

Room-temperature storage of medications labeled for refrigeration

VICTOR COHEN, SAMANTHA P. JELLINEK, LEFTHERIOS TEPERIKIDIS, ELLIOT BERKOVITS,
AND WILLIAM M. GOLDMAN

The U.S. Pharmacopeia's Medmarx medication-error-reporting system has received nearly 1000 reports involving errors associated with refrigerated medications.¹ Many of these reports were a result of nursing staff not realizing that certain medications required refrigeration. Subsequent errors involved delayed administration of medications to patients and inappropriate storage of expensive medications (e.g., epoetin alfa). Recommendations based on a review of these errors suggested displaying a table on the outside of the refrigerator door listing common refrigerated items for that particular unit.¹

Inappropriate vaccine storage has been implicated in numerous reports of vaccine-related adverse events.² For example, two days after receiving a pneumococcal polysaccharide vaccination that had not been refrigerated, a patient developed dizziness, racing heart, jerking of the limbs, and "pins and needles" from head to toe, resulting in a persistent and significant disability. In another case, a patient developed a cluster of 20 painful and itchy vesicles on an erythematous base

Purpose. Data regarding the recommended maximum duration that refrigerated medications available in hospital pharmacies may be stored safely at room temperature were collected and compiled in a tabular format.

Methods. During May and June of 2006, the prescribing information for medications labeled for refrigeration as obtained from the supplier were reviewed for data addressing room-temperature storage. Telephone surveys of the products' manufacturers were conducted when this information was not available in the prescribing information. Medications were included in the review if they were labeled to be stored at 2–8 °C and purchased by the pharmacy department for uses indicated on the hospital formulary. Frozen antibiotics thawed in the refrigerator and extemporaneously compounded medications were excluded. Information was compiled and arranged

in tabular format. The *U.S. Pharmacopeia's* definition of room temperature (20–25 °C [68–77 °F]) was used for this review.

Results. Of the 189 medications listed in *AHFS Drug Information 2006* for storage in a refrigerator, 89 were present in the pharmacy department's refrigerator. Since six manufacturers were unable to provide information for 10 medications, only 79 medications were included in the review. This table may help to avoid unnecessary drug loss and expenditures due to improper storage temperatures.

Conclusion. Information regarding the room-temperature storage of 79 medications labeled for refrigerated storage was compiled.

Index terms: Errors, medication; Labeling; Pharmacy, institutional, hospital; Stability; Storage; Temperature

Am J Health-Syst Pharm. 2007; 64:1711-5

on the midposterior lateral forearm after receiving varicella vaccine that was not properly refrigerated.²

In 1975, Wolfert and Cox³ recognized that pharmacists were often asked about the stability of refrigerated medications that are accidentally stored at room-temperature. However, because product labeling

was insufficient regarding room-temperature stability and pharmacists were not routinely able to predict stability based on the physicochemical properties of the medications, the authors surveyed manufacturers about room-temperature storage of selected medications labeled for refrigeration. This information was

VICTOR COHEN, PHARM.D., BCPS, is Clinical Pharmacy Manager, Departments of Emergency Medicine and Pharmaceutical Sciences, Maimonides Medical Center (MMC), Brooklyn, NY, and Assistant Professor of Pharmacy Practice, Arnold & Marie Schwartz College of Pharmacy and Health Sciences, Long Island University (LIU), Brooklyn. SAMANTHA P. JELLINEK, PHARM.D., BCPS, is Clinical Pharmacy Manager, Medication Reconciliation and Safety, and Clinical Coordinator, Pharmacy Practice Residency Program; LEFTHERIOS TEPERIKIDIS, PHARM.D., is Pharmacy Resident; and ELLIOT BERKOVITS, PHARM.D., is Pharmacy Resident, MMC. WILLIAM GOLDMAN, PHARM.D.,

is Associate Director, Pharmacy for Clinical and Educational Services, MMC, and Clinical Assistant Professor of Pharmacy, Arnold & Marie Schwartz College of Pharmacy and Health Sciences, LIU.

Address correspondence to Dr. Cohen at the Department of Pharmaceutical Sciences, Maimonides Medical Center, 4802 Tenth Avenue, Brooklyn, NY 11219 (vcohen@maimonidesmed.org).

Copyright © 2007, American Society of Health-System Pharmacists, Inc. All right reserved. 1079-2082/07/0802-1711\$06.00.

