



Drug and Biologic Coverage Policy

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Opioid Therapy – Individual and Family Plans

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Related Coverage Resources

- [Quantity Limitations - \(1201\)](#)
- [Transmucosal Fentanyl - \(1018\)](#)

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for ALL of the following:

- Immediate-release opioid analgesics (refer to [Appendix 1](#) for products)
- Extended-release opioid analgesics (refer to [Appendix 2](#) for products)
- Injectable opioid analgesics (refer to [Appendix 3](#) for products)

Additional criteria that support the review for medical necessity exceptions of non-covered products are located in the [Non-Covered Product Table](#) by the respective plan type and drug list where applicable.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Medical Necessity Criteria

Opioid analgesics are considered medically necessary when the following are met:

- I. Immediate-release opioid analgesics in an opioid naïve individual are considered medically necessary when the individual meets ONE of the following:

1. Documented diagnosis of active cancer treatment (defined as receiving antineoplastic or antitumor therapy) requiring treatment for cancer-related pain, end-of-life care (including hospice or palliative care), sickle cell disease, **OR** receiving medication-assisted treatment for opioid addiction (this applies to prior authorization for methadone only)
 1. Non-Covered Product Criteria is met, refer to below table

2. **For the management of acute pain (for example, pain lasting less than 90 days).** Individual meets **ALL** of the following:
 - A. Attestation that the history of controlled substance prescriptions has been checked using the state prescription drug monitoring program (PDMP)
 - B. **ONE** of the following:
 - i. For the management of acute dental pain: Attestation that an initial treatment regimen exceeding 3 days is medically necessary (for example, the individual is not a candidate for less than 3 days of therapy)
 - ii. For the management of acute non-dental pain: Attestation that an initial treatment regimen exceeding 7 days is medically necessary (for example, the individual is not a candidate for less than 7 days of therapy)
 - C. Non-Covered Product Criteria is met, refer to below table

3. **For the management chronic pain (for example, pain lasting more than 90 days).** Individual meets **ALL** of the following:
 - A. Failure, contraindication, or intolerance to nonopioid pharmacologic therapies intended to treat pain
 - B. Attestation that the history of controlled substance prescriptions has been checked using the state prescription drug monitoring program (PDMP)
 - C. Attestation that opioids will be prescribed in accordance with current clinical practice guidelines **AND** that an assessment of risks, harms, and goals consistent with an opioid agreement (or comprehensive treatment plan) has been undertaken
 - D. Non-Covered Product Criteria is met, refer to below table

Immediate-Release Opioid Analgesic Non-Covered Products and Criteria:

Non-Covered Product	Criteria
Acetaminophen/caffeine/dihydrocodeine	In addition to the criteria detailed above, ONE of the following: <ol style="list-style-type: none"> 1. Established therapy for an individual in hospice or end of life care or active cancer treatment 2. Documentation of failure, contraindication, or intolerance to BOTH of the following short acting narcotics: <ol style="list-style-type: none"> A. hydrocodone / acetaminophen B. oxycodone / acetaminophen (generic for Percocet)
Apadaz™ (benzhydrocodone / acetaminophen) tablet	In addition to the criteria detailed above, ONE of the following: <ol style="list-style-type: none"> 1. Established therapy for an individual in hospice or end of life care or active cancer treatment 2. Documentation of failure, contraindication, or intolerance to BOTH of the following short acting narcotics: <ol style="list-style-type: none"> A. hydrocodone / acetaminophen B. oxycodone / acetaminophen (generic for Percocet)
Dilaudid® (hydromorphone) oral solution	In addition to the criteria detailed above, ONE of the following: <ol style="list-style-type: none"> 1. Established therapy for an individual in hospice or end of life care or active cancer treatment 2. Documentation of BOTH of the following: <ol style="list-style-type: none"> A. Trial of hydromorphone oral solution (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive

