What’s New in Drug Therapy?
2016 Update

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Objectives

1. List new drugs approved by the FDA in 2015. For each drug the participant will be able to describe the approved indication, unapproved uses of the medication, common adverse effects and drug interactions. For each new medication, identify pertinent information regarding each, including drug indication(s), usual dosing, contraindications, major warnings/precautions, and major drug interactions.

2. For each new relevant medication approved in 2015, describe the burden to-benefit ratio and the role of the medication in caring for patients with advanced illness.

3. Analyze important drug alerts and breaking drug news and their relevance to drug therapies commonly used in hospice and palliative care patients.

4. Describe three intriguing tips and tricks in medication management in advanced illness.
51 New Drugs in 2015!

DiABETES
Concentrated Insulin Glargine (Toujeo)

- A more concentrated form of insulin glargine
  - 300 IU/ml (Lantus = 100 IU/ml); disposable prefilled pen
- More gradual and prolonged release from SQ site than Lantus – even more peakless!
- Injected once daily at same time
  - Same dose if switching from other QD LA insulin
    - May need 10-15% more Toujeo vs. Lantus
    - If switching from NPH, start at 80% TDD NPH

<table>
<thead>
<tr>
<th>Insulin</th>
<th>Price/Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Humulin N</td>
<td>$278</td>
</tr>
<tr>
<td>Novolin N</td>
<td>$219</td>
</tr>
<tr>
<td>Novolin N (Walmart)</td>
<td>$50</td>
</tr>
<tr>
<td>Levemir</td>
<td>$298</td>
</tr>
<tr>
<td>Lantus</td>
<td>$298</td>
</tr>
<tr>
<td>Toujeo</td>
<td>$335</td>
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</tbody>
</table>

Insulin Degludec (Treshiba)

- Once-daily ULTRA long-acting insulin (42 hours)
- A1c lowering ~ insulin glargine
- ~$450/month (vs. ≤ $400 for Lantus, Levemir, Toujeo; vs. $40 for NPH)
- Use same time each day
- Reserve for patients who need over 80 units/injection
  - Tresiba200 units/ml pen delivers up to 160 units/dose
- Basaglar (insulin glargine) approved
SGL T2 Inhibitor News

• Empagliflozin/Metformin – Synjardy – T2DM
• Empagliflozin vs. placebo
  – No difference in MI or CVA
  – 32-38% risk reduction in CV deaths, hospitalization from HF, or death from any cause
• Canagliflozin increased fracture rate (decreased bone mineral density)
• Ketoacidosis risk
  – T2DM
  – MOA unknown

<table>
<thead>
<tr>
<th>Drug</th>
<th>Trade (all $363/mo)</th>
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</thead>
<tbody>
<tr>
<td>Canagliflozin</td>
<td>Invokana</td>
</tr>
<tr>
<td>Canagliflozin/Metformin</td>
<td>Invokamet</td>
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<tr>
<td>Dapagliflozin</td>
<td>Farxiga</td>
</tr>
<tr>
<td>Dapagliflozin/Metformin</td>
<td>XigduoXR</td>
</tr>
<tr>
<td>Empagliflozin</td>
<td>Jardiance</td>
</tr>
<tr>
<td>Empagliflozin/Metformin</td>
<td>Synjardy</td>
</tr>
</tbody>
</table>


Liraglutide (Saxenda) for Weight Loss

• GLP-1 receptor agonist (Victoza for T2DM)
• Approved at higher dose as Saxenda for chronic weight management (3 mg SQ once daily)
  – Adults with BMI ≥ 30 or BMI ≥ 27 (with HTN, dyslipidemia, DM)
• MOA – decreases caloric intake; unknown
• Adverse effects – nausea, vomiting, diarrhea, constipation, headache, anorexia, dyspepsia
  – Acute pancreatitis, cholelithiasis, ARFx/CRFx, suicidal thoughts, neuropsychiatric reactions, thyroid C tumors (rats)
  – Pregnancy category X
• Weight loss – 6 kg after one year; $1068/month (!)
Who’s With Me?
(Who Slipped Out for a Donut?)

Which of the following insulin products has the LONGEST duration of action?

A. Toujeo (concentrated insulin glargine)
B. Treshiba (insulin degludec)
C. Basaglar (insulin glargine)
D. NPH insulin
Sacubitril/Valsartan (Entresto)

- **Sacubitril** - converted to LBQ657 (active metabolite)
  - Neprilysin inhibitor – increases natriuretic peptides and bradykinin
  - Reduces vasoconstriction and sodium retention
- **Valsartan** - ARB
  - Inhibits angiotensin II and release of aldosterone
  - CV and renal benefits
- **Indication** – to reduce risk of CV death and hospitalization for HF in NYHA Class II-IV and reduced EF
  - Used with other HF therapies, in place of an ACEI or ARB

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**PARADIGM-HF**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Enalapril 10 mg BID</th>
<th>Sacubitril/Valsartan 97 mg/103 mg BID</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary endpoint: First hospitalization for worsening HF or CV death</td>
<td>26.5%</td>
<td>21.8%</td>
</tr>
<tr>
<td>First hospitalization for worsening HF</td>
<td>15.6%</td>
<td>12.8%</td>
</tr>
<tr>
<td>Death from CV causes</td>
<td>16.5%</td>
<td>13.3%</td>
</tr>
<tr>
<td>All cause mortality</td>
<td>19.8%</td>
<td>17.0%</td>
</tr>
</tbody>
</table>

Sacubitril/Valsartan (Entresto)

- Film-coated, unscored, ovaloid-shaped tablet

<table>
<thead>
<tr>
<th>Strength</th>
<th>Sacubitril</th>
<th>Valsartan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Entresto 50</td>
<td>24 mg</td>
<td>26 mg</td>
</tr>
<tr>
<td>Entresto 100</td>
<td>49 mg</td>
<td>51 mg</td>
</tr>
<tr>
<td>Entresto 200</td>
<td>97 mg</td>
<td>103 mg</td>
</tr>
</tbody>
</table>

- **Dosing**
  - Starting dose Entresto 100 twice daily
  - Increase every 2-4 weeks to target dose
  - Reduce starting dose (Entresto 50 twice daily) if no ACEI or ARB previously, severe renal impairment (CLcr < 30ml/min) or moderate hepatic impairment
  - 36 hour wash out from ACEI

