



April 2016 Issue

## From the Front Lines

AlixRx Clinical Pharmacists Address Everyday Challenges in Long-Term Care

### New Insulin Products – Concentration is Key

Insulin is available in multiple forms and is typically dispensed in a vial or pen device. Recent products introduced to the market have varying concentrations of insulin. Insulin concentrations are listed as units per milliliter (ml). Insulin with a concentration of 100 units/ml will be labeled as U100, an insulin product with a concentration of 200 units/ml will be labeled as U200, and so on. Identifying the concentration of the insulin product ordered and administered is essential to safe use. Until recently, insulin was available at a concentration of 100 units/ml or 500 units/ml, U100 and U500 insulin respectively.

Insulin pen devices with varying concentrations of insulin are currently available. Toujeo® is long-acting insulin glargine at a concentration of 300 units/ml, a more concentrated form of Lantus®. Tresiba® is an ultra long-acting insulin available in concentrations of 100 and 200 units/ml. Even rapid acting Humalog® is now available in 100 and 200 units/ml concentrations via the Humalog KwikPen® device. U500 insulin has only been available in a vial until the approval of the Humulin R U-500 KwikPen® this year.

U500 insulin is 5x as concentrated as U100 insulin (500 units/ml vs 100 units/ml). Concentrated insulin allows for less injection volume per unit which decreases variability in absorption at high dosages. Health care providers should also be aware that unlike U100 regular insulin with an approximate onset of action of 30 minutes and duration of 1-3 hours, U500 insulin acts more like a 70/30 mix of NPH and regular insulin. It is typically dosed BID with an onset of 30 minutes but an extended duration of action up to 24 hours. Dosing errors can lead to significant adverse reactions including death. Recently Eli Lilly received approval from the FDA for Humulin R U-500 KwikPen® for patients that require more than 200 units of insulin per day.

The U-500 KwikPen® should provide a safer dosing medium compared to using a vial of U-500 insulin and converting dosages with a U100 insulin syringe or a TB syringe. The U-500 KwikPen® dials in increments of 5 units and has 1500 units of insulin per pen. Once the pen is used it may be stored at room temperature for up to 28 days. Unopened pens should be stored in the refrigerator.

When non-conventional insulin products are ordered, transcription and order entry into electronic health records is vitally important. Ensure all orders are double checked and exactly match the pharmacy label attached to the insulin product. All orders should include an insulin concentration and dose for clarity, since dosing errors can be fatal. Don't hesitate to ask your AlixaRx Pharmacy Team for clarification and guidance related to insulin products and their safe use.

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## Reducing the Risks of Relief: The CDC Opioid-Prescribing Guideline

Beginning in the 1990s, efforts to improve treatment of pain failed to adequately take into account opioids' addictiveness, low therapeutic ratio, and lack of documented effectiveness in the treatment of chronic pain. Deaths from prescription opioid overdose have increased dramatically in the United States, quadrupling in the past 15 years. It has become increasingly clear that opioids carry substantial risks and uncertain benefits.

On March 15, 2016, the Centers for Disease Control and Prevention (CDC) released a "Guideline for Prescribing Opioids for Chronic Pain" to chart a safer, more effective course. The guideline is designed to support clinicians caring for patients outside the context of active cancer treatment, palliative, or end-of-life care.

Most placebo-controlled, randomized trials of opioids have lasted 6 weeks or less. The few randomized trials to evaluate opioid efficacy for longer than 6 weeks had consistently poor results. In fact, several studies have showed that use of opioids for chronic pain may actually worsen pain and functioning, possibly by potentiating pain perception.

Three key principles underlie the guideline's 12 recommendations:

1. Non-opioid therapy is preferred for chronic pain outside the context of active cancer, palliative, or end-of-life care.
2. When opioids are used, the lowest possible effective dose should be prescribed to reduce the risks of opioid use disorder and overdose.
3. Clinicians should exercise caution when prescribing opioids and should monitor all patients closely.

### The CDC Opioid-Prescribing Guidelines – Twelve Recommendations for Clinicians

1. Non-pharmacologic therapy and non-opioid pharmacologic therapy are preferred for chronic pain. Clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient. If opioids are used, they should be combined with non-pharmacologic therapy and non-opioid pharmacologic therapy, as appropriate.
2. Before starting opioid therapy for chronic pain, clinicians should establish treatment goals with all patients, including realistic goals for pain and function. They should also consider how therapy will be discontinued if benefits do not outweigh risks. Clinicians should continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety.
3. Before starting and periodically during opioid therapy, clinicians should discuss with patients known risks and realistic benefits of opioid therapy and patient and provider responsibilities for managing therapy.
4. When starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids.
5. When opioids are started, clinicians should prescribe the lowest effective dosage. Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when increasing dosage to  $\geq 50$  morphine milligram equivalents (MME) per day, and should avoid increasing dosage to  $\geq 90$  MME per day or carefully justify a decision to titrate dosage to  $\geq 90$  MME per day.
6. Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. Three days or less will often be sufficient; more than 7 days will rarely be needed.
7. Clinicians should evaluate benefits and harms with patients within 1–4 weeks of starting opioid therapy for chronic pain or of dose escalation. Clinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently. If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids.
8. Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid-related harms. Clinicians should incorporate into the management plan strategies to mitigate risk,

including considering offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages ( $\geq 50$  MME/day), or concurrent benzodiazepine use are present.

