

MEDICATION

A MONTHLY PUBLICATION FROM VA MEDSAFE:
VA'S COMPREHENSIVE PHARMACOVIGILANCE CENTER

SAFETY IN SECONDS

Helping to achieve safe medication use

ACETAMINOPHEN SAFETY

A recent Office of Inspector General (OIG) report highlighted the potential for VA patient harm from prescribing higher than recommended doses of acetaminophen in combination opioid products.¹ Results from this OIG study may have implications for clinical practice, especially in patients prescribed acetaminophen for pain control as a component of analgesic combinations for scheduled as well as as-needed use or in patients taking over-the-counter (OTC) acetaminophen preparations. Severe liver injury, including cases of acute liver failure resulting in liver transplant and death, has occurred with the use of high doses of acetaminophen.

FDA recommends a maximum dose of **4 g per 24 hours** for prescription acetaminophen products (mainly combination formulations with opioids). An FDA-imposed limit of 325 mg per dosage unit in prescription combination products minimizes the risk of acetaminophen overdose and toxicity, but currently does not apply to OTC acetamino-

phen products. The recommended maximum dose of OTC acetaminophen may vary by formulation, strength, and manufacturer but still should not exceed 4 g per day.²

Earlier this year, VA PBM and MedSAFE released a drug safety alert that addressed the risk of severe liver damage with the use of high doses of acetaminophen exceeding the recommended dose of 4 g within a 24-hour period. FDA actions as well as provider recommendations to reduce the risk of accidental acetaminophen overdose were also discussed in this educational piece.³ Details are available in the [National PBM Bulletin](#) issued this past June.

As of June 1, 2014, it was estimated that approximately 527,153 patients in the VA during fiscal year quarter 3 to date received an outpatient prescription for acetaminophen. Roughly 2% of patients with a prescription for an acetaminophen product have a dose greater than 4 g, and around 8%

(continued on page 4)

IN THIS ISSUE:

- ▶ ACETAMINOPHEN SAFETY...1, 4
- ▶ MEDICATION SAFETY NEWS FROM THE VA NATIONAL PHARMACY BENEFITS MANAGEMENT SERVICES [PBM] AND THE FOOD AND DRUG ADMINISTRATION [FDA].....1
- ▶ HYDROMORPHONE SAFETY CONSIDERATIONS.....2-4



VA PHARMACY BENEFITS MANAGEMENT SERVICES (PBM)

PBM maintains VA's national drug formulary, as well as promotes, optimizes, and assists VA practitioners with the safe and appropriate use of all medications.

VA CENTER FOR MEDICATION SAFETY (VA MedSAFE)

VA MedSAFE performs pharmacovigilance activities; tracks adverse drug events (ADEs) using spontaneous and integrated databases; enhances education and communication of ADEs to the field; and promotes medication safety on a national level.

EDITOR-IN-CHIEF

Marie Sales, Pharm.D.
VA Pharmacy Benefits Management Services [PBM] & Center for Medication Safety [VA MedSAFE]; 1st Avenue—1 Block North of Cermak Road | Building 37; Room 139 | Hines, Illinois | 60141; www.pbm.va.gov

NEWSWORTHY...

from the pbm

- UPDATE: Niacin Study Results and Implications – 08/29/2014 - [National PBM Bulletin](#)

Getting the most from our safety surveillance

HYDROMORPHONE SAFETY CONSIDERATIONS

In a recent complicated clinical case, a single high dose of hydromorphone (10 mg given intravenously) may have led to, or acted as a contributing factor to, a serious adverse event. In reviewing this case, VA's Center for Medication Safety and its consultants, raised concerns regarding provider awareness with respect to the relative potency of this medication and that some Centers may not fully utilize available safeguards to reduce use of high doses of hydromorphone, as well as other opioids, by providers without knowledge or expertise in pain management.

According to the equianalgesic potency ratios provided in the hydromorphone product labeling, one dose of 10 mg of hydromorphone administered parenterally is *approximately* equivalent to 30 - 55 mg of oral hydromorphone; or 200 - 450 mg of oral morphine; or 50 - 75 mg of parenteral morphine delivered in a single administration. Product information goes on to caution that if an intravenous route is clinically indicated, the hydromorphone injection should be given very slowly, over at least 2-3 minutes, since rapid intravenous injection of opioid analgesics increases the possibility of side effects such as hypotension and respiratory depression. In addition, a boxed warning in the product labeling advises to not confuse the high potency hydromorphone parenteral formulation (10 mg/mL ampules and vials) with standard parenteral formulations of hydromorphone (1, 2, and 4 mg/mL ampules) as overdose and death could result due to the more concentrated solution. Doses at this level warrant careful consideration and consultation with providers experienced in pain management with high-dose and/or high-potency opioids.