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Sacubitril/Valsartan (Entresto)

- **Adverse effects**
  - Hypotension (18%), hyperkalemia (12%), cough (9%), dizziness (6%), renal failure/acute renal failure (5%)

- **Contraindications**
  - History of angioedema from ACEI or ARB
  - Concomitant use of ACEI or ARB
  - Concomitant use of aliskiren in patients with diabetes
  - Severe hepatic impairment
  - Do not use during pregnancy

- **Commentary**
  - BB, ACEI or ARB, aldosterone antagonist, +/- diuretic
  - $375/month
Ivabradine (Corlanor)

• **Indication** – reduction of hospitalization in patients with chronic HF with the following:
  – Stable, symptomatic HF
  – LVEF of ≤ 35%
  – Sinus rhythm with resting HR of ≥ 70 bpm
  – On maximum tolerated doses of beta blockers, or contraindication to beta blockers

• **Mechanism of action** – slows HR by inhibiting the cardiac pacemaker If current.
  – No effect on ventricular repolarization or myocardial contractility

Ivabradine (Corlanor)

• **Clinical Trials**
  – SHIFT – 6,558 adults, NYHA II-IV HF, h/o hospitalization
  – On standard therapy +/- ivabradine; 22.9 months f/u
    • Worsening HF or CV death – 24% vs. 29%
    • Hospitalization for worsening HF – 16% vs. 21%
    • Death due to HF – 3% vs. 5%
    • Cardiovascular death – 14% vs. 15% (not significant)
  – BEAUTIFUL – no difference in outcomes
  – SIGNIFY – no difference in outcomes

• **Adverse Effects** – bradycardia, hypertension, atrial fibrillation, visual disturbances

Ivabradine (Corlanor)

- **Contraindications to therapy**
  - Acute decompensated HF
  - BP < 90/50 mmHg
  - Sick sinus syndrome, sinoatrial block, 3rd degree AV block (without functioning pacemaker)
  - Resting heart rate < 60 bpm before treatment
  - Severe hepatic impairment (Child-Pugh C)
  - Pacemaker dependence
  - Concomitant use of strong 3A4 inhibitors
  - Do not use in pregnancy

- **Dosage** – 5 mg bid with meals; increase per HR
- **Cost** - ~ $375/month


Cangrelor Kengreal

- IV platelet inhibitor
- Adjunct to percutaneous coronary intervention
  - If not pre-treated with a platelet inhibitor (clopidogrel, prasugrel, ticagrelor) and not on a glycoprotein IIb/IIIa inhibitor (abciximab, eptifibatide, tirofiban)
- **Dose** – 30 mcg/kg as IV bolus before PCI, then 4 mcg/kg/min IV infusion for duration of procedure or for 2 hours, whichever is longer. Start platelet inhibitor after stopping cangrelor.
- **Efficacy** – as good or better than clopidogrel
- **Adverse effect** - bleeding
Vorapaxar (Zontivity)

- **First protease-activated receptor-1 antagonist**
  - Inhibits platelet aggregation for about 4 weeks
  - PARs facilitate the action of thrombin in the formation of thrombi.
  - PAR-1 has a high affinity for thrombin and is found primarily on platelets, smooth muscle cells, endothelial cells
  - Vorapaxar is a selective, reversible antagonist

- **Indication** – For use with low-dose aspirin and/or clopidogrel after MI in in patients with PAD

- **Dose** – 2.5 mg once a day

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Vorapaxar (Zontivity)

- **Contraindications:**
  - History of CVA, TIA, intracranial hemorrhage, active pathologic bleeding
  - Increased risk of bleeding, use of anticoagulants, NSAIDs, SSRIs, SNRIs
  - Severe hepatic impairment, 3A4 inhibitors

- **Precautions:**
  - Do not use as monotherapy
  - Do not combine with Effient or Brilinta (not studied)
  - LONG half-life – no antidote to reverse its antiplatelet effects – may require transfusion

- **Cost** - ~ $300/month
New Class Lipid-Lowering Drugs

• PCSK9 Inhibitors (proprotein convertase subtilisin/kexin type 9)

• **Indication** – Adjunct to diet and maximally tolerated statin therapy for adults with heterozygous familiar hypercholesterolemia or clinical atherosclerotic CV disease who require additional LDL-C lowering

<table>
<thead>
<tr>
<th>Generic</th>
<th>Trade</th>
<th>Dose</th>
<th>Cost/Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alirocumab</td>
<td>Praluent</td>
<td>75 – 150 mg SC q2weeks</td>
<td>$13,440</td>
</tr>
<tr>
<td>Evolocumab</td>
<td>Repatha</td>
<td>140 mg SC q2weeks or 420 mg SC once/month</td>
<td>$13,015</td>
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</table>

New Class Lipid-Lowering Drugs

• PCSK9 Inhibitors (proprotein convertase subtilisin/kexin type 9)

• **Mechanism** – PCSK9 binding to LDL receptors on hepatocytes:
  – Promotes receptor degradation
  – Prevents LDL-C clearance from blood
  – Increases serum concentration of LDL-C

• PCSK9 are monoclonal antibodies that target PCSK9, preventing binding to LDL receptors and increasing uptake of LDL-C.

• Lower LDL-C 40-60%; effects on CV outcomes unknown
Yay! ONE NOAC Reversal Agent

- **Idarucizumab** (Praxbind)
- First reversal agent for one of the NOAC’s (novel oral anticoagulant) – **dabigatran (Pradaxa)**
- Dabigatran is a **thrombin inhibitor**
  - Won’t work for factor Xa inhibitors (rivaroxaban [Xarelto], apixaban [Eliquis], edoxaban [Savaysa])
- Reverses dabigatran in most patients within 4 hours, stops bleeding within about 11 hours
- Used for life-threatening bleeding, or when reversal is needed within 8 hours for emergency surgery
- **Dose** – 5 grams (2 x 2.5 g) IV; $3500

24 Hour Extended-Release Aspirin (Durlaza)

- **WHAT?**
- Indicated for secondary prevention of MI and CVA
- Efficacy was shown from EARLIER clinical trials of low-dose ASA in preventing secondary CV events, and bioequivalence compared to IR aspirin
- 162.5 mg capsules; take one daily
- $6 per capsule; Rx only
- No evidence it’s as safe or effective as low dose IR aspirin in preventing CV events!
Hepatitis C

