March 24, 2016 ■ Volume 21 Issue 6

Acute Care
ISMP Medication Safety Alert!®
Educating the Healthcare Community About Safe Medication Practices

Do not let "Depo-" medications be a depot for mistakes

PROBLEM: Today, several longstanding medications are available on the market with names that begin with the prefix "Depo-," meaning they are administered via a *depot injection* that deposits the drug into localized tissue from which it is gradually absorbed by surrounding tissue. These injections, typically subcutaneous, intramuscular, or intra-articular, allow the active compound to be released consistently over a longer period of time. Many of these medications with the prefix "Depo-" have been on the market for 30 to 50 years, some even longer. Misadministration of these medications by the intravenous (IV) route has been consistently reported throughout the years, as has confusing one "Depo-" medication with another. More recently, mix-ups between different strengths and volumes of containers of a "Depo-" drug have occurred. The "Depo-" medications most often involved in these wrong route, wrong drug, or wrong strength/volume errors include:

- **DEPO-PROVERA**, **DEPO-PROVERA** Contraceptive Injection, and **DEPO-SUBQ PROVERA 104** (medroxy**PROGESTER**one acetate): an intramuscular or subcutaneous progestin used as a contraceptive, or to treat endometriosis or endometrial carcinoma.
- **DEPO-MEDROL** (methyl**PREDNIS**olone acetate): an anti-inflammatory or immunosuppressive corticosteroid given via intramuscular or intra-articular injection.
- **DEPO-TESTOSTERONE** (testosterone cypionate): an intramuscular androgen used to treat male hypogonadism.

Examples of error reports submitted to the US Food and Drug Administration (FDA) Adverse Event Reporting System (FAERS) and/or the ISMP National Medication Errors Reporting Program (MERP) are provided below.

Depo-Provera vs. Depo-Medrol

In early 2015, FAERS received a report involving a 44-year-old man with shoulder pain (non-impingement) who received an intra-articular injection of Depo-Provera instead of Depo-Medrol. A box of Depo-Provera had been stored inadvertently in the bin where Depo-Medrol was usually kept in a medication cabinet. Other than size, the medication cartons do not look similar, but both drug names start with "Depo-…" and appear in the same black font (**Figure 1**). The physician performing the shoulder injection reached into the bin and removed a box of the correct medication, Depo-Medrol, and read the label and concentration. He set that carton aside, and a moment later, he inadvertently reached back into the bin and removed another box, but this one contained Depo-Provera. Believing he had previously confirmed the drug and concentration, the physician withdrew the desired amount of an opaque white liquid similar in appearance to Depo-Medrol (**Figure 2**, page 2). The physician injected about



Figure 1. Both "Depo-" products have been mixed up, despite dissimilar carton labels.

continued on page 2—"Depo-" drugs >

SAFETY briefs

Mistake in argatroban dosing table. A physician stopped by the pharmacy with a pharmacy-dispensed carton of argatroban for a coronary artery bypass graft (CABG) patient with heparin-induced thrombocytopenia. The physician pulled out the package insert to ask the pharmacist about one of the tables, which had weight-based dosing rates listed in mg/min (minute). He wanted to be sure that he wasn't misunderstanding the dosing. The pharmacist double checked the math in that table and realized that the mg/min dosing rates would cause a 1,000-fold overdose. The values should have been stated as mcg/min. The rate in mL/hr was correct if diluted per the manufacturer recommendations. **Figure 1** shows the part of Table 2 in the package insert that lists mg/min in error.

Infusion Dosing
For ACT 300-450 seconds
25 mcg/kg/min

Continuous Infusion Dose (mg/min)	Continuous Infusion Rate (mL/hr)
1250	75
1500	90
1750	105
2000	120
2250	135
2500	150
2750	165
3000	180
3250	195
3500	210

Figure 1. Argatroban continuous infusion dose should be mcg per minute, not mg per minute.

What is also worrying is that every package insert we looked at from other manufacturers of this product (Sandoz, Teva, GSK, Fresenius, West-Ward, and Eagle) had the same error, except for Par Pharmaceutical. An error in magnitude of 1,000 was overlooked by multiple drug companies, drug package insert reviewers, the US Food and Drug Administration (FDA) approval channels, and many others who missed the error.

continued on page 2—SAFETY briefs >

> "Depo-" drugs—continued from page 1

three-quarters of the 1 mL volume he had withdrawn into the syringe (about 112 mg of Depo-Provera). A medical assistant discovered the error while cleaning up after the patient had left the office. Within 3 days of injection, the patient experienced a lack of libido and had erectile dysfunction, which required prolonged use of testosterone and **CIALIS** (tadalafil). Since making the error, the physician learned that others have made the same error, mixing up Depo-Medrol and Depo-Provera.