To assist in reducing high dose usage in general, the VA implemented new order checks for maximum single dosing in June 2014. A software upgrade to the Medication Order Check Healthcare Application (MOCHA) within VA's computerized provider drug-order entry system will generate an alert to notify a prescriber when the single maximum dose ordered of any drug, including opioids, exceeds the recommended maximum dose according to the First Databank drug database. This is accomplished by imposing upper limit medication dose checks when an order is entered by a VA provider. Version 2.1 (V2.1) includes total daily dose checks, scheduled to be implemented by the end of fiscal year (FY) 2015. In the case of hydromorphone, the trigger of single dose is set to 6 milligrams, as displayed in Figure 1 (page 3).

However, while this is an important step, and might, for example, help stop the use of a single high dose opioid, dosing still can be quite high, depending on the medication chosen. In addition, providers can over-ride order checks and/or could use multiple doses thus skirting around the high dose trigger. Hence, VA's Center for Medication Safety suggests additional measures that can be employed that can help.

To further ensure safe and appropriate opioid therapy, providers and/or facilities should consider options such as:

- Enhancing competencies through education and training regarding opioid potency and equivalency; consider, for example, teaching prescribers how to use opioid equivalency tables properly and giving them access to feature-rich online opioid calculators.
- Promoting opioid therapy concordant with clinical practice guidelines. (See below)
- Obtaining consultation and guidance from pain management specialists on high dose opioid use and/or whenever pertinent questions on initiating, titrating, or transitioning between opioids arise.
- Utilizing existing CPRS and order entry tools in addition to resources to promote system improvements such as:
 - ◇ Using limited default dosing (i.e., limited pre-populated dose selections available in a drop-down pick-and-choose format for opioids identified to be of high-risk, high-dose, or with an identified safety issue). This allows providers to carefully, within defined parameters, individualize opioid dose for each patient when these agents are ordered.
 - ◇ Restricting certain opioids (such as methadone) to pain and palliative care (and other selected) specialists for initiation and/or titration.
 - ◇ Limiting high opioid doses to pain and palliative care (and other selected services) for use or approval (e.g., hydromorphone > 3 mg).
 - ◇ Utilizing quick orders with relevant information (Figure 2, page 3); and/or drug text display restrictions\guidelines (Figure 3, page 4) to promote dosing safety across the board for opioids.

Materials and links that may assist in opioid related education and management include:

- VA's Pain Management Directive—VHA Directive 2009-053 (available at : <http://www.va.gov/PAINMANAGEMENT/docs/VHA09PainDirective.pdf>).
- VA/DoD Evidence-Based Clinical Practice Guidelines on Management of Opioid Therapy for Chronic Pain (available at: http://vaww1.va.gov/PAINMANAGEMENT/docs/CPG_opioidtherapy_fulltext.pdf).
- Pharmacy Benefits Management Initiatives and Clinical Guidance (available at: <http://www.pbm.va.gov/clinicalguidance.asp>).

Contributed by:

Peter A. Glassman, MBBS, MSc, FACP

Norwan J. Moaleji, Pharm.D., BCPP

Robert Silverman, Pharm.D.

and Marie Sales, Pharm.D.

(continued on page 3)

Getting the most from our safety surveillance

HYDROMORPHONE SAFETY CONSIDERATIONS

(continued from page 2)

Figure 1.
With the MOCHA software implemented, when a 10mg dose is free-texted in an inpatient or outpatient order, the provider (and pharmacist) receives this maximum single dose exceeded warning.

