Introduction

In America, 75 million people experience chronic pain,1 which the International Association for the Study of Pain (IASP) defines as pain without apparent biological value continuing beyond the normal tissue healing time (3 months).2 Chronic pain eases physical, psychological, and social well-being, and patients frequently experience sleep disturbance, depression, and anxiety.3 Thus, healthcare professionals (HCPs) who seek to treat pain must utilize therapies that not only reduce pain but also improve function and sleep.

Chronic Pain Management

The 2007 joint guidelines from the American Pain Society (APS) and American College of Physicians (ACP),4 and recommendations from the IASP Neuropathic Pain Special Interest Group stated that opioid analgesics are an effective and safe treatment option for chronic pain conditions of moderate to severe intensity. Effective chronic pain management requires balancing analgesia and adverse effects to attain a net improvement in function.5

Short-acting opioid (SAO) formulations are appropriate when frequent titration is indicated, as in occasional or breakthrough pain, or in determining optimum dosing at therapy initiation.7 Long-acting opioid (LAO) formulations are appropriate when continuous and uniform pain control is desired, as when pain is persistent or chronic.7 Patients receiving LAO formulations report better pain control, improved function, less pain-induced anxiety over time, a better adjustment to disease and treatment, and improved strength.7

Relevance of Consistent Plasma Opioid Levels and 24-Hour Pain Control

Oral LAO formulations range in dosing intervals from 2 to 3 times per day (controlled-release [CR] and extended-release [ER] morphine, CR oxycodone, and oxymorphone ER) to once-daily (AVINZA® [morphine sulfate extended-release capsules, King Pharmaceuticals, Inc]; ER morphine). LAO formulations with longer dosing intervals provide more consistent plasma levels (few peak-to-trough fluctuations) over 24 hours compared with shorter dosing intervals.4

In patients who would benefit from treatment with a long-acting morphine formulation, AVINZA® once daily provides consistent plasma opioid levels, and fewer peak-to-trough fluctuations over 24 hours compared with immediate-release (IR) morphine dosed 6 times daily (Figure 1), twice-daily CR morphine, and twice-daily CR oxycodone.8,9

Other treatment options that may be beneficial for certain patients with persistent pain are long-acting formulations of oxycodone, oxymorphone, tramadol, and fentanyl.

Analgesics in Various Chronic Pain Conditions: Pain Relief

The around-the-clock therapy offered by LAOs can provide effective, safe, and tolerable analgesia in various chronic pain conditions with moderate to severe baseline pain, and may improve the patient’s ability to function and sleep.7

Low-back Pain

Chronic low-back pain (LBP) occurs in 5% to 8% of the general US population and is the second leading symptom prompting visits to HCPs—19% of working adults report chronic LBP.10 In the United States, back pain is associated with healthcare costs of more than $90 billion per year.12 Recent ASP and ACP clinical practice guidelines suggest that opioids, including long-acting formulations of morphine, oxycodone, fentanyl (transdermal), and oxymorphone, are indicated for LBP in patients with severe, disabling pain that is not (or is unlikely to be) controlled with acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs).13,14 As seen in 2 studies, AVINZA® also provides around-the-clock pain control in patients with chronic LBP (Figure 2), and has been associated with improvements in function and sleep in this patient population.15,16

OSTEOPATHITIS

The prevalence of arthritis in the United States is projected to increase from 47.8 million adults in 2005 to 67 million adults by 2030, with nearly 40% of these individuals suffering from arthritis-attributed activity limitations.15 Osteoarthritis (OA)-related pain can lead to physical and psychosocial disability, sleep problems, and decreased quality of life.16

APS guidelines (2002) suggested that opioids, alone or in combination with NSAIDs or acetylsalicylic acid, are indicated in patients with moderate to severe OA pain that does not respond to other treatments such as acetaminophen, NSAIDs, or topical agents.17 AVINZA® improves pain control, physical function, and sleep quality in patients with OA.16

NEUROPATHIC PAIN

In the United States, more than 3 million people are thought to have painful diabetic peripheral neuropathy (DPN) and approximately 1 million people suffer from postherpetic neuralgia (PHN).18 Recently published (2007) evidence-based recommendations for the pharmacologic management of neuropathic pain suggested that opioid analgesics and tramadol, alone or in combination with a first-line therapy, are recommended as second-line therapy for patients who do not respond to other treatments, including tricyclic antidepressants, serotonin and norepinephrine reuptake inhibitors, gabapentin and pregabalin, and topical lidocaine.3 They are recommended as first-line therapy when rapid pain relief is needed, such as during titration of a first-line medication or for episodic exacerbations of severe pain, acute neuropathic pain, or neuropathic cancer pain.1

