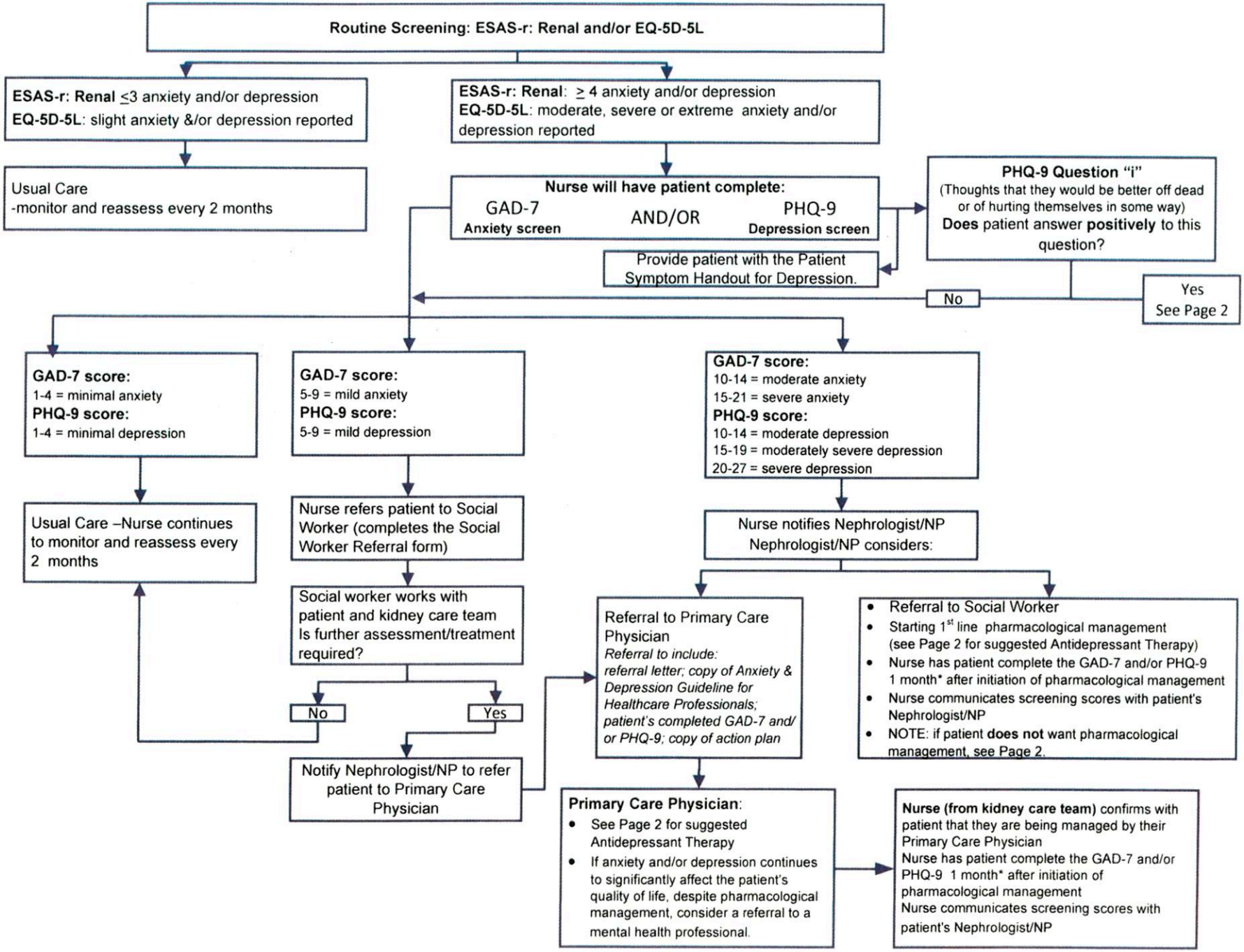
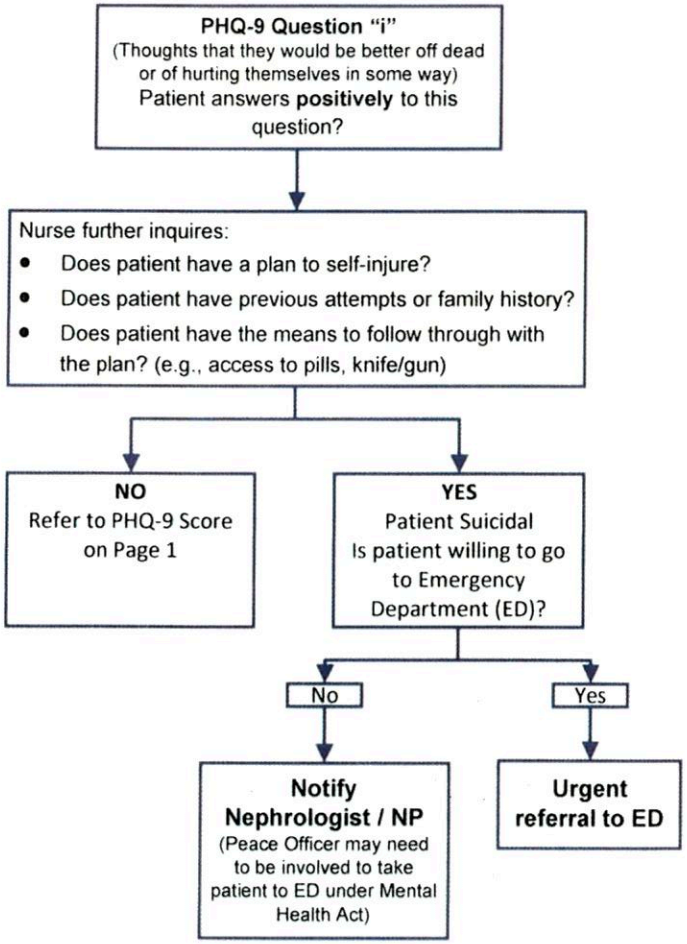
Anxiety & Depression Guideline for Healthcare Professionals