Non-Covered Product	Criteria
	<p>ingredient(s) which would result in a significant allergy or serious adverse reaction</p> <p>B. Failure, contraindication, or intolerance to FOUR of the following short acting narcotics:</p> <ul style="list-style-type: none"> i. hydrocodone / acetaminophen ii. morphine iii. oxycodone iv. oxycodone / acetaminophen (generic for Percocet) v. oxymorphone
<p>Dilaudid® (hydromorphone) tablet</p>	<p>In addition to the criteria detailed above, ONE of the following:</p> <ol style="list-style-type: none"> 1. Established therapy for an individual in hospice or end of life care or active cancer treatment 2. Documentation of BOTH of the following: <ul style="list-style-type: none"> A. Trial of hydromorphone tablet (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction B. Failure, contraindication, or intolerance to FOUR of the following short acting narcotics: <ul style="list-style-type: none"> i. hydrocodone / acetaminophen ii. morphine iii. oxycodone iv. oxycodone / acetaminophen (generic for Percocet) v. oxymorphone
<p>Hycodan® (hydrocodone / homatropine) oral solution</p>	<p>In addition to the criteria detailed above, ONE of the following:</p> <ol style="list-style-type: none"> 1. Established therapy for an individual in hospice or end of life care or active cancer treatment 2. Documented trial of hydrocodone/homatropine oral solution (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction
<p>Hycodan® (hydrocodone / homatropine) tablet</p>	<p>In addition to the criteria detailed above, ONE of the following:</p> <ol style="list-style-type: none"> 1. Established therapy for an individual in hospice or end of life care or active cancer treatment 2. Documented trial of hydrocodone/homatropine tablet (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction
<p>Nalocet® (oxycodone / acetaminophen) tablet</p>	<p>In addition to the criteria detailed above, ONE of the following:</p> <ol style="list-style-type: none"> 1. Established therapy for an individual in hospice or end of life care or active cancer treatment 2. Documentation of BOTH of the following: <ul style="list-style-type: none"> A. Intolerance to oxycodone / acetaminophen (generic for Percocet) B. Failure, contraindication, or intolerance to hydrocodone / acetaminophen
<p>Nucynta® (tapentadol) tablet</p>	<p>In addition to the criteria detailed above, ONE of the following:</p> <ol style="list-style-type: none"> 1. Established therapy for an individual in hospice or end of life care or active cancer treatment

Non-Covered Product	Criteria
	2. Documentation of Failure, contraindication, or intolerance to ALL of the following: <ul style="list-style-type: none"> A. hydrocodone / acetaminophen B. morphine C. oxycodone D. oxycodone / acetaminophen (generic for Percocet) E. oxymorphone
Oxaydo® (oxycodone tablet)	In addition to the criteria detailed above, ONE of the following: <ul style="list-style-type: none"> 1. Established therapy for an individual in hospice or end of life care or active cancer treatment 2. Documentation of BOTH of the following: <ul style="list-style-type: none"> A. Intolerance to oxycodone B. Failure, contraindication, or intolerance to ALL of the following short acting narcotics: <ul style="list-style-type: none"> i. hydrocodone / acetaminophen ii. hydromorphone iii. morphine iv. oxymorphone
Oxycodone / Acetaminophen 2.5 mg/ 300 mg, 5 mg/ 300 mg, 7.5 mg/ 300 mg, 10 mg/ 300 mg tablets and capsules	In addition to the criteria detailed above, ONE of the following: <ul style="list-style-type: none"> 1. Established therapy for an individual in hospice or end of life care or active cancer treatment 2. Documentation of BOTH of the following: <ul style="list-style-type: none"> A. Intolerance to generic oxycodone / acetaminophen tablets (generic for Percocet) B. Failure, contraindication or intolerance to hydrocodone / acetaminophen
Oxycodone / Acetaminophen 5 mg / 325 mg oral solution	In addition to the criteria detailed above, ONE of the following: <ul style="list-style-type: none"> 1. Established therapy for an individual in hospice or end of life care or active cancer treatment 2. Documentation of ONE of the following: <ul style="list-style-type: none"> A. Intolerance to generic oxycodone / acetaminophen tablets (generic for Percocet) B. Inability to swallow tablets
Percocet® (oxycodone / acetaminophen) tablet	In addition to the criteria detailed above, ONE of the following: <ul style="list-style-type: none"> 1. Established therapy for an individual in hospice or end of life care or active cancer treatment 2. Documentation of BOTH of the following: <ul style="list-style-type: none"> A. Trial of oxycodone/acetaminophen tablet (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction B. Failure, contraindication, or intolerance to hydrocodone / acetaminophen
Prolate® (oxycodone/ acetaminophen) oral solution	In addition to the criteria detailed above, ONE of the following: <ul style="list-style-type: none"> 1. Established therapy for an individual in hospice or end of life care or active cancer treatment 2. Documentation of ONE of the following: <ul style="list-style-type: none"> A. Intolerance to generic oxycodone / acetaminophen tablets (generic for Percocet)

