

# Pharmacological Symptom Management Tips in Advanced CKD/ESRD

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Renal Pharmacists Network Education Evening  
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## Learning Objectives

- Review pharmacological treatment and management algorithm for ...
  - Insomnia
  - Pruritus
  - Pain

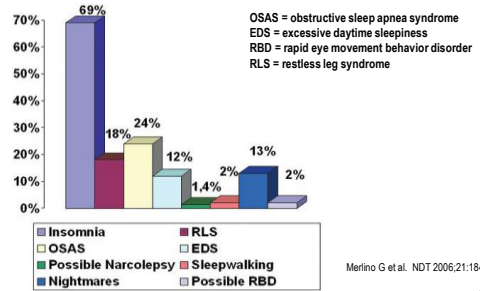


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## Insomnia



## Prevalence



Merlino G et al. NDT 2006;21:184-90.

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## Consequences

- Excessive daytime sleepiness
- Associated with
  - decreased quality of life
  - increased morbidity
  - increased hospitalization
  - increased mortality



Novak M et al. Sem Dial 2006;19:25-31  
 Kosmadakis GC. Int J Artif Organs 2008;31:919-27

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## Contributing Factors



### Pathophysiologic

- Acid-base disorders
- Electrolyte disturbances
- Iron deficiency
- Uremic toxins
- Renal anemia
- Renal neuropathy
- Altered melatonin metabolism
- Others:**
  - Alcohol and caffeine
  - Smoking

### Psychologic

- Mood disorders
- Anxiety
- Sexual problems
- Psychosocial problems

### Lifestyle-related

- Sedentary lifestyle
- Napping during dialysis
- Getting up too early for HD

Novak M et al. Sem Dial 2006;19:25-31

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## Good Sleep Hygiene



- Maintain regular schedule for bedtime and awakening
- Avoid daytime naps or going to bed too early in evening
- Avoid caffeine, nicotine, alcohol, heavy meals, chocolate, excessive sugar or fluid before bedtime
- Exercise regularly during the day but avoid vigorous exercise within 3 hrs of bedtime
- Minimize noise, light & extreme temp in bedroom
- Develop relaxing bedtime rituals, e.g. reading, music
- Get the clock out of visible range to avoid clock watching
- Go to bed only when sleepy
- Get out of bed if unable to sleep within 20 minutes. Return when sleepy

Navak M et al. Sem Dial 2006;19:25-31  
[http://phc.eduhealth.ca/PHC\\_PDFs/FMFM.900.SI82.PHC.pdf](http://phc.eduhealth.ca/PHC_PDFs/FMFM.900.SI82.PHC.pdf)

## Pharmacotherapy of Insomnia



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## Benzodiazepines



	Half life (hr)	Dose	Adverse Effects	Drug Interactions
<b>Short – for early insomnia – onset 15-30 min ** NOT recommended **</b>				
Triazolam	2-5	0.125-0.25 mg	Amnesia, rebound Drowsiness, dizziness, incoordination	No active metabolite; Metabolized by CYP 3A4
<b>Intermediate – for sleep-maintenance insomnia – onset 1-2 hrs</b>				
Lorazepam	10-20	0.5-2 mg	Amnesia, drowsiness, dizziness, incoordination	No active metabolite; Glucuronidation
Oxazepam	5-20	10-30 mg		No active metabolite; Glucuronidation
Temazepam	9.5-12	15-30 mg		No active metabolite; Glucuronidation
<b>Long – ** NOT recommended **</b>				
Diazepam	20-50	2-5 mg	Amnesia, drowsiness, dizziness, incoordination	Active metabolites;
Flurazepam	40-114	15-30 mg		Active metabolites; CYP 3A4/2D6

Estivill E et al. Clin Drug Invest 2003;23:351-85 10

## Non-benzodiazepine GABA agonists

	Zopiclone	Zolpidem	Zaleplon*
Onset	30-60 min	30 min	15-30 min
Duration	5-8 hrs	6-8 hrs	2-4 hrs
Elimination t <sub>1/2</sub>	~5 hrs	2.5-3 hrs	1 hr
Indications	Early and middle insomnia	Early and middle insomnia	Early insomnia
Dosing	5-10mg	10mg (If ≤ 4 hr sleep left 1.75mg ; 3.5mg ;)	7.5-15 mg
Dosing in Elderly	3.75-5mg	5mg*	5 mg
Metabolism	CYP 3A4	CYP 3A4	Aldehyde oxidase

