alixaRx

July 2015 Issue

From the Front Lines

AlixaRx Clinical Pharmacists Address Everyday Challenges in Long-Term Care

What's All the Fuss About Antipsychotic Use

Before a prescription drug manufacturer can promote a medication for a specific indication they must conduct extensive clinical trials demonstrating safety and effectiveness. The FDA (Food and Drug Administration) then reviews the data and approves an indication if warranted. While the FDA controls approval of medications in this country, they do not regulate their prescribing. If a drug is used for an unapproved indication then it is referred to as "off label" use. In the United States, greater than 1 out of 5 medications are prescribed for an off label use.

Off label use tends to evolve over time as a growing number of prescribers gain knowledge of potential medication benefits either through their own practice, that of their peers or through journal reports. The expense associated with conducting clinical trials for FDA drug approval is a barrier to manufacturers seeking official indications for use.

In this issue:

Many of the medications commonly used in our nursing facilities do not have FDA approval for the indication prescribed. Examples of this would include carbidopa/levodopa (Sinemet) for restless leg syndrome, mirtazapine (Remeron) for appetite stimulation, trazodone (Desyrel) for insomnia and antipsychotics such as risperidone (Risperdal), quetiapine (Seroquel) and olanzapine (Zyprexa) for behavioral and psychotic symptoms of dementia (BPSD).

In the case of antipsychotic use for dementia related conditions there have been attempts by the major drug manufacturers to gain FDA approval for this indication. However, these clinical trials did not demonstrate significant benefit in the majority of patients and their approval was denied. One thing that these clinical trials did demonstrate was that there was an increased risk of death associated with their use in individuals with dementia. This risk has been estimated at a 1.6-1.7 time greater risk of death than individuals with dementia not receiving antipsychotics. More recent studies conducted within the VA system have suggested an even higher risk. These deaths are most frequently associated with cardiovascular or respiratory complications. Because of this significant risk, the FDA has mandated that all antipsychotics carry a "Black Box Warning" if used for BPSD.

It is because of the significant risk associated with antipsychotic use for BPSD, and limited clinical data supporting their benefit, that they come under increased scrutiny during Department of Health survey visits to nursing facilities.

Nuedexta In The Nursing Home

Nuedexta® (dextromethorphan hydrobromide and quinidine) was the first medication approved by the FDA for the treatment of pseudobulbar affect (PBA). Pseudobulbar affect is a specific neurological disorder characterized by sudden, uncontrollable laughing and/or crying that does not represent the patient's true emotions at the moment of outburst. Patients may present with PBA secondary to many neurological disorders including: dementia, Alzheimer's disease, stroke, traumatic brain injury, Parkinson's disease, multiple sclerosis, and amyotrophic lateral sclerosis (ALS). PBA is often misdiagnosed as depression due to the frequent outbursts of crying, so many patients are placed on antidepressants.

Nuedexta® is manufactured by Avanir Pharmaceuticals and is available as 20/10 mg capsules at a cost of over $600 for a one-month supply. The usual dosage is one capsule every 12 hours, following a one capsule daily titration period of 7 days. It is important for patients, prescribers, and nurses (in the LTC setting) to observe for signs and symptoms of adverse effects during the titration period. (see below)

To date, there have been 25 clinical trials completed. The results of several clinical trials have been clinically insignificant due to small sample size. In one clinical trial, Nuedexta® showed statistically significant improvement in reducing PBA symptoms after 12 weeks in patients with ALS and MS but, its safety and efficacy has yet to be established in patient with any other neurological disorders. It is worth noting that in this "pivotal" trial, even the placebo group had a remission rate of 30%, which may suggest the symptoms of PBA may be more transient and less chronic.

There is some concern to the long-term and off-label use of Nuedexta® in the elderly for other neurological or psychological conditions with affective instability. Nuedexta® is not indicated and has not been studied as a treatment for the behavioral and psychological symptoms of dementia (BPSD). In clinical trials, only 2% of participants were 75 years old or older. More data from head-to-head clinical trials and post-marketing adverse event reporting is needed to know how safe and effective Nuedexta® will be in other neurological conditions as well as in the older population. As with all new medications, healthcare providers should exercise caution when initiating Nuedexta® and monitor closely for adverse effects.