22 November 2018

Anxiety & Depression Guideline for Healthcare Professionals



Patient does not want pharmacological management:

- Nurse has patient complete the GAD-7 and/or PHQ-9 in 1 month* to assess if patient is staying stable or getting worse
- If staying stable: patient completes the GAD-7 and/or PHQ-9 in 1 month*
- If getting worse: continue to have patient complete GAD-7 and/or PHQ-9 in 1 month* or sooner, based on clinical judgement
- Nurse communicates screening scores with patient's Nephrologist/NP

Suggested Antidepressant Therapy

NOTE: It is recommended to begin therapy using minimum effective dose and to titrate after 1-2 weeks. If there is SOME CHANGE, continue dose and agent for 2-3 months to assess effect achieved.

- First Line therapies: Selective Serotonin Reuptake Inhibitors (SSRIs), consider:
  - Sertraline (Zoloft) 25-200 milligrams by mouth daily
  - Citalopram (Celexa) 5-20 milligrams by mouth daily. Can be increased to 40 milligrams by mouth daily after one month of therapy if no strong cyp2c19 inhibitors (risk of QTc prolongation)
  - Escitalopram (Cipralex) 5-10 milligrams by mouth daily (risk of QTc prolongation; twice as potent as Citalopram)
  - Paroxetine (Paxil) 10 milligrams by mouth daily (most anticholinergic activity; has been used for pruritus)
- Non-first Line therapies, consider:
  - Serotonin/Norepinephrine Reuptake Inhibitors (SNRIs)
    - Venlafaxine (Effexor) 37.5 – 112.5 milligrams by mouth daily
    - Duloxetine (Cymbalta) 30-60 milligrams by mouth daily
  - Other Antidepressants
    - Bupropion XL (Wellbutrin) 150 milligrams by mouth daily (risk of accumulation of toxic metabolites causing dysrhythmia)
    - Mirtazapine (Remeron) 15-30 milligrams by mouth daily (has been used for pruritus; can be used for concomitant insomnia, anxiety, and to increase appetite)

* Does not replace individualized care and clinical expertise

22 November 2018

Breathlessness Guideline for Healthcare Professionals

Guiding Principle: Treat the patient's breathlessness **if it is affecting** their quality of life.

Step 1: Assess for and address any other potential treatable causes *(e.g. anxiety, anemia, infection)*

- Breathlessness is a subjective discomfort involving the patient's perceptions and reaction to feeling breathless. It can often be one of the most distressing symptoms of ESKD.

Step 2: If the patient is intravascularly volume overloaded:

- The most common cause for breathlessness in this patient population is **pulmonary edema**.
- Assess patient's dry weight.
- If dry weight has been lowered, watch for hypotension

Step 3: Consider non-pharmacological management:

- Explore with patient contributing and alleviating factors
- Review intradialytic weight gains
- Consider referral to dietitian for consultation on fluid and salt management
- Sit in an upright position (45°)
- Position by an open window
- Have a fan blow air gently across the face (stimulation of the trigeminal nerve V2 branch has central inhibitory effects on dyspnea)
- Maintain humidity in room
- Pursed lip breathing
- Supplemental oxygen: Provide oxygen and titrate to relieve symptoms rather than to achieve a particular oxygen level. Be cautious providing high flow oxygen to patients with COPD, as the drive for breath depends on their carbon dioxide level. (note that the patient must be hypoxic at rest in order to qualify for coverage at home)
- Meditation, mindfulness, music and/or relaxation therapy
- Provide reassurance
- See: Feeling Short of Breath Patient Handout and Swelling Patient Handout

Step 4: If the patient is still short of breath, consider combination therapy (low-dose metolazone and high-dose oral furosemide (Lasix))

- Metolazone 2.5–5 mg PO daily, in addition to individual's furosemide (Lasix) regime up to 120 mg PO BID x 2-5 days, then re-evaluate.