Figure 2. Vials look dissimilar except for the "Depo-" part of the drug name and the opaque white liquid inside the vial.

Depo-Medrol vs. Depo-Provera

Several years ago, ISMP received a report of a similar mix-up, again leading to patient harm, but in this case, the patient was supposed to receive Depo-Provera but received Depo-Medrol in error. A 19-year-old woman went to a clinic to receive an injection of Depo-Provera for contraception, which was to be repeated every 12 weeks. After providing a negative pregnancy test, the young woman was mistakenly given an intramuscular injection of Depo-Medrol. The lot number of the vial of medication was recorded in her medical record. The woman returned in 12 weeks and reported a positive home pregnancy test. An ultrasound confirmed the pregnancy, with an estimated date of conception about 3 ½ weeks after her first injection. The error was uncovered when the documented lot number was found to be associated with Depo-Medrol.

In this case, Depo-Medrol and Depo-Provera had previously been stored in separate cabinets. However, a few days before the event, the medication cabinets had been consolidated, and the medications were stored alphabetically in bins. The stock in the consolidated cabinet had been labeled with Depo-Provera and Depo-Medrol, which were stored next to each other. Working with only a verbal order for the drug, the clinic staff had accidentally selected a vial of Depo-Medrol instead of the intended Depo-Provera.

Wrong strength Depo-Testosterone

ISMP has received reports regarding potential errors with Depo-Testosterone for which the wrong strength or volume of the drug might be administered to patients. This drug is available in two strengths: 100 mg/mL and 200 mg/mL. The 200 mg/mL strength is available in a 1 mL vial and a 10 mL vial. However, the vial sizes are extremely hard to differentiate when looking at the medication cartons (**Figure 3**).



Figure 3. Can you see the difference? The labeling on cartons of Depo-Testosterone makes it difficult to notice that one contains a 1 mL vial (L) and the other a 10 mL vial (R).

Wrong route Depo-Medrol

In late 2015, a patient received 100 mg of Depo-Medrol IV. The route of administration was not specified on the written order given to the nurse, who assumed the drug should be administered IV, like the other medications the patient was receiving. The nurse did not recall seeing the statement, "Not for IV Use" on the back of the vial label; the statement is in a very small font size. Fortunately, the patient was not harmed. The reporting pharmacist found many case reports of similar errors published in the literature.

Other errors involving Depo-Medrol being administered IV instead of intramuscularly have resulted from mix-ups between **SOLU-MEDROL** (methyl**PREDNIS**olone sodium succinate) and Depo-Medrol, often due to stocking errors. Depo-Medrol's milky white

continued on page 3—"Depo-" drugs >

> SAFETY briefs cont'd from page 1

An independent check of the dosing tables and their calculations might have identified the error immediately. It's an important lesson, because the same thing could easily happen at a hospital when developing order sets, forms, tables, and so on. Please check to make sure this table was not copied into an order set or is otherwise being used to guide therapy. We thank the doctor and pharmacist who picked up this error AND reported it. You showed us the importance of speaking up about the errors you find.

Ask about safety caps. An elderly patient with multiple myeloma suffered a spiral fracture of the humerus with 15 mm of posterior displacement while trying to remove the child-resistant cap on her medication bottle. The simple act of trying to push down and twist broke the weakened bone and caused the fracture. These bottles are designed to protect children from accidental overdoses but, in this case, ended up harming an elderly woman (**Figure 1**). The point is, pharmacists need to talk to patients periodically to discuss any problems they may have accessing their medications. If difficulty is expressed, patients should be offered the choice of having their prescription(s) dispensed in a bottle without a safety cap. Some pharmacists never ask about this while others routinely ask when filling a prescription for a new patient. This type of information, which is often overlooked, needs to be updated periodically. When safety caps are not used, it is critically important to educate patients about the risk of accidental poisonings of children and safe medication storage (www.upandaway.org).



Figure 1. Fractured humerus clearly visible on X-ray.

Safety opportunities with NY e-Rx requirement. Beginning March 27, 2016, prescribers in New York (NY) State *must* utilize

continued on page 3—SAFETY briefs >

© 2016 ISMP. Reproduction of the newsletter or its content for use outside your facility, including republication of articles/excerpts or posting on a public-access website, is prohibited without written permission from ISMP.

> "Depo-" drugs—continued from page 2

appearance rarely gives pause anymore before administration given the wide variety of other cloudy or opaque medications that are administered IV.

