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ISMP
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Educating the Healthcare Community About Safe Medication Practices

The dark side—safety issues when protecting medications from light

The phrase, "protect from light," is poorly defined in commonly accessed prescribing information and many drug references. Inconsistencies exist in understanding what "protect from light" means and the necessary measures that should be taken during the various phases of the medication-use process. ISMP recently researched this topic to "shed more light" on it for our readers. Our findings and recommendations are presented below.

Types of Light Vulnerabilities

There are different types of light (e.g., the visible spectrum, infrared, ultraviolet) that can affect pharmaceutical products. Certain medications, such as biologics, chemotherapeutics, and protein-containing and protein-derived products (e.g., vaccines, immune globulin) are particularly susceptible to wavelengths from ultraviolet or blue light. Medications that require a prolonged intravenous (IV) infusion time are also most vulnerable to light.

Few Medications Need Protection from Light During Administration

We recently searched Lexicomp monographs for "protect from light" and found more than 800 results mentioning the phrase—sometimes referring to when being stored, sometimes during administration, and sometimes specifically for both. Of those, less than 2% specified that protection from light was needed during administration.

Light Protection Testing

According to the US Food and Drug Administration (FDA) *Guidance for Industry: Q1A (R2) Stability Testing of New Drug Substances and Products* (www.ismp.org/ext/1304), photostability testing is recommended during product development to determine appropriate manufacturing conditions and container closure systems. The FDA *Guidance for Industry: Q1B Photostability Testing of New Drug Substances and Products* (www.ismp.org/ext/1305) further recommends that it may be appropriate to test certain products (e.g., infusions) to support their photostability in-use. However, this is left to the manufacturer's discretion. Medication labeling often does not provide adequate information on the duration of light exposure that may result in medication degradation to assist practitioners in determining if medications require protection from light exposure during specific parts of the medication-use process (e.g., administration).

Light Protection Responsibility

Several light-protective mechanisms exist, such as foil-shielding blister packaging, amber vials, overwrap bags, and tablet film coatings. Some of these mechanisms are put in place by the manufacturer, while in other cases, pharmacy or the practitioner administering the medication may need to implement them to limit light exposure during each applicable step in the medication-use process. Without specific information, medications that degrade with short exposure to light may not be sufficiently protected. On the other hand, overuse of light-protective containers (e.g., bags, overwraps) that hinder the practitioner's ability to read the medication label, or other related processes (e.g., affixing labels with barcodes to the outer bag and scanning the applied label instead of the actual product) can increase the risk of error.

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Warning! Manufacturer's dexmedeTOMIDine premixed IV bags may be packaged in an overwrap labeled as acetaminophen! A prescriber ordered an acetaminophen 1,000 mg/100 mL infusion for a patient. The nurse removed what she thought was an acetaminophen infusion bag from the automated dispensing cabinet (ADC), scanned the barcode on the overwrap, and administered the infusion to the patient. Approximately 15 minutes later, the patient experienced bradycardia and bradypnea. The nurse looked at the empty bag hanging on the intravenous (IV) pole and discovered that it was labeled "dexmede**TOM**idine hydrochloride injection, 400 mcg/100 mL" (lot number 24070461, expiration date 03/2026). Dexmede**TOMID**ine is an alpha-2 agonist used for sedation of ventilated patients and is not typically stored in ADCs on general patient care units. The infusion bag label had a different font from the typical product and contained statements in French with ISMP Canada's tall man lettering (i.e., dexmede**TOM**idine) (www.ismp.org/ext/1394) which differs from the tall man lettering (i.e., dexmede**TOMID**ine) on ISMP ***List of Look-Alike Drug Names with Recommended Tall Man (Mixed Case) Letters*** (www.ismp.org/node/136) (**Figure 1**). The nurse notified the prescriber and provided supplemental oxygen to the patient who was closely monitored for a few hours. Fortunately, the patient recovered.

Figure 1. An infusion bag (left) found inside the acetaminophen injection overwrap by Hikma, was labeled dexmede**TOM**idine 400 mcg/100 mL with Canadian labeling and a different font compared to the US product labeling (right).

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Examples of Medication Safety Issues

Below are a few examples of medication safety issues reported to ISMP that involved protecting medications from light.