DOI 10.2146/ajhp060262

Table 1. Acceptable Duration of Room-Temperature Storage for Medications Labeled for Refrigeration

Drug Product	Brand Name (Manufacturer)	Acceptable Duration of Storage at Room Temperature	Source of Information
Abciximab 2-mg/mL injection	Reopro (Centocor B.V. [Lilly])	8 days	Manufacturer
Allergen extract concentrate	NA ^a (Greer)	28 days	Manufacturer
Alprostadil injection	Prostin VR Pediatric (Sicor)	34 days at 20 °C 26 days at 30 °C	Manufacturer
Alteplase	Cathflo Activase (Genentech)	4 mo	Manufacturer
Atracurium injection	Tracrium (Catalytica Pharmaceuticals)	14 days	Prescribing information
Becaplermin 0.01%	Regranex topical gel (Ortho-McNeil-Janssen)	6 days	Manufacturer
Botulinum toxin type-A 100 units	Botox (Allergan)	5 days	Manufacturer
Calcitonin injection	Miacalcin (Novartis)	14 days	Manufacturer
Calcitonin nasal spray	Miacalcin (Novartis)	35 days	Prescribing information
Calcitonin salmon intranasal	Fortical (Upsher-Smith)	7 days	Manufacturer
<i>Candida albicans</i> skin test	Candin (Allermed Laboratories)	7 days	Manufacturer
Cisatracurium injection	Nimbex (Abbott)	21 days	Prescribing information
Conjugated estrogens injection	Premarin IV (Wyeth)	7 days	Manufacturer
Dacarbazine for injection	DTIC-Dome (Ben Venue Laboratories)	3 mo	Manufacturer
Daptomycin for injection	Cubicin (Cubist Pharmaceuticals)	12 mo	Manufacturer
Darbepoetin alfa	Aranesp (Amgen)	7 days	Manufacturer
Digoxin immune fab (ovine)	Digibind (GlaxoSmithKline)	30 days	Prescribing information
Diphtheria and tetanus toxoids and acellular pertussis adsorbed, hepatitis B (recombinant) and inactivated poliovirus vaccine combined	Pediarix (GlaxoSmithKline)	24 hr	Manufacturer
Diphtheria and tetanus toxoids and acellular pertussis vaccine adsorbed	Infanrix (GlaxoSmithKline)	72 hr	Manufacturer
Dornase alfa	Pulmozyme (Genentech)	24 hr	Prescribing information
Epoetin alfa multidose	Procrit (Ortho Biotech)	7 days	Manufacturer
Epoetin alfa single dose	Procrit (Ortho Biotech)	14 days	Manufacturer
Eptifibatid 2 mg/mL	Integrilin (Schering)	60 days	Prescribing information
Erythromycin ethylsuccinate oral suspension	EES (Abbott)	14 days	Prescribing information
Etanercept powder	Enbrel (Immunex Corporation [Amgen and Wyeth Pharmaceuticals])	7 days	Manufacturer
Etanercept prefilled syringe	Enbrel (Immunex Corporation [Amgen and Wyeth Pharmaceuticals])	4 days	Manufacturer
Etoposide injection	Vepesid (Gensia/Sicor)	24 mo	Prescribing information

Continued on next page

Table 1 (continued)

Drug Product	Brand Name (Manufacturer)	Acceptable Duration of Storage at Room Temperature	Source of Information
Exenatide	Byetta (Amylin Pharmaceuticals [Lilly])	Repeated periods of exposure for a combined maximal duration of 6 days	Manufacturer
Famotidine	Pepcid (Bedford)	3 mo	Manufacturer
Fligrastrim vials and Singleject prefilled syringes	Neupogen (Amgen)	7 days	Manufacturer
Fosphenytoin sodium injection	Cerebix (Pfizer)	48 hr	Prescribing information
Glatiramer acetate injection	Copaxone (Teva Neuroscience)	7 days	Prescribing information
Hepatitis A vaccine, inactivated	Havrix (GlaxoSmithKline)	72 hr	Manufacturer
Hepatitis A vaccine, inactivated	Vaqta (Merck)	12 mo at 37 °C	Manufacturer
Hepatitis B immune globulin (human)	Hyperhep B S/D (Bayer)	Cumulative exposure for 7 days	Manufacturer
Hepatitis B vaccine (recombinant)	Engerix-B (GlaxoSmithKline)	72 hr	Manufacturer
Immune globulin (human)	Gamastan S/D (Bayer)	Cumulative exposure for 7 days	Manufacturer
Influenza virus vaccine	Fluarix (GlaxoSmithKline)	72 hr	Manufacturer
Insulin aspart (rDNA origin) injection	Novolog (Novo Nordisk)	28 days	Prescribing information
Insulin glargine (rDNA origin) vial or cartridge	Lantus vial or cartridge (Sanofi-Aventis)	28 days	Prescribing information
70% insulin aspart protamine suspension and 30% insulin aspart injection (rDNA origin) pen fill cartridge	Novolog Mix 70/30 pen fill cartridge (Novo Nordisk)	14 days	Prescribing information
70% insulin aspart protamine suspension and 30% insulin aspart injection (rDNA origin) vial	Novolog Mix 70/30 vial (Novo Nordisk)	28 days	Prescribing information
Lente human insulin (rDNA origin) zinc suspension	Humulin L (Lilly)	28 days	Prescribing information
Insulin lispro (rDNA origin) vial	Humalog vial (Lilly)	28 days	Prescribing information
NPH, human insulin isophane suspension (rDNA origin)	Novolin N vial (Novo Nordisk)	30 days	Prescribing information
Regular human insulin injection (rDNA origin)	Novolin R vial (Novo Nordisk)	30 days	Prescribing information
Humulin Ultralente human insulin (rDNA origin) extended zinc suspension	Humulin U (Lilly)	28 days	Prescribing information
Hyaluronic acid	Healon (AMO Advanced Medical Optics)	14 days	Manufacturer
Interferon beta-1a i.m. injection	Avonex (Biogen Idec)	30 days	Prescribing information
Interferon beta-1a s.c. injection	Rebif (Serono)	30 days	Prescribing information
Latanoprost 0.005% ophthalmic solution	Xalatan (Pharmacia and Upjohn)	6 wk	Prescribing information
Lopinavir/ritonavir capsules	Kaletra capsules (Abbott)	60 days	Prescribing information
Lopinavir/ritonavir oral solution	Kaletra solution (Abbott)	60 days	Prescribing information
Melphalan 2-mg tablets	Alkeran (GlaxoSmithKline)	7 days	Prescribing information
Methylergonovine maleate injection	Methergine (Novartis)	14 days	Manufacturer
Neomycin sulfate–polymixin B sulfate solution for irrigation	Neosporin G.U. Irrigant Sterile (Monarch Pharmaceuticals)	6 mo if undiluted	Manufacturer
Octreotide acetate injectable suspension	Sandostatin (Novartis)	14 days	Prescribing information