- FDA approved **daclatasvir** (Daklinza) – oral direct-acting anti-viral drug
  - Daclatasvir 60 mg po qd + sofosbuvir (Sovaldi) 400 mg for 12 weeks ($147,000)
  - For hepatitis C genotype 3 (<10% HCV in US)
- FDA approved **Technivie** (ombitasvir + paritaprevir + ritonavir) – HCV genotype 4 – 12 weeks $76,000
  - Ombitasvir/paritaprevir/ritonavir + dasabuvir = Viekira Pak for HCV 1 genotype
  - Caution with moderate to severe hepatic impairment
- **Harvoni** (ledipasvir + sofosbuvir) approved for HCV genotypes 4, 5 and 6 (in addition to type 1)
Ferric Citrate (Auryxia)

- **Indication** – Oral phosphate binder used to treat hyperphosphatemia in chronic kidney disease on dialysis.
- **Mechanism** – Ferric iron binds to dietary phosphate in the GI tract; precipitate is eliminated in the stool.
- **Adverse effects** – Diarrhea (21%), nausea, vomiting, constipation, cough (> 5%). Increases iron stores.
- **Dose** – 2 g tid with meals (up to 12 g qd)
- **Cost** - ~$1100/month

Patiromer (Veltassa)

- **Indication** – Chronic hyperkalemia
- **Mechanism** – Potassium binder; exchanges calcium instead of sodium to bind potassium
- **Cost** - ~$20/day
- **Administration** – must be spaced 6 hours from ALL other oral meds to avoid binding.
  - Powder in single-use packets (8.4 gm, 16.8 g, 25.2 g)
  - Store in refrigerator
Deoxycholic Acid (Kybella)

• **Indication** – SC injection used to improve appearance of moderate to severe convexity or fullness associated with submental fat (double chin) in adults. This is a firstie!

• **Mechanism** – Deoxycholic acid – endogenous bile acid that solubilizes dietary fat in the gut.
  – Injected into SC fat tissue, solubilizes lipids in adipocyte membranes.
  – Induces inflammatory response that clears cell debris.

• **Adverse effects** – 20%; edema, bruising, pain, numbness, erythema, induration at injection site

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Deoxycholic Acid (Kybella)

• **Dosage**
  – Each 2 ml vial contains 20 mg deoxycholic acid
  – Dose is 2 mg/cm² administered as 0.2 ml injections, 1 cm apart
  – Inject into SC fat tissue
  – May receive up to 6 treatments, spaced at least 1 month apart, no more than 50 injections (10 ml) given in a single treatment session.
  – One 2 ml vial = $300
  – Six treatment sessions ~ $9,000!
Flibanserin (Addyi)

• **Indication** – Treatment of premenopausal women with acquired, generalized hypoactive sexual desire disorder (HSDD). Another firstie!

• **HSDD** – A deficiency or lack of sexual thoughts or desire that causes personal distress or interpersonal difficulty.
  – Up to 14% of premenopausal woman 20-49 years old

• **Mechanism** – Unknown. 5-HT1A agonist; 5-HT2A antagonist.
  – Animal models – decreases serotonin and increases norepinephrine and dopamine in pre-frontal cortex

Flibanserin (Addyi)

• **Dose** – 100 mg once daily at bedtime

• **Efficacy** - ~ 10% premenopausal women reported “much” or “very much” improvement in their condition, vs. placebo.

• **Adverse effects** – hypotension, syncope, CNS depression; alcohol exacerbates

• **Drug interactions** – many

• **Cost** – $800/month
## Miscellaneous New Molecular Entities

<table>
<thead>
<tr>
<th>Brand</th>
<th>Generic</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alecensa</td>
<td>Alectinib</td>
<td>Oral kinase inhibitor for NSCLC</td>
</tr>
<tr>
<td>Avycaz</td>
<td>Ceftazidime/avibactam</td>
<td>Cephalosporin/beta-lactamase inhibitor for complicated intra-abdominal and UTI</td>
</tr>
<tr>
<td>Bridion</td>
<td>Sugammadex</td>
<td>IV agent for reversal of neuromuscular blockade by rocuronium or vecuronium</td>
</tr>
<tr>
<td>Cholbam</td>
<td>Cholic acid</td>
<td>Bile acid for patients with certain genetic metabolic conditions</td>
</tr>
<tr>
<td>Cotellic</td>
<td>Cobimetinib</td>
<td>Oral kinase inhibitor for advanced melanoma</td>
</tr>
<tr>
<td>Cresemba</td>
<td>Isavuconazonium</td>
<td>Azole antifungal for invasive aspergillosis and mucormycosis</td>
</tr>
<tr>
<td>Farydk</td>
<td>Panobinostat</td>
<td>Histone deacetylase inhibitor for multiple myeloma</td>
</tr>
<tr>
<td>Genvoya</td>
<td>Elvitegravir, cobicistate, emtricitabine, tenofovir, alafenamide</td>
<td>Fixed dose combo for HIV-1 infection</td>
</tr>
</tbody>
</table>

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</thead>
<tbody>
<tr>
<td>Ibrance</td>
<td>Palbociclib</td>
<td>Akinase inhibitor for advanced breast cancer</td>
</tr>
<tr>
<td>Lenvima</td>
<td>Lenvatinib</td>
<td>A kinase inhibitor for advanced thyroid cancer</td>
</tr>
<tr>
<td>Lonsurf</td>
<td>Tipiracil/trifluridine</td>
<td>New oral combination formulation for metastatic colorectal cancer</td>
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<tr>
<td>Ninlaro</td>
<td>Ixazomib</td>
<td>An oral proteasome inhibitor for multiple myeloma</td>
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<tr>
<td>Odomzo</td>
<td>Sonidegib</td>
<td>An oral hedgehog pathway inhibitor for advanced basal cell carcinoma</td>
</tr>
<tr>
<td>Tagrisso</td>
<td>Osimertinib</td>
<td>An oral kinase inhibitor for metastatic non-small cell lung cancer</td>
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<tr>
<td>Uptravi</td>
<td>Selexipag</td>
<td>A prostacyclin receptor agonist for PAH</td>
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<tr>
<td>Viberzi</td>
<td>Eluxadoline</td>
<td>A mu-receptor agonist for IBS-D</td>
</tr>
<tr>
<td>Vraylar</td>
<td>Cariprazine</td>
<td>An atypical antipsychotic for schizophrenia</td>
</tr>
</tbody>
</table>
Naloxegol (Movantik)