A patient who was undergoing surgery began decompensating due to vasodilation. The patient was given a dose of ***ADRENALIN*** *(****EPINEPH****rine) from a 1 mg/mL injection vial, with no clinical effect. A practitioner noted that the vial used, along with several others, were discolored, indicating degradation of the product.* ***EPINEPH****rine solution is light sensitive and deteriorates rapidly when exposed to light, turning pink, and then brown.* ***EPINEPH****rine vials are available in clear glass that may not protect the medication from light (****Figure 1****). A subsequent dose was administered from a vial of* ***EPINEPH****rine that was not discolored with good clinical response.*

Figure 1. Adrenalin (**EPINEPH**rine) 1 mg/mL injection by Par Pharmaceutical should be protected from light, but it comes in a clear vial.

*A patient was prescribed a ni****CAR****dipine infusion to control blood pressure, but a norepinephrine infusion prescribed for a different patient was accidentally administered. The pharmacy dispensed both infusions in brown opaque bags to protect them from light. The pharmacy system was set up to print two patient-specific labels with barcodes; one to affix to the compounded infusion, and the other to be placed on the brown bag. At some point, the IV bags were accidentally switched. The nurse who inadvertently administered norepinephrine to the patient reviewed the label and scanned the barcode on the brown bag prior to administration but did not notice a different patient's medication inside the bag. The patient recovered, but the organization reported that similar events have occurred.*

Recommendations

Organizations should consider the following strategies to safeguard medications that need to be protected from light.

Develop a "protect from light" list based on phases that require light protection. Review prescribing information, published literature, and drug information resources to identify medications on your organization's formulary that require protection from light during storage, preparation, and/or administration. Refer to resources such as *Hospital Pharmacy's Light-Sensitive Injectable Prescription Drugs—2022* (www.ismp.org/ext/1248), which includes a comprehensive list of medications that require protection from light during specific steps of the medication-use process. Ensure there is a process to routinely review the list as manufacturers and prescribing information are continually modified and updated. Include this designation on monograph templates for new formulary requests. Ensure all clinicians can easily access this list.

Evaluate light-protective products and usage. Bags available to reduce the amount of light transmission to medications have various opacities. Consider purchasing products (e.g., amber bags) that meet the requirements for light protection but allow practitioners to read the medication label through the bag and still have visibility of the inner product for monitoring the infusion during administration. For medications that are recommended to be stored in the original carton to "protect from light" until preparation, consider using amber-lidded bins to contain the vials if the carton is to be disposed of on receiving (e.g., disposal of the carton before stocking).

Label the product directly. Practitioners should scan the manufacturer's barcode directly on the product to prevent the risk of a false positive barcode scan from a pharmacy-applied or patient label. If a pharmacy-generated label with a barcode is needed (e.g., compounded infusion), affix it directly on the product (e.g., syringe, infusion bag). Do not include barcodes on pharmacy-generated labels placed on the outer containers or bags to force scanning of the actual product.

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After the event, the hospital reported that the nurse retrieved the overwrap from the top of the trash bin that she had scanned prior to administration, which was labeled acetaminophen 1,000 mg/100 mL (Hikma, NDC 0143-9386-01, lot number 24070381, expiration date 09/2025) (**Figure 2**). The hospital quarantined the overwrap and infusion bag and notified Hikma. The hospital did not find any additional infusion bags with this issue.

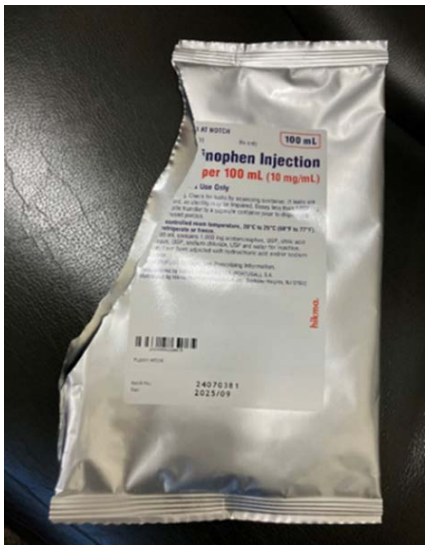

Figure 2. A hospital reported that Hikma's overwrap labeled acetaminophen injection 1,000 mg/100 mL contained an infusion bag labeled dexmede**TOM**idine 400 mcg/100 mL.

We reached out to the US Food and Drug Administration (FDA) and the manufacturer, Hikma, to notify them of this concern. Soon after, on July 22, 2024 Hikma announced a nationwide recall of infusion bags of acetaminophen injection 1,000 mg/100 mL (lot number 24070381) (www.ismp.org/ext/1408).