Aggregate reports

Analysis of aggregate data regarding mix-ups between Depo-Medrol and Depo-Provera between 1999 and 2015 identified 5 additional cases reported to FAERS and 4 more reported to the ISMP MERP database, for a total of 11 reports. One of the events occurred as recently as December 2015, although no harm occurred when the patient received an injection of Depo-Medrol instead of Depo-Provera. Date ranges for the reported errors were distributed evenly between 1999 through 2015; therefore, we did not find any trends in the occurrence of the errors over time. In most of the cases (n=7), Depo-Provera was the intended drug and Depo-Medrol was administered instead. The errors occurred in a variety of settings, so it is difficult to associate patterns of error within a specific clinical setting (e.g., clinic vs. hospital). Five of the reports identified the Pfizer Depo-Medrol 80 mg/mL vials, and 2 involved the Pfizer Depo-Provera 150 mg/mL vials (both distributed by Pharmacia & Upjohn, a division of Pfizer). In four of the 11 cases, both products were available as unit stock. This may have contributed to errors due to the similarities in the names. For example, confusion may have occurred if staff misread the correct drug name when stocking the drug product (i.e., stocked in the wrong bin) and then the wrong drug was selected prior to administration, leading to a medication error. Other than name similarity, none of the reports identified container labels or carton labeling similarities as a contributing factor.

Another analysis of aggregate data regarding IV administration of a "Depo-" medication shows that the most frequent wrong route errors were associated with Depo-Medrol (n=11 out of 12 total IV administrations). In 5 of these cases, the route of administration was misunderstood, and Depo-Medrol was administered intravenously. In the remaining 6 cases, Depo-Medrol was administered in error when the order was for IV Solu-**MEDROL**. It should be noted that there is also a product named **DEPO-ESTRADIOL** (estradiol cypionate), although we have only one error report for this drug indicating that it was given by the IV route instead of intramuscular route of administration.

The recent close calls associated with Depo-Testosterone (n=2) were both caused by volume or strength confusion due to look-alike labeling and packaging.

Safe Practice Recommendations: Today, the "Depo-" naming convention would be a concern for FDA based on its proprietary name review criteria (www.ismp.org/sc?id=423). However, when these drugs were first approved, the risk associated with this prefix was not considered. It would be very difficult to change the names of these products today—it may even make the risk of errors greater since these drug names are widely recognized. However, there are steps manufacturers, regulatory agencies, and healthcare practitioners can take to reduce the risk of potentially harmful mix-ups between these medications, strengths/container volumes, and routes of administration.

Manufacturers and regulatory agencies

Clarify labeling. Address the look-alike labels and packages of Depo-Testosterone as soon as possible. Most people look at the 1 mL and 10 mL vials and fail to realize that they are not the same.

Enhance warnings. Make warnings against IV use of depot products more prominent. The warnings should be clearly visible on the front label panel of cartons and vials, not on the back.

continued on page 4—"Depo-" drugs >

> SAFETY briefs

cont'd from page 2

electronic prescribing (e-Rx) or face fines, license revocation, or even prison. Except in emergencies or a few other exceptions, handwritten and printed prescriptions will soon become a thing of the past in NY (www.ismp.org/sc?id=1697). Other states will likely follow suit. Minnesota already has such a rule, although without consequences for noncompliance. The NY law requires a secure, encrypted, or encoded system for electronic transmission from prescriber to pharmacy, computer to computer. Emailed prescriptions are not allowed; a faxed prescription for non-controlled drugs is allowed under certain circumstances.

This is a well-intentioned rule that will likely reduce errors due to poor handwriting and will hopefully provide prescribers with clinical decision support. However, as with most changes, the law could also result in unintended consequences. For example, the risk is elevated for errors due to selecting the wrong medication among several look-alike drug names from a drop-down list. This type of error would be hard to detect without knowing the intended purpose of a newly prescribed medication. Strategies that would help, such as communicating each medication's purpose, using tall man lettering, and counseling patients, are not mentioned in the legislation. We hope healthcare practitioners will keep these strategies in mind.

Also missing is a provision for ensuring that patients receive a printout at the prescriber's office that lists newly prescribed medications. Otherwise, how will patients know what they're supposed to receive? The prescriber doesn't always communicate the name, strength, and directions for using the prescribed medication; if they do, patients sometimes forget. Ideally, with e-prescribing, the prescriber should give the patient verbal instructions, offer an opportunity to ask questions, and provide the patient with a corresponding printout that lists the prescribed medication, dose, and directions for use. As long as the printout isn't on official NY State prescription paper, once the e-Rx is sent electronically, the law does not prohibit a printout of current medications. This is a

continued on page 4—SAFETY briefs >

> "Depo-" drugs—continued from page 3

Healthcare practitioners

Keep vials apart. Separate the storage of Solu-**MEDROL**, Depo-Medrol, and Depo-Provera vials in the pharmacy and in all clinical settings where these drugs are stocked. Store only one medication in each bin or other storage container. Evaluate whether all three drugs need to be stocked in patient care units.