- **Indication** – Treatment of opioid-induced constipation in adults with chronic noncancer pain. (Only oral antagonist approved for this indication)
- **Mechanism** – Block mu opioid receptors in gut (PAMORA); pegylation reduces the ability of naloxegol to cross the blood-brain barrier
Naloxegol (Movantik)

- **Adverse Effects** – abdominal pain, diarrhea, nausea, flatulence, vomiting
- **Drug Interactions** – Strong 3A4 inhibitors; ketoconazole increases exposure to naloxegol 13X (may cause opioid withdrawal)
  - Avoid grapefruit or grapefruit juice
  - Strong 3A4 inducers lower naloxegol serum levels
- **Dose** – DC all maintenance laxatives before starting naloxegol (may restart after 3 days)
  - CrCl < 60 ml/min – 12.5 mg po qd
  - Otherwise 25 mg po qd
  - In morning, 1 hour before, or 2 hours after meal

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Trial 1</th>
<th>Trial 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naloxegol 12.5 mg</td>
<td>41%</td>
<td>35%</td>
</tr>
<tr>
<td>Naloxegol 25 mg</td>
<td>44%</td>
<td>40%</td>
</tr>
<tr>
<td>Placebo</td>
<td>29%</td>
<td>29%</td>
</tr>
</tbody>
</table>

- ~ $300.00/month
- Conclusion – no direct comparisons to other bowel regimens, not studied in cancer pain.
- More traditional bowel regimens should be tried first.
### Irritable Bowel Syndrome w/Diarrhea

**Rifaximin (Xifaxan)**
- Minimally absorbed oral antibiotic
- $1200/month

**Eluxadoline (Viberzi)**
- Mu-opioid receptor agonist and delta-opioid receptor antagonist
- C-IV – supratherapeutic oral and intranasal doses > placebo but < oxycodone to induced euphoria
- $960/month

### Rolapitnant (Varubi)

**Indication** – Oral substance P/neurokinin 1 (NK1) receptor antagonist for use with other antiemetics for prevention of CINV.
- Aprepitant (Emend) and netupitant (with palonosetron as Akynzeo) – comparison unclear

- Usually used in highly emetogenic regimens
- **Dose** – 180 mg (2 tablets) taken 1-2 hours before each cycle of moderately or highly emetogenic chemotherapy. Do not take more than once every two weeks.
- **Cost** – 90 tablets ~ $530
PPI Info

• Article published in NY Times May 1, 2015 listed top 10 Medicare covered drugs
• $2.53 billion – PPI esomeprazole (Nexium)
• No compelling evidence one PPI is better than another. Consider OTC!
  • FDA approved dextansoprazole (Dexilant SoluTab) – melts in your mouth [not in your hand! It had to be said!]
  • Indication – heartburn associated with GERD
  • Take 30 minutes before a meal

You’re up at bat!

• Idarucizumab is used to reverse bleeding associated with which of the following anticoagulants?
  A. Dabigatran
  B. Rivaroxaban
  C. Apixaban
  D. Edoxaban
Antipsychotic Agents

- Two new long-acting injectable formulations of second-generation antipsychotic agents
- Aripiprazole (Aristada) – every 4-6 weeks
- Paliperidone palmitate (Invega Trinza) – every 3 months
### Long Acting Injectable Antipsychotics for Schizophrenia

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Price/Mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluphenazine decanoate</td>
<td>12.5-12 mg IM or SC q2-3 weeks</td>
<td>$145</td>
</tr>
<tr>
<td>Haloperidol decanoate</td>
<td>10-15 x previous oral dose IM q4weeks</td>
<td>$33</td>
</tr>
<tr>
<td>Aripiprazole (Abilify Maintena)</td>
<td>400 mg IM qmonth</td>
<td>$1646</td>
</tr>
<tr>
<td>Aripiprazole (Aristada)</td>
<td>441-882 mg IM qmonth, or 882 mg IM q6weeks</td>
<td>Unknown</td>
</tr>
<tr>
<td>Olanzapine (Zyprexa Relprevv)</td>
<td>150-300 mg IM q2weeks or 300-405 mg IM qmo</td>
<td>$842</td>
</tr>
<tr>
<td>Paliperidone (Invega Sustenna)</td>
<td>117 mg IM qmonth</td>
<td>$1004</td>
</tr>
<tr>
<td>Paliperidone (Invega Trinza)</td>
<td>410 mg IM q3months</td>
<td>$3014</td>
</tr>
<tr>
<td>Risperidone (Risperdal Consta)</td>
<td>25 mg IM q2weeks</td>
<td>$723</td>
</tr>
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### Brexpiprazole (Rexulti)

- Oral, once-daily, second-gen antipsychotic
- Treatment of schizophrenia and adjunctively for MDD
- More effective than placebo in short-term trials, generally well tolerated
- Dosage adjustment with 3A4 inducers/inhibitors and 2D6 inhibitors
- No comparisons with other antipsychotics, long-term safety unknown
- No compelling reason to use over generic aripiprazole
- $865/month
Namzaric (memantine + donepezil)

- What can I say? Heave, sigh...
- No new efficacy data were required for approval of combination, only bioequivalence
- Study by Howard et al showed no benefit in AD of either drug in patients with MMSE ≤ 9
  - End points MMSE and BADLS
- Likely of marginal/no benefit in FAST 7
- Adverse effects can be significant

Buprenorphine

- **Bunavail** – buprenorphine + naloxone (2.1/0.3; 4.2/0.7; 6.3/1)
  - Buccal film, maintenance treatment of opioid dependence
  - Manufacturer claims superiority over SL formulation due to better absorption → lower dose
    - P’kin study showed 4.2/0.7 mg buccal ~ 8/2 mg SL tablet (Suboxone)
  - Dosage range = 2.1/0.3 mg – 12.6/2.1 mg/day
    - Recommended target maintenance dosage = 8.4/1.4 mg QD
  - Moisten inside of cheek with tongue, place side of film imprinted with dosage marking against cheek
    - Avoid drinking or eating until film dissolves
- Target maintenance dose (all brands) ~ $422.40/month
Belbuca (buprenorphine film)

• Buccal film contains buprenorphine, a partial opioid agonist

• Indicated for management of pain severe enough to require daily, around the clock, long-term opioid treatment for which there are no other options.