9. Where permissible by law, Clinicians should review the patient's history of controlled substance prescriptions using state prescription drug monitoring program (PDMP) data to determine whether the patient is receiving opioid dosages or dangerous combinations that put him or her at high risk for overdose. Clinicians should review PDMP data when starting opioid therapy for chronic pain and periodically during opioid therapy for chronic pain, ranging from every prescription to every 3 months.
10. When prescribing opioids for chronic pain, clinicians should use urine drug testing before starting opioid therapy and consider urine drug testing at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs.
11. Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible.
12. Clinicians should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies) for patients with opioid-use disorder.

Reference: Frieden TR and Houry D. Reducing the Risks of Relief — The CDC Opioid-Prescribing Guideline. NEJM 10.1056/NEJMp1515917 March 15, 2016

## My Resident's INR is Elevated!

What is the recommended treatment? What should I expect?

Guidelines for anticoagulant therapy have been updated and changed slightly over the past few years. Below is a simplified table for your reference:

**INR < 4.5 with no significant bleeding:** Decrease or hold warfarin dose and monitor INR more frequently. Reinitiate therapy at a lower dose once a therapeutic INR is reached. If slightly above the therapeutic range, no dose reduction may be required.

**INR  $\geq 4.5$  and  $\leq 10$  with no evidence of bleeding:** Clinical practice guidelines recommend against the routine use of vitamin K. Hold the next 1 or 2 doses of warfarin, monitor the INR more frequently, and reinitiate therapy at a lower dose once a therapeutic INR is reached.

**INR > 10 with no significant bleeding:** Vitamin K1 (Mephyton, Phytonadione) 2.5–5 mg PO with the expectation that the INR would be reduced substantially in 24–48 hours. Hold warfarin therapy. Monitor INR more frequently. If the INR is still elevated, additional vitamin K may be given. Reinitiate therapy at a lower dose once a therapeutic INR is reached.

**Serious bleeding at any elevation of INR:** Vitamin K1 5–10 mg IV by slow infusion in addition to 4-factor prothrombin complex concentrate. Hold warfarin therapy.

### \*\*\*Nursing Pearl\*\*\*

Large doses of Vitamin K can lead to warfarin resistance for up to a week after vitamin K is discontinued. Therefore, your resident's INR may remain "low" or subtherapeutic for up to a week after vitamin K is administered, regardless of the warfarin dose. This is especially true if a large dose ( $>5$ mg) of Vitamin K has been administered.

### What is available in my AlixaRx Electronic Medication Cabinet (EMC)?

Mephyton (Phytonadione, Vitamin K1) 5mg tablet.

For additional questions please contact your AlixaRx Clinical Pharmacist.

## Controlled Substance Prescriptions Procedure

Medications included in the Drug Enforcement Administration (DEA) classification as controlled substances, and medications classified as controlled substances by state law, are subject to special ordering.

According to DEA regulations, pharmacies can accept prescriptions from nurses in LTC facilities who are designated as an authorized agent of the physician. However, this requires an executed written agreement between the prescriber and nurse.

### Schedule III-IV controlled medications

Prescriptions can only be filled by the provider pharmacy if a valid prescription is received from the prescriber.

1. Verbal prescriptions can be phoned into the pharmacy by the prescriber.
2. Written prescriptions signed by the prescriber may be faxed by the prescriber.

### Schedule II controlled medications

Generally speaking, the pharmacy must have a signed prescription by the physician prior to dispensing. A signed prescription for a C-II drug may be faxed to the provider pharmacy in accordance with the state laws by the prescriber. The one exception to these requirements is outlined below for emergency situations.

1. Verbal prescriptions may be accepted only for a short term emergency supply of C-II prescriptions. These can ONLY be phoned in to the pharmacist by the prescriber. A written copy of the prescription, to cover the verbal authorization, must be delivered to the dispensing pharmacy within 7 days per DEA regulations.
2. If the medication is required beyond the emergency period, a continuation prescription should then be faxed or mailed to AlixaRx.

### AlixarX's role in obtaining a NEW prescription order from the prescriber

An order is written or faxed to the pharmacy for a medication that requires a prescription from the prescriber:

1. If it is a new admission, the pharmacy will first call the facility to see if they have the prescription.
2. If the facility does not have the prescription, the pharmacy will either fax or call the prescriber to request a prescription.
3. The pharmacy will follow up by either via fax or phone call in 24 hours if there is no response and again in 48 hours if there is still no response. \*\*Please note that some prescribers will not allow AlixaRx to contact them via phone\*\*
4. If AlixaRx does not receive a prescription from the prescriber, the pharmacy does not normally call the facility to let them know. After 3 attempts, the narcotic technician will e-mail the Director of Nursing at the facility to notify them of the prescriptions that are needed.

### AlixarX's role in obtaining refill prescriptions of controlled substances

1. The Hub pharmacy will run the controlled reorders report to determine if any orders will expire in the next 2 weeks or have less than a 10 day supply remaining.
2. The Hub pharmacy will then send RX blanks to the prescriber for a new prescription.
3. Once the prescriber responds, the Hub pharmacy will fill or retain the prescription for future use.
4. If no response is obtained from the prescriber, the Hub pharmacy will contact the prescriber via phone or fax every 2 days.
5. If no response from the prescriber is obtained after the 3rd attempt, the Hub pharmacy will contact the facility, who can then contact their medical director for direction.
6. If no response is obtained after the facility's attempt, the facility can begin working through their call tree to obtain the necessary authorization for the prescription.

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