Clinical Algorithm & Preferred Medications to Treat Pain in Dialysis Patients

Developed by the Mid-Atlantic Renal Coalition and the Kidney End-of-Life Coalition

September 2009

This project was supported, in part, under CMS Contract #HHS-500-2006-NW005C. The contents of this document do not necessarily reflect CMS policy.
• Assess pain intensity on a 0-10 scale in which 0 = no pain at all and 10 = the worst pain imaginable. Determine if the pain is mild (1-4), moderate (5-6), or severe (7-10).
• Prescribe pain medications and dosages according to the World Health Organization 3-Step Analgesic Ladder adapted for patients with chronic kidney disease (see page 2).
• Assess the character of the patient's pain and determine whether it is nociceptive, neuropathic, or both. Patients may have more than one type of pain; each pain syndrome should be diagnosed and treated.
• Nociceptive pain involves intact pain receptors and is described by patients as aching, dull, throbbing, cramping, or pressure. Neuropathic pain involves injury to pain receptors and is described by patients as tingling, burning, stabbing, or numb (see pages 3 & 4). Treatment of severe neuropathic pain usually requires opioid medications in addition to gabapentin or pregabalin, or other medications specific for neuropathic pain.
• Assess pain regularly for site, relieving and aggravating factors, and temporal relationships, and assess treatment regularly for effect on functioning and quality of life.
• Believe the patient's report of pain.
• Refer for non-pharmacological interventions as appropriate.
• Use adjuvant medications to reduce pain and side effects.
• Anticipate and treat constipation.
• Always consider depression as a potential contributor.
• Screen for opioid abuse.

RECOMMENDED PRACTICES

A Educate patient/caregivers on pain assessment and charting at home, goals of therapy, management plan, and potential complications.

B Aim to achieve control at a level acceptable to the patient; it may not be necessary or possible to make the patient completely pain-free. Provide prn doses for breakthrough pain.

C For chronic pain, schedule doses over 24 hours on a regular basis. Additional "breakthrough" medication should be available on an "as needed" basis.
WHO 3-STEP ANALGESIC LADDER

**Severe Pain (7-10)**
- Hydromorphone – start at 1 mg PO q 4h + 1 mg prn for breakthrough pain q 2h

**Moderate Pain (5-6)**
- Hydrocodone – start at 5 mg po q 4h prn
- Oxycodone – start at 5 mg po q 4h prn
- Tramadol – start at 25 mg po q d
- ± Nonopioid analgesics ± Adjuvants

**Mild Pain (1-4)**
- Acetaminophen
- Avoid NSAIDS
- ± Adjuvants

Titrates upwards, increasing the dose until either analgesia or intolerable side effects occur. For mild-moderate pain, increase dose by 25-50%; for severe pain, increase dose by 50-100%.

Do not exceed 4g of the acetaminophen per day to avoid hepatotoxicity.

Adjuvants include medications such as anticonvulsants for neuropathic pain. It may also refer to medications that are administered to manage an adverse effect of an opioid, or to enhance analgesia, such as steroids for pain from bone metastases.
Algorithm to Treat Severe Chronic Pain in Dialysis Patients

Hydromorphone:

- Start at 0.5 -1 mg PO q 4 hours plus 1 mg PO q 2 hours prn pain. Titrate dosage every 2 – 3 days.
- If pain is not controlled, is continuous, and 24-hour dose exceeds 12 mg, substitute transdermal fentanyl 25mcg/h for regular dose of hydromorphone.
- If further “as needed” hydromorphone exceeds 12 mg/24 hours, increase dose of fentanyl patch by further 25 mcg. Titrate upwards in similar manner if pain is not controlled.
- Caution: Toxic metabolite, H3G, accumulates if dialysis is stopped.

Fentanyl Transdermal Patches:

- Useful for patients with chronic, stable pain. Start after immediate-release opioid dose is established. Analgesia may not be obtained for 12-24 hours, so continue previous prn analgesics for 12 hours to ensure a smooth transition.
- Initial dose for opioid-naïve patients is 12 mcg/h (increase dose every 3 – 6 days as needed for pain). Useful choice if dialysis non-adherence or stopping dialysis are concerns.
- Fentanyl patches above 12 mcg/hr should not be used in opioid-naïve patients due to risk of respiratory depression.
- Prescribe medication for breakthrough pain.

Methadone:

- Only recommended to be used by knowledgeable physicians.
- Use if unable to control pain with hydromorphone or fentanyl (opioid-allergy, adverse effects, or refractory pain).
- Obtain baseline QTc (methadone may prolong QT interval) and repeat EKG if daily dose > 100 mg. QTc < 450 ms considered safe.
- Beware of multiple drug interactions and adjust dose.
- Consult www.hopweb.org for opioid conversions from hydromorphone or fentanyl to methadone.
**Nociceptive Pain Treatment**

*Note: Monitor for opioid toxicity (sedation, hallucinations, myoclonus and/or asterixis) and opioid adverse effects (constipation, nausea, and vomiting).*

- Confirm patient is able to swallow oral medications.
- Long-acting opioids should be started after the needed dosage to control pain is established with short-acting opioids.
- A rescue dose equivalent to 10% of the 24-hour dose of opioid should be available to be taken every 1-2 hours prn for breakthrough pain. Remember to recalculate the rescue dose when increasing the base dose (long-acting dose).
- If the patient is experiencing pain when he/she takes the long-acting opioid, he/she should take a rescue dose at the same time and not expect the long-acting opioid to relieve the breakthrough pain.

