EDUCATION MODULE

PRESCRIBING OPIOIDS FOR PATIENTS WITH BIPOLAR DISORDER OR SCHIZOPHRENIA*

*This module provides additional details about bipolar disorder or schizophrenia as risk factors for opioid overdose, and specific risk-reduction guidance. It **supplements** but does not replace the general best practices for opioid prescribing presented in the "**Considerations for Safe and Responsible Opioid Prescribing**" module.*

Background

1. Chronic pain and mental health disorders are common in the general population, and they are often comorbid.[1-3] Patients with co-occurring chronic pain and mental health disorders:

    a. Have greater intensity and longer duration of pain, poorer clinical outcomes, and increased health care utilization compared with those with either condition alone.[4-7]
    b. Are more likely to be treated with opioids, to receive a higher potency opioid or a higher opioid dose, and/or to have a longer duration (>90 days) of opioid therapy than those without mental health disorders.[8-10]

2. There is high prevalence of lifetime alcohol and substance use disorders among patients with bipolar disorder or schizophrenia.[11-13]

Bipolar disorder, schizophrenia, and opioid overdose

1. Individuals with a mental health disorder have greater risk for drug overdose.[4,14-18]

2. Bipolar disorder is associated with impulsive behavior, recklessness, and generally increased risk-taking behavior.[19]

    a. Lack of insight combined with poor judgment leads an individual to engage in risky activities, partly explaining medication non-adherence during a manic episode, and an increased risk of overdose due to combined use of prescribed and misused drugs.[20]
    b. During manic or hypomanic episodes, patients with co-occurring substance use disorder commonly self-medicate with opioids or other central nervous system (CNS) depressants such as alcohol.[19] Frequently referred to as "chemical coping," this may be an attempt to counter rage, aggression, or dysphoria during such episodes.[21]
    c. In bipolar disorder, mixed states represent dangerous and potentially deadly combinations of depressed affect, impaired cognition and judgment, dysphoria, and increased energy level and impulsivity.[19]

3. Many psychotherapeutic medications that are commonly used to treat bipolar disorder or schizophrenia are sedating, and can increase the risk of CNS and respiratory depression when used with opioids. Examples include benzodiazepines, sedatives/hypnotics, and certain antipsychotics, antidepressants, anticonvulsants, and anticholinergics.[17,18] (see also: FDA label)

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4. In patients with inadequately treated pain, emotional or psychological distress is common and may be accentuated in patients with co-occurring mental health disorders. Pain is often resolved or reduced if the psychiatric comorbidity is well-managed.[22]

Risk-mitigation interventions to consider when prescribing opioids for patients with bipolar disorder or schizophrenia:
(Refer to the full prescribing information in the FDA label for important product-specific details)

1. Avoid concurrent use of other medications or substances that are CNS depressants, such as benzodiazepines, sedatives/hypnotics, and alcohol in opioid-treated patients with bipolar disorder and schizophrenia. These combinations can result in profound sedation, respiratory depression, coma, and death, and should be restricted to the minimum required dosage and duration in patients for whom alternative treatment options are inadequate or contraindicated.[16,22,23] (see also: FDA label)

2. Before considering opioids to manage chronic non-cancer pain in individuals with acute psychiatric instability, consult or refer to a behavioral/mental health specialist.[14,16,22,24]

3. Co-manage with a behavioral/mental health specialist (psychiatrist) those patients with bipolar disorder or schizophrenia who also have pain severe enough to require opioids.[16,22,25]

4. Prescribe a lower initial dose of an opioid for patients who are already taking a CNS depressant.[26]

5. If the patient is already taking an opioid, prescribe a lower initial dose of the psychotherapeutic medication(s) than otherwise would be indicated.

    a. NOTE: Anticonvulsants to treat epilepsy are the exception.

6. If necessary, slowly titrate the dose of the opioid (or psychotherapeutic medication) to optimize outcomes (adequate analgesia and control of bipolar disorder or schizophrenia, with adequate tolerability/minimal adverse effects).

7. Closely monitor the patient for respiratory depression or over-sedation during opioid initiation and after dosage escalation. The risk for overdose is greatest at this time because tolerance to an opioid's respiratory depressant effects is slower to develop and less complete than tolerance to its analgesic or euphoric effects.[16,23,27,28] Incorporate bio-behavioral approaches to limit opioid misuse and abuse by patients with co-morbid mental health issues.

8. Check the PDMP to confirm that the patient is not obtaining controlled medications from multiple prescribers (or pharmacies). Check that the patient is securely storing and safely disposing of unused controlled medications.[16] (see "**Considerations for Safe and Responsible Opioid Prescribing**" module)

9. Determine whether a caregiver is needed to responsibly co-manage medication therapy.[16] Collaborate closely with the patient, patient's caregiver (if applicable), and pharmacist to ensure safe use of opioids and other medications.

10. If tapering or discontinuing opioid therapy in patients with bipolar disorder or schizophrenia, monitor closely for emergent anxiety, depression, destabilization of the mental health disorder, suicidality, or unmasked opioid use disorder (i.e., aberrant opioid use behaviors), especially in patients treated with opioids long-term or at high opioid dosages.[16,23]

11. Co-manage opioid tapering with a behavioral/mental health specialist. Refer patients who experience destabilization or serious challenges in tapering to a structured multidisciplinary program, if local resources are available.[25]

12. Consider prescribing take-home naloxone to opioid-treated patients with bipolar disorder or schizophrenia to reverse life-threatening respiratory depression if an overdose occurs. Educate the patient, family/household members, and caregivers about signs and symptoms of opioid overdose and train them to properly use naloxone if an opioid-related overdose is suspected.[16,30]

Additional Resources

**The information presented in this module highlights some fundamental concepts of opioid prescribing for adult outpatients. It excludes certain populations (pediatrics, pregnancy, patients with active cancer or receiving palliative or end-of-life care) and settings (perioperative, emergency, in-patient). The information provided is intended to support safe and effective opioid therapy and minimize serious adverse outcomes, particularly overdose. It is not intended to be exhaustive nor substitute for consulting a medication's full prescribing information for complete details and warnings. Links and references to selected, more comprehensive clinical and prescribing resources are provided to facilitate safe and effective opioid prescribing.*

1. FDA-approved drug label information: FDA Online Label Repository or Daily Med (NIH/National Library of Medicine)
2. Bipolar disorder guideline. APA 2010.
3. Bipolar disorder treatment guidelines. British Association for Psychopharmacology 2016
4. Schizophrenia practice guideline. APA 2010
5. Depression and Bipolar Support Alliance
6. International Society for Bipolar Disorders
7. Schizophrenia Research Forum

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25. U.S. Department of Veterans Affairs. VA/DoD clinical practice guideline for opioid therapy for chronic pain. Washington, DC: US Department of Veterans Affairs; 2017. VA/DOD 2017
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