Non-Covered Product	Criteria
	B. Inability to swallow tablets
Qdolo® (tramadol) oral solution	In addition to the criteria detailed above, ONE of the following: <ol style="list-style-type: none"> 1. Established therapy for an individual in hospice or end of life care or active cancer treatment 2. Documentation of BOTH of the following: <ol style="list-style-type: none"> A. 18 years of age or older B. Inability to swallow tramadol 50 mg immediate-release tablets
Tramadol oral solution (generic for Qdolo)	In addition to the criteria detailed above, ONE of the following: <ol style="list-style-type: none"> 1. Established therapy for an individual in hospice or end of life care or active cancer treatment 2. Documentation of BOTH of the following: <ol style="list-style-type: none"> A. 18 years of age or older B. Inability to swallow tramadol 50 mg immediate-release tablets
Roxicodone® (oxycodone)	In addition to the criteria detailed above, ONE of the following: <ol style="list-style-type: none"> 1. Established therapy for an individual in hospice or end of life care or active cancer treatment 2. Documentation of BOTH of the following: <ol style="list-style-type: none"> A. Trial of oxycodone tablet (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction B. Failure, contraindication, or intolerance to FOUR of the following short acting narcotics: <ol style="list-style-type: none"> i. hydrocodone / acetaminophen ii. hydromorphone iii. morphine iv. oxycodone / acetaminophen (generic for Percocet) v. oxymorphone
RoxyBond™ (oxycodone)	In addition to the criteria detailed above, ONE of the following: <ol style="list-style-type: none"> 1. Established therapy for an individual in hospice or end of life care or active cancer treatment 2. Documentation of ONE of the following: <ol style="list-style-type: none"> A. An abuse-deterrent short-acting opioid is required B. BOTH of the following: <ol style="list-style-type: none"> i. Intolerance to oxycodone tablets ii. Failure, contraindication, or intolerance to ALL of the following short acting narcotics: <ol style="list-style-type: none"> a) hydrocodone / acetaminophen b) hydromorphone c) morphine d) oxymorphone
Seglentis® (celecoxib and tramadol)	In addition to the criteria detailed above, ONE of the following: <ol style="list-style-type: none"> 1. Established therapy for an individual in hospice or end of life care or active cancer treatment 2. Documentation of BOTH of the following: <ol style="list-style-type: none"> A. 18 years of age or older B. Inability to use tramadol tablets and celecoxib capsules concurrently

Non-Covered Product	Criteria
Tramadol 100 mg tablet	In addition to the criteria detailed above, ONE of the following: <ol style="list-style-type: none"> 1. Established therapy for an individual in hospice or end of life care or active cancer treatment 2. Documentation of intolerance or inability to use tramadol 50 mg immediate-release tablets
Trezip™ (dihydrocodeine / acetaminophen / caffeine) tablet	In addition to the criteria detailed above, ONE of the following: <ol style="list-style-type: none"> 1. Established therapy for an individual in hospice or end of life care or active cancer treatment 2. Documentation of BOTH of the following: <ol style="list-style-type: none"> A. Intolerance to generic dihydrocodeine / acetaminophen / caffeine capsules B. Failure, contraindication, or intolerance to BOTH of the following short acting narcotics: <ol style="list-style-type: none"> i. hydrocodone / acetaminophen ii. oxycodone / acetaminophen (generic for Percocet)

II. **Extended-release opioid analgesics are considered medically necessary when the individual meets ONE of the following:**

1. Documented diagnosis of active cancer treatment (defined as receiving antineoplastic or antitumor therapy) requiring treatment for cancer-related pain, end-of-life care (including hospice or palliative care), sickle cell disease, **OR** receiving medication-assisted treatment for opioid addiction (this applies to prior authorization for methadone only)
 - A. Non-Covered Product Criteria is met, refer to below table
2. Diagnosis of pain severe enough to require daily, around-the-clock, long-term opioid treatment. Individual meets **ALL** of the following:
 - A. Failure, contraindication, or intolerance to a minimum one week trial of immediate-release opioids
 - B. Failure, contraindication, or intolerance to nonopioid pharmacologic therapies intended to treat pain
 - C. Attestation that the history of controlled substance prescriptions has been checked using the state prescription drug monitoring program (PDMP)
 - D. Documentation that opioids will be prescribed in accordance with current clinical practice guidelines **AND** that an assessment of risks, harms, and goals consistent with an opioid agreement (or comprehensive treatment plan) has been undertaken
 - E. Non-Covered Product Criteria is met, refer to below table