\*available in US only

Bain KT Am J Geriatr Pharmacother 2006;4:168-92 11

## Complex Sleep-Related Behaviors

- e.g. sleep-driving, making phone calls, preparing & eating food while asleep
- No recollection of event
- 90% had some alcohol prior



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## Sedating Antidepressants

### Trazodone

- Usual initial dose: 25-50 mg po HS
- Commonly used in antidepressant-induced insomnia, pts +/- depression
- Adverse effects: orthostatic hypotension, blurred vision, atrial & ventricular arrhythmias, priapism, risk of serotonin syndrome

### Tricyclic antidepressants

- e.g. doxepin, amitriptyline
- Inappropriate for elderly
- Adverse effects: anticholinergic effects, orthostatic hypotension, weight gain, cardiac arrhythmias, increased risk of falls

### Mirtazepine

- Adverse effects: weight gain, anticholinergic effects

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## Sedating Antipsychotics

- e.g. methotrimeprazine, chlorpromazine, olanzapine, quetiapine
- Studies demonstrating the usefulness of these medications for either short- or long-term management of insomnia are lacking
- Not recommended due to risk of long term side effects



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## Sedating Antihistamines

- Diphenhydramine or doxylamine
  - Inappropriate for elderly
    - Anticholinergic effects, increased risk of falls
  - Tolerance after 1-2 wks of continuous use
  - No systematic evidence for efficacy and there are significant concerns about risks of these medications.



<http://consensus.nih.gov>; Bain KT. Am J Geriatr Pharmacother 2006;4:168-92

## Herbal Supplements

- Lack of regulation
  - Large variations in formulation, purity & potency
- Valerian (*Valeriana officinalis*)
- Kava kava (*Piper methysticum*)
  - Safety data limited; case reports of hepatotoxicity in persons taking herbal products containing these



<http://naturalstandard.com>  
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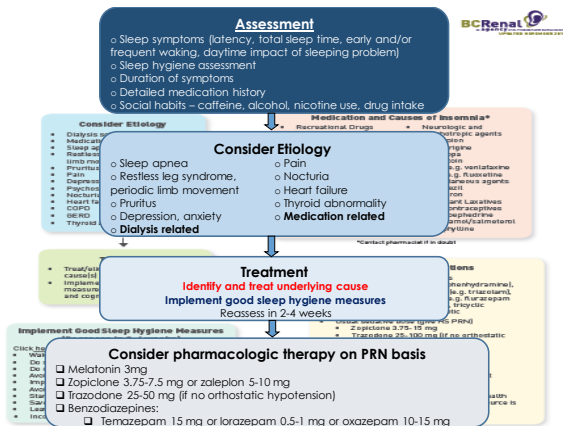
## Melatonin

- Natural hormone produced by the pineal gland
- Little evidence exists for efficacy in the treatment of insomnia or its appropriate dosage, time of administration, toxicity and limited to short term
- 1 DB, PC, x-over study in 24 HD pts using 3mg po HS x 6 wks showed ↓ sleep latency and ↑ sleep efficiency

## L-Tryptophan

- Extremely limited evidence supporting its use
- Concerns with possible toxic effects, esp. in combination with certain psychiatric medications

Estvil E et al. Clin Drug Invest 2003;23:351-85  
Koch BC et al. Br J Clin Pharmacol 2009;67:68-75  
17



Medication causes of insomnia	
<b>Recreational Drugs</b> Alcohol Caffeine Nicotine Amphetamines and Methamphetamines Drug withdrawal Cardiovascular agents Diuretics Beta blockers Endocrine agents Corticosteroids Thyroid hormone Stimulants Methylphenidate Dextroamphetamine	<b>Neurologic and psychotropic agents</b> Levodopa Phenytoin Lamotrigine Bupropion SSRI, e.g. fluoxetine SNRI, e.g. venlafaxine <b>Miscellaneous agents</b> Theophylline Oral Contraceptives Cimetidine Pseudoephedrine Stimulant Laxatives Interferon Donepezil