Adapted from the CKM Breathlessness Guideline for Healthcare Professionals (2018) for the EMPATHY Trial
Last updated: 11 May 2018

Acronym Legend

Acronym:	Intended Meaning:
ATC	Around the Clock
BID	Twice Daily
CKD	Chronic Kidney Disease
CKM	Conservative Kidney Management
COPD	Chronic Obstructive Pulmonary Disease
CO2	Carbon Dioxide
EOL	End of Life
ESA	Erythropoietin Stimulating Agent
ESKD	End Stage Kidney Disease
GFR	Glomerular Filtration Rate
GI	Gastrointestinal
g/L	Grams per litre
HgB	Hemoglobin
IN	Intranasal
IU	International Units
IV	Intravenous
kg	Kilogram
mcg	Microgram
mg	Milligram
mL	Millilitre

Acronym:	Intended Meaning:
mmol/L	Millimoles per Litre
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PO	By Mouth
PRN	As Needed
NSAID	Non-steroidal Anti-inflammatory Drugs
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q(1-8)h	Every (Time Eg, 4) Hours
q(1-8)weeks	Every (Time Eg. 2) Weeks
QHS	At Bedtime
RLS	Restless Leg Syndrome
SC	Subcutaneous
SL	Sublingual
SNRI	Serotonin and Norepinephrine Reuptake Inhibitors
SSRI	Selective Serotonin Reuptake Inhibitors
TCA	Tricyclic Antidepressant
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Adapted from the CKM Breathlessness Guideline for Healthcare Professionals (2018) for the EMPATHY Trial
Last updated: 11 May 2018

Constipation Guideline for Healthcare Professionals

Guiding Principles: Constipation is common in people with kidney disease. Constipation is described as difficult, hard, incomplete or infrequent emptying of the bowels. Constipation is **subjective in nature**, aligned with the normal frequency of an individual's bowel movements. If patients are on regularly scheduled opioids, consider ordering a regular bowel routine. The primary objective of managing constipation is to **support patients in having regular and adequate bowel movements**, based on the individual's preference and functional status.

Step 1: Assess for possible factors contributing to constipation, and address as appropriate:

- Decreased mobility
- Advanced age
- Depression, stress and anxiety
- Low fibre intake
- Low fluid intake
- Adverse effects of medications (e.g. opioids, oral iron supplements, antacids, calcium supplements)
- Metabolic disturbances (e.g. hypercalcemia, hypokalemia, hypothyroidism, diabetes)
- Bowel Conditions (e.g. Irritable Bowel Syndrome)
- Neurological Conditions (e.g. Parkinson's, Multiple Sclerosis, Spinal cord injury)
- Mechanical obstruction of the bowel or rectum

Assessment: When assessing constipation, **rule out a bowel obstruction**. Signs and symptoms of a bowel obstruction may include: nausea/vomiting, high pitched/absent bowel sounds, distended abdomen and abdominal cramping/pain. If a bowel obstruction is suspected, consider obtaining an abdominal flat plate x-ray.

Step 2: Consider non-pharmacological management:

- Exercise (if appropriate).
- Increasing fibre intake (if appropriate).
    - Some higher fibre foods such as bran, beans, lentils, nuts and seeds are also high in phosphorus and potassium and may need to be limited.
    - Consider a referral to a Registered Dietician (RD) for nutritional counselling.
- Ensure adequate hydration management.
- Prunes/prune juice (if appropriate as prunes are high in potassium), Caffeinated coffee/tea.
- Toileting upon waking and post meals; proper positioning over the toilet in contrast to using a bedpan.
- See: Constipation Patient Handout

Step 3: If the patient is still experiencing constipation, consider pharmacological management:

