Care Guide: *Cancer Pain*

Key Points: Cancer Pain

1. Pain is defined as "an independent and emotional experience associated with actual or potential tissue damage or described in terms of such damage." Pain occurs in approximately 25% of patients with newly diagnosed malignancies, 33% of patients undergoing treatment, and 75% of patients with advanced cancer. Most importantly, pain is what the patient says it is, and it needs to be addressed adequately in order to improve quality of life.

2. Unrelieved cancer pain denies patients of comfort and greatly affects their activities, motivation, interactions with family and friends, and overall quality of life.

3. Studies have revealed that most physicians underestimate the level of their patient's pain. It is recommended that all cancer patients should be screened for pain during their initial visit, at regular intervals and whenever new therapy is initiated.

4. Most patients can have their cancer pain successfully controlled with appropriate techniques and safe drugs if the pain management algorithms are applied, monitored, and tailored to the needs of the individual.

5. Pain medications not recommended for use in cancer patients by the NCCN because of inadequate pain control include:

- Meperidine (Demerol)
- Placebos
- Partial agonists (buprenorphine)
- Mixed agonist-antagonists (albuphine, pentazocine)

Specific Pain Problems

1. For pain associated with inflammation, a trial of NSAIDs or glucocorticoids is indicated.

2. Bone pain without oncologic emergency.

- Trial of opioids and/or NSAIDs
- Consider radiation therapy or nerve block for local bone pain
- For diffuse bone pain: Consider trial of bisphosphonates, hormonal chemotherapy or radioisotopes for responsive tumors
- Consider physical medicine evaluation
- For resistant pain, consider anesthetic procedures

3. Nerve compression or inflammation – trial of glucocorticoids.

4. Neuropathic pain:

- Trial of tricyclic antidepressants
- Trial of anticonvulsants-neurontin, tegretrol, lyrica
- Consider topical agents

Consider referral to a pain specialist and/or interventional strategies.

5. Consider trial of radiation, hormones or chemotherapy for painful lesions

Key Points: Cancer Pain Management

Numerical Patient Rating Scale:

Verbal: What number describes your worst pain in the past 24 hours? _____
Scale from 0 (no pain) to 10 (worst imaginable pain)

Written: Circle the number that best describes your worst pain in the past 24 hours.
No pain 0 1 2 3 4 5 6 7 8 9 10 Worst imaginable pain

Categorical: What is the worst pain you have had in the past 24 hours?
☐ None (0) ☐ Mild (1–3) ☐ Moderate (4–6) ☐ Severe (7–10)

COMPREHENSIVE PAIN ASSESSMENT

The self-reporting of pain is the standard. The assessment should consist of an evaluation of the following:

► Pain experience
- Location, pattern, radiation
- Intensity (last 24 hours, current, at rest, with movement)
- Interference with activities (mood, relationships, sleep, appetite)
- Timing: Onset, duration, course, persistent, or intermittent
- Description or quality (aching, gnawing, sharp, etc)
- Aggravating and alleviating factors
- Other current symptoms
- Current pain management plan (pharmacologic and non-pharmacologic)
- Response to current therapy
- Prior pain therapies
- Special issues (meaning and consequences of pain, knowledge, beliefs, culture, goals and expectations)

► Psychosocial
- Distress
- Support
- Psychiatric history including substance abuse
- Risk factors for inappropriate use of pain medication
- Risk for under treatment of pain

► Medical history
- Current or prior oncologic treatment, illnesses, conditions
- Pre-existing chronic pain

► Physical examination

► Laboratory and/or imaging evaluations

►Establish "pain diagnosis" (etiology and pathophysiology) and individualized treatment plan

OPIOID PRESCRIBING: TITRATION AND MAINTENANCE

General Principles

- Morphine is the international "gold standard" for first-line treatment of cancer pain.
- The appropriate dose will relieve the patient's pain throughout its dosing interval without causing unmanageable side effects.
- Calculate increase based on total opioid dose (around the clock, scheduled or as needed) taken in the previous 24 hours.
- Increase both around the clock and as needed doses. The rapidity of dose escalation should be related to the severity of the symptoms.

