ASCO® Guidelines

Use of Opioids for Adults with Pain from Cancer or Cancer Treatment: ASCO Guideline				
Clinical Question	**Recommendation**	**Type**	**Evidence Quality**	**Strength**
In what circumstances should opioids be offered?	**1.1.** Opioids should be offered to patients with moderate-to-severe pain related to cancer or active cancer treatment unless contraindicated.	EB	M	S
	1.2. Prior to initiating opioid therapy, clinicians, patients, and caregivers should discuss goals regarding functional outcomes, shared expectations, and pain intensity, as well as any concerns about opioids.	IC	N/A	S
Which opioids should be offered?	**2.1.** For patients who are candidates to begin opioid treatment (Recommendation 1.1), clinicians may offer any of the opioids approved by the FDA or other regulatory agencies for pain treatment.	EB	M – L	W
	Qualifying Statement: The decision of which opioid is most appropriate should be based on factors such as pharmacokinetic properties, including bioavailability, route of administration, half-life, neurotoxicity, and cost of the differing drugs. Tramadol and codeine have limitations that may make them less desirable than other opioids in this setting. Tramadol is a pro-drug, has limitations in dose titration related to a low threshold for neurotoxicity, and has potential interactions with other drugs at the level of cytochrome P450 (CYP) 2D6, 2B6, and 3A4.[1,2] Codeine is a pro-drug, requiring CYP2D6 to allow it to be metabolized to morphine to achieve analgesic effects.[2]			
	2.2. Clinicians with limited experience with methadone prescribing should consult palliative care or pain specialists when initiating or rotating to methadone.	IC	N/A	S
How should opioids be initiated and titrated?	**3.1.** Opioids should be initiated at the lowest possible dose to achieve acceptable analgesia and patient goals.	IC	N/A	S
	3.2. Opioids should be initiated as immediate release and PRN (as needed) to establish an effective dose, with early assessment and frequent titration.	IC	N/A	S
	3.3. Patients who have been taking other analgesics, such as NSAIDs, may continue these analgesics after opioid initiation if these agents provide additional analgesia and are not contraindicated.	IC	N/A	W
	3.4. Evidence remains insufficient to recommend for or against the use of genetic testing, such as for polymorphism of CYP2D6, to guide opioid dosing.	N/A	N/A	N/A
	3.5. Evidence remains insufficient to recommend any single set of ranges for dose escalation in opioid titration.	N/A	N/A	N/A
	Note: In general, the minimum dose increase is 25-50%, but patient factors such as frailty, comorbidities, and organ function must be evaluated and considered when changing doses.			

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	3.6. For patients with a substance use disorder, clinicians should collaborate with a palliative care, pain, and/or substance use disorder specialist to determine the optimal approach to pain management.	IC	N/A	S
How should opioid-related adverse events be prevented or managed?	**4.** Clinicians should proactively offer education and strategies to prevent known opioid-related adverse effects, monitor for the development of these adverse effects, and manage these effects when they occur.	IC	N/A	S
	Note: Strategies for the prevention and management of common opioid-induced adverse effects are provided in Table 1 of the guideline publication.			
How should opioid use be modified in patients with renal or hepatic impairment?	**5.1.** For patients with renal impairment currently treated with an opioid, clinicians may rotate to methadone, if not contraindicated, as this agent is excreted fecally. Opioids primarily eliminated in urine, such as fentanyl, oxycodone, and hydromorphone, should be carefully titrated and frequently monitored for risk or accumulation of the parent drug or active metabolites. Morphine, meperidine, codeine, and tramadol should be avoided in this population, unless there are no alternatives.	IC	N/A	S
	5.2. For patients with renal or hepatic impairment who receive opioids, clinicians should perform more frequent clinical observation and opioid dose adjustment.	IC	N/A	S
How should breakthrough pain be managed?	**6.1.** In patients receiving opioids around the clock, immediate-release opioids at a dose of 5-20% of the daily regular morphine equivalent daily dose should be prescribed for breakthrough pain.	IC	N/A	S For prescribing immediate-release opioids for breakthrough pain W For dosing
	6.2. Evidence remains insufficient to recommend a specific, short-acting opioid for breakthrough pain.	N/A	N/A	N/A
When and how should opioids be switched (rotated)?	**7.** Opioid rotation should be offered to patients with pain that is refractory to dose titration of a given opioid, poorly managed side effects, logistical or cost concerns, or trouble with the route of opioid administration or absorption.	EB	M	S

Abbreviations. EB, evidence based; FDA, US Food and Drug Administration; H, high; IC, informal consensus; L, low; M, moderate; N/A, not applicable; NSAIDs, nonsteroidal anti-inflammatory drugs; S, strong; W, weak

References.

1. Grond S, Sablotzki A: Clinical pharmacology of tramadol. Clin Pharmacokinet 43:879-923, 2004
2. Crews KR, Monte AA, Huddart R, et al: Clinical Pharmacogenetics Implementation Consortium Guideline for CYP2D6, OPRM1, and COMT Genotypes and Select Opioid Therapy. Clin Pharmacol Ther 110:888-896, 2021