Belbuca (buprenorphine film)

• **Dose**
  – Opioid-naïve – Belbuca 75 mcg one daily or q12h; after 4 days increase to 150 mcg every 12 hours
  – Opioid-tolerant – Taper opioid down to 30 mg OME or less.
    • < 30 mg oral MSE – start Belbuca 75 mcg po qd-q12h
    • 30-89 mg oral MSE – start Belbuca 150 mcg q12h
    • 90-160 mg oral MSE – start Belbuca 300 mcg q12h
    • 160 mg oral MSE – consider alternate therapy

• **Availability** – 75, 150, 300, 450, 600, 750, 900 mcg

• **Cost** - ~$150 for 75 mcg; ~$350 for 900 mcg
Probuphine (buprenorphine implant)

- Rod-shaped implant – up to six months delivery of buprenorphine
  - 4 rods implanted
- Maintenance treatment for stable, opioid-dependent patients receiving 8 mg or less of buprenorphine per day
- Non-inferiority vs. 8 mg SL buprenorphine-naloxone daily
  - Primary outcome – at least 4 months free of illicit opioid use – 96.4% implant vs. 87.6% SL

Naloxone (Narcan) Nasal Spray

- Available to first responders, relatives, close friends of persons using heroin or prescription opioids
  - Used intranasally off-label
  - IM/SC auto-injector (Evzio)
- Bioavailability
  - IN 4 mg (1 dose) or 8 mg (2 doses) > 0.4 mg IM naloxone
- Narcan NS supplied in carton containing two 4 mg/0.1 ml single-use nasal spray devices

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Onset</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV</td>
<td>1-2 minutes</td>
</tr>
<tr>
<td>IM/SC</td>
<td>2-5 minutes</td>
</tr>
<tr>
<td>Intranasal</td>
<td>8-13 minutes</td>
</tr>
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</table>
Naloxone (Narcan) Nasal Spray

<table>
<thead>
<tr>
<th>Drug</th>
<th>Formulation</th>
<th>Usual Dosage</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Generic parenteral</td>
<td>0.4 mg/ml vials and syringes</td>
<td>0.2 mg IV, IM, SC</td>
<td>$17.40</td>
</tr>
<tr>
<td>Evzio</td>
<td>0.4 mg/0.4 ml prefilled auto-injector</td>
<td>0.4 mg IM or SC</td>
<td>$375.00</td>
</tr>
<tr>
<td>Narcan NS</td>
<td>4 mg/0.1 ml NS</td>
<td>4 mg IN</td>
<td>$62.50</td>
</tr>
</tbody>
</table>

Intravenous Diclofenac (Dyloject)

- **Indication** – Monotherapy for mild to moderate pain, or in combination with opioids for moderate to severe pain.
  - Ibuprofen (Caldolor), Ketorolac, Acetaminophen (Ofirmev)
- **New formulation** – Diclofenac has poor aqueous solubility.
  - Dyloject complexes diclofenac with an inert solubility enhancer that releases diclofenac immediately on injection.
  - Peak serum levels in 5 minutes
- **Dose** – 37.5 mg IV bolus over 15 seconds q6h prn
Saucy Tips and Medication Tricks

Those new diabetes drugs...
### A1c Lowering by Class/Drug

<table>
<thead>
<tr>
<th>Drug/Class</th>
<th>Expected A1c Lowering</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alpha-glucosidase inhibitor (acarbose [Precose], miglitol [Glyset])</td>
<td>0.5-1%</td>
</tr>
<tr>
<td>Amylin analog (pramlintide [Symlin])</td>
<td>0.5-1%</td>
</tr>
<tr>
<td>Biguanide (metformin [Glupophage])</td>
<td>1-1.5%</td>
</tr>
<tr>
<td>Dipeptidyl peptidase-4 (DPP-4) inhibitor (alogliptin [Nesina], linagliptin [Tradjenta], saxagliptin [Onglyza], sitagliptin [Januvia])</td>
<td>0.5-1%</td>
</tr>
<tr>
<td>GLP-1 agonists or incretin mimetic (albiglutide [Tamzei], dulaglutide [Trulicity], exenatide [Byetta], exenatide XR [Bydureon], liraglutide Victoza)</td>
<td>1-1.5%</td>
</tr>
<tr>
<td>Insulin (rapid, short, intermediate, long-acting)</td>
<td>1.5-3.5%</td>
</tr>
<tr>
<td>Meglitinide (nateglinide [Starlix], repaglinide [Prandin])</td>
<td>0.5-1%</td>
</tr>
<tr>
<td>Sodium-glucose co-transporter 2 (SGLT2) inhibitor (canagliflozin [Invokana], dapagliflozin [Farxiga], empagliflozin [Jardiance])</td>
<td>0.5-1%</td>
</tr>
<tr>
<td>Sulfonylurea – first generation and second generation (chlorpropamide, tolazamide, tolbutamide, glyburide, glipizide, glimepiride)</td>
<td>1-1.5%</td>
</tr>
<tr>
<td>Thiazolidinedione (pioglitazone [Actos], rosiglitazone [Avandia])</td>
<td>1-1.5%</td>
</tr>
</tbody>
</table>

### A1c and eAG (mg/dl)

<table>
<thead>
<tr>
<th>A1c (%)</th>
<th>eAG (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>97</td>
</tr>
<tr>
<td>6</td>
<td>126</td>
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<tr>
<td>7</td>
<td>154</td>
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<tr>
<td>8</td>
<td>183</td>
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<td>9</td>
<td>212</td>
</tr>
<tr>
<td>10</td>
<td>240</td>
</tr>
<tr>
<td>11</td>
<td>269</td>
</tr>
<tr>
<td>12</td>
<td>298</td>
</tr>
</tbody>
</table>

**eAG = estimated average glucose**
### A1c Lowering by Class/Drug

<table>
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</tr>
</tbody>
</table>

### DPP-4 Inhibitors and Pain

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Generic name(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Januvia</td>
<td>sitagliptin</td>
</tr>
<tr>
<td>Janumet</td>
<td>sitagliptin and metformin</td>
</tr>
<tr>
<td>Janumet XR</td>
<td>sitagliptin and metformin extended release</td>
</tr>
<tr>
<td>Onglyza</td>
<td>saxagliptin</td>
</tr>
<tr>
<td>Kombiglyze XR</td>
<td>saxagliptin and metformin extended release</td>
</tr>
<tr>
<td>Tradjenta</td>
<td>linagliptin</td>
</tr>
<tr>
<td>Glyxambi</td>
<td>linagliptin and empagliflozin</td>
</tr>
<tr>
<td>Jentadueto</td>
<td>linagliptin and metformin</td>
</tr>
<tr>
<td>Nesina</td>
<td>alogliptin</td>
</tr>
<tr>
<td>Kazano</td>
<td>alogliptin and metformin</td>
</tr>
<tr>
<td>Oseni</td>
<td>alogliptin and pioglitazone</td>
</tr>
</tbody>
</table>

Severe persistent joint pain. Occurs from 1 day to 1 year after starting tx. Usually resolves within 1 month after DC.