**Neuropathic Pain Treatment**

**Gabapentin:**
- Start 100 mg po q hs and increase weekly by 100 mg per night to a maximum of 300 mg q hs. Occasionally doses up to 600 mg a day can be safely used.
- If ineffective at maximum tolerated dose, discontinue and start Pregabalin.

**Pregabalin:**
- 25 mg q hs and increase every few days to 100 mg a day.
- If pain control is inadequate at target dose for 2 to 4 weeks, or intolerable adverse effects, discontinue and start Desipramine.

**Desipramine:**
- 10 mg po q hs. Titrate to adequate pain control or maximum dose of 150 mg q hs.
- If pain control still remains inadequate, institute WHO 3-Step Analgesic Ladder (see page 2).
**Management of Opioid Adverse Effects**

**Acute:**

**Excessive sedation, compromised respiration with low O₂ saturation**
- Dilute 0.4 mg of Naloxone in 10 ml NS and administer 1 ml IV q 1-2 minutes until patient arouses.
- Continue to monitor for return of sedation or slowed respirations (half-life of Naloxone is shorter than half-life of opioids).

**Chronic:**

**Nausea and/or vomiting**
- Prochlorperazine 2.5 to 10 mg PO, SC or PR QID prn.
- Haloperidol 0.5 to 1 mg PO, SL, SC, IV BID-TID prn (Haloperidol solution is flavorless).
- Metoclopramide 5 to 10 mg PO, SC, IV QID prn.
- Dimenhydrinate may be used 25 to 50 mg PO, SC, IV but is less effective, except if secondary to motion/dizziness. It also reduces opioid-induced pruritus.
- Ondansetron 4-8 mg PO or IV q8H prn.

**Constipation**
- Start docusate sodium and stimulant laxative (e.g. Senna, Bisacodyl) at same time as opioids as preventative therapy.
- Lactulose at 15-30 ml po daily to BID is more effective for opioid-induced constipation but patients may prefer medication in pill form.

**Cognitive impairment**
- Try decreasing the opioid dose to determine if function improves. If it does, consider using a lower dose or a different pain medication.

References for this document can be found on the Kidney End-of-Life Coalition website: [www.kidneyeol.org](http://www.kidneyeol.org).
## Preferred Medications in CKD

<table>
<thead>
<tr>
<th>Recommended</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Fentanyl</td>
<td></td>
</tr>
<tr>
<td>Methadone</td>
<td></td>
</tr>
<tr>
<td>Hydromorphone</td>
<td></td>
</tr>
<tr>
<td>Acetaminophen</td>
<td></td>
</tr>
<tr>
<td>Gabapentin</td>
<td>Doses up to 300 mg/d are generally considered safe in ESRD, but doses up to 600 mg should be used with caution; note that gabapentin use for neuropathic pain is off-label but effectiveness has been documented.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Use with Caution</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Tramadol</td>
<td>Limit dose to 50 mg BID. Higher doses have been used but caution needs to be taken since pharmacokinetics are not well established.</td>
</tr>
<tr>
<td>Hydrocodone/Oxycodone</td>
<td>Insufficient pharmacokinetic evidence to establish safety in CKD, but literature reports use without major adverse effects.</td>
</tr>
<tr>
<td>Desipramine/Nortriptyline</td>
<td>Alternative to treat neuropathic pain, but more adverse effects than gabapentin and pregabalin.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>DO NOT USE</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td></td>
</tr>
<tr>
<td>Codeine</td>
<td></td>
</tr>
<tr>
<td>Meperidine</td>
<td></td>
</tr>
<tr>
<td>Propoxyphene</td>
<td>Morphine, codeine, meperidine, propoxyphene: Renally excreted metabolites accumulate in CKD causing neurotoxicity.</td>
</tr>
</tbody>
</table>
**PAIN ASSESSMENT**

Instructions: Please have your patient describe his/her level of pain by circling the appropriate number or the face that best describes the intensity of pain. Determine if the pain is nociceptive or neuropathic by the descriptors the patient uses to describe the pain (see algorithm below). Repeat the pain assessment on subsequent patient visits.

1. "Are you having any pain?"
   - Verbal: "How much pain are you having, from 0 (no pain) to 10 (worst pain imaginable)?"
   - Written: "Circle the number that describes how much pain you are having."

2. "Where is the pain located?"
   - Record, screen and address each site.

3. "How much pain are you having?"
   - Use Pain Screening Tool—Numerical Scale or Categorical Faces/R Scale (for cognitively impaired).

4. "What is the character of the pain?"

5. "What relieves the pain?", "What aggravates the pain?"

### Instructions:
- Please have your patient describe his/her level of pain by circling the appropriate number or the face that best describes the intensity of pain. Determine if the pain is nociceptive or neuropathic by the descriptors the patient uses to describe the pain (see algorithm below). Repeat the pain assessment on subsequent patient visits.

### Algorithm:
- **No pain**
- **Mild (1-4)**
- **Moderate (5-6)**
- **Severe (7-10)**

### Pain Descriptors:
- Nociceptive: aching, dull, throbbing, cramping, pressure.
- Neuropathic: tingling, numbness, burning, stabbing, increased pain to light touch.

### Pain Assessment
- **None (0)**
- **Mild (1-4)**
- **Moderate (5-6)**
- **Severe (7-10)**

### PPPAINAINAIN ASSESSMENTSSESSMENTSSESSMENT