

June 12, 2007

Florida Department of Elder Affairs
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To Whom It May Concern:

excelleRx appreciates this opportunity to respond to the Florida Department of Elder Affairs proposed rule 58A-2.005(3)5.d, which addresses the use of experimental medications as well as FDA-approved medications when used for non-approved indications. Under the current form of the rule, the use of such medications shall not be undertaken without the consent of the patient, patient's legal representative, surrogate, or proxy. Furthermore, the hospice program will be responsible for providing information related to any risks of the proposed intervention as well as procuring written consent from the patient or caregiver prior to instituting such therapies.

Company Background: excelleRx, Inc. is the leading medication management company for hospices in the nation, with licensed pharmacy facilities in Philadelphia, PA, Memphis, TN and Tempe, AZ. The company was established in 1996 as Hospice Pharmacia and has grown from serving 200 patients to serving approximately 85,000 hospice patients residing in homes, long term care facilities, assisted living facilities, and hospital based and free standing hospice inpatient units across the United States. Our staff actively monitors and studies medications used in the palliation process, continually updating our proprietary medication use guidelines as new information becomes available regarding drug efficacy and more importantly, drug appropriateness for hospice related illnesses and symptoms. Additionally, on a daily basis we work with hospice nurses, doctors, and medical directors to provide appropriate drug regimens for all hospice patients.

Policy Issue:

While we recognize that the proposed rule does not prevent the use of medication for off-label indications, the uniform requirement of written consent for their use is a potential grave barrier to adequate and appropriate care at patient end of life. The need for procuring and achieving written consent for each one of these therapies poses significant burden for patients and their caregivers, nurses, and physicians. Achievement of such written consent may unnecessarily delay treatment and create or prolong patient suffering. Additionally, the complexity of associated consent forms may also act as a barrier for patients to receive the most appropriate care.

Many of the examples listed further below are commonly used when a patient is within 72 hours of death or when cognition is severely impaired. It may not be possible to

achieve patient consent in many patients, written or verbal. Of these patients, many may not have a caregiver that is easily accessible who can provide timely written consent for therapies needed emergently.

FDA-approved indications are defined as those disease(s) a given drug might treat effectively based on the drug's known effects on the body. Upon determining that enough evidence exists for a given therapy to be effective and appears to be safe for use, the FDA allows the pharmaceutical manufacturer to claim that the medication is effective for the given indication and therefore allow this information to market their drug to the public.

Non-approved indications (i.e., off-label) for the FDA are those indications or diseases for which the pharmaceutical company has not invested the time and resources to study in order to market the drug for use as being safe and effective. Reasons for not pursuing such indications are primarily financial in nature, as either the sales for the indication will not generate enough revenue, similar preparations already exist in the marketplace that are approved for the indication in question, or the off-label use of the medication is so common that FDA-approval for such uses will not make much of a difference in a drug's utilization and/or associated revenue generated.

Many of the therapies used for palliation of symptoms in the terminally ill have existed in the market for a long time and are therefore, off-patent and available in a generic form. Therefore, no incentives exist for pharmaceutical manufacturers to perform studies on these agents. That does not mean that such therapies do not have utility for indications or populations that they were not intended to address. Below is a non-exhaustive list of therapies and their off-label indications commonly used in hospice and palliative care:

- Amitriptyline (Elavil[®]) for neuropathic pain, diabetic neuropathy, and post herpetic neuralgia
- Methylphenidate (Ritalin[®]) for depression and fatigue
- Dexamethasone (Decadron[®]) for bone pain and cachexia
- Octreotide (Sandostatin[®]) for the treatment of bowel obstruction
- Nebulized morphine for the treatment of dyspnea
- Haloperidol (Haldol[®]) for the treatment of agitation, delirium, dementia, nausea/vomiting, hiccups
- Ibuprofen (Motrin[®]) and other NSAIDs for the treatment of bone pain
- Hyoscyamine (Levsin[®]) and other antimuscarinics for the management of terminal secretions (e.g., "death rattle")

As this abbreviated list illustrates, many off-label therapies are used on a daily basis in addressing symptoms of terminally ill patients. Numerous studies and case reports exist in the primary literature justifying the use of these therapies in the hospice population. In many cases, such medications are considered to be the current standard of care. Research in vulnerable populations such as hospice or the elderly is challenging and often lags behind other disciplines of medicine. Despite this, off-label use is frequently necessary as no FDA-approved therapies are indicated specifically for the population that hospice and palliative care clinicians provide care for. In addition, a case can be made for the inadequacy of the current FDA system of medication approval secondary to its inability

to protect the public from serious adverse events from agents recently approved for a given indication; Thiazolidinediones, rofecoxib (Vioxx[®]), and tegaserod (Zelnorm[®]) are recent examples of this.

Recommendation:

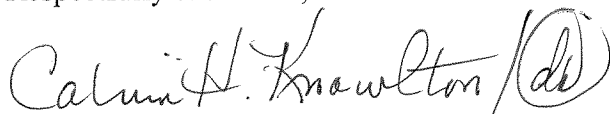
We appreciate the concern that the FDEA has for the safety of all patients receiving hospice care, and agree that safe medication prescribing should be the highest priority when providing care for this vulnerable population. However, we believe that hospice patients can and will continue to receive safe, appropriate palliative care drug therapy in lieu of resorting to signed written consents.

In addition, documentation of adverse reactions secondary to medications will be part of the forthcoming changes in the proposed Medicare Conditions of Participation (CoP), ensuring that all hospices are held to a universal standard in providing adequate attention and oversight to this crucial issue.

For these reasons and the other reasons listed above, we strongly recommend that FDEA not impose a requirement of written consent prior to off-label prescribing for palliative treatment in the hospice population. Instead, we ask FDEA to consider witnessed verbal authorization from a patient or patient's caregiver adequate or in the alternative, allow patients and/or their caregivers to provide written consent to off-label treatments at the onset of hospice treatment. Such prior written consent could include explanations of most commonly used off-label therapies and their most common side effects as well as a secondary verbal consent at the time particular therapies are to be used for the palliative care of the hospice patient.

It is our belief that incorporation of these suggestions will both adequately protect patients and their caregivers, as well as nurses and physicians while not impeding the palliative treatment provided for hospice patients at the end of life.

Respectfully submitted,

Handwritten signature of Calvin H. Knowlton in black ink, with a circled 'd' at the end of the signature.

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CEO
excelleRx, Inc.