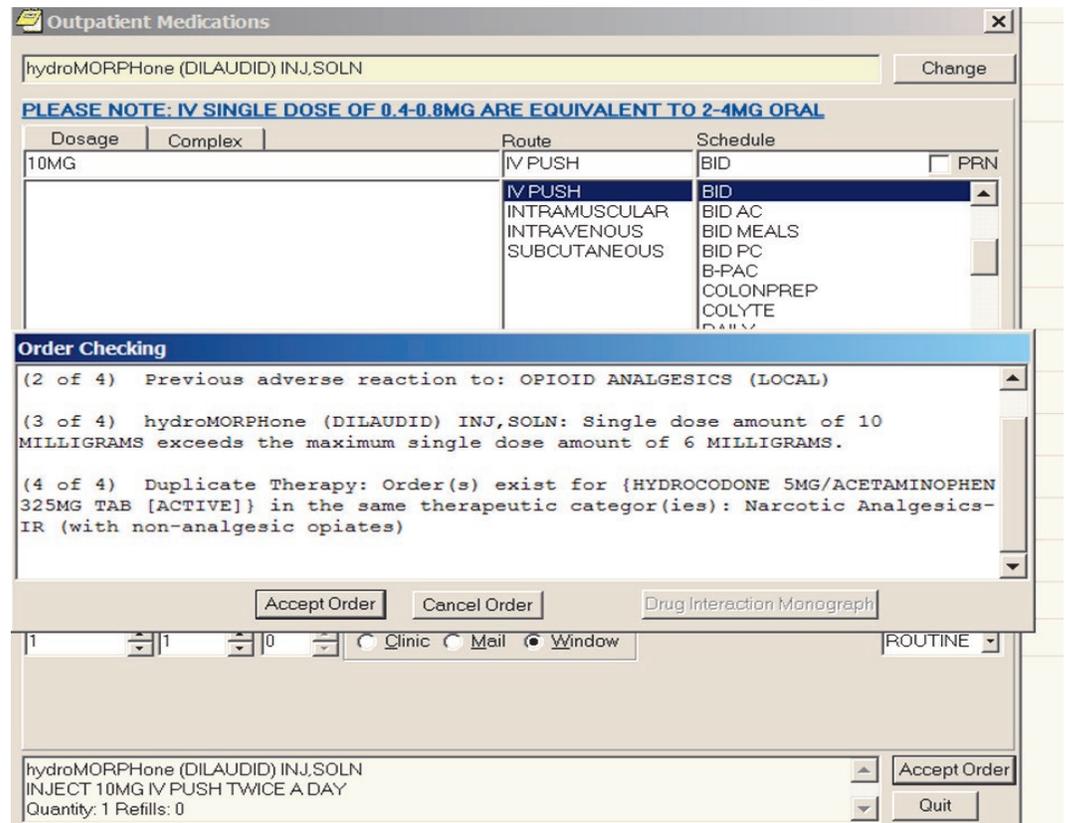
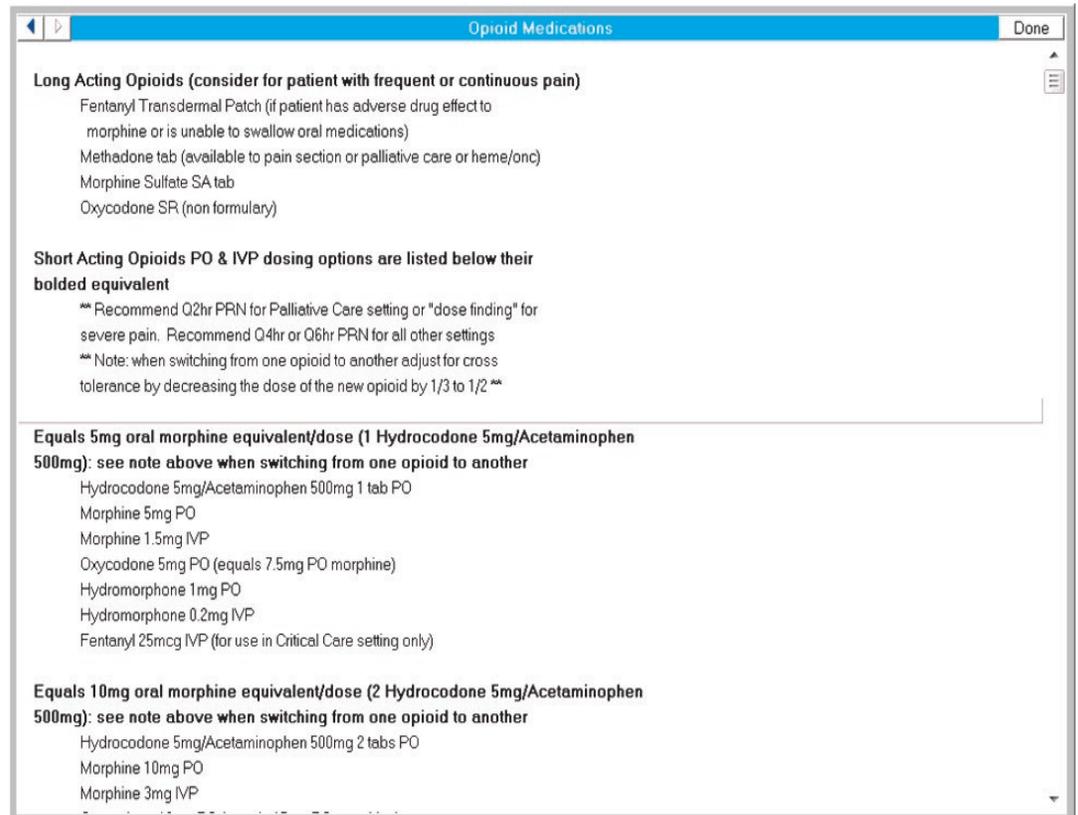


