Do not let “Depo-” medications be a depot for mistakes

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** (medroxyPROGESTERone acetate): an intramuscular or subcutaneous progestin used as a contraceptive, or to treat endometriosis or endometrial carcinoma.
- **DEPO-MEDROL** (methylPREDNISolone 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).

Consider the following recommendations to prevent errors with “Depo-” medications:

- **Keep vials apart.** Separate the storage of Solu-MEDROL, Med-Drol, 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 products.** Ask pharmacy to 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, continued on page 2—check it out >
“Depo-” medications—continued from page 1

The physician injected about 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 the 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.

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 3½ 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).

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.

Express generic names safely. Use tall man letters when expressing the generic names of Depo-Medrol and Depo-Provera (i.e., methylPREDNISolone, medroxy-PROGESTERone) to prevent confusion. When expressing generic names for SolumEDROL and Depo-Medrol, include the correct form of methylPREDNISolone (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 wires

“Floaters” in liquid melatonin. We received a report about floating numbers found in liquid melatonin. Pharmacists preparing doses of Natrol Melatonin 1 mg/4 mL in oral syringes saw what appears to be the number 2 or 5 floating in the filled syringe (Figure 1, top of page 3). Appar-
Other errors involving Depo-Medrol being administered IV instead of intramuscularly have resulted from mix-ups between SOLU-MEDROL (methylPREDNISolone sodium succinate) and Depo-Medrol, often due to stocking errors. Depo-Medrol’s milky white 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 the patient was not harmed after receiving 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.

### Conclusions

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 can take to clarify the labels and enhance the warnings against IV use of depot products so they are clearly visible on the front label of cartons and vials.

While we have suggested specific label enhancements to manufacturers, until label changes happen, consider the recommendations in the check it out column (starting on page 1, right column) to reduce the risk of potentially harmful mix-ups between these medications, strengths/container volumes, and routes of administration.

Bone density may decline, and fractures may occur as a result of osteoporosis.

#### Unsafe labeling—Caution advised.

The labeling of VistaPharm potassium chloride oral solution 10% in unit dose cups is misleading as to the exact quantity in the container. The container prominently lists the strength as 20 mEq per 15 mL, but the cup actually contains 30 mL, or 40 mEq. The actual amount in milliequivalents is not stated. Other companies, including Pharmaceutical Associates, have safer labeling to indicate that the cup delivers either 15 or 30 mL and 20 or 40 mEq (Figure 1). We’ve contacted VistaPharm to suggest a label change that shows the exact quantity in the container (delivers 30 mL with strength of 40 mEq per 30 mL).
Your Reports at Work

Label improvement for CutisPharma vancomycin kit. ISMP appreciates the improved labeling that CutisPharma has begun to use for its FIRST brand vancomycin oral solution compounding kit. In the past, the diluent and powder container listed the drug name and strength at the top of both bottles (Figure 1), making it difficult to tell these apart. In fact, in our acute care newsletter, October 22, 2015 issue, we wrote about a nurse who gave only the diluent to her patient, thinking it contained the liquid vancomycin. It was not easy to tell the diluent container from the drug container without reading the full label with great care, which doesn’t happen often enough!

But now, CutisPharma has revised the container labels by doing what we suggested last fall: print “Diluent” in large, bold text on the diluent label and “vancomycin hydrochloride Powder” on the powder label (Figure 2). They also made distinct color changes to help make each container look different. These changes will likely help to avoid similar errors.

We thank CutisPharma for making this change. The company told us that it is systematically revising other compounding kit labels, too, including omeprazole and lansoprazole.

FREE ISMP Resources

Consumer leaflets in Spanish. We now have Spanish translations of our consumer leaflets for 11 high-alert medications, including insulin analogs, methotrexate, fentaNYL patches, enoxaparin, warfarin, and others. The leaflets provide consumers with important safety tips for taking each medication safely. The leaflets are freely available (www.ismp.org/sc?id=1709) and can be reproduced for distribution to patients.

> SAFETY wires continued from page 3

Cup with wrong measurement marking. A 30 mL dosing cup distributed by Essential Medical Supply (model # C1108) has an incorrect marking of 5 mL at the 10 mL gradation. The cup has the correct mL markings for the other gradations, but sequentially, the markings are listed as 2.5 mL, 5 mL, 7.5 mL, and 5 mL (Figure 1). These cups have primarily been distributed to outpatient pharmacies, but please be certain you are not using them. Both the pharmacist at the hospital who reported the error and ISMP have contacted the distributor. We also notified the US Food and Drug Administration (FDA), and the Center for Devices and Radiological Health (CDRH) is investigating the issue. ISMP believes that a recall is in order, but it has not yet occurred. Two-fold dosing errors, which could cause serious harm depending on the drug, are inevitable given the incorrectly marked gradation on the cup.

Oral devices with mL-only dosing marks. Progress continues with manufacturers making syringes with metric-only dose scales. NeomEd has had mL-only syringes for some time. We also have heard from BD and Baxter regarding their plans to provide mL-only oral syringes. Medi-Dose and Health Care Logistics are advertising metric-only devices. Dosage cups that measure in mL-only are becoming available, although the ones we have seen so far have scales that are embossed on clear plastic, making them difficult to read with certain liquids. We expect improvements soon. Thanks for your efforts in converting to the metric system to improve patient safety.