SGLT-2 Inhibitors

- FDA warns about reports of:
  - Ketoacidosis
  - Serious UTI’s (urosepsis)

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Generic Name(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Invokana</td>
<td>Canagliflozin</td>
</tr>
<tr>
<td>Invokamet</td>
<td>Canagliflozin and metformin</td>
</tr>
<tr>
<td>Jardiance</td>
<td>Empagliflozin</td>
</tr>
<tr>
<td>Glyxambi</td>
<td>Empagliflozin and linagliptin</td>
</tr>
<tr>
<td>Synjardy</td>
<td>Empagliflozin and metformin</td>
</tr>
<tr>
<td>Farxiga</td>
<td>Dapagliflozin</td>
</tr>
<tr>
<td>Xigduo XR</td>
<td>Dapagliflozin and metformin</td>
</tr>
</tbody>
</table>

http://www.fda.gov/Drugs/DrugSafety/ucm475463.htm

Canagliflozin

- Canagliflozin (Invokana, Invokamet)
- Reduced bone mineral density
- Increased risk of bone fracture
  - Falling from standing height
- Can occur as early as 12 weeks after starting therapy
- Evaluating risk with empagliflozin and dapagliflozin

http://www.fda.gov/Drugs/DrugSafety/ucm461449.htm
Improving Diabetes Care for Hospice Patients

• **Recommendation 1** – Upon enrollment into hospice, providers should discuss goals of care with patients and their families (and be reimbursed for these discussions), including the likely trajectory of glycemic treatment.

• **Recommendation 2a** – Research focusing on patients with a limited life expectancy, including hospice patients, should determine the levels of hyperglycemia that commonly leads to symptoms.

• **Recommendation 2b** – While we await results of research on glucose levels that leads to symptoms in hospice patients, we recommend a blood glucose target between 200 and 300 mg/dL to balance the twin goals of minimizing the risk of hypoglycemia while avoiding symptomatic hyperglycemia.

• **Recommendation 3a** – Hemoglobin A1c levels should not be ordered in hospice patients. Hemoglobin A1c levels are used to determine average glucose levels over 3 months and guide treatment decisions. However, for hospice patients for whom the primary goal of treatment is to avoid symptomatic hyper- and hypoglycemia, average glucose-level data provided by Hemoglobin A1c tests are unlikely to be helpful.
Improving Diabetes Care for Hospice Patients

- **Recommendation 3b** – Providers should be educated that hospice patients are now excluded from HEDIS glycemic control quality indicators. We applaud the move by the National Committee for Quality Assurance to exclude members with a hospice benefit from 2014 HEDIS reporting as well as efforts by the National Quality Forum to identify and define quality indicators for palliative and end of life care. Outreach efforts should be initiated to ensure that providers are aware of this change in glycemic control quality indicators.


---

Warfarin and the FAB-4

- **F** – Fluconazole (Diflucan)
- **A** – Amiodarone (Cordarone)
- **B** – Bactrim (trimethoprim/sulfamethoxazole)
- **F**(our) – Flagyl (metronidazole)

Inhibit warfarin metabolism within 24 hours!
Warfarin and the FAB-4!

• If a patient is taking warfarin, and a prescriber orders Fluconazole, Amiodarone, Bactrim or Flagyl – say “Hold the phone! As you know, this medication is a strong inhibitor of warfarin and the INR will likely go up, increasing the risk of bleeding. Do you want to empirically reduce the warfarin dose?”

Prophylactic Anticonvulsants in CNS Malignancy

• “Multiple studies have demonstrated no clear benefit from prophylactic antiepileptic drug (AED) therapy for patients who have CNS tumors and no prior history of seizures. Therefore, initiating AED prophylaxis is not recommended for such patients, and if a patient is currently receiving an AED, it should be tapered and discontinued.”

Lorazepam 0.5 (to 1.0mg) po tid-qid
Lorazepam 1 mg (to 2 mg) po q5min, up to 4 doses for seizure activity

Fast Facts

Where For Art Thou?

http://www.mypcnow.org/
FAST FACTS AND CONCEPTS #311
OPIOIDS FOR CHRONIC PAIN IN PATIENTS WITH HISTORY OF SUBSTANCE USE DISORDERS
PART 1: ASSESSMENT AND INITIATION
Amy J. Kennedy MD, Robert M. Arnold MD, Julie W. Childers MD.

When is it appropriate to use opioids in the palliative care setting for a patient with a history of a substance use disorder (SUD)? This Fast Fact addresses strategies for initiating opioids for patients with a history of SUD; Fast Fact #312 will address maintenance therapy.

Definitions:
SUD: A maladaptive pattern of substance use that is characterized by a continued use of a substance despite the occurrence of physical or psychological harm from the substance use or other important problems in a person's life (1).
Opioid: A class of medications that act on specific receptors in the body to produce analgesia (pain relief) and other effects (2).

Opioid Therapy in Patients with SUD:
- Addiction: Overwhelming involvement with illicit drug use, compulsive drug use, and use despite knowledge of harmful consequences.
- Risks of Opioid Therapy in Patients with SUD:
  - Inability to achieve effective analgesia.
  - Adverse opioid effects with higher doses.
  - Aberrant drug behaviors including drug diversion.

Patient Monitoring:
- Adherence checklists and individual or group counseling can reduce opioid abuse in high-risk patients (1). Only one clinician and pharmacy should be utilized in providing opioids. Regular follow-up visits should be scheduled to assess the “Four A’s of Pain” before and after every intervention (2).
- Fast Fact #311 discussed the assessment and initiation of opioid therapy in patients with a history of a substance use disorder (SUD). This Fast Fact will highlight expert suggested strategies for opioid monitoring in this patient population.
- Pain assessment should include an evaluation of the patient’s physical, psychological, and social well-being.
- Pain monitoring should include regular assessment of pain intensity, functional status, and overall well-being.