Figure 2.
Example of a quick order used at one site that has opioid equivalents clearly stated.



(continued on page 4)

Getting the most from our safety surveillance

HYDROMORPHONE SAFETY CONSIDERATIONS

(continued from page 3)

Figure 3.
Example of a drug text display restriction/guideline that displays as blue text on the screen when ordering. In this instance, one facility created a drug text display restriction/guideline that alerts providers to potential look-alike sound-alike confusion between certain opioid agents.

Dosage / Rate	Complex	Route	Schedule (Day-Of-Week)
0.2MG/0.1ML	0.13156	IV	5X-DAILY
0.3MG/0.15ML	0.19734		7X-DAILY (INPT)
0.4MG/0.2ML	0.26312		7X-DAILY (OUTPT)
0.5MG/0.25ML	0.3289		AT BEDTIME
0.6MG/0.3ML	0.39468		AT BEDTIME PRN
0.8MG/0.4ML	0.52624		BID
1MG/0.5ML	0.6578		BID (TOPICAL)
			BID/FOOD
			BID-DIURETIC
			BID-INSULIN
			BID-RT
			BISACODYL-BE
			CONTINUOUS VIA PUMP
			DAILY
			DAILY (TOPICAL)
			DAILY AT-1800
			DAILY-0700
			DAILY-AFTER MEAL
			DAILY-DIGOXIN

REFERENCES:

1. Dilaudid® and Dilaudid-HP® Injection (hydromorphone hydrochloride) product package insert. Lake Forest, IL: Hospira, Inc.; June 2008.
2. VHA Directive 2009-053, *Pain Management*, October 28, 2009.
3. *Management of Opioid Therapy for Chronic Pain*. Washington, DC: Office of Quality and Performance and the Veterans Affairs and Department of Defense Development Work Group, Veterans Health Administration, Department of Veterans Affairs; May 2010. Office of Quality and Performance publication 306-1.

Helping to achieve safe medication use

ACETAMINOPHEN SAFETY

(continued from page 1)

have a dose in between 3 g to 4 g. Close to 90% of patients prescribed acetaminophen have a dose less than 3 g.⁴

REFERENCES:

1. Department of Veterans Affairs Office of Inspector General. Healthcare Inspection – VA Patterns of Dispensing Take-Home opioids and Monitoring Patients on Opioid Therapy (Report No. 14-00895-163). May 14, 2014. Washington, DC. Available at: <http://www.va.gov/oig/pubs/VAOIG-14-00895-163.pdf>. Accessed May 16, 2014.
2. FDA Drug Safety Communication: Prescription Acetaminophen Products to be Limited to 325 mg Per Dosage Unit; Boxed Warning Will Highlight Potential for Severe Liver Failure. 1-13-2011. Available at: <http://www.fda.gov/Drugs/DrugSafety/ucm239821.htm>.
3. *National PBM Bulletin*. Acetaminophen Safety. Washington, DC: Pharmacy Benefits Management Services, the Medical Advisory Panel, and the Center for Medication Safety, Veterans Health Administration, Department of Veterans Affairs. June 10, 2014.
4. Internal data.