ORIGINS® PHARMACY SOLUTIONS

Outlook

WINTER 2015

Tramadol in the Hospice Setting

Tramadol is frequently prescribed for the treatment of pain in the palliative care setting. Various reasons that contribute to its popularity include its low cost and ease of prescribing as it is a Schedule IV medication rather than a more highly regulated Schedule II product. However, prescribers need to be aware of its pharmacology and adverse effects in order to make prudent decisions regarding its use in the hospice setting.

The mechanism of action attributed to tramadol involves both activity as a mu-opioid agonist and weak inhibition of reuptake of norepinephrine and serotonin. Though its side effect profile is fairly similar to other opioids, its pharmacology makes it less likely to cause respiratory depression and be abused but necessitates that several cautions be taken into consideration when it is being considered for use in a hospice patient.

⚠ CAUTION #1: Consider Hepatic and Renal Status

Recommendations are that tramadol dosing be adjusted in patients with significant renal impairment and/or hepatic impairment. When patients' creatinine clearance falls below 30 mL/min, it is prudent to increase the dosing interval to 12 hours and not exceed the maximum daily dose of 200 mg. Dosing in cirrhosis patients should not exceed 50 mg every 12 hours. Regardless of whether or not renal and hepatic statuses are known, patients over 75 years of age should not exceed a total of 300 mg per day due to the greater risk for adverse effects.

⚠ CAUTION #2: Consider Potential Drug Interactions Affecting Metabolism

Tramadol functions as a prodrug, with the majority of its effects being from its pharmacologically active metabolite O-desmethyltramadol (M1). Because the metabolism of tramadol to M1 depends upon CYP2D6, tramadol interacts significantly with other CYP2D6 inhibitors (such as fluoxetine, paroxetine, bupropion, and quinidine). Such inhibitors decrease the plasma concentrations of M1. Though the clinical significance of this interaction is not known, it may lead to a decrease in therapeutic response to tramadol since M1 demonstrates 6 times the analgesic effects of tramadol.

Interactions with CYP3A4 inhibitors (such as clarithromycin, verapamil, and diltiazem) are also significant as such inhibition increases plasma concentrations of tramadol and M1, increasing the risk of seizures and serotonin syndrome.

It may be appropriate to adjust dosing and clinical effects of tramadol when drugs altering its metabolism are added or withdrawn.

⚠ CAUTION #3: Consider Seizure Risk

Higher than recommended dosing of tramadol can result in seizure, as can concomitant use of other medications that lower the seizure threshold, such as SSRIs, SNRIs, and MAOIs. Use caution in patients with a history of seizures or with a risk of seizures related to other medical conditions (i.e. head trauma, CNS malignancy, or drug/ethanol withdrawal). (Cont'd on Page 2)

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⚠ CAUTION #4: **Consider Risk for Serotonin Syndrome**

When tramadol is concomitantly used with other serotonergic drugs, serotonin syndrome can occur. The characteristic changes in cognitive, neuromuscular, and autonomic function typically occur within six to eight hours of an increase in dose or initiation of a serotonergic medication.

⚠ CAUTION #5: **Risk of Clinically Significant Hypoglycemia**

A large UK study found a significant increase in risk of hospitalization for hypoglycemia in those patients taking tramadol compared with those utilizing codeine. Ensure that caregivers are aware to report any signs of hypoglycemia regardless of whether diabetic medications are being used

References:

1) Frank C. Recognition and treatment of serotonin syndrome. Can Fam Physician. 2008 Jul; 54(7): 988–992.
2) Fournier J, et. al. Tramadol use and the risk of hospitalization for hypoglycemia in patients with noncancer pain. JAMA Intern Med. 2015;175(2):186-193.

When Discontinuing Medications is Continuing Compassionate Care

If ever there is a time for compassionate medicine, it is when a patient is nearing the end of life. Unfortunately, when hospice becomes involved in patient care and recommendations are made for the discontinuation of medications, patients and caregivers alike can feel abandoned. They may feel as though the discontinuations will hasten death, worsen symptoms, or imply the patient is not worth treating any longer.