Continued on next page

Table 1 (continued)

Drug Product	Brand Name (Manufacturer)	Acceptable Duration of Storage at Room Temperature	Source of Information
Palivizumab powder and solution	Synagis (MedImmune)	Lifetime cumulative exposure for 14 days	Manufacturer
Pancuronium bromide injection	Pavulon (Gensia/Sicor)	6 mo	Prescribing information
Peg-interferon alfa-2a vial	Pegasys vial (Roche)	14 days	Manufacturer
Peg-interferon alfa-2a vial pre-filled syringe	Pegasys pre-filled syringe (Roche)	6 days	Manufacturer
Penicillin G benzathine injection suspension	Bicillin LA (Monarch Pharmaceuticals)	7 days at 77 °F 1 day at 104 °F	Manufacturer
Penicillin G benzathine and penicillin G procaine injection suspension	Bicillin CR (Wyeth)	7 days at 77 °F 1 day at 104 °F	Manufacturer
Pneumococcal 7-valent conjugate vaccine (diphtheria CRM ₁₉₇ protein)	Prevnar (Wyeth)	7 days	Manufacturer
Propracaine hydrochloride ophthalmic solution	Alcaine (Alcon Research Ltd.)	30 days	Manufacturer
Quinupristin-dalfopristin for injection	Synercid (DSM Pharmaceuticals)	7 days	Manufacturer
Rabies immune globulin (human) solvent/detergent treated	Hyperab S/D (Talecris)	Cumulative exposure for 7 days	Manufacturer
Rabies vaccine	Rabavert (Chiron)	6.2% loss after 12 mo	Manufacturer
Ritonovir capsules	Norvir (Abbott)	30 days	Prescribing information
Rh ₀ D immune globulin (human)	Hyperrho SD (Bayer)	Cumulative exposure for 7 days	Manufacturer
Rocuronium bromide	Zemuron (Organon USA)	60 days	Prescribing information
Saquinavir soft gelatin capsules	Fortovase (Roche)	90 days	Prescribing information
Succinylcholine chloride multidose	Anectine (GlaxoSmithKline)	14 days	Prescribing information
Tetanus immune globulin human solvent/detergent treated	Hypertet S/D (Talecris)	Cumulative exposure for 7 days	Manufacturer
Tipranavir capsules	Aptivus capsules (Boehringer-Ingelheim)	60 days if opened	Prescribing information
Tobramycin inhalation solution	Tobi (Chiron)	28 days	Prescribing information
Trifluridine ophthalmic solution	Viroptic (Monarch Pharmaceuticals)	14 days	Manufacturer
Vinorelbine tartrate injection	Navelbine (Pierre Fabre Pharmaceuticals)	72 hr	Prescribing information
Vitamin A	Aquasol-A parenteral (Aai Pharma/Mayne)	4 wk	Manufacturer

^aNA = not applicable.

then compiled into a table for use as a guide to control drug storage within the authors' institution.