# Restless Leg Syndrome (RLS)



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# RLS Medication Options



- **Dopamine precursor**
  - Levodopa/carbidopa 100mg/25mg to 200mg/50mg po HS
  - Risk of augmentation, nausea, orthostatic hypotension
- **Dopamine agonists**
  - Decreased risk for augmentation
  - Increased incidence of hypotension and nausea
  - Caution re sleep attack
    - Pramipexole 0.125-0.75mg po HS
    - Ropinirole 0.25-2mg po HS

Molnar MZ et al. Drugs 2006;66:607-24; Miranda M et al. Neurology 2004;62:831-2; Pellicchia MT et al. Clin Neuropharmacol 2004;27:178-81; de Oliveira MM et al. Movement Dis 2010;25:1335-42 21

# RLS Refractory Symptoms

- **Gabapentin**
  - 100mg po HS (max 300mg po HS)
- **Benzodiazepine**
  - Clonazepam 0.5mg po HS
  - Questionable efficacy and potential for dependency and risk of falls
- **Clonidine**
  - 0.05mg po HS
  - Watch hypotension



Molnar MZ et al. Drugs 2006;66:607-24; de Oliveira MM et al. Movement Dis 2010;25:1335-42; Thorp ML. AJKD 2001;38:104-8; Mcozokadioglu H. Ren Fail 2004;26:393-7 22

<p><b>Assessment</b></p> <ul style="list-style-type: none"> <li>• Rule out mimic disorders</li> <li>• Rule out drug-induced RLS</li> <li>• Assess risk/contributing factors                     <ul style="list-style-type: none"> <li>• Iron deficiency</li> <li>• Sleep deprivation</li> <li>• Positive family history</li> <li>• Rheumatoid arthritis or Sjogren's</li> <li>• Pregnancy</li> </ul> </li> </ul>	<p><b>Mimic Conditions</b></p> <ul style="list-style-type: none"> <li>• Movement disorders: akathisia, ADHD</li> <li>• Restlessness secondary to anxiety, depression, psychotic disorders</li> <li>• Local leg pathology: e.g. peripheral neuropathy, myelopathy, peripheral venous congestion</li> <li>• Positional discomfort</li> </ul>
<p><b>Initial Recommendation</b></p> <ul style="list-style-type: none"> <li>• Discontinue or reduce offending drug, if feasible</li> <li>• Correct iron deficiency – may prevent initial augmentation with dopaminergic therapy</li> <li>• Encourage good sleep hygiene (see insomnia flowchart) <a href="http://phc.eduhealth.ca/PHC_PDFs/FM/FM.900.S182.PHC.pdf">http://phc.eduhealth.ca/PHC_PDFs/FM/FM.900.S182.PHC.pdf</a></li> </ul>	<p><b>Drug-induced RLS</b></p> <ul style="list-style-type: none"> <li>• Dopamine antagonists:                     <ul style="list-style-type: none"> <li>• Antipsychotics: pimozide, haloperidol, olanzapine, risperidone</li> <li>• Metoclopramide, promethazine</li> </ul> </li> <li>• Antidepressants:                     <ul style="list-style-type: none"> <li>• Mirtazapine (up to 28%)</li> <li>• SSRI (&lt;5%) e.g. citalopram, escitalopram, fluoxetine, paroxetine, sertraline</li> <li>• SNRI's (&lt;5%), e.g. duloxetine, venlafaxine</li> </ul> </li> </ul> <p>Stimulants: alcohol, caffeine, nicotine Others: TCA's, carbamazepine, lithium</p>
<p><b>Medication options</b></p> <ul style="list-style-type: none"> <li>• Avoid opioids and quinine</li> <li>• For intermittent RLS: Levodopa/carbidopa</li> <li>• For daily RLS; dopamine agonist</li> <li>• For RLS with painful neuropathy: gabapentin</li> </ul>	<p><b>Refractory Symptoms</b></p> <ul style="list-style-type: none"> <li>• Clonazepam</li> <li>• Clonidine</li> </ul>

variable efficacy and adverse effects due to clonazepam's 20% 7.2 mg po HS 23

# Pruritus



# Prevalence

- Predialysis: 15-49%
- Hemodialysis or peritoneal dialysis: 50-90%
- 84% daily or nearly daily itch
- 46% rated itch as moderate or severe
- 59% reported ongoing itch for > 1 year