- **Osmotic Laxatives:**
    - Polyethylene Glycol 3350 (Lax-A-Day) PO 17-34g daily (doses can be divided).
    - Lactulose 15-30ml PO Daily to TID.
- **Peristaltic Stimulants:**
    - Sennosides 8.6mg 1-2 tablets PO qHS, then increase to 2-4 tablets BID PRN if needed.
    - Bisacodyl 5-15mg PO Daily.
- **Typical Laxative Regime** if a patient taking opioids has **not** had a bowel movement in three days or is **unable to take oral** laxatives:
    - Glycerin suppository per rectum once daily PRN.
    - If glycerine suppository ineffective, give bisacodyl 10mg suppository per rectum q3d PRN.
    - If bisacodyl suppository is ineffective, give High Mineral Oil enema per rectum PRN, wait 4-8 hours, then administer Soap Suds enema per rectum x1 PRN ***Sodium phosphate enemas (Fleet enemas) should be avoided with ESKD patients.**
- Consider a bowel clean-out of Golytely or Colyte 3-4L
    - Can be spaced out over a week if the patient is frail.
- **Methylnaltrexone (Relistor)** is used for acute management of opioid-induced constipation when oral and rectal laxatives are not effective. Consider cost when prescribing this medication. In kidney failure, reduce dose by half.
        - e.g. Methylnaltrexone (Relistor) 4mg SC (38kg-62kg), 6mg SC (62-114kg); administer once every 2 days.

Adapted from the CKM Constipation Guidelines for Healthcare Professionals (2018) for the EMPATHY Trial
Last updated: 11 May 2018

Acronym Legend

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Fatigue and Sleep Disturbances Guideline for Healthcare Professionals

Guiding Principles: Fatigue is a very common symptom in ESKD and it is often multifactorial. Treat the patient's tiredness and/or daytime drowsiness **if it is affecting** their quality of life.

Step 1: Assess for possible modifiable factors contributing to fatigue:

- Vitamin D deficiency
- Metabolic acidosis
- Hypothyroidism/hyperthyroidism
- Anemia
- Uremia: ensure patient is adequately dialyzed
- Malnutrition: consider referral to a registered dietitian
- Mood disorders such as anxiety, depression
- Sleep disorders and symptoms affecting sleep

Step 2: If the patient reports ongoing difficulties with falling and/or staying asleep, consider the following possible contributing factors:

- Restless Legs Syndrome
- Pruritus
- Pain
- Breathlessness
- Cognitive Impairment
- Medications
- Generalized insomnia
- Mood disorders such as anxiety, depression
- Apnea

Step 3: Consider non-pharmacological management:

- Exercise (if appropriate)
- Nutrition and hydration management
- Cognitive and psychological approaches (eg. relaxation therapy, hypnosis, stress management, delegating and setting limits)
- Complementary treatments such as acupressure/acupuncture (no high quality evidence to support this; no lasting adverse effects)
- Energy Conservation Strategies (See: Tiredness Patient Handout)
- Promote good sleep hygiene (See: Sleep Patient Handout)
- Incorporate relaxation techniques
- Consider suggesting to your patient:
  - Wake up at the same time every morning
  - Do not go to bed until you feel sleepy
  - Do not "try" to fall asleep
  - Avoid napping during the day
  - Avoid caffeine in the evening
  - Save your bedroom for sleep (and sex) only
  - Leave your day's dilemmas at the door

Step 4: If the patient continues to report tiredness +/- drowsiness, consider pharmacological management:

- Reassess medications prescribed for the treatment of insomnia after 2-4 weeks. Avoid OTC sleep aids and benzodiazepines if possible.
- Consider low-dose gabapentin (*particularly if the patient has concomitant symptoms of* ***neuropathic pain, RLS, or uremic pruritus***):
  - **Gabapentin 50-100 mg PO nightly**. If not effective, it can be further titrated by 100 mg every 7 nights to a maximum of 300mg PO at bedtime. It should be taken **2-3 hours before bed due to delay of peak onset.**
- If ineffective, cautiously consider:
  - Mirtazapine (Remeron) 7.5 mg PO at bedtime (not if taking Tramadol or antidepressants)
  - Doxepin 10 mg PO at bedtime (monitor carefully for anticholinergic side effects and cardiac arrhythmias)
  - Zopiclone 3.75-5 mg PO at bedtime for short term use
  - Melatonin 2-5 mg PO at bedtime (although the evidence is somewhat limited and inconclusive)

Adapted from the CKM Fatigue and Sleep Disturbances Guideline for Healthcare Professionals (2018) for the EMPATHY Trial
Last updated: 11 May 2018

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Adapted from the CKM Fatigue and Sleep Disturbances Guideline for Healthcare Professionals (2018) for the EMPATHY Trial
Last updated: 11 May 2018

Nausea & Vomiting Guideline for Healthcare Professionals

Guiding Principle: Treat the patient's nausea/vomiting **if it is affecting** their quality of life.