The difficulty of appropriately communicating rationale for drug discontinuation often results in continuation of unnecessary polypharmacy in order to avoid those difficult discussions. However, if approached appropriately, these discontinuations can be made while assuring patients and caregivers of a desire to improve quality of life.

Careful consideration must be made when determining what medications to discontinue in hospice patients.

HELPFUL QUESTIONS TO ASK INCLUDE:

- Does a medication's risks outweigh its benefits?
- Is the therapeutic benefit diminished to the extent that the medication no longer provides benefit?
- Is there a lack of evidence to support the continuation of therapy?
- Does this medication help meet goals of care for this patient?
- If the medication was recently added, is the time to benefit longer than life expectancy?
- Has the medication been effective?
- Does the medication interact with other products or disease states?
- Are there therapeutic duplications in the patient's drug regimen?
- Could the medication be treating a side effect of another medication?
- Is the patient and/or caregiver over-burdened with current drug regimen?
- Is there a clear indication for the medication?

However, when there is no time to taper medications, ensure staff and caregivers are aware to monitor patients for withdrawal symptoms, such as rebound hypertension when blood pressure medications are discontinued or agitation when antipsychotics are stopped.

Discussions regarding discontinuation of medications can be intimidating for case managers to initiate, but educating staff on the benefits of appropriate discontinuation can give staff more confidence in their presentation of such recommendations. As hospice staff knowledge increases regarding issues surrounding the continuation versus discontinuation of risky medications, case managers are more likely to seize the opportunity to discuss the benefits of timely discontinuation. Are family members

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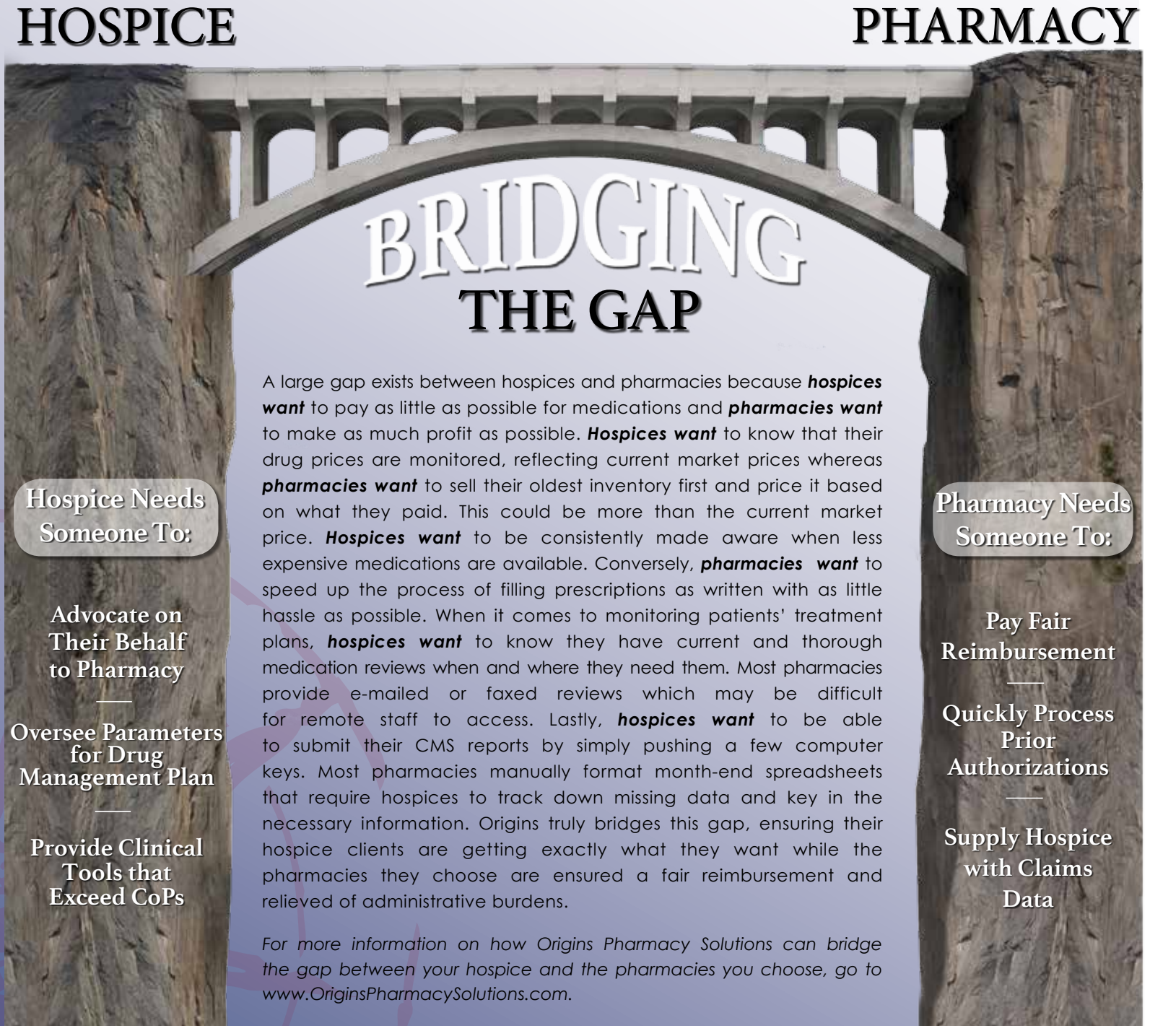
recognizing the patient's decline? Consider discontinuing unnecessary medications. Is the patient experiencing troublesome side effects that decrease quality of life? Consider discontinuation of offending medications. Are medications becoming ineffective? Consider stopping those drugs that are no longer providing benefit.