Mathur VS et al. CJASN 2010;5:1410-9; Narita I et al. J Nephrol 2008;21:161-5 25

## Consequences

- Decreased Quality of life
- Insomnia
  - 70% complained of insomnia due to itch with score  $\geq 7$
- Mood disorders
- Increased mortality associated with high itch score

Narita I et al. J Nephrol 2008;21:161-5  
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## Pathogenesis

- Stimulating influences
  - Ca/P deposits in epidermis
  - Secondary hyperparathyroidism
  - Sensitivity to dialysis products
- Dermatological abnormalities
- Immune system derangement
- Imbalance of endogenous opioidergic system
- Neuropathic injury

Narita I et al. J Nephrol 2008;21:161-5  
Patel TS et al. AJKD 2007;50:11-20  
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## Non-Drug Measures

- Use gentle soap
- Apply soap only to axillae and groin/perineum (except if visibly dirty)
- Avoid excessive bathing or bathing with hot water – use only lukewarm water
- Eliminate wool or irritating clothing
- Keep finger nails trimmed



Headley CM et al. Nephrol Nurs J 2002;29:525-41

## Emollient

- Cream with high water content
- NO lotion
- NO fragrance
- NO or few preservatives
- Apply liberally at least BID and after bathing



Headley CM et al. Nephrol Nurs J 2002;29:525-41

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## Topical

- **Capsaicin 0.025% cream TID-QID**
  - Mechanism: depletes substance P
  - Side effects: local burning, stinging, erythema
  - Localized area only
- **Topical steroids**
  - Localized area only
  - Lack of studies
- **$\gamma$ -linoleic acid (GLA) 2.2% cream or GLA rich evening primrose oil TID-QID**
  - Mechanism:  $\downarrow$  lymphocyte proliferation and lymphokine production



Tang DC et al. Nephron 1996;72:617-22;  
Chen YC et al. AJKD 2006;48:69-76  
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## Systemic

- **Antihistamine**
  - Sedating antihistamine, e.g. hydroxyzine
    - Marginal benefit
    - Lack of studies
  - Non-sedating antihistamine – not effective
- **gabapentin**
  - Dose: 100mg PO post dialysis x 4 wks, titrate to effect (max: 300mg post HD for dialysis pts)
  - Side effects: dizziness, somnolence, ataxia



Keith-Reddy SR et al. KI 2007;72:373-7  
Patel TS et al. AJKD 2007;50:11-20  
Gunal AI. NDT 2004;19:3137-9  
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## Others...

- **Active Charcoal**
  - Mechanism: bind pruritogens in intestinal lumen
  - Dose: up to 6g/day
  - Side effects: adsorption of other meds, tolerability
- **Cholestyramine**
  - Dose: 5g po bid
- **Conflicting evidence:**
  - Naltrexone, ondansetron, epoetin
- **Difficult to access:**
  - Thalidomine, nalfurafine

Mettang T et al. NDT 2002;17:1558-63  
32

## Evidence...or lack of...

Treatment	Study Type	n	Response
Emollient	Open noncontrolled	21	Remission in 9
Capsaicin 0.025% cr TID x 2wks 0.03% oint QID x 4wks	DB, x-over R,DB,PC,x-over	19 34	Remission in 5; ↓ in 9 ↓84% in pruritus score
γ-linolenic acid 2.2% cr	R,DB,PC, x-over	16	↓40% in pruritus score
Gabapentin 300mg post HD 400mg twice/wk 100mg post HD	R,DB,PC,x-over R,DB,PC,x-over DB,PC,x-over	25 34 25	↓85% in VAS ↓79% in pruritus score ↓94% in pruritus score
Pregabalin 25mg po HS	Open, noncontrolled	12	↓77% in VAS
Activated charcoal 6g/day x 8 wks	PC, x-over	11 23	↓33% in pruritus score Remission in 10, ↓ in 10
Cholestyramine 5g bid	PC, DB	10	↓47% in pruritus score in 4 treated

Morton CA et al NDT 1996;11:2031-6. Chen YC et al AJKD 2006;48:69-76. Tang DC et al Nephron 1996;72:817-22. Goral AI et al NDT 2004;19:3137-9. Nami AA et al Saudi J Kidney Dis Transpl 2007;18:378-81. Marcell L et al NDT 2005;20:1278-9. Saegren E et al Ren Failure 2005;31:65-69. Kozars G et al Ren Care 2010;36:186-9. Pedersen JH et al Ann Intern Med 1980;93:446-8. Giovannetti S et al Nephron 1995;70:193-6. Silverberg DS et al BMJ 1977;1:752-3. Lugon JR, Jr 2006;9:180-8  
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### Assessment