Aberrant Drug Behaviors: Aberrant drug behaviors are not all the same; each behavior should be evaluated based on the specific patient and situation. Clinicians should assess the degree of risk involved with the aberrant drug behaviors.

FAST FACTS AND CONCEPTS #312
OPIOIDS FOR CHRONIC PAIN IN PATIENTS WITH HISTORY OF SUBSTANCE USE DISORDERS
PART 2: MANAGEMENT AND MONITORING
Amy J. Kennedy MD, Robert M. Arnold MD, Julie W. Childers MD.

Fast Fact #311 discussed the assessment and initiation of opioid therapy in patients with a history of a substance use disorder (SUD). This Fast Fact will highlight expert suggested strategies for opioid monitoring in this patient population.

Patient Monitoring:
- Adherence checklists and individual or group counseling can reduce opioid abuse in high-risk patients (1). Only one clinician and pharmacy should be utilized in providing opioids. Regular follow-up visits should be scheduled to assess the “Four A’s of Pain” before and after every intervention (2,3).
- Pain assessment should include an evaluation of the patient’s physical, psychological, and social well-being.
- Pain monitoring should include regular assessment of pain intensity, functional status, and overall well-being.

Aberrant Drug Behaviors: Aberrant drug behaviors are not all the same; each behavior should be evaluated based on the specific patient and situation. Clinicians should assess the degree of risk involved with the aberrant drug behaviors.

Overview:
- Levorphanol, a “forgotten” potent opioid agonist, has unique attributes (1). This Fast Fact summarizes its pharmacology and role in pain management.

Pharmacology:
- Levorphanol is a unique opioid, with both similarities to and important differences from methadone (see Fast Facts #75, 86, 171 about methadone pharmacology).
- It is an agonist at the mu, kappa, and delta opioid receptors, an NMDA antagonist, and a monoamine reuptake inhibitor of norepinephrine and serotonin (10).
- Similar to methadone, levorphanol analgesic half-life is 0-3 hours, and its elimination half-life is longer than its analgesic duration of action (patients can still have significant tissue and serum levels of levorphanol even after its analgesic effect has waned). However, its elimination half-life of ~11 hours is more predictable than methadone’s (9). Accumulation and toxicity can occur if levorphanol’s dose is increased too quickly, without waiting for steady-state to occur (~5 elimination half-lives or 2-3 days).
- Drug concentrations peak 20 minutes after parenteral injection and 1 hour after oral doses.
- An oral dose undergoes approximately 50% first-pass clearance.
- Levorphanol is metabolized via conjugation to a glucuronide in the liver; however, the cytochrome P450 system does not appear to be involved with levorphanol. Hence it may have less drug interactions than methadone. Like methadone, it has no known active metabolites. Side effects are similar to other opioids. There are no documented studies showing QT interval prolongation or Torsades de Pointes.

Clinical Uses:
- Several properties of levorphanol make it of interest as an analgesic:
- Similar to methadone, levorphanol’s longer duration of action is not affected by crushing, and it can be safely
There’s Gotta Be an App for That!

Goodrx.com
Levorphanol 2 mg po tid #90 ~$150-170 per month
Nocturnal Hypoglycemia

• The NiteBite® Timed-release Glucose Bar™
  – Formulated to avoid nocturnal hypoglycemia
• NiteBite contains three sources of glucose that are absorbed at different times:
  – Sucrose in NiteBite is readily converted to glucose, and is absorbed quickly.
  – Protein in NiteBite is converted to glucose more slowly and absorbed around 2.5 to 5 hours after eating.
  – Uncooked cornstarch begins to appear in the blood as glucose immediately after ingestion. However, due to its complexity, it continues to appear in the blood for 6 or more hours.

http://www.childrenwithdiabetes.com/d_08_c10.htm
What?? $$$ Thorazine??

- Price of chlorpromazine increased 1100%
- Delirium, nausea/vomiting, hiccups – haloperidol
- Combative restlessness -phenobarbital

<table>
<thead>
<tr>
<th>Antipsychotic</th>
<th>Sedating Effects</th>
<th>Anticholinergic Effects</th>
<th>Extrapyramidal Side Effects</th>
<th>Hypotensive Effects</th>
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</thead>
<tbody>
<tr>
<td>Chlorpromazine</td>
<td>High</td>
<td>High</td>
<td>Low</td>
<td>IM – High</td>
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<tr>
<td>(Thorazine)</td>
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<td></td>
<td></td>
<td>PO – Moderate</td>
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<tr>
<td>Haloperidol</td>
<td>Very low</td>
<td>Very low</td>
<td>Very high</td>
<td>Very low</td>
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<tr>
<td>(Haldol)</td>
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<td></td>
</tr>
<tr>
<td>Thioridazine</td>
<td>High</td>
<td>High</td>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>(Mellaril)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

“I don’t feel very much like Pooh today," said Pooh.

"There there," said Piglet. "I’ll bring you tea and honey until you do.”

_A.A. Milne, Winnie-the-Pooh_
Honey for a Cough

• A 2014 Cochrane Review concluded that “honey may be better than ‘no treatment’ for reducing cough frequency, cough severity and improving sleep quality for both children and parents.”
  – This conclusion was based on results from four randomized controlled trials of the efficacy of honey for treatment of acute cough in children aged 12 months to 18 years (no data in adults).
  – Dose ranged from 2.5 ml for the youngest child, to 10 ml for the oldest, given 30 minutes before bedtime.
  – Results showed honey was better than no treatment, but neither better nor worse than nonprescription antitussives.

New Drugs of Abuse!