Step 1: Consider the underlying causes of nausea, and address as appropriate:

- Metabolic disturbances (eg. uremia- ensure patients is adequately dialyzed)
- Medications (eg. opioids, SSRI antidepressants)
- Gastrointestinal disturbances (eg. constipation, delayed gastric emptying)

Step 2: Consider non-pharmacological management:

- Manage/avoid constipation (See: Constipation Guideline)
- Encourage good oral hygiene
- Offer smaller amounts of food more frequently and adjust timing of meals as necessary. Eat slowly
- Do not drink alcohol. Try to drink fluids 30-60 minutes before or after meals instead of with meals
- Minimize aromas (cooking odours, perfumes, smoke, etc.)
- Avoid foods that are greasy, spicy, or excessively sweet
- Encourage patient to relax in an upright position after eating to facilitate digestion
- Apply a cool damp cloth to forehead or nape of neck
- Suggest loose fitting clothing
- Consider complementary therapies such as relaxation, imagery, acupressure, or acupuncture, and the use of ginger
- See: Nausea & Vomiting Patient Handout

Step 3: If the patient continues to report nausea +/- vomiting, consider pharmacological options:

The below suggestions have been dose-adjusted for the ESKD patient and some of the medications are being used off-label for nausea.

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- **Ondansetron (Zofran)** 4 mg PO TID (Can titrate to 8 mg PO TID). Ondansetron (Zofran) can be constipating
  NOTE: If nausea is due to gastroparesis, consider Metoclopramide as first choice before using Ondansetron.
- **IF ineffective:**
  - consider replacing with:
    - **Metoclopramide (Metonia)** 2.5 mg PO q4h ATC and/or PRN*
      Metoclopramide (Metonia) crosses the blood-brain barrier and stimulates the CTZ. Extrapyramidal symptoms are possible.

  IF nausea persists:
  - Consider replacing with:
    - **Haloperidol (Haldol)** 0.5 mg PO q8h ATC and q4h PRN* Haloperidol (Haldol) has a higher risk of extrapyramidal symptoms than metoclopramide (Metonia) and Olanzapine (Zyrexa).
    - **Olanzapine (Zyprexa)** 2.5 mg PO q8h ATC and q4h PRN* It is available in an orally disintegrating formulation but still needs to be absorbed via the lower GI tract.

  IF previous options were ineffective:
  - Consider increasing: **Haloperidol (Haldol)** to 1 mg PO q8h ATC and q1h PRN (to a maximum 5 mg in 24 hours)

  IF previous options were ineffective:
  - Consider adding or replacing with: **methotrimeprazine (Nozinan)** 5 mg PO q8h ATC
    - **NOTE**: Increasing the dose of methotrimeprazine (Nozinan) may lead to levels of drowsiness that the patient may find unacceptable. This should be discussed with the patient before the dose is increased.

Adapted from the CKM Nausea & Vomiting Guideline for Healthcare Professional (2018) for the EMPATHY Trial
Last updated: 07 June 2018

Haloperidol (Haldol), metoclopramide (Metonia), and olanzapine (Zyprexa) are all dopamine antagonists – avoid prescribing them together. They can also exacerbate Restless Legs Syndrome (See: Restless Legs Syndrome Guideline)

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	Neuropathic Pain	Nociceptive Pain
▶ Determine type and cause of pain – have the patient complete the Initial Pain Assessment	**Neuropathic pain** is commonly described as **numbness, tingling, burning, stabbing, shooting.** • Patients with ESKD may experience pain from a variety of causes. They might have neuropathic and/or nociceptive pain. If patient experiences both types of pain, treat the neuropathic pain first.	**Nociceptive pain** is most commonly described as **aching, dull, gnawing, throbbing, cramping.** • Determine cause for pain and consider appropriate investigations. • Step 1 analgesics at full dose can be added to Step 2 & 3. Adjuvants may be added to all 3 steps. **For severe pain, consider starting both non-opioid & opioid agents simultaneously.**
	• Consider using the Follow-up Pain Assessment Tool weekly to monitor effect of pain management. • See: Pain Patient Handout	

	Neuropathic Pain	Nociceptive Pain
▶ **Step 1:** Start with adjuvant therapy	1st Line: • **Gabapentin 50-100 mg PO nightly**. If not effective, titrate by 100 mg every 7 nights to a maximum of 300 mg nightly. It should be taken **2-3 hours before bedtime due to delay of peak onset.** Or • **Pregabalin** 25 mg PO nightly. Titrate by 25 mg every 7 nights to a maximum of 75 mg PO nightly. It should be taken 2 hours before bedtime. (Pregabalin is **not covered** by the Seniors' or Basic Alberta Blue Cross plans). 2nd Line: • TCA antidepressant (unless contraindications i.e. conduction abnormalities on ECG, or excess weight gain) • Amitriptyline (Elavil) 10-25 mg PO nightly (max dose 75 mg daily). Titrate by 10-25 mg every week as required. **Is pain now adequately controlled?** • Yes: Reassess at least monthly using the Follow-up Pain Assessment Tool • No benefit: STOP Adjuvant and START Non-Opioid/Weak Opioid (Step 3) • Some benefit but inadequate: ADD Non-Opioid/Weak Opioid (Step 3)	N/A