While this is an unusual situation, we thought it was important to share with nurses. Prior to medication administration, the best practice is to scan the barcode *directly on an infusion bag* (not the overwrap). In addition, it is important to take time to read the infusion bag label prior to barcode scanning and administration, especially when removing the product from an overwrap. If any issues are noted, immediately report them within your organization and to ISMP (www.ismp.org/report-medication-error) and FDA (www.ismp.org/ext/544).

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Additionally, for drugs that require protection from light, FDA should consider label revisions to require more detailed information on the duration of light exposure that may result in medication degradation to ensure appropriate light protection of medications during the entire medication-use process.

what's in a Name?

The "-caine" drug stem name

Medications ending in "-caine" are classified as local anesthetics (LA). (Please note that there are other medications that fall within the class of LAs that do not include the "-caine" stem; those medications will not be discussed in this article.) These medications work by reversibly inhibiting nerve transmission. There are currently 11 medications in the class of LAs available in the United States (**Table 1**, page 4). Because of their usefulness in inhibiting pain sensations, medications in this class can be administered topically to the skin, mucous membranes, cornea, and conjunctiva; or injected into an area of the body to infiltrate the tissue as a peripheral or central (e.g., caudal, lumbar, thoracic) nerve block; or as spinal anesthesia (epidurally).

LAs are available as creams, ointments, gels, topical solutions, solutions for nebulization, sprays, patches, and injectable solutions. Lidocaine is unique in that it is the only LA approved for intravenous use in the treatment of ventricular arrhythmias and in the off-label treatment of chronic pain.

Medications in this class can be further categorized based on potency, speed of onset, duration of action (short, intermediate, or long), or chemical group (amide or ester). The chemical group is important when evaluating the use of LAs in patients with reported allergies.

Several injectable LAs are available in combination with fixed doses of **EPINEPH**rine which produces local vasoconstriction. This in turn decreases local bleeding during procedures and decreases systemic absorption of the anesthetic, which helps prolong the duration of anesthesia. Although important, the combination products are beyond the scope of this article and are not included in the table.

Many injectable LAs are available in multiple-dose vials that contain preservatives. Therefore, it is important to identify appropriate preservative free (PF), or methylparaben free (MPF), single-use formulations for use in neuraxial anesthesia (e.g., spinal, epidural). Single-dose vials typically state, "for infiltration and nerve block including epidural and caudal" compared to multi-dose vials with preservatives that typically state, "for infiltration and nerve block. NOT FOR EPIDURAL OR CAUDAL USE."

In addition, some of the "-caine" drugs are commonly found in over-the-counter (OTC) pain medications in the form of patches, creams, throat lozenges, and other formulations. These OTC products are used for dermal irritation, hemorrhoids, mouth and gum irritation, poison ivy/sumac, sunburn, and a sore throat/mouth. Benzocaine is used in many OTC products (i.e., **ANBESOL MAXIMUM STRENGTH**), which is important to note due to its risk of precipitating a life-threatening condition called methemoglobinemia, which affects how red blood cells deliver oxygen to cells and tissues, particularly in young children. This risk prompted a US Food and Drug Administration (FDA) safety announcement in 2018, with recommended labeling changes by manufacturers (www.ismp.org/ext/1071). Benzocaine is not recommended for teething and mouth pain in infants and children less than 2 years.

While the intended actions of LAs are meant to be local, systemic absorption of these agents can lead to adverse effects that can range from discomfort at the injection site and tingling sensations as the effects wear off, to dizziness, headaches, blurred vision, twitching muscles or shivering,

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Magnesium sulfate almost administered instead of dexmedeTOMIDine. A nurse obtained a bag of what she thought was dexmede**TOMID**ine injection (400 mcg/100 mL) from an automated dispensing cabinet (ADC) in the intensive care unit. The nurse scanned the barcode prior to administration, and identified it was actually a bag of magnesium sulfate injection (4 g/100 mL). A pharmacy technician had mistakenly stocked the magnesium sulfate bag in the dexmede**TOMID**ine bin in the ADC during the stocking process; it was not reported if barcode scanning had been used during this process. Both products, made by Amneal, come in 100 mL bags and have nearly identical outer wrappers with similar colors, fonts, and designs (**Figure 1**).

Figure 1. Magnesium sulfate 4 g/100 mL (left) and dexmede**TOMID**ine 400 mcg/100 mL (right) injection bags by Amneal look nearly identical.

The pharmacy had previously purchased these medications from different manufacturers, and the look-alike packaging was not identified when the new products were brought into the organization. The pharmacy now purchases magnesium sulfate from a different manufacturer to avoid mix-ups.

