	iso-osmotic
m	month(s)
min	minute(s)
RTU	ready to use from manufacturer
unspec.	unspecified
w	week(s)
y	year(s)

Solution Abbreviations

BWFI	Bacteriostatic water for injection
D	Dextrose solution (percentage unspecified)
D2.5	Dextrose 2.5% in water
D2.5$^1/_2$S	Dextrose 2.5% in sodium chloride 0.45%
D5LR	Dextrose 5% in lactated Ringer's
D5$^1/_4$S	Dextrose 5% in sodium chloride 0.225%
D5$^1/_2$S	Dextrose 5% in sodium chloride 0.45%
D5S	Dextrose 5% in sodium chloride 0.9%
D10S	Dextrose 10% in saline
D5W	Dextrose 5% in water
D7W	Dextrose 7% in water
D10W	Dextrose 10% in water
DXN-6	Dextran 6%
IS	Invert sugar to
LR	Ringer's injection, lactated
M10	Mannitol 10%
NS	Sodium chloride 0.9%
R	Ringer's solution
$^1/_2$S	Sodium chloride 0.45%
$^1/_4$S	Sodium chloride 0.22%
W	Sterile water for injection

Reference

1. United States Pharmacopeial Convention. Chapter <795> Pharmaceutical Compounding—Nonsterile Preparations. Official August 1, 2008.