For example:

Pain 7-10 Consider increasing dose by 50-100%
Pain 4-6 Consider increasing dose by 25-50%
Pain 1-3 Consider increasing dose by 25%

- Switch from fixed-combination opioids to single-entity opioids when acetaminophen dose > 4 g/d.
- If patient is experiencing unmanageable side effects and pain is < 4, consider downward dose titration by approximately 25% and re-evaluate.
- Equilibrium achieved in about 5 half-lives.

Principles of Maintenance Opioid Therapy

Consider converting from short-acting to sustained release opioids for control of chronic persistent pain when 24 h opioid requirement is stable. Examples include:

- Extended-release morphine sulfate tablets q 8-24 h depending on brand. Capsules q 8-24 h.
- Extended-release oxycodone hydrochloride tablets q8-12 h.
- Transdermal fentanyl delivery system q 48-72 h.

Provide rescue doses of short-acting opioids for pain not relieved by sustained release opioids including acute exacerbations of pain, activity, or position-related pain or pain at the end of dosing interval:

- Use short-acting form of sustained release opioid whenever possible.
- Allow immediate-release rescue doses of 10-20% of 24 h oral dose (mg) every 1 h prn.
- The 24 h adult oral morphine dose equivalent of transdermal fentanyl is 2 x mcg/h dose.
- Consider oral transmucosal fentanyl citrate for brief episodes of acute exacerbation of pain not attributed to inadequate dosing of around the clock opioid. Data does not support a specific transmucosal fentanyl dose. Initiate with a 200 mcg unit.

Increase dose of sustained-release opioid if, (a) patient persistently needs doses of as needed opioids, or (b) dose of around the clock opioid fails to relieve pain at peak effect or at end of dose.

Approximate Oral and Parenteral Dose Equivalents of Opioids Based on Single Dose Data

Opioid Analgesic	Oral Dose	Parental Dose	Typical Dose Frequency	Transdermal Dose	Half Life
Codeine	100 mg	50 mg	q 3 – 4 h		2.9 h
Hydrocodone	15 mg	N/A	q 3 – 4 h		3.8 ± .3 h
Oxycodone	7.5 – 10 mg	N/A	q 3 – 4 h		3.2 h
Morphine	15 mg	5 mg	q 3 – 4 h		1.5 – 2 h
Hydromorphone	4 mg	0.75 – 1.5 mg	q 3 – 4 h		2.5 h
Levorphanol	2 mg	1 mg	q 6 – 8 h		11 – 30 h
Methadone	10 mg	5 mg	q 6 – 8 h		15 – 30 h
Fentanyl	N/A	50 mcg	q 2 – 3 h	q 48 – 72 h Transdermal	1 – 3 h

World Health Organization (WHO) 3-Step Pain Ladder *

STEP 1 Medications (*similar to Visual pain scale 1-3*)
(Note: Potential adverse effects should be noted, particularly the renal and gastrointestinal adverse effects of the NSAIDs

- ASA (Aspirin)
- Acetaminophen (Tylenol)
- NSAIDs (nonsteroidal anti-inflammatory drugs)
  Ibuprofen (Advil, Motrin)
  Naproxen (Alleve, Naprosyn)
  Celecoxib (Celebrex)
  Ketorolac (Toradol)
- Tramadol (Ultram)

STEP 2 Medications (*similar to Visual pain scale 4-6*)

- Codeine preparations with/without Tylenol
- Acetaminophen + Hydrocodone (Vicodin)
- Aspirin + Oxycodone (Percodan)
- Acetaminophen + Oxycodone (Percocet)

STEP 3 Medications (*similar to Visual pain scale 7-10*)