Adapted from the CKM Neuropathic and Nociceptive Pain Guidelines for Healthcare Professionals (2017) for the EMPATHY Trial
Last Updated: 23 August 2018

	Neuropathic Pain	Nociceptive Pain
▶ **Step 2: Start or add a non-opioid +/- adjuvant therapy**	**ADD non-opioid to adjuvant therapy:** • Acetaminophen (Tylenol) 500-1000 mg PO q6-8 hours (max 3 grams/24hrs)	**Start non-opioid:** • Acetaminophen (Tylenol) 500-1000 mg PO q6-8 hours (max 3 grams/24hrs) **If pain localized to small joint:** • Consider a topical NSAID (e.g. Diclofenac (5% or 10%) gel); Apply to affected area BID to TID
	Is pain now adequately controlled? Yes: Reassess at least monthly using the Follow-up Pain Assessment Tool Inadequate: ADD strong opioid (Step 3)	
▶ **Step 3: Add a strong opioid and titrate slowly as tolerated to adequate pain relief**	**Can continue with step 1 and ADD a strong opioid.**	**Can continue with step 2 and ADD a strong opioid.**
	Review the opioid risk tool score recorded on the Initial Pain Assessment and order a **bowel routine** (See: Constipation Guideline) and give patient Constipation Handout. Start with low doses and titrate slowly to effect. • **Methadone** 1-2 mg/daily PO • **Hydromorphone (Dilaudid)** 0.5 mg PO q4h. Due to the accumulation of metabolites, monitor closely for toxicity. • **Fentanyl Transdermal Patch** (for controlled pain) 12 mcg/h q72hours. Not recommended in opioid naïve patients (see Opioid Conversion Table). • **Buprenorphine Transdermal Patch** (for controlled pain) 5 mcg/h q7days (see Opioid Conversion Table). Is not covered by Alberta Blue Cross. Access may be limited.	

Is pain now adequately controlled?

- Yes: Reassess at least monthly using the Follow-Up Pain Assessment Tool
- No: Refer to Chronic Pain Clinic

Considerations for Opioid Titration:

- Ongoing pain re-assessment is **critical**.
- Titrate analgesics every 3-7 days as needed and tolerated. Slower titration may be required.
- **Titrating up the regular Opioid dose**:
  1. Add the total amount of opioid used in the last 24 hours (regular and breakthrough doses). Divide the total dose by 6 and prescribe this amount every 4 hours (q4H).

     OR
  2. For ongoing pain exceeding patients pain control targets, adjust as follows:
     - For pain rated 3-6, increase dose of opioid by 25%
     - For pain rated 7-10, increase dose of opioid by 50%
- **Breakthrough (PRN) dose prescription**: 10% of total 24-hour opioid dose q 1-2 hrs PRN.
- If the patient is also taking benzodiazepines, consider titrating down the dose, while opioids are being increased. If not, titrate opioids more slowly.

Opioid Conversion Table (for patients on chronic opioids**)

Drug	Parenteral	Oral
Hydromorphone	2 mg	4 mg
Oxycodone	N/A	20 mg
Fentanyl	100 µg (0.1 mg)	N/A
Fentanyl Patch	** see below	
Buprenorphine Patch	** see below	
Methadone	N/A	

* As per PHC/VCH opioid conversion table (last update Jan 15/2010)
** Recommended conversion from PO daily hydromorphone equivalent to fentanyl and buprenorphine
***conversion doses are patient dependent

Hydromorphone (mg/24 hrs)	Fentanyl (µg/hr)	Buprenorphine (µg/hr)
<6	-	5
6-12	12	10
13-26	25	20
27-35	37	
36-44	50	
45-53	62	
54-62	75	
63-71	87	
72-80	100	

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Uremic Pruritus Guideline for Healthcare Professionals

Guiding Principle: Treat the patient's daily pruritus **if it is impairing** their sleep or quality of life.

Step 1: Address possible contributing factors:

- Uremia: ensure patient is adequately dialyzed
- Correct iron deficiency (See: Anemia Guideline).
- Other: xerosis, drug hypersensitivities, allergies, infestations, contact dermatitis, or inflammation.