Common Adverse Events	Contraindications	Concerns for LTCFs
• Dizziness • Cough • Vomiting • Asthenia • Peripheral edema • Urinary Tract Infection • Influenza • Elevated liver enzymes • Gas	• Hypersensitivity to either component • Use with Quinidine, Quinine, or Mefloquine • MAOIs (must discontinue use 14 days before initiating Nuedexta®) • Prolonged QT interval • Congential long QT syndrome • History of torsades de pointes • Heart failure • Hepatitis • Use with CYP2D6 drugs that prolong QT interval • AV block w/o pacemaker and high risk for complete AV block	• Increased fall risk • Anticholinergic effects of quinidine • Drug-drug interactions with current psychoactive treatment o Serotonin syndrome o QTc prolongation • Drug-disease interactions o AV block • Long-term use has not been studied

References: 1. Pioro EP, Brooks BR, Cummings J, et al. Dextromethorphan plus ultra low-dose quinidine reduces pseudobulbar aff ect. Ann Neurol 2010; 68: 693–702. 2. Nuedexta [package insert]. Aliso Viejo, CA: Avanir Pharmaceuticals, Inc.; Revised January 2015.

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, pharmacy may accept prescriptions from nurses in LTC facilities, provided that they are designated as an authorized agent of the physician. 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

The pharmacy must have a signed prescription by the physician prior to dispensing, required by law. A signed prescription for a C-II drug may be faxed to the provider pharmacy in accordance with the state laws by the prescriber.

1. Verbal prescriptions are accepted only for short term emergency supply of C-II prescriptions. These can my phoned in to the pharmacist ONLY by the prescriber. A written copy of the prescription must be delivered to the dispensing pharmacy within 7 days per DEA regulations.
2. If additional therapy is needed, a continuation prescription should then be faxed or called into 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:

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 either via fax or phone call in 24 hours if no response and again in 48 hours if there is still no response.**Note: Some prescribers will not allow AlixaRx to call them**
4. After 3 attempts, the narcotic technician will e-mail the Director of Nursing 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 via Amalga to determine if any orders will expire in the next 2 weeks or have less than 1 fill remaining.
2. The Hub pharmacy will then notify the prescriber if new or continuance prescriptions are needed.
3. Once the prescriber responds, the Hub pharmacy will fill or store the prescription.
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 will then contact their medical director for direction.
6. If no response is obtained after the facility attempt, the facility will implement their call tree.

Drug-Induced Vitamin B-12 Deficiency

A guiding principle in geriatrics is to assume that any symptom in an elderly adult is a drug side effect until proven otherwise.

Diabetic patients often experience symptoms of neuropathy, either as pain or loss of feeling in the lower extremities. Many older adults experience cognitive decline especially those with dementia. In both cases Vitamin B-12 deficiency should be ruled out before assuming the symptoms are due to disease progression. If not treated, Vitamin B-12 deficiency can cause pernicious anemia, neuropathy, and cognitive decline.

Metformin is considered a first-line treatment for adult-onset (Type II) diabetes. However, metformin can cause malabsorption of Vitamin B-12. This is thought to be due to a decrease in bile acid secretion resulting in bacterial overgrowth that causes decreased intestinal absorption. Vitamin B-12 levels can be restored by stopping metformin, B-12 supplementation, or administration of doxycycline or calcium.

Vitamin B-12 absorption can also be reduced by drugs that reduce stomach acidity including proton pump inhibitors (PPIs) and histamine receptor antagonists (HRAs). Commonly prescribed PPIs include omeprazole and pantoprazole while the most utilized HRAs are famotidine and ranitidine. Higher doses and longer duration of treatment with these drugs increases the risk for malabsorption of not only Vitamin B-12, but also calcium carbonate, iron, and magnesium.

AlixaRx Clinical Pharmacists routinely evaluate the need for continued treatment, especially with higher doses of PPIs and will make recommendations to optimize therapy. Utilizing the lowest effective dose for the shortest duration will avoid complications such as malabsorption of critical vitamins and minerals.

Nurses and prescribers should consult their AlixaRx Clinical Pharmacist for a change of condition medication review if they suspect patient symptoms may be drug-induced or if they cannot rule out a drug cause.