- Morphine preparations
- Fentanyl (Duragesic)
- Hydromorphone (Dilaudid)
- Methadone (Dolophine)
- Levorphanol (Levo-Dromoran)

* American College of Physicians Guidelines on Cancer Pain

MANAGEMENT OF OPIOID SIDE EFFECTS

Side effects usually improve over time with the exception of constipation. A multi-system assessment is necessary.
Pain is rarely treated in isolation in patients with cancer and side effects may be from other treatments or cancer itself

Constipation

Preventive measures:

- Prophylactic medications
  - ► Stimulate laxative + stool softener (senna + docusate, 2 tablets q am)
  - ► Increase dose of laxative when increasing dose of opioids
- Maintain fluids
- Maintain dietary fiber (psyllium compounds are unlikely to control opioid induced constipation and are **not** recommended)
- Exercise, if appropriate

If constipation develops:

- Assess for cause and severity of constipation
- Rule out obstruction
- Treat other causes
- Titrate as needed to maximal dose of laxative (senna + docusate, 4 tablets bid) with goal of one non-forced bowel movement q 1-2 days
- Consider co-analgesic to allow reduction of the opioid dose

If constipation persists:

- Reassess for cause and severity of constipation
- Check for impaction
- Consider adding another agent such as magnesium hydroxide, 30-60 mL qd; bisacodyl, 2-3 tablets PO qd, or 1 rectal suppository qd; lactulose, 30-60 mL qd; sorbitol, 30 mL q2 h x 3, then prn, or magnesium citrate, 8 oz PO qd, polyethelene glycol (1 capful/8 oz water PO bid)
- Fleet, saline or tap water enema
- Consider use of a prokinetic agent (e.g., metoclopramide, 10-20 mg PO qid)
- When response to laxative therapy has not been sufficient for opioid-induced constipation in patients with advanced illness, consider Methylnaltrexone, 0.15 mg/kg sq, maximum one dose per day
- Consider neuraxial analgesics or neuroablative techniques to potentially reduce opiate dose

Nausea *(Refer to Antiemesis Care Guide)*

Sedation

If sedation develops and persists for more than 1 week after initiating opioids:

- Assess for other causes of sedation (e.g., CNS pathology, other sedating medications, hypercalcemia, dehydration, sepsis, hypoxia)
- Decrease the dose of opioid if pain control can be maintained at a lower dose
- Consider changing the opioid
- Consider co-analgesic to allow reduction of the opioid dose
- Consider a lower dose of opioid given more frequently to decrease peak concentrations
- Consider the addition of caffeine, 100-200 mg PO q6; methylphenidate, 5-10 mg 1 – 3 /day; or dextroamphetamine, 5-10 mg PO 1 – 3 /day; or modafinil, 100 – 200 mg PO qd. (Limit dosing to morning and early afternoon to avoid insomnia)

If sedation persists despite several changes of opioids and the above measures:

- Reassess cause and severity of sedation
- Consider neuraxial analgesics or neuroablative techniques to potentially reduce opiate dose

Delirium

- Assess for other causes of delirium including hypercalcemia, CNS, metastases, other psychoactive medications, etc.
- Consider changing the opioid
- Consider co-analgesic to allow reduction of the opioid dose
- Consider haloperidol, 0.5-2 mg PO q4-6 h or alternative neuroleptic agents

Motor and Cognitive Impairment

- Studies have shown that stable doses (>2 wk) are not likely to interfere with psychomotor and cognitive function but should be monitored

Respiratory Depression

- Use reversing agents cautiously.
- If respiratory problems or acute changes in mental status occur, consider naloxone administration. Consider another reason for neurological status changes if unresponsive to naloxone.