Extended-Release Opioid Analgesic Non-Covered Products and Criteria:

Non-Covered Product	Criteria
Conzip™ (tramadol extended-release capsule)	In addition to the criteria detailed above, ONE of the following: <ol style="list-style-type: none"> 1. Established therapy for an individual in hospice or end of life care or active cancer treatment 2. Documentation of failure, contraindication, or intolerance to BOTH of the following: <ol style="list-style-type: none"> A. tramadol 50 mg tablets B. tramadol 100 mg, 200 mg, OR 300 mg extended-release tablets

Non-Covered Product	Criteria
Tramadol extended-release capsule (generic for Conzip)	In addition to the criteria detailed above, ONE of the following: <ol style="list-style-type: none"> 1. Established therapy for an individual in hospice or end of life care or active cancer treatment 2. Documentation of failure, contraindication, or intolerance to BOTH of the following: <ol style="list-style-type: none"> A. tramadol 50 mg tablets B. tramadol 100 mg, 200 mg, OR 300 mg extended-release tablets
Hysingla™ ER (hydrocodone bitartrate)	In addition to the criteria detailed above, ONE of the following: <ol style="list-style-type: none"> 1. Established therapy for an individual in hospice or end of life care or active cancer treatment 2. Documentation of BOTH of the following: <ol style="list-style-type: none"> A. Trial of hydrocodone bitartrate ER (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction B. Failure, contraindication, or intolerance to Xtampza ER
MS Contin® (morphine sulfate) extended-release tablet	In addition to the criteria detailed above, ONE of the following: <ol style="list-style-type: none"> 1. Established therapy for an individual in hospice or end of life care or active cancer treatment 2. Documentation of BOTH of the following: <ol style="list-style-type: none"> A. Trial of morphine sulfate ER (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction B. Failure, contraindication, or intolerance to ALL of the following: <ol style="list-style-type: none"> i. hydrocodone bitartrate ER ii. hydromorphone ER iii. oxymorphone ER iv. Xtampza ER
Nucynta® ER (tapentadol)	In addition to the criteria detailed above, ONE of the following: <ol style="list-style-type: none"> 1. Established therapy for an individual in hospice or end of life care or active cancer treatment 2. Documentation of failure, contraindication, or intolerance to BOTH of the following: <ol style="list-style-type: none"> A. hydrocodone bitartrate ER B. Xtampza ER
Oxycontin® (oxycodone HCl)	In addition to the criteria detailed above, ONE of the following: <ol style="list-style-type: none"> 1. Established therapy for an individual in hospice or end of life care or active cancer treatment 2. 11 years of age to 17 years of age 3. Documentation of failure, contraindication, or intolerance to BOTH of the following: <ol style="list-style-type: none"> A. hydrocodone bitartrate ER B. Xtampza ER
Oxycodone extended-release tablet	In addition to the criteria detailed above, ONE of the following: <ol style="list-style-type: none"> 1. Established therapy for an individual in hospice or end of life care or active cancer treatment 2. 11 years of age to 17 years of age

Non-Covered Product	Criteria
	3. Documentation of failure, contraindication, or intolerance to BOTH of the following: A. hydrocodone bitartrate ER B. Xtampza ER

III. **Methadone and Fentanyl Transdermal Patches are considered medically necessary when the individual meets ONE of the following:**

1. Documented diagnosis of active cancer treatment (defined as receiving antineoplastic or antitumor therapy) requiring treatment for cancer-related pain, end-of-life care (including hospice or palliative care), sickle cell disease, **OR** receiving medication-assisted treatment for opioid addiction (this applies to prior authorization for methadone only)
2. **ALL** of the following:
 - A. Diagnosis of pain severe enough to require daily, around-the-clock, long-term opioid treatment
 - B. Failure, contraindication, or intolerance to a minimum one week trial of immediate-release opioids
 - C. Opioid tolerant [required daily dosage for pain management exceeds 60 morphine milligram equivalents (MME)]
 - D. Alternative treatment options are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain
 - E. Attestation that the history of controlled substance prescriptions has been checked using the state prescription drug monitoring program (PDMP)
 - F. Documentation that opioids will be prescribed in accordance with current clinical practice guidelines **AND** that an assessment of risks, harms, and goals consistent with an opioid agreement (or comprehensive treatment plan) has been undertaken
 - G. Medication prescribed by, or in consultation with, a board certified pain management specialist