Source: http://www.diabetesincontrol.com/articles/diabetes-news/17898-neuropathy-due-to-vitamin-b-12-deficiency-not-diabetes

Contributing authors:

Matt Palmer, CGP, PharmD – AlixaRx Clinical Pharmcist

Jenny Rowley-Funk, RPh, CGP – AlixaRx Clinical Pharmacist

Al Barber, PharmD,CGP – Director of Pharmacy

Holly Vesely PharmD, CGP – AlixaRx Clinical Pharmacist

Brian Dressing, R.Ph. – AlixaRx Clinical Pharmacist

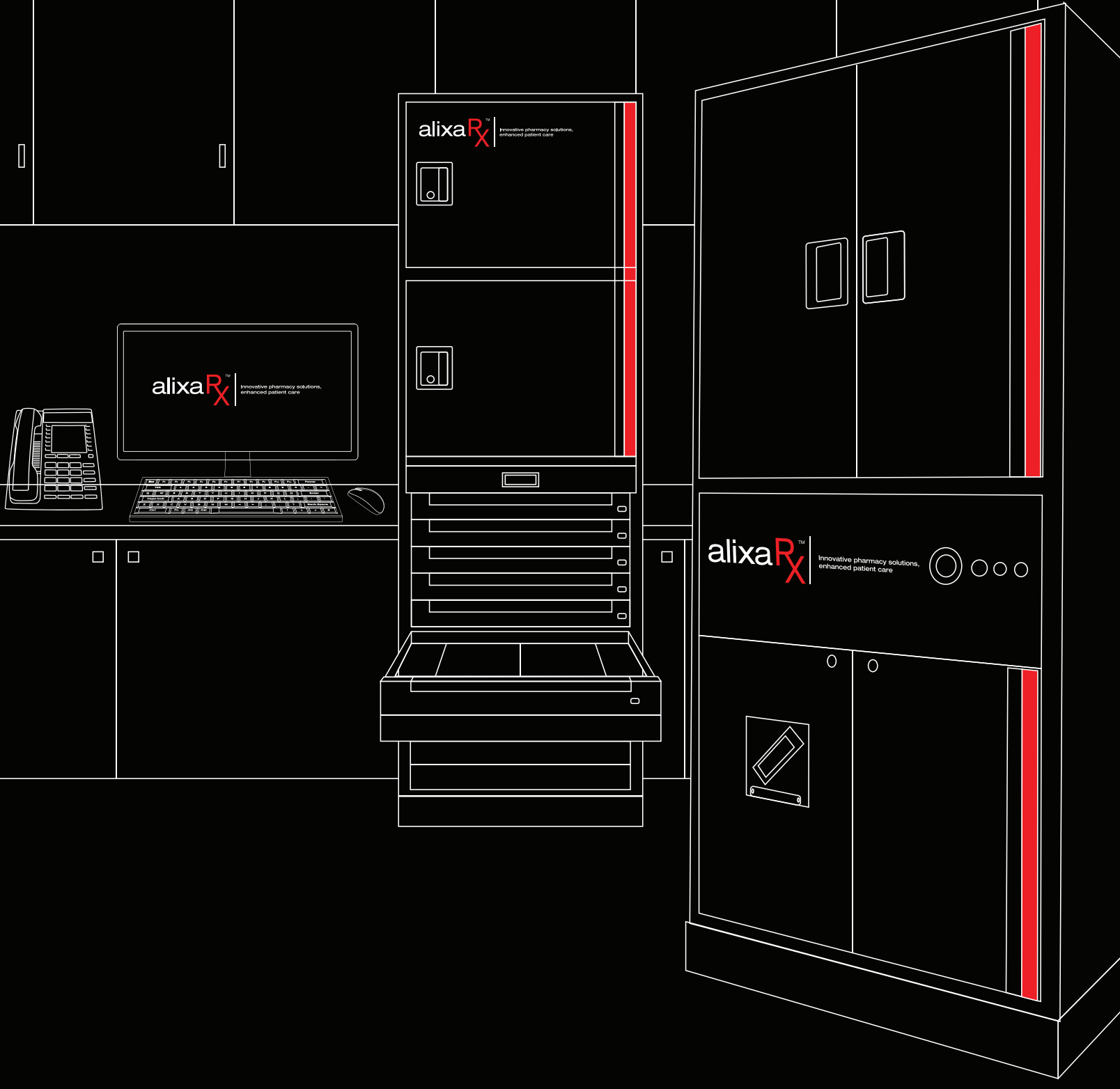
Veronica Posey, PharmD – AlixaRx Clinical Pharmacist

Jason Sutton, DPh. – National Director of Clinical Pharmacy Service

Blake Griese, PharmD, JD – Editor

alixaRx Innovative pharmacy solutions, enhanced patient care

6400 Pinecrest Drive, Suite 200
Plano, TX 75024
www.alixarx.com



alixaRX™ | Innovative pharmacy solutions, enhanced patient care

6400 Pinecrest, Suite 200
Plano, TX 75024