Pruritus

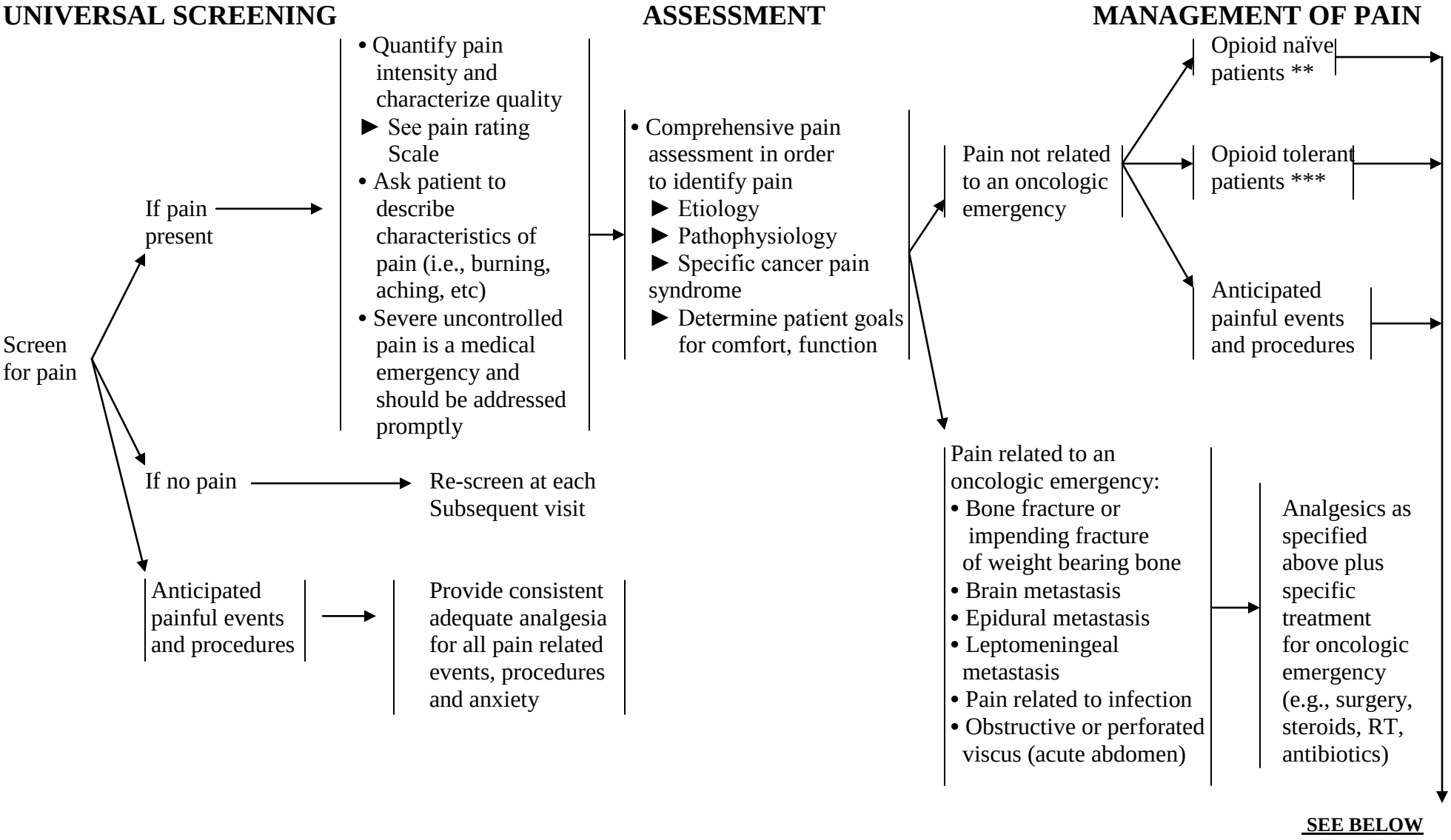
If pruritus develops

- Assess for other causes (other medications, etc)
- Consider antihistamine administration