In 1983, Vogenberg and Souney⁴ compiled a similar table describing the acceptable duration of storage of medications labeled for refrigeration when refrigerated (2–8 °C) after 24 hours of storage at room-temperature, when stored in a cool place (8–15 °C), and when stored at room-temperature (15–30 °C).

In 1987, Sterchele⁵ described the frequency of drug information requests received concerning room-temperature storage of drug products labeled for refrigeration. The author reported that this information was not easily retrievable and often incomplete and compiled an updated table to supplement the previously available information on the topic. Only 22 of 36 manufacturers replied with information about 39 products, and most manufacturers did not provide data for storage in “a cool place,” as it was unrecognized as a method for storage. In 1990, Dalton-Bunnow and Halvachs⁶ updated the available data. In 2006, Cobos Campos et al.⁷ compiled written information from drug manufacturers about the room-temperature storage of 83 medications labeled for refrigeration. This information was limited by the fact that it was collected outside of the United States and published in the Spanish medical literature.

The objective of this study was to provide an updated table of the maximum acceptable duration that medications labeled for refrigeration may be stored at room-temperature.

Methods

During May and June of 2006, we reviewed the prescribing information for medications labeled for refrigeration as obtained from the supplier for data addressing room-temperature storage. The *U.S. Pharmacopeia's* definition of room-temperature (20–25 °C [68–77 °F]) was used.⁸ Telephone surveys and follow-up inquiries of the products' manufacturers were con-

ducted when information about room-temperature storage was not available in the prescribing information.

Medications were included in the review if they were labeled to be stored at 2–8 °C and purchased by our pharmacy department for uses indicated on the hospital formulary. Frozen antibiotics thawed in the refrigerator and extemporaneously compounded medications were excluded. Information was compiled and arranged in tabular format.

Results

Of the 189 medications listed in *AHFS Drug Information 2006* for storage in a refrigerator,⁹ 89 were present in our pharmacy department's refrigerator and were included in this review. The information for 34 of these medications (38%) was obtained from the official prescribing information. A total of 44 manufacturers were contacted and asked to provide the relevant information for the remaining 55 medications (62%). Since 6 manufacturers were unable to provide information for 10 medications, information was compiled and tabulated for 79 medications (Table 1).

Discussion

The table is limited by our hospital pharmacy's formulary; however, our purpose was to update the current literature.

The table is intended for use as a guide when medications labeled for refrigerated storage are inadvertently exposed to room-temperature. This may occur during routine excursions, power outages, compressor failures, natural disasters, and inadvertent storage at room-temperature if the need for refrigeration is unknown. According to the manufacturers surveyed, the medications included in the table may be returned to the refrigerator within the time period listed without affecting stability or expiration date. This table may help to avoid unnecessary drug loss and expenditures due to improper storage temperatures.

Although a full discussion of methods of stability information is beyond the scope of this article, the methods to evaluate temperature-related storage recommendations for medications are required to be reported to the Food and Drug Administration as part of current good manufacturing practices.

While recommended temperature-related storage data were easily retrievable from the medications' prescribing information, the effects of temporary excursions from refrigeration were not always addressed. Retrieving this information from each manufacturer was complicated by prolonged response times, lack of available data, and the inability of some manufacturers to release the information for legal reasons.

Conclusion

Information regarding the room-temperature storage of 79 medications labeled for refrigerated storage was compiled.

References

1. Santell JP, Cousins D. Refrigerated medications at risk for errors. www.uspharmacist.com/index.asp?show=article&page=8_1144.htm (accessed 2006 Aug 10).
2. Centers for Disease Control and Prevention. VAERS public data. <http://vaers.hhs.gov/scripts/data.cfm> (accessed 2007 May 22).
3. Wolfert RR, Cox RM. Room temperature stability of drug products labeled for refrigerated storage. *Am J Hosp Pharm.* 1975; 32:585-7.
4. Vogenberg FR, Souney PF. Stability guidelines for routinely refrigerated drug products. *Am J Hosp Pharm.* 1983; 40:101-2.
5. Sterchele JA. Update on stability guidelines for routinely refrigerated drug products. *Am J Hosp Pharm.* 1987; 44:2698, 2701.
6. Dalton-Bunnow MF, Halvachs FJ. Update on room-temperature stability of drug products labeled for refrigerated storage. *Am J Hosp Pharm.* 1990; 47:2522-4.
7. Cobos Campos R, Salvador Collado P, Gomez Gener A et al. [Maximum stability of thermolabile drugs outside the refrigerator.] *Farm Hosp.* 2006; 30:33-43. In Spanish.
8. The United States pharmacopeia, 25th rev., and The national formulary, 20th ed., Rockville, MD: United States Pharmacopoeial Convention; 2002:9.
9. McEvoy GK, ed. *AHFS drug information 2006*. Bethesda, MD: American Society of Health-System Pharmacists; 2006.