Additional education regarding optimal discontinuation methods can prevent undesirable withdrawal symptoms. Tapering may be necessary, especially in discontinuation of:

- Antipsychotics
- Baclofen & Tizanidine
- Corticosteroids
- Benzodiazepines
- Paroxetine & Venlafaxine
- Beta-blockers
- Clonidine
- Anti-seizure medications

Ultimately, goals of care should always center around providing the most excellent care for the hospice patient. As medication decisions are made, ensure that both the patient's and physician's goals of care are met. Honest, open communication with the patient, family, and caregivers as well as among participants of IDG will help guide decision-making and result in the medication regimen most appropriate for the compassionate care of each patient.



About Origins Pharmacy Solutions

Our mission is to simplify the pharmacy benefit process for end-of-life care

Origins Pharmacy Solutions® partners with hospice organizations, allowing them to provide exceptional patient care while controlling pharmacy costs. By providing a comprehensive, evidence-based formulary and competitive pricing along with unique partnerships with local pharmacies, Origins helps hospices to guarantee quality service and compassionate care.

We at Origins provide numerous cost reports and customized reports including the CR 8358 report that can be formatted to fit directly into your EMR. A Geriatric Certified Doctor of Pharmacy performs all Medication Therapy Reviews (MTRs) and Nationally Certified Pharmacy Technicians are available 24 hours a day, seven days a week, 365 days a year, providing exceptional customer service to hospice staff and pharmacies.

Origins Pharmacy Solutions® provides an extensive list of services, including:

- **Pharmaceutical Expense Management**
- **Clinical Consulting Services**
- **Formulary Guidance**
- **CR8358 Reports formatted to fit your EMR software**
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We strive to keep our relationships strong with local pharmacies; we do not offer mail-order services which keeps your business in your community. Origins is contracted with over 60,000 pharmacies nationwide – several in your immediate area- making it simple to use a network pharmacy.

We offer several pricing and formulary options including our Manual of Appropriate Pharmacotherapies® (MAPs®) which allows you to select the most cost-effective, evidence based hospice-related medications available. Our goal is to keep your drug costs low, simplify the pharmacy process for end-of-life care, and provide other much needed pharmacy-related services, all while exceeding your expectations in customer service. Call today for an individualized proposal that addresses your specific area(s) of need!

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