If pruritus persists

- Consider changing to another opioid if other management has failed
- Consider adding to analgesic regimen: nalbuphine, 0.5 – 1 mg IV every 6 hours as needed

Consider continuous infusion of naloxone for the relief of pruritus without decreasing analgesic effect


UNIVERSAL SCREENING
ASSESSMENT
MANAGEMENT OF PAIN
Screen for pain
If pain present
• Quantify pain intensity and characterize quality
► See pain rating Scale
• Ask patient to describe characteristics of pain (i.e., burning, aching, etc)
• Severe uncontrolled pain is a medical emergency and should be addressed promptly
• Comprehensive pain assessment in order to identify pain
► Etiology
► Pathophysiology
► Specific cancer pain syndrome
► Determine patient goals for comfort, function
Pain not related to an oncologic emergency
Opioid naïve patients **
Opioid tolerant patients ***
Anticipated painful events and procedures
If no pain
Re-screen at each Subsequent visit
Anticipated painful events and procedures
Provide consistent adequate analgesia for all pain related events, procedures and anxiety
Pain related to an oncologic emergency:
• Bone fracture or impending fracture of weight bearing bone
• Brain metastasis
• Epidural metastasis
• Leptomeningeal metastasis
• Pain related to infection
• Obstructive or perforated viscus (acute abdomen)
Analgesics as specified above plus specific treatment for oncologic emergency (e.g., surgery, steroids, RT, antibiotics)
SEE BELOW

** Opioid-Naïve Patients

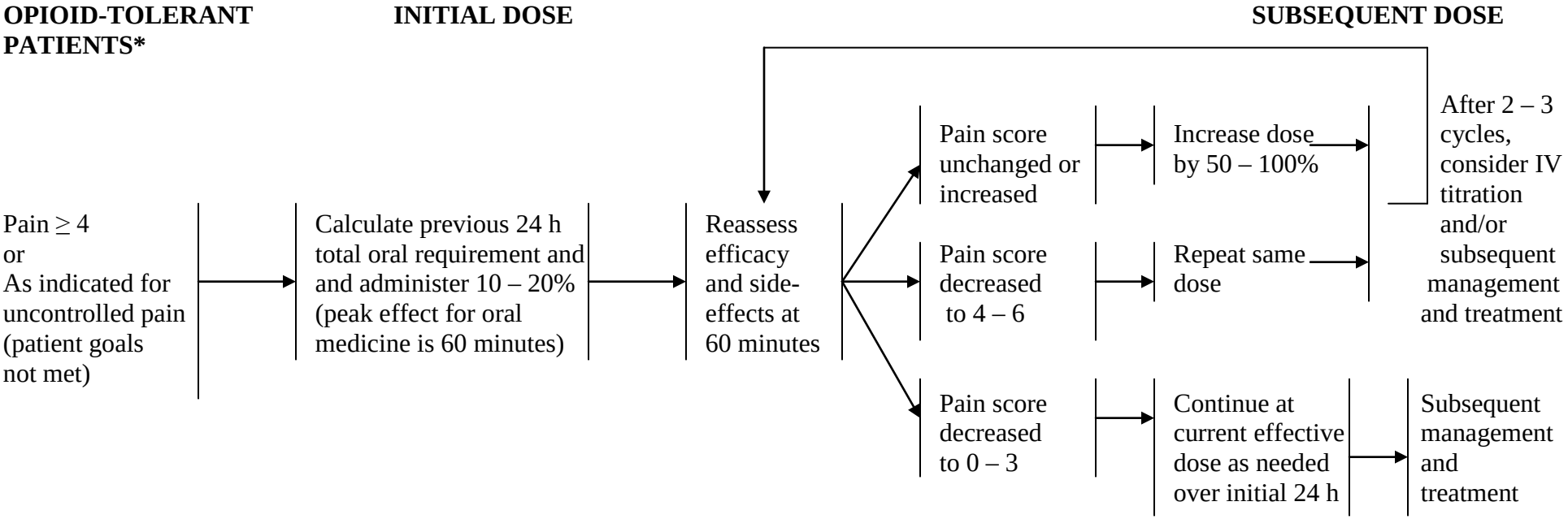
PAIN INTESITY	MANAGEMENT OF PAIN IN OPIOID-NAÏVE PATIENTS*
For *ALL* levels of pain	• Recognize and treat analgesic side effects • Consider adding co-analgesics for specific pain syndrome • Provide psychosocial support • Provide patient and family education • Optimize non-pharmacologic interventions
Severe Pain 7 – 10	• Manage for all levels of pain as above **AND** • Rapidly titrate short-acting opioid ► Oral peak effect in 60 minutes ► 5 – 15 mg short-acting morphine sulfate Or equivalent ► Increase or decrease dose based on pain score ♦ Begin bowel regimen
Moderate Pain 4-6	• Manage for all levels of pain as above **AND** • Titrate short-acting opioid ♦ Begin bowel regimen
Mild Pain 1 -3	• Manage for all levels of pain as above **AND** • Consider non-steroidal anti-inflammatory drugs (NSAIDs) or acetaminophen without opioid if patient is not on analgesics **or** • Consider titrating short-acting opioid ♦ Begin bowel regimen