IV. **Daily dose of all opioid analgesics exceed 120 morphine milligram equivalents (120 MME), opioid analgesics are considered medically necessary when the individual meets ONE of the following:**

1. Documented diagnosis of active cancer treatment (defined as receiving antineoplastic or antitumor therapy) requiring treatment for cancer-related pain, end-of-life care (including hospice or palliative care), sickle cell disease, **OR** receiving medication-assisted treatment for opioid addiction (this applies to prior authorization for methadone only)
2. **ALL** of the following:
 - A. Failure, contraindication, or intolerance to nonopioid pharmacologic therapies intended to treat pain
 - B. Attestation that the history of controlled substance prescriptions has been checked using the state prescription drug monitoring program (PDMP)
 - C. Documentation that opioids will be prescribed in accordance with current clinical practice guidelines **AND** that an assessment of risks, harms, and goals consistent with an opioid agreement (or comprehensive treatment plan) has been undertaken
 - D. Consideration of additional precautions intended to reduce the risk of serious harm associated with high dose opioids (for example, education and provision of naloxone)
 - E. Quarterly reassessment of opioid therapy benefits and risks specific to diagnosis and treatment goals
 - F. Medication prescribed by, or in consultation with, a board certified pain management specialist

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- V. **Daily dose of all opioid analgesics exceed 200 morphine milligram equivalents (200 MME), opioid analgesics are considered medically necessary when the individual meets ONE of the following:**
1. Documented diagnosis of active cancer treatment (defined as receiving antineoplastic or antitumor therapy) requiring treatment for cancer-related pain, end-of-life care (including hospice or palliative care), sickle cell disease, **OR** receiving medication-assisted treatment for opioid addiction (this applies to prior authorization for methadone only)
 2. **ALL** of the following:
 - A. Failure, contraindication, or intolerance to nonopioid pharmacologic therapies intended to treat pain
 - B. Attestation that the history of controlled substance prescriptions has been checked using the state prescription drug monitoring program (PDMP)
 - C. Documentation that opioids will be prescribed in accordance with current clinical practice guidelines **AND** that an assessment of risks, harms, and goals consistent with an opioid agreement (or comprehensive treatment plan) has been undertaken
 - D. Quarterly reassessment of opioid therapy benefits and risks specific to diagnosis and treatment goals
 - E. Consideration of additional precautions intended to reduce the risk of serious harm associated with high dose opioids (for example, education and provision of naloxone)
 - F. The provider has performed an individualized behavioral health screening to assess the risks and benefits of the opioid dose (for example, PHQ-9, GAD-7, PC-PTSD)
 - G. The provider has screened for substance abuse risk to assess the risks and benefits of the opioid dose (for example, DIRE, ORT, PDUQ, PMQ)
 - H. Medication prescribed by, or in consultation with, a board certified pain management specialist

Resources for calculating morphine milligram equivalents can be found in [Appendix 4](#)

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Reauthorization Criteria

Opioid analgesics are considered medically necessary for continued use when the above medical necessity criteria are met **AND** there is documentation of beneficial response.

Authorization Duration

Initial approval duration is up to 12 months
Reauthorization approval duration is up to 12 months

Background

OVERVIEW

All of the long-acting opioids are indicated for the **management of pain severe enough to require daily, around-the-clock, long-term opioid treatment** and for which alternative treatment options are inadequate.¹⁻¹⁶ OxyContin is the only product specifically indicated in pediatric patients 11 years to 18 years of age.⁶ Nucynta ER is the only product also indicated for the management of neuropathic pain associated with diabetic peripheral neuropathy in adults.¹ Methadone has additional indications for the treatment and maintenance treatment of opioid addiction (i.e., heroin or other morphine-like drugs).¹⁶ Note that methadone products, when used for the treatment of opioid addiction in detoxification or maintenance programs, shall be dispensed only by opioid treatment programs (and agencies, practitioners, or institutions by formal agreement with the program sponsor)

certified by the Substance Abuse and Mental Health Services Administration and approved by the designated state authority.