**General History**

- Generalized vs localized pruritus
- Duration of pruritus
- Character of pruritus (e.g paroxysmal, continuous)
- Exacerbating and relieving factors
- Detailed drug history

**Physical Examination**  
(check for signs of severe pruritus)

- Physi
- Erupt
- Pruri
- Liche

### Consider Etiology

**Uremia Related:**

- Xerosis
- HD adequacy
- Anemia (CKD or iron-deficiency)
- Secondary hyperparathyroidism

**Unrelated:**

- Infections (scabies, lice, etc)
- Allergy

**Check Ca/P/PP**

**Consider and adjust PRN:**

Hydroxyzine or Diphenhydramine or Mefenorex or Citrasate

### Non-Pharmacological Measures

- Use gentle soap e.g. Dove
- Apply soap only to axillae and groin/perineum (arms or legs are visibly dirty)
- Avoid excessive bathing or bathing with hot water
- Eliminate used or irritating clothing

**Localized Itchiness**

- Topical steroids cream vs ointment
- low vs very high potency
- Capsaicin

**Generalized Itchiness**

- Oral Antihistamines hydroxyzine diphenhydramine
- Gabapentin

**Refractory Symptoms**

- Doxepin
- Dermatology Consult



## Prevalence in Renal Patients

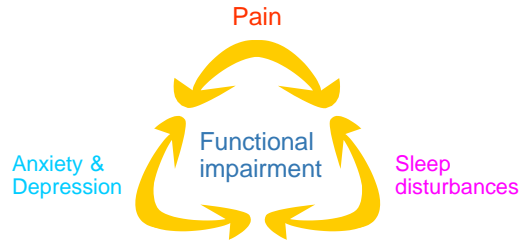
Literature suggests:

- ~37-50% hemodialysis (HD) pts report pain
- 20-30% pts rated their pain as severe
- 50% of pts who withdrew from HD had significant pain and other distressing symptoms



Davison BN JAASN 2003;42:1239-47  
Davison BN JAASN 2002;31:590A  
Cohen LM AJKD 2000;36:140-4

## Decreased Quality of Life (QoL)



# Multifactorial Causes



## Non-Renal Related

- DM neuropathy
- PVD with ischemic limbs
- Musculoskeletal e.g. arthritis
- Others...

## Renal Related

- Renal bone disease
- Osteomyelitis & discitis
- HD related
  - Needling
  - Muscle cramps
  - Headaches
  - Steal syndrome
  - Amyloid arthropathy
- PD related
  - abdominal distension/back pain
  - peritonitis
- Calcific uremic arteriolopathy
- Polycystic Kidney

Davison SN. J Palliative Med 2007;10:1277-87

# What are specific issues related to renal patients?



# A typical renal patient has...

- Multiple co-morbidities
- Polypharmacy
- Reduced clearance for some drugs
- Increased dialysis clearance for some drugs



## Sensitivity to medications!!!

Ferro CJ et al. Management of pain in renal failure In: Supportive Care for the Renal Patient. EJ Chambers, M Germain, EA Brown (eds) Davison SN. J Palliative Med 2007;10:1277-87

# Barriers to Adequate Pain Relief



- Pts may under-report pain
  - assuming pain is part of underlying condition or dialysis
- Lack of research in pain management in renal pts
- Lack of analgesic pharmacokinetic/ pharmacodynamic data in renal pts
- Lack of training in pain management
- Adverse effects of analgesics may mimic uremic symptoms

Ferro CJ et al. Management of pain in renal failure In: Supportive Care for the Renal Patient. EJ Chambers, M Germain, EA Brown (eds) Davison SN. J Palliative Med 2007;10:1277-87

Opioids	Comments
<b>Mild Pain</b>	
codeine	~10% pts lack the enzyme to convert codeine to morphine. May cause more nausea & constipation than other narcotics
<b>Moderate Severe Pain</b>	
morphine	Active metabolites renally cleared and may accumulate in ESRD. Caution with chronic use in renal pts
hydromorphone	Slightly shorter duration than morphine. Less accumulation than morphine in pts with renal failure
oxycodone	Limited data in renal dysfunction – caution
fentanyl	<ul style="list-style-type: none"> <li>• Causes less nausea or histamine release</li> <li>• Transdermal patch is not recommended for acute pain or narcotic naive pts; patch may last up to 72 hrs but small # of pts may require q48hr dosing</li> </ul>
methadone	Accumulates with repeated dosing, esp on days 2-5. Variable half-life (17-128hrs), longer to titrate. Use with caution in elderly. Blocks NMDA receptor; slow development of tolerance.
Meperidine	Not recommended for post-op or chronic pain management. Neurotoxic and seizure risk. Metabolites accumulate in renal dysfunction.