→ Re-evaluate pain at each contact and as needed to meet patient goals for comfort and function

* Opioid naïve patients are those who do not meet the criteria for opioid tolerant patients described by the U.S. FDA.

*** MANAGEMENT OF PAIN IN OPIOID-TOLERANT PATIENTS

Monitor for acute and chronic adverse effects



* U.S. FDA: "patients considered opioid tolerant are those who are taking at least: 60 mg oral morphine/day, 25 mcg transdermal fentanyl/hour, 25 mg oral oxymorphone/day, or an equianalgesic dose of another opioid for one week or longer."

SUBSEQUENT PAIN MANAGEMENT AND TREATMENT IN OPIOID-TOLERANT PATIENTS*

For **ALL** pain Levels
- Provide psychosocial support
- Provide patient and family education

Severe Pain 7 – 10
- See management for *all* levels of pain above AND
- Re-evaluate opioid titration
- Re-evaluate working diagnosis with a comprehensive pain assessment
- Consider specific pain syndrome problems
- Consider pain specialist consultation
- Re-evaluate co-analgesics, as indicated

Moderate Pain 4 - 6
- See management for *all* levels of pain above AND
- Continue opioid titration
- Consider specific pain syndrome problems
- Consider pain specialist consultation
- Continue co-analgesic titration

Mild Pain 0 - 3
- See management for *all* levels of pain above AND
- Re-assess and modify regimen to minimize side-effects
- Co-analgesics as needed