Differentiate the products. Consider stocking Depo-Provera in prefilled syringes for single patient use instead of single-dose vials. Depo-SubQ Provera 104 is available in single use 0.65 mL (104 mg) prefilled syringes for subcutaneous injections, and Depo-Provera 1 mL (150 mg) is available in prefilled syringes for intramuscular injections. Since Depo-Medrol is not supplied in prefilled syringes, this may increase differentiation between the two products, but only if staff know to expect Depo-Provera in a syringe. Thus, staff awareness is a necessary component of this differentiation strategy.

Limit access. Attempt to limit inventory of Depo-Testosterone to a single strength and vial size. Also evaluate which "Depo-" medications need to be stocked in patient care units, and limit access to those that can be dispensed as needed from the pharmacy.

Include auxiliary labels. Highlight or circle important information on labels to draw attention to it, or add an auxiliary label if necessary. For example, given the small font of the warning on Depo-Medrol vials, an auxiliary label that states, "IM Use Only" or "Intra-articular Use Only" may be required. For Depo-Testosterone labels, circle or point an arrow toward the total volume in each vial.

Express generic names safely. Use tall man letters when expressing the generic names of Depo-Medrol and Depo-Provera (i.e., methyl**PREDNIS**olone, medroxy**PROG-ESTER**one) to prevent confusion. When expressing generic names for Solu-**MEDROL** and Depo-Medrol, include the correct form of methyl**PREDNIS**olone (i.e., acetate, sodium succinate) to help differentiate the drugs.

Highlight the route. Always include the route of administration, easily visible in a prominent location, on orders and medication administration records.

Use barcode scanning. Implement barcode scanning to verify medications when stocking and restocking medications in automated dispensing cabinets, and prior to drug administration at the bedside as a method to help mitigate confusion that may lead to wrong drug medication errors. When used at the bedside, this technology confirms not only the drug but also the patient's identity, dose, time, and dosage form of the medication being delivered. Track scanning compliance to ensure that staff is using the technology.

Increase staff awareness. Assess staff understanding of the term "depot," and increase their understanding regarding why "Depo-" medications should not be administered IV. Be sure staff know the risk of confusion between "Depo-" products with similar names, such as mix-ups between Depo-Provera and Depo-Medrol, or the risk of errors related to labeling and packaging similarities with Depo-Testosterone.

> SAFETY briefs cont'd from page 3

practice that should be encouraged, and not just in NY! Patients can know what to expect, read about the drugs, and formulate any questions they may have for their pharmacists, or contact their physicians if they have concerns about taking the medications.

The new law may also impact the way patients choose a pharmacy. Since electronic prescriptions are sent to a specific pharmacy, and printed prescriptions are no longer used, patients may have difficulty bringing the prescription to different pharmacies to get the best price and/or service.

Special Announcements

Free CE for pharmacists

ISMP has 4 new opportunities for pharmacists to earn FREE continuing education credits online:

- *Making Smart Pumps More Intelligent*
- *Improving the Safety of Compounding Sterile Products*
- *Advancing Medication Safety for Adult Patients Receiving IV Push Therapy*
- *Medication Safety in Radiology: Often Unrecognized Issues*

Access all 4 programs from our homepage at: www.ismp.org.

ISMP webinar

Join us on **April 19** for our next webinar, ***Smart Pump Technology: Capturing the Full Safety Potential.*** It is important for organizations to maximize the safety value of these devices and prepare for smart pump integration. Join the dialogue with our faculty from **WellStar Health System** and **Cook Children's Health Care System** as they describe the lessons learned with full implementation of smart pumps throughout their organizations. For details, please visit: www.ismp.org/sc?id=349.

If you would like to subscribe to this newsletter, visit: www.ismp.org/sc?id=382

ISMP INSTITUTE FOR SAFE MEDICATION PRACTICES

ISMP Medication *Safety Alert!* Acute Care (ISSN 1550-6312) © 2016 Institute for Safe Medication Practices (ISMP). Subscribers are granted permission to redistribute the newsletter or reproduce its contents within their practice site or facility only. Other reproduction, including posting on a public-access website, is prohibited without written permission from ISMP. This is a peer reviewed publication.

Report medication and vaccine errors to ISMP: Please call 1-800-FAIL-SAF(E), or visit our website at: www.ismp.org/MERP or www.ismp.org/VERP. ISMP guarantees the confidentiality of information received and respects the reporters' wishes regarding the level of detail included in publications.

Editors: Judy Smetzer, BSN, RN, FISMP; Michael Cohen, RPh, MS, ScD (hon), DPS (hon); Ann Shastay, MSN, RN, AOCN; Russell Jenkins, MD; Ronald S. Litman, DO. ISMP, 200 Lakeside Drive, Suite 200, Horsham, PA 19044. Email: ismpinfo@ismp.org; Tel: 215-947-7797; Fax: 215-914-1492.