Ferro CJ et al. Management of pain in renal failure In: Supportive Care for the Renal Patient. EJ Chambers, M Germain, EA Brown (eds) Davison SN. J Palliative Med 2007;10:1277-87

# Opioids



Adverse Effects	Management
<b>CNS</b>	
Sedation/dizziness	Slow titration; Not to drive
Myoclonus	↓ Dose or Switch to hydromorphone
Confusion/delirium	↓ Dose or Switch to hydromorphone
<b>CVS</b>	
Hypotension/bradycardia	↓ Dose; atropine
<b>Resp</b>	
Respiratory depression	↓ Dose; naloxone
<b>GI</b>	
Nausea/vomiting	Antiemetics
Constipation	Fluid; exercise; bulking agent; stool softener; stimulant
<b>Pruritus</b>	Switch opioids; antihistamines

Lynch ME et al. Pain Res Manage 2006;11:11-38

## Antidepressants

- Tricyclic Antidepressants
  - Most literature support for amitriptyline
  - Similar analgesic effects between agents
  - Differs in degree of adverse effects
  - Caution in elderly, heart conduction abnormality
  - Titrate doses slowly
  - Medications for symptom relief
- Serotonin norepinephrine-reuptake inhibitors (SNRIs)
  - venlafaxine (Effexor®), duloxetine (Cymbalta®)
  - Effective in neuropathic pain
  - Better tolerated than TCAs
  - Renal dose adjustment needed
- Selective serotonin-reuptake inhibitors (SSRIs)
  - fluoxetine (Prozac®), paroxetine (Paxil®)
  - Less effective analgesia

Lynch ME et al. Pain Res Manage 2006;11:11-38; Ferro CJ et al. Management of pain in renal failure In: Supportive Care for the Renal Patient. EJ Chambers, M Germain, EA Brown (eds), Davison SN. J Palliative Med 2007;10:1277-87

## Tricyclic Antidepressants

Side Effects	Amitriptyline (Elavil®)	Imipramine (Tofranil®)	Nortriptyline (Aventyl®)	Desipramine (Norpramin®)
Sedation	++++	+++	+	+/-
Confusion	++++	+++	+	+
Orthostatic Hypotension	+++	+++	+	++
Arrhythmia	++	++	++	++
Anticholinergic	++++	+++	++	+
Weight Gain	++++	+++	++	++

Most ADRs  Fewest ADRs

Lynch ME et al. Pain Res Manage 2006;11:11-38

## Anticonvulsants

- Gabapentin first line
- Adverse effects: Somnolence, dizziness, ataxia

	gabapentin	pregabalin
<b>Absorption</b>	Saturable	Non-saturable across dose range
<b>Oral bioavailability</b>	60% 900mg 47% 1200mg 34% 2400mg 33% 3600mg	≥ 90%
<b>Renal Elimination</b>	70-80%	90-99%
<b>Renal Impairment</b>	Dosage adjustment	Dosage adjustment
<b>Dialyzability</b>	Yes	Yes
<b>Onset of action</b>	≥ 9 days	1-3 days

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## Topiramate

- Limited evidence for analgesia
- Adverse effects:
  - CNS: fatigue, nervousness, confusion, mood changes, dizziness, cognitive dysfunction, speech disorders, ataxia, paresthesias
  - kidney stones, altered taste, acute angle glaucoma
- Renal dose adjustment needed

## Nabilone

- Synthetic cannabinoid
- Adverse effects:
  - Sedation, euphoria, poor concentration, vertigo, dysphoric mood, hypotension, dry mouth, visual disturbances
- No renal dosage adjustment needed
- Start with 0.5mg PO HS