→ Re-evaluate patient's goals of comfort and function at each contact

→ Achieved → See **Ongoing Care**

→ Not achieved → Re-screen and re-assess; Consider interventional strategies

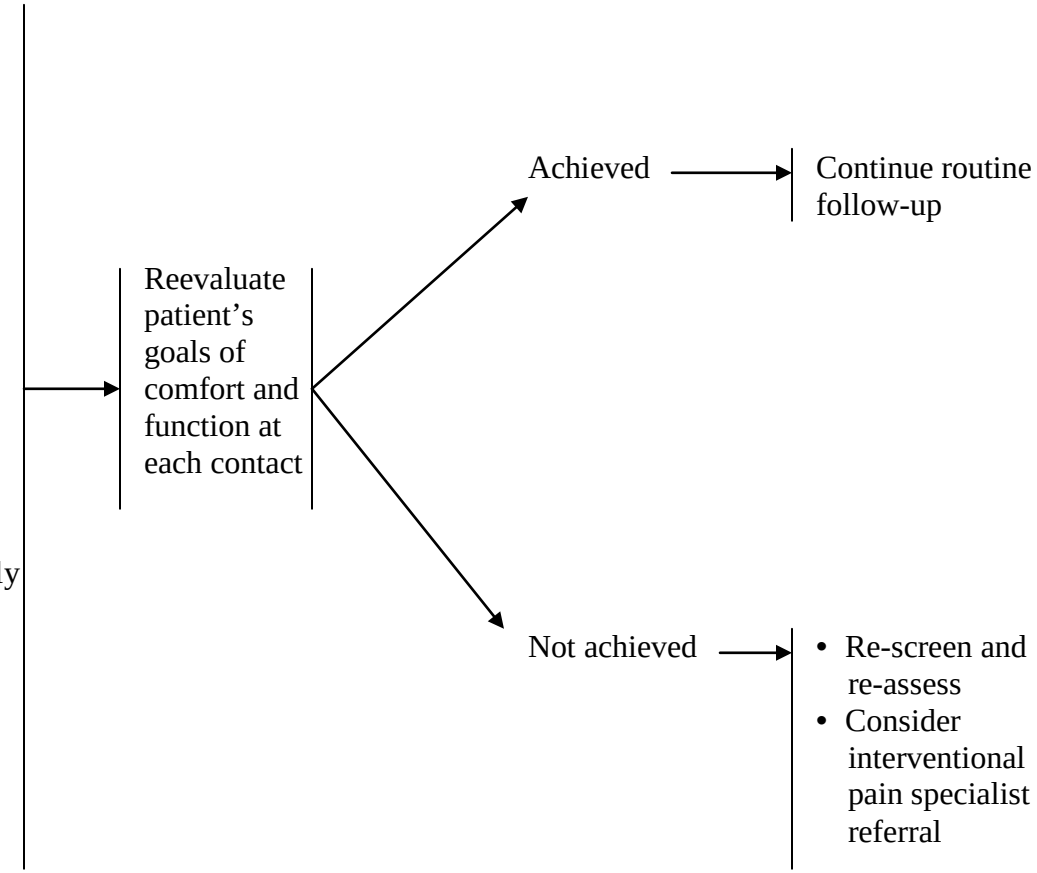
* Opioid tolerant includes patients who <u>are</u> chronically receiving opioid analgesic on a daily basis

ONGOING CARE

Clinician responsibilities

- Convert to oral medications (if feasible) including extended-release agent with rescue doses
- Routine follow-up
  - ► Assess pain during each outpatient contact or at least each day for inpatients or more frequently based on:
    - Δ Patient's condition
    - Δ Institutional standards
    - Δ Regulatory requirements
- Provide written follow-up plan, including prescribed medications
- Ensure adequate access to prescribed medications, especially during transition between sites of care
- Instruct the patient on the importance of the following:
  - ► Follow documented pain plan
  - ► Maintain clinic appointments
  - ► Contact clinician if pain worsens or side effects inadequately controlled
- Process realistic goals, revise, and review
- Address system barriers
  - ► Obtain assistance from social workers
- Maintain communication and coordinate care with pain specialist and relevant providers
- On-call/as needed availability

GOALS OF TREATMENT



References:

1. NCCN: Practice Guidelines in Oncology Adult Cancer Pain - v. 1. 2010

2. Cohen MZ et al. Cancer pain management and the JCAHO's pain standards: an institutional challenge. J Pain Symptom Manage 25(6): 519-527, 2003.

3. Stjernsward J et al. The WHO Cancer Pain and Palliative Care program: Past, present, and future. J Pain Symptom Manage 12; 65-72, 1996

4. Serlin RC et al. When is cancer pain mild, moderate or severe? Grading pain severity by its interference with function. Pain 61: 277-284, 1995.

5. Cherny NI. The pharmacologic management of cancer pain. Oncology 18(12): 1499-1515, 2004.

6. Portenoy RK et al. management of cancer pain. Lancet 353: 1695-1700, 1999.