The currently available long-acting opioids are buprenorphine, fentanyl, hydrocodone, hydromorphone, methadone, morphine sulfate, oxycodone, oxymorphone, tapentadol, and tramadol.¹⁻¹⁶

Short-acting opioids are indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.¹⁷

Guidelines

In 2022, the **Centers for Disease Control (CDC)** published an updated guideline for prescribing opioids for pain.¹⁷ Nonopioid therapies are at least as effective as opioids for many common types of acute pain, and nonopioid therapies are preferred for subacute and chronic pain. Clinicians should maximize the use of nonpharmacologic and nonopioid pharmacologic therapies as appropriate for the specific condition and patient and only consider initiating opioid therapy if expected benefits for pain and function are anticipated to outweigh risks to the patient. Multiple noninvasive nonpharmacologic interventions (e.g., aerobic, aquatic, or resistance exercises, weight loss, psychological therapy, spinal manipulation, low-level laser therapy, massage, mindfulness-based stress reduction, yoga, tai chi, qigong, acupuncture, cognitive behavioral therapy, and spinal manipulation) are associated with improvements in pain, function, or both, that are sustained after treatment and are not associated with serious harms. Non-opioid drugs (e.g., tricyclic antidepressants, serotonin and norepinephrine reuptake inhibitor [SNRI] antidepressants, duloxetine, selected anticonvulsants (e.g., pregabalin, gabapentin, oxcarbazepine), capsaicin and lidocaine patches, and nonsteroidal anti-inflammatory drugs [NSAIDs]) are associated with small to moderate improvements in chronic pain and function for certain chronic pain conditions.

Before initiating opioid therapy for patients with pain, clinicians should discuss with patients the realistic benefits and known risks of opioid therapy.¹⁷ Before starting ongoing opioid therapy for patients with subacute or chronic pain, clinicians should work with patients to establish treatment goals for pain and function and consider how opioid therapy will be discontinued if benefits do not outweigh risks. When opioids are initiated, clinicians should prescribe the lowest effective dosage of immediate-release opioids for no longer than needed for the expected duration of pain severe enough to require opioids. During ongoing opioid therapy, clinicians should collaborate with patients to evaluate and carefully weigh the benefits and risks of continuing opioid therapy and exercise care when increasing, continuing, or reducing opioid dosage. The guideline recommends that clinicians should not initiate opioid treatment with LA opioids for patients who are opioid-naïve and should not prescribe LA opioids for intermittent use. LA opioids should be reserved for severe, continuous pain. Before starting and periodically during continuation of opioid therapy, clinicians should evaluate the risk for opioid-related harms and should work with patients to incorporate relevant strategies to mitigate risk, including offering naloxone and reviewing potential interactions with any other prescribed medications or substances used. When prescribing initial opioid therapy and periodically during opioid therapy, clinicians should review the patient's history of controlled substance prescriptions using state prescription drug monitoring program (PDMP) data to determine whether the patient is receiving opioid dosages or combinations that put the patient at high risk for overdose. When prescribing opioids for subacute or chronic pain, clinicians should consider the benefits and risks of toxicology testing to assess for prescribed medications as well as other prescribed and nonprescribed controlled substances.

The 2020 **American Society of Hematology** guideline for the management of acute and chronic pain in patients with sickle cell disease states that pain causes significant morbidity for those living with sickle cell disease and manifests as acute intermittent pain, chronic daily pain, and acute-on-chronic pain.¹⁸ For adults and children with chronic pain who are receiving chronic opioid therapy, are functioning well, and have perceived benefit, the guideline suggests shared decision making for continuation of chronic opioid therapy. For adults and children with chronic pain who are receiving chronic opioid therapy, are functioning poorly, or are at high risk for aberrant opioid use or toxicity, the guideline suggests against continuation of chronic opioid therapy.

Appendix 1

Immediate-release opioid analgesics include the following:

Acetaminophen/codeine tablet

Benzhydrocodone/acetaminophen (Apadaz™)
Butorphanol tartrate spray
Codeine sulfate tablets and solution
Codeine/carisoprodol/aspirin
Dihydrocodeine/acetaminophen/caffeine (Dvorah, Trezix™)
Dihydrocodeine/aspirin/caffeine
Hydrocodone/acetaminophen (Lorcet®, Lorcet® HD, Lorcet® Plus, Lortab®, Stagesic-10, Zydone®)
Hydrocodone/ibuprofen
Hydromorphone tablets, solution, suppositories (Dilaudid®)
Levorphanol tablets
Meperidine tablets and solution
Morphine sulfate tablets, solution, suppositories
Nucynta® (tapentadol)
Opium Tincture
Opium/Belladonna alkaloids (Belladonna-Opium) suppository
Oxycodone hydrochloride capsules, concentrate, solution, tablets (Oxaydo®)
Oxycodone/acetaminophen (Endocet, Nalocet, Percocet®, Primlev™; Prolate)
Oxycodone/aspirin tablets
Oxycodone/ibuprofen tablets
Oxymorphone tablets
Pentazocine/naloxone
Roxicodone® (oxycodone) tablets
Tramadol (Qdolo and its Authorized Generic) solution, (Ultram®) tablets
Tramadol/acetaminophen (Ultracet®) tablets