Step 2: Consider non-pharmacological management:

- **Good skin care and moisturizers are considered first line treatment. Some general principles to follow:**
  - Baths are better than showers (daily in lukewarm water for at least 15 minutes).
  - Avoid harsh soaps, body washes, bubble baths, etc. Try gentle cleansers (eg. Cerave, Cetaphil), and only in limited places such as the axilla and groin areas.
  - Post bath: **pat dry** and moisturize skin within **two minutes** of getting out. Skin will still be damp. Ideally, use hypoallergenic moisturizers with ceramides (eg. Cerave) that are free from fragrance and additives. Do not use the moisturizers on areas of broken skin.
- **Other skin care strategies include the following**:
  - Keep skin cool by wearing light and cool clothing.
  - Avoid scratching – keep fingernails short, encourage massaging rather than scratching, wear gloves at night.
  - Maintain a humid home environment, especially in the winter.
- See: Itch Patient Handout

Step 3: If non-pharmacological interventions are not successful, and if the pruritus is localized, consider topical therapies:

- **Pramoxine**
  - Gold Bond Medicated Anti-Itch products (OTC) – contain pramoxine, dimethicone, menthol
  - Pramox HC (hydrocortisone 1%/pramoxine 1%) - apply two times a day for 4 weeks
- **Capsaicin 0.025% or 0.03% ointment**
  - Zostrix 0.025% and Zostrix Hp 0.075%
  - Can be applied 2-4 times a day to affected areas.
  - *It may initially cause burning to the area.*
- **Menthol, Camphor and Phenol** are separate products that can be added to most creams, typically in the range of 0.3-1.0%
  - All three may be added together, commonly with a 0.3% concentration for each.
  - *Must be compounded by pharmacy.*
- **Gamma-Linolenic acid (GLA) 2.2% cream**
  - Apply cream twice daily to identified dry skin.
  - *May not be easily accessible in Alberta.*

Step 4: If topical therapies are not successful, or if the pruritus is generalized, consider systemic therapies:

Many of the following medications have been dose-adjusted for the ESKD patient and some are being used off-label for pruritus.

Note that gabapentin is not commercially available in 50 mg capsules, but can be compounded for patients if the recommended low starting dose is desired.

Antihistamines are not recommended in the treatment of uremic pruritus.

- **Gabapentin**
  - A recommended **starting dose is 50 -100 mg nightly.** If not effective, it can be further titrated by 100mg every 7 nights to a maximum of 300mg PO qhs. It should be taken **2-3 hours before bedtime due to delay of peak onset.**
  - The most common side effects are drowsiness, dizziness, confusion, and fatigue. Peripheral edema may also be a side effect.
- **Pregabalin:** Similar to gabapentin, but more expensive and **not covered** by Seniors' or Basic Alberta Blue Cross plans. Other private plans may cover the cost. Pregabalin can be initiated at 25 mg PO nightly and titrated by 25 mg every 7 nights to a maximum of 75 mg PO qhs. It should be taken 2 hours before bedtime. Potential side effects are similar to those of gabapentin.

Adapted from the CKM Uremic Pruritus Guideline for Healthcare Professionals (2018) for the EMPATHY Trial
Last updated: 23 August 2018

- **Doxepin**
  - Doxepin 10 mg PO QHS as tolerated.
  - Doxepin is a tricyclic antidepressant. A randomized control trial found that it may be effective.
  - Potential adverse effects: dizziness, blurred vision, constipation, urinary retention. Particularly in older adults, there is an increased risk of confusion and sedation.
- **Phototherapy:** Not much is known about the long term effects of UVB, but a trial of three times a week for 3 weeks may provide some relief for a period of time. Requires referral to Dermatology.
- **Acupuncture:** Although there is a lack of good evidence about its efficacy, patients may wish to consider this as an alternative or complementary treatment option.

Acronym Legend

Acronym:	Intended Meaning:
ATC	Around the Clock
BID	Twice Daily
CKD	Chronic Kidney Disease
CKM	Conservative Kidney Management
COPD	Chronic Obstructive Pulmonary Disease
CO2	Carbon Dioxide
EOL	End of Life
ESA	Erythropoietin Stimulating Agent
ESKD	End Stage Kidney Disease
GFR	Glomerular Filtration Rate
GI	Gastrointestinal
g/L	Grams per litre
HgB	Hemoglobin
IN	Intranasal
IU	International Units
IV	Intravenous
kg	Kilogram
mcg	Microgram
mg	Milligram
mL	Millilitre