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## Recommended Analgesics

- |   |  |
|---|--|
| <p><b>YES</b></p> <ul style="list-style-type: none"> <li>• acetaminophen</li> <li>• Topical NSAIDs</li> <li>• Opioids                             <ul style="list-style-type: none"> <li>• hydromorphone</li> <li>• oxycodone</li> <li>• fentanyl</li> <li>• methadone</li> </ul> </li> <li>• tramadol*</li> <li>• Anticonvulsants*</li> <li>• Antidepressants                             <ul style="list-style-type: none"> <li>• TCAs</li> <li>• SNRIs*</li> </ul> </li> <li>• Cannabinoids</li> </ul> | <p><b>NO</b></p> <ul style="list-style-type: none"> <li>• NSAIDs</li> <li>• codeine</li> <li>• morphine</li> <li>• meperidine</li> </ul> <p>* Dosing adjustment may be required for some medications</p> |
|---|--|

Ferro CJ et al. Management of pain in renal failure In: Supportive Care for the Renal Patient. EJ Chambers, M Germain, EA Brown (eds)

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**Renal Analgesic Brochure**

**OPIOID**  
Hydromorphone (Dilaudid® and Hydromorphon®)

**Indications**  
Not indicated to treat nociceptive or musculoskeletal pain.  
Acute or chronic pain.  
Neuropathic pain – higher doses.

**Mechanisms of Action**  
Mu receptor agonist.

**Pharmacokinetics**  
Normal half life 2.5 hrs. Oral bioavailability 10%; Extensive hepatic metabolism; +12% excreted unchanged in urine; Clearance: metabolites are excreted renally.

**Adverse Effects**  
Opioid related adverse drug reactions (see hydromorphone). May have less adverse effects than morphine in some patients, e.g. constipation, dizziness, nausea, vomiting, blur of vision and dry mouth with renal impairment due to active hydromorphone-3- glucuronide metabolite.

**Dosing Guidelines (normal)**  
Start low and titrate to effect, e.g. 0.5 to 1 mg PO q2-4h, sustained release 3 mg PO bid. Available PO, transdermal release, sustained release (e.g. hydromorphone Control® and Hydromorphone Transdermal® – SPC/DA).

	>50 (ml/min)	10 to 50 (ml/min)	<10 (ml/min)
	100%	75%	50%

**Renal Dosing**

	HD	PD
	No	No

**HD/PD Dose**

**Coverage**  
Hydromorphone 0-90%  
Hydromorphone IR - Not licensed for patients in Patient Care Program or Special Authority required for patients using extended or intrathecal hydromorphone IR or morphine IR.

**Cost**  
Hydromorphone IR 3 mg PO q2h, 527.60  
Hydromorphone IR 3 mg PO bid, 145.40

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## Nociceptive Pain

**Pain Score 1-4**  
Acetaminophen  
Topical NSAID or capsaicin

**Pain not controlled or initial pain > 3**

**ADD OPIOID**  
Avoid morphine or meperidine

- Hydromorphone 0.25-0.5 mg PO or oxycodone 1.25-2.5mg PO Q3-4H prn
- Once stable, consider CR formulation or fentanyl patch
- + breakthrough 1/10<sup>th</sup> total daily dose PO Q2H prn

**Alternatives**  
Tramadol (Ultracet) - If has opioid tolerance, avoid tramadol.  
PO bid (Tolma)  
Acetaminophen  
Maximum (daily)

- Tramadol
- Buprenorphine
- Methadone

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## Neuropathic Pain

**Pain Score 1-4**  
Gabapentin 100 mg PO HS  
Topical capsaicin

**Pain not controlled or initial pain > 3**

**Ineffective or intolerable side effects**

- Add nortriptyline/desipramine 10mg PO daily
- Consider opioid – hydromorphone or oxycodone
- Alternatives:
  - nabilone
  - topiramate
  - pregabalin
  - THC:CBD spray (Sativex®)

Previous Opioid Algorithm

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## ESAS Scores at Baseline and 1 Year at St. Paul's Hosp HD unit

• Mean scores reduced for all symptoms after 1 year of ESAS assessment (n=187)

• Statistically significant decreases with tiredness, depression and drowsiness

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## Percentage of Pts with SEVERE Symptoms at Baseline vs 1 Year

• % patients with severe scores reduced for all symptoms (except for itchy) after 1 year of ESAS assessment (n=187)

54