Appendix 2

Extended-release opioid analgesics include the following:

Conzip™ (tramadol ER capsules)
Fentanyl patches
Hydrocodone bitartrate ER (generic for Hysingla ER)
Hydromorphone hydrochloride ER tablets
Hysingla® ER (hydrocodone bitartrate)
Kadian® (morphine sulfate)
Levorphanol tablets
Morphabond ER™ (morphine sulfate)
MS Contin® (morphine sulfate)
Nucynta® ER (tapentadol)
Oxycodone hydrochloride ER tablets
Oxycontin® (oxycodone HCl)
Oxymorphone hydrochloride ER tablets
Tramadol hydrochloride ER capsules/tablets
Xtampza® ER (oxycodone myristate)

Appendix 3

Alfentanil ampule
Hydromorphone ampule
Hydromorphone carpject
Hydromorphone Isecure syringe
Hydromorphone syringe (Dilaudid)
Hydromorphone vial
Hydromorphone / Bupivacane
Hydromorphone / Ropivacaine / Sodium chloride

Hydromorphone / Sodium chloride
Hydromorphone / Water
Meperidine ampule (Demerol)
Meperidine carpject (Demerol)
Meperidine vial (Demerol)
Meperidine / Sodium chloride
Methadone vial
Morphine ampule (Duramorph, Infumorph)
Morphine auto-injector
Morphine carpject
Morphine Isecure syringe
Morphine syringe
Morphine vial (Mitgo)
Morphine / Sodium chloride
Morphine / D5W
Remifentanil vial (Ultiva)
Sufentanil ampule
Sufentanil vial

Appendix 4

Morphine Milligram Equivalent (MME) Dose Calculation

A commonly used method to compare opioid analgesic doses is to calculate its dose in terms of morphine milligram equivalents. To calculate the morphine milligram equivalent (MME) dose one starts by adding the total daily milligram amount of each opioid an individual takes. Next, each opioid total dose should be converted to a morphine milligram equivalent by multiplying the total dose by the conversion factor associated with the identity of the patients' opioid. The conversion factors are shown in the table below. Once all opioid doses have been converted to a morphine milligram equivalent dose, they should be added together to calculate a total MME dose per day. It is important to note that this calculation should only be used as an approximation for comparative purposes. If using a similar conversion to switch an individual to a different opioid, a dose reduction must be made to account for incomplete tolerance and prevent an overdose.

Opioid	Conversion Factor
Codeine	0.15
Fentanyl (transdermal) in mcg / hr	2.4
Hydrocodone	1
Hydromorphone	4
Methadone	
1 – 20 mg / day	4
21 – 40 mg / day	8
41 – 60 mg / day	10
≥ 61 – 80 mg / day	12
Morphine	1
Oxycodone Hydrochloride	1.5
Oxycodone Myristate (Xtampza ER)	1.67
Oxymorphone	3
Tapentadol	0.4

Source: Adapted from CDC Guideline for Prescribing Opioids for Chronic Pain

Example: An individual is using 20 mg of extended-release oxycodone twice daily and 5 mg / 300 mg of immediate-release hydrocodone / acetaminophen three times daily.

- 1) Calculate the total daily dose of each opioid
 - a. 20 mg oxycodone twice daily = 40 mg oxycodone
 - b. 5 mg hydrocodone three times daily = 15 mg hydrocodone
- 2) Convert to a morphine milligram equivalent dose by multiplying the total daily dose of each opioid by the conversion factor
 - a. 40 mg oxycodone x 1.5 = 60 morphine milligram equivalents
 - b. 15 mg hydrocodone x 1 = 15 morphine milligram equivalents
- 3) Add the morphine milligram equivalent doses to calculate the total morphine milligram equivalent dose per day
 - a. 60 + 15 = 75 morphine milligram equivalents per day

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