Acronym:	Intended Meaning:
mmol/L	Millimoles per Litre
OTC	Over the Counter
PO	By Mouth
PRN	As Needed
NSAID	Non-steroidal Anti-inflammatory Drugs
q(1-8)d	Every (Time Eg, 2) Days
q(1-8)h	Every (Time Eg, 4) Hours
q(1-8)weeks	Every (Time Eg. 2) Weeks
QHS	At Bedtime
RLS	Restless Leg Syndrome
SC	Subcutaneous
SL	Sublingual
SNRI	Serotonin and Norepinephrine Reuptake Inhibitors
SSRI	Selective Serotonin Reuptake Inhibitors
TCA	Tricyclic Antidepressant
TID	Three Times a Day
>	Greater Than
≥	Greater Than or Equal To
<	Less Than
≤	Less Than or Equal To

Guiding Principle: Treat the patient's restless legs syndrome (RLS) **if it is affecting** their sleep or quality of life.

Step 1: Address contributing factors:

- Correct anemia and iron deficiency
- Correct hyperphosphatemia
- Correct Vitamin D deficiency
- Uremia: ensure patient is adequately dialyzed
- **Remove drugs** which may contribute to or cause RLS:
  - **Dopamine antagonists:**
    - antipsychotics: pimozide, haloperidol (Haldol), olanzapine (Zyrexa), risperidone, quetiapine (Seroquel), methotrimeprazine (Nozinan)
    - other: metoclopramide (Metonia), promethazine
  - **Antidepressants**
    - Mirtazapine (Remeron)
    - SSRIs: e.g. citalopram, escitalopram, fluoxetine (Prozac), paroxetine (Paxil), sertraline (Zoloft)
    - SNRIs: e.g. duloxetine (Cymbalta), venlafaxine (Effexor)
    - Others: Topiramate; opioids may also exacerbate RLS in this population

Step 2: Consider non-pharmacological management:

- A trial of **abstinence from stimulants** such as alcohol, caffeine and nicotine.
- Consider the following changes to the dialysis prescription: low-temperature dialysis, morning treatment time for patient
- A trial of **mental alerting activities**, such as video games or crossword puzzles, to reduce symptoms at times of boredom.
- The promotion of good sleep hygiene:
  - Wake up at the same time every morning.
  - Do not go to bed until you feel sleepy.
  - Do not "try" to fall asleep.
  - Avoid napping during the day.
  - Avoid caffeine in the evening.
  - Save your bedroom for sleep (and sex) only.
  - Leave your day's dilemmas at the door.
  - Incorporate relaxation techniques.
- If realistic for the patient, encourage **aerobic exercise, walking, stretching, and/or gentle leg massage.**
- See: Fatigue and Sleep Disturbances Guideline
- See: Restless Legs Patient Handout

Step 3: If the patient continues to report restless legs syndrome, consider pharmacological options:

Many of the following medications have been dose-adjusted for the ESKD patient and some are being used off-label for RLS. *Note that gabapentin is not commercially available in 50 mg capsules, but can be compounded for patients if the lower starting dose is desired.

- **Gabapentin:** A recommended **starting dose is 50-100 mg nightly**. If not effective, it can be further titrated by 100 mg every 7 nights to a maximum of 300 mg PO qhs. It should be taken **2-3 hours before bedtime due to delay of peak onset.**
  The most common side effects are drowsiness, dizziness, confusion and fatigue. Peripheral edema may also be a side effect.
- **Pregabalin:** Similar to gabapentin, but more expensive and **not covered** by the Seniors' or Basic Alberta Blue Cross plans. Other private plans may cover the cost. Pregabalin can be initiated at 25 mg PO nightly and titrated by 25 mg every 7 nights to a maximum of 75 mg PO qhs. It should be taken 2 hours before bedtime. Potential side effects are similar to those of gabapentin.
- **Non-ergot derived dopamine agonists:** These have shown success in reducing RLS symptoms in idiopathic RLS and there are a few limited studies that have examined their role in uremic RLS.
  Note that **all dopamine agonists should be taken 2 hours before sleep due to delay of onset.** Side effects might include headache, insomnia, and nausea; augmentation may occur with long-time usage.

  - Rotigotine transdermal patch 1 mg/24 h applied once daily, may increase by 1 mg/24 h weekly up to a maximum 3 mg/24 h. Requires tapering if discontinuing.
  - Pramipexole 0.125 mg PO 2 hours prior to HS; may increase by 0.125 mg PO Q7days to effect up to a maximum of 0.75 mg/day.
  - Ropinirole 0.25 mg PO 2 hours prior to HS; may increase by 0.25 mg PO Q5-7 days to effect up to a maximum of 2 mg/day.

Adapted from the CKM Restless Legs Guideline for Healthcare Professionals (2018) for the EMPATHY Trial
Last updated: 23 August 2018

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