

# Nonopioid Medications for Pain



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## KEYWORDS

- Opioid • NSAID • Acetaminophen • Antidepressant • Anticonvulsant
- Benzodiazepine • Neuropathic pain • Central sensitization

## KEY POINTS

- Although there is evidence supporting the analgesic efficacy of opioids, other classes of medications seem to be equally effective, and are often safer to use.
- Nonsteroidal antiinflammatory drugs are most likely to be effective in the setting of nociceptive or inflammatory pain.
- Antidepressants and anticonvulsants are the most effective agents for neuropathic pain or pain from central sensitization.
- Unless there is clear evidence of spasticity, muscle relaxers, including benzodiazepines, and antispasticity agents add limited, if any, benefits in the management of chronic pain.
- Benzodiazepines should not be used in conjunction with opioids.
- An important early target for pharmacologic management should be improvement in the patient's ability to sleep.

## INTRODUCTION

Treatment of pain, particularly chronic pain, requires multimodal analgesia that includes pharmacologic and nondrug therapies as well as a large measure of clinician-guided patient self-management. This article emphasizes the point that pain medicine is more than opioid management; that chronic pain treatment should rarely if ever be opioid monotherapy. The conflation of pain care with opioid

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prescribing has, since the mid 1990s, displaced the initial tenets of multidisciplinary pain care that were fundamentally about functional and behavioral retraining without opioids and other central nervous system depressants. Recent population-based trends document that significant increases in opioid prescribing without increases in other drug categories<sup>1</sup> have directly contributed to the pain-related distress experienced not only by patients with chronic pain but by providers of pain care, and health systems.<sup>2</sup> Understanding the basic pharmacologic principles and comparative effectiveness of so-called adjuvant drugs in the management of chronic pain should increase not only success of pharmacologically based pain treatments but also reduce over-reliance on opioids and the associated challenges of opioid-related side effects such as accidental overdoses, dependency and addiction, and most importantly poor pain care outcomes.

### ***Principles and Definitions***

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A key principle guides this article: chronic pain is a complex multidimensional disorder that is different from acute pain in both pathoanatomic and psychosocial domains. Although many commonly encountered chronic pain disorders do involve continuing nociceptive triggers (nociceptive pain results when tissue injury or disease leads to stimulation of nociceptors at peripheral sensory nerve endings located in the skin, muscle, joints, and viscera), the persistence of pain beyond 3 to 6 months alters peripheral and central nervous function and, with additional behavioral and functional modifications, adds the insult to the original injury. This pathophysiologic process involves sensitization, whereby the intrinsic neuroplasticity of the nervous system disrupts previously normal (or worsens previously abnormal) neurochemical and structural function of the peripheral and central nervous system, altering neuronal activity, their synapses, and the brain's regional connectivity.<sup>3,4</sup> Current functional imaging data support the emerging understanding that, over time, nearly all chronic nociceptive stimulation, especially persistent and repetitive high input, becomes transformed in a process called chronification.<sup>5</sup> In addition, susceptibility to chronification varies by complex mechanisms determined by an increasingly well-understood overlay of genetic predisposition, epigenetic biological processes, psychological responses, and sociologic exposures.<sup>6</sup> Hence pain, an "unpleasant sensory and emotional experience that is commonly associated with actual or potential tissue damage,"<sup>7</sup> is an emergent experience, shaped by the complex interplay of genetics, past experiences, setting, affect, cognitive context, and cultural and social expectations. Patients with both acute and chronic pain thus present with a wide range of responses to seemingly identical injuries, and effective treatment requires a clinical toolbox capable of multidimensional therapies.

### ***Assessing Effectiveness***

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Consideration of effectiveness is essential to clinicians' proper selection of pain treatments. An expanded appreciation and more detailed understanding of the complex nature of pain entail multimodal assessment of pain beyond a simple numeric pain intensity score (numerical rating scale [NRS]) of 0 to 10 out of 10. Although pain rating is useful in acute pain, in which reduction in pain intensity can be achieved quickly and effectively with opioids, nerve blocks, and general anesthetics, successful chronic pain care requires demonstration of improved measures of physical, emotional, and social function, and thus overall quality of life. Hence, this article references treatment goals beyond how much it hurts; successful pain management requires careful tracking of outcomes across key domains of physical (including sleep), psychological, and social function.

High-quality multidisciplinary pain care also reduces overall health care costs by adding system value. Literature since the 1970s has supported the positive effects

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