We have received additional reports and reached out to the US Food and Drug Administration (FDA) and the manufacturer to recommend changes to the infusion bag labels, such as using color differentiation. In addition, nurses should use bedside barcode scanning technology to confirm that medications selected for administration match those included on the patient's medication administration record.

Dialysis bags may rupture during mixing. We received reports of NxStage PureFlow Bicarbonate Solution Bags (**Figure 1**, page 4) rupturing when practitioners attempted to break the seal between compartments in the dual chamber bag. The

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prolonged numbness, or difficulty urinating (typically with neuraxial use). At higher systemic levels, LAs can also lead to seizures and cardiac arrest. The latter reactions are most commonly the result of inadvertent venous or arterial injection or overdoses of topical or orally administered preparations. Institutions should have protocols for managing these toxicities including antidotes such as methylene blue (for methemoglobinemia) and intravenous lipid emulsion (for severe cardiac toxicity).

In some cases, allergic reactions ranging from contact dermatitis and local swelling to generalized urticaria and anaphylaxis can occur but are often rare. When possible, patients should be referred for testing to determine if the allergy is from the LA or to other ingredients or excipients. In more urgent situations, choosing an LA from a different chemical group (e.g., amide, ester) is recommended.

Table 1. Medications with the "-caine" drug stem that are available in the United States.

Generic	Brand	Form(s)	Amide/Ester
benzocaine*	multiple brands available	topical	ester
BUPivacaine	**BUPIVACAINE FISIOPHARMA**, **BUPIVACAINE SPINAL**, **MARCAINE**, **MARCAINE PRESERVATIVE FREE**, **MARCAINE SPINAL**, **POSIMIR**, **SENSORCAINE-MPF**, **XARACOLL**	implant, injection	amide
BUPivacaine (liposomal)	**EXPAREL**	injection (postsurgical analgesia)	amide
chloroprocaine	**CLOROTEKAL**, **NESACAINE**, **NESACAINE-MPF**, **IHEEZO** (ophthalmic)	injection, topical	ester
cocaine	**GOPRELTO**	topical	ester
dibucaine*	**NUPERCAINAL**	topical	amide
lidocaine*	Systemic: **XYLOCAINE**, **XYLOCAINE-MPF**	injection, ophthalmic, otic, topical	amide
	Ophthalmic: **AKTEN**		
	Otic: **EAR PAIN MD**, **EAR PAIN MD FOR KIDS**		
	Topical: multiple brands available		
mepivacaine	**CARBOCAINE**, **POLOCAINE**, **POLOCAINE DENTAL**, **POLOCAINE-MPF**, **SCANDONEST 3% PLAIN**	injection	amide
proparacaine	**ALCAINE**	ophthalmic	ester
ROPivacaine	**NAROPIN**	injection	amide
tetracaine	generic (spinal), **ALTACAINE** (ophthalmic)	injection, ophthalmic	ester

*OTC formulations available

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smaller chamber contains a salt solution (pH less than 2, acidic), and the larger chamber contains a bicarbonate buffer (alkaline) solution. Practitioners must apply pressure to the bags to break the seal between the compartments to mix before use. In one report, when the nurse was applying pressure to break the seal, the bag ruptured splashing contents on her face. She had to be treated for eye exposure.

Figure 1. NxStage PureFlow Bicarbonate Solution bag has a seal between the compartments that needs to be broken so the solution can be mixed prior to administration.

In May 2024, NxStage notified customers that they were voluntarily recalling 724 lots of NxStage PureFlow Bicarbonate Solution (www.ismp.org/ext/1410, refer to Appendix A). Our affiliate, ECRI, released a hazard alert (www.ismp.org/ext/1411) with recommendations that should be followed when these products are used. Anytime nurses need to manipulate products like these, the following general safety practices can be utilized to prevent exposure should the bag rupture.

1) Don personal protective equipment before breaking the seal, including protective eyewear and gloves to reduce the risk of eye and skin exposure.
2) Consider placing a towel over the bag before compressing it to break the seal.
3) After the seal is broken and the components are mixed, verify that the towel is dry and the bag is not leaking.
4) Do not use the product if the bag is leaking or has ruptured.
5) If skin exposure occurs, rinse thoroughly with water. For eye exposure, flush the eyes thoroughly for 15 minutes and consult a physician.
6) Report problems to the manufacturer, ECRI (www.ismp.org/ext/1162), and FDA.

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