• Gabapentin and pregabalin popular drugs of abuse
• Euphoric and sedative effect (especially with opioid)
• Misuse of gabapentin increased by 90%
• 20% of patients misuse gabapentin

### Comparison

<table>
<thead>
<tr>
<th>Medication</th>
<th>NNT</th>
<th>+SBMs/week over placebo</th>
<th>Extra BMs/month</th>
<th>Cost (30 days)</th>
<th>Cost per BM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polyethylene glycol</td>
<td>3</td>
<td>+2.7</td>
<td>11</td>
<td>$13-$39</td>
<td>$1.20-$3.50</td>
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<tr>
<td>Docusate</td>
<td>N/A</td>
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<td>Linaclotide*</td>
<td>6-10*</td>
<td>+2</td>
<td>8</td>
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<td>Lubiprostone</td>
<td>12</td>
<td>+0.9</td>
<td>3.6</td>
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<tr>
<td>Methylnaltrexone</td>
<td>3-5**</td>
<td>+0.6-1.6</td>
<td>2.4-6.4</td>
<td>$80/dose $1200</td>
<td>$80-$500</td>
</tr>
<tr>
<td>Naloxegol</td>
<td>5-9.7</td>
<td>+0.5-1</td>
<td>2-4</td>
<td>$297</td>
<td>$74-$148</td>
</tr>
</tbody>
</table>

*CIC data  **in CNCP patients

Slide courtesy of Dr. Kashelle Lockman
PEG $17-50 $1.20-3.50 per BM

Lubiprostone $360 $100 per BM

Methylnaltrexone $1200 $74-$148 per BM

Naloxegol $297 $500 per BM

Slide courtesy of Dr. Kashelle Lockman
Approach to Constipated Patient

- Ensure there is no impaction or obstruction
- Minimize constipating risk factors; use nonpharmacologic approaches
- Optimize traditional oral regimens (e.g., senna, polyethylene glycol)
- Don’t forget about rectal therapy when appropriate!
- Methylnaltrexone or naloxegol for OIC despite optimized prophylactic & non-PAMORA treatment therapy

Bristol Stool Chart

Type 1: Separate hard lumps, like nuts (hard to pass)
Type 2: Sausage-shaped but lumpy
Type 3: Like a sausage but with cracks on its surface
Type 4: Like a sausage or snake, smooth and soft
Type 5: Soft blobs with clear-cut edges (passed easily)
Type 6: Fluffy pieces with ragged edges, a mushy stool
Type 7: Watery, no solid pieces. Entirely Liquid

Slide courtesy of Dr. Kashelle Lockman
Exhaled Fentanyl

• “...in addition to hepatic biotransformation and elimination via urine and faeces, fentanyl is also eliminated unchanged by the lungs.”

• “Potential risk to operating theatre personnel from long-term exposure to exhaled anaesthetic agents following intravenous administration during surgery warrants further research.”

Uh-Oh!

• INTENSOL: A highly concentrated oral medication solution (1 ml in buccal area)
• My “six pack” includes:
  – Morphine 20 mg/ml
  – Oxycodone 20 mg/ml
  – Methadone 10 mg/ml
  – Haloperidol 2 mg/ml
  – Lorazepam 2 mg/ml
  – Dexamethasone 1 mg/ml

Answer is...

• “Why yes, I happen to look good in orange. Why do you ask?”
Question is...

- “If you start an IV infusion of morphine at 2 mg/hour and order “titrate to comfort,” the consequences may beg the question how you look in orange.”

“Titrate to Comfort” is not a good look

- Half-life of morphine
  - General population 2-3 hours
  - Pediatrics 2-9 hours

<table>
<thead>
<tr>
<th>Number t ½</th>
<th>% of Steady State Achieved</th>
<th>2 hour t ½</th>
<th>3 hour t ½</th>
<th>4 hour t ½</th>
<th>8 hour t ½</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>50</td>
<td>2</td>
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There’s gotta be a better way....
(Why yes, there is, thanks for asking)
1. Give morphine 1 mg IV loading dose, then start IV morphine infusion at 1 mg/hour.
2. PRN RN IV bolus 1 to 2 mg morphine every 15 minutes if needed for uncontrolled pain.
3. If patient is uncontrolled by PRN RN IV boluses, increased continuous infusion by 50-10% every 12-24 hours and increase PRN RN IV bolus to amount equal to the new hourly infusion dose.
4. Call MD for poorly controlled pain, if more than 3 dose escalations are necessary, if patient is unexpectedly very difficult to arouse, or for questions on how to safely increase dose.

http://prc.coh.org/pdf/Titrate5-10.pdf

“Titrate to Comfort” is not a good look

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<th>Number t ½</th>
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- More aggressive – increase continuous infusion in 8-12 hours
“Titrate to Comfort” is not a good look

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- Most aggressive – increase continuous infusion in 8-10 hours
- More conservative – increase continuous infusion in 12-24 hours

JR and Clozapine REMS

- JR is a 48 year old man admitted to hospice with NSCLC; his prognosis is about 3 months.
- JR also has a history of schizophrenia that has been very difficult to manage. The only antipsychotic agent that seems to provide an acceptable response is clozapine.
- JR is too weak to go to his PCP’s office for blood draws (to assess risk of neutropenia) and he is a TOUGH stick.
JR and Clozapine REMS

- What is your best option for JR?

A. Insert a central line for blood draws
B. Switch from clozapine to a different antipsychotic, knowing the response will not be nearly as good.
C. Call a darned good-looking pharmacist who has the answer to your prayers (ok that would be me!).

www.clozapinerems.com

1. Click on “Resources”
2. Click on “Program Materials”
3. Select REMS ANC Lab Reporting Form
Section 3: Prescriber Authorization

Treatment Rationale:

Complete this section if the patient has moderate neutropenia (ANC 500-999/µL for the General Population) or severe neutropenia (ANC < 500/µL for General Population and Patients with BEN) and you want to continue treatment.

The treatment rationale is (check one and sign below):

- Benefits of continuing clozapine treatment outweigh risk of neutropenia
- Until next ANC Lab
- Until (MM/DD/YYYY)
- No more than 6 months from today
- Patient has Benign Ethnic Neutropenia (BEN) (No Expiration)

Hospice Care:

For hospice patients (i.e., terminally ill patients with an estimated life expectancy of six months or less), the prescriber may reduce the ANC monitoring frequency to once every 6 months, after a discussion with the patient and/or their caregivers.

If you want to change the monitoring frequency to once every 6 months for a hospice patient, check the box and sign below:

- This is a hospice patient.

Authorizing Prescriber Information (All Fields Required)

Name: 
NPI or DEA: 
Authorizing Prescriber Signature: 
Date (MM/DD/YYYY):

*Authorizing Prescriber Signature is required for a change in treatment rationale, and/or for a hospice care patient.
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• Entirely online, interprofessional (students and faculty)
• Earn up to two graduate certificates
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