Improved Function and Sleep

LAOs can improve physical and mental function in patients with OA, LBP, and neuropathic pain, including painful DPN and PHN.14,15,16-18 AVINZA® once daily has been associated with improvements in physical function in patients with OA, and both physical and mental function in patients with chronic LBP.14 In patients with neuropathic pain, long-acting morphine has been associated with improvements in physical and mental function.2,19

Pain-related sleep disturbance affects an estimated 70% of patients with chronic pain.1 There are benefits and risks of opioid therapy for patients experiencing pain-related sleep disturbances. A benefit in subjective measures of pain-related sleep disturbance has been noted for several LAOs, including formulations of once-daily morphine, oxycodone, oxymorphone, and tramadol.16,17,20-27 Randomized controlled trials demonstrate that LAOs may be associated with less trouble falling asleep,16 improvements in sleep quality by 25%,21,26,27-30 increased sleep duration,30 less need for sleep medication,16 and reduced pain-related sleep disturbance.15,20,26,31

A recent study reported that reduction of chronic pain in patients with OA treated with AVINZA® once daily concurrently improved objective sleep measures (polysomnography).22 This supports reports of subjective sleep improvement in patients with pain-related sleep disturbance receiving AVINZA® once daily.26,27 The benefits of analgesia for sleep, however, must be balanced with the sleep-related risks of opioids, specifically, an increased presence of sleep-disordered breathing (including sleep apnea) in some patients treated with chronic opioid therapy.21,24,25 The risk of increased presence of sleep apnea was directly correlated with methadone dosage but not with the dosage of nonmethylene opioids.24

Pain control has clear benefits for pain-related sleep disturbance, but the risks should be considered, especially in patients who have risk factors for sleep apnea such as a sedentary lifestyle or a high body mass index.26

![Figure 1. Mean Steady-state Plasma Morphine Concentrations Following Once-daily Administration of AVINZA® Capsules (Long-acting) or 6 Times Daily Administration of Morphine Solution (Short-acting).](image-url)
Risk Minimization in the Clinical Setting

All therapies have risks that must be managed. Risks may include adverse effects, the intentional or unintentional misuse of opioid therapies, and abuse. For any of these potential risks, patients may be considered at low, medium, or high risk, the level of risk will affect treatment decisions. When considering opioid therapy, some patients, such as those with cognitive impairment, may be at increased risk of reduced psychomotor performance.

Furthermore, those with a prior history of substance abuse may be at increased risk of opioid abuse, misuse, and diversion. It is recommended that patients be triaged by risk level at initiation of therapy, reassessed periodically, and managed according to risk level through a “Universal Precautions” approach to pain management, in which those at highest risk of abuse and misuse receive additional monitoring and management.

However, the efficacy of this approach has not yet been assessed in a clinical trial.

Conclusion

LAOs are an effective treatment option for a broad range of chronic pain conditions, including OA and chronic LBP. AVINZA® once daily provides consistent 24-hour plasma opioid concentrations and stable 24-hour pain control in these disease states, which in turn can help patients to improve function and sleep.

Important Safety Information

AVINZA® (morphine sulfate extended-release capsules) is a modified-release formulation of morphine sulfate indicated for once-daily administration for the relief of moderate to severe pain requiring continuous, around-the-clock opioid therapy for an extended period of time.

AVINZA® capsules are to be swallowed whole or the contents of the capsules sprinkled on applesauce. The capsule beads are not to be chewed, crushed, or dissolved due to the risk of rapid release and absorption of a potentially fatal dose of morphine. Patients must not consume alcoholic beverages while on AVINZA® therapy. Additionally, patients must not use prescription or nonprescription medications containing alcohol while on AVINZA® therapy. Consumption of alcohol while taking AVINZA® may result in the rapid release and absorption of a potentially fatal dose of morphine.

The most common serious adverse events reported with administration of AVINZA® capsules were vomiting, nausea, death (in patients treated for pain due to underlying malignancy), dehydration, dyspnea, sepsis, constipation, somnolence, and headache. Serious adverse events caused by morphine include respiratory depression, apnea, and to a lesser degree, circulatory depression, respiratory arrest, shock, and cardiac arrest.

AVINZA® is NOT intended for use as a prn analgesic. The safety and efficacy of using AVINZA® in a postoperative setting has not been evaluated. AVINZA® is not indicated for postoperative use. If the patient has been receiving the drug prior to surgery, resumption of the pre-surgical dose may be appropriate once the patient is able to take the drug by mouth. Physicians should individualize treatment, moving from parenteral to oral analgesics as appropriate.

See the American Pain Society guidelines. Morphine sulfate is a Schedule II controlled substance that can be abused in a manner that is different from the manner intended. Abuse may lead to dependence.

References


