DELTA CARE
Hospice Pharmacy. Innovation. Partnership.

Drug Shortages: A Critical Look at Alternatives and Drugs with Multiple Uses

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Acknowledgement

There are no financial conflicts of interest. The information to be presented is consistent with information that can be obtained from peer reviewed journals/studies and well documented literature.

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First things first

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Introduction

"The U.S. Government Accountability Office reports that the total number of active drug shortages, including both new and ongoing shortages from the prior year, has increased since 2007. According to one study looking at these shortages, more than 80% of drugs in short supply are generics. Of those, 80% are injectables that treat cancer, cardiovascular disease, infection, central nervous system conditions and pain."

Heather Cooley, Director of Supply Chain Services, McKesson

& Cathy Leventis, Director of Clinical Services, McKesson

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Objectives

1. Identify current trends in drug shortages, what may be causing them, and how to stay 'in the know'
2. Discuss patient safety concerns as a result of drug shortages
3. Review suggestions of strategies to mitigate shortages
4. Evaluate alternative medications that could be utilized when others are on shortage
5. Apply knowledge gained to patient case

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Objective 1: Identify current trends in drug shortages and what may be causing them

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Objective 1: Identify current trends in drug shortages and what may be causing them

First things first:

- Drug shortages are not new
- Some things are outside of the FDA's control
- There are actually less drugs that go on shortage today than there was before mitigation strategies were introduced.
- Approx 1% of prescriptions written are affected by drug shortages

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Objective 1: Identify current trends in drug shortages and what may be causing them

What is the FDA doing about this?

- Prioritize reports based on medical necessity
- Attempts to address the underlying issue causing shortage
- Evaluate the public health risk
- Advise and offer help to manufacturers
- Involve other manufacturers to see if they have the capacity/willingness to assist in production
- Expedite reviews/inspections
- Import medications

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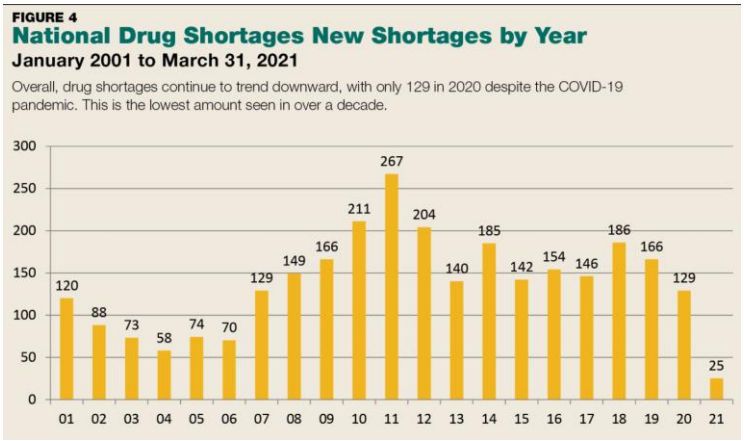
Objective 1: Identify current trends in drug shortages and what may be causing them
By the numbers:



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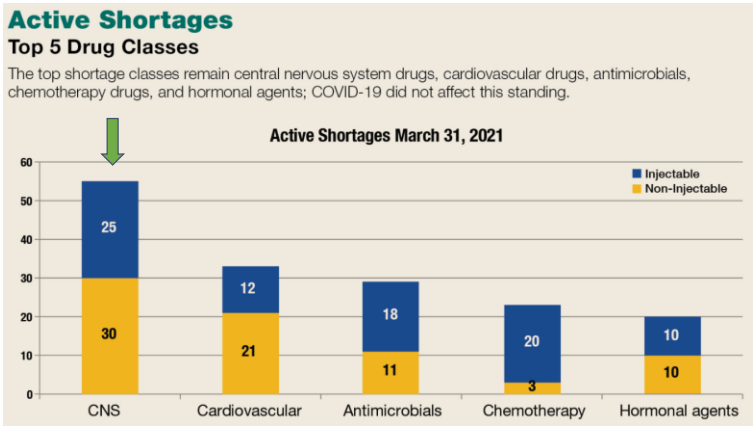

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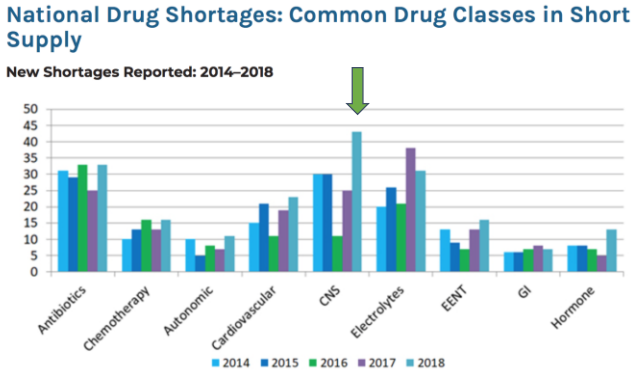

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Objective 1: Identify current trends in drug shortages and what may be causing them

Common causes:

- Sourcing limitations
- Global recalls
- Manufacturing issues
- Generic deflation
- Discontinuations
- Pricing Strategies
- API issues
- Disasters

Drug manufacturing is a business!

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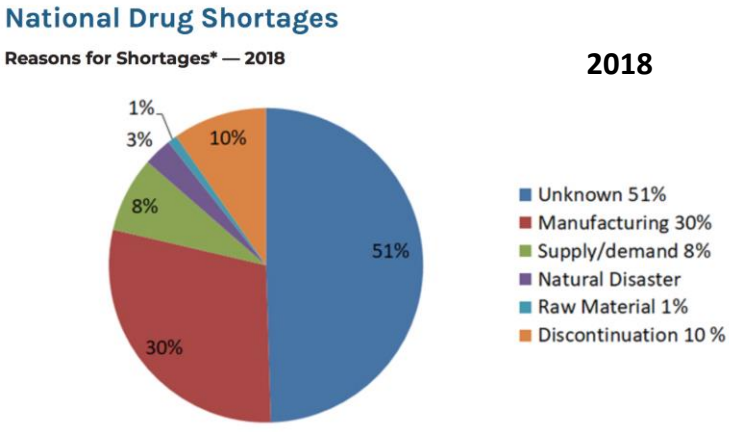
Objective 1: Identify current trends in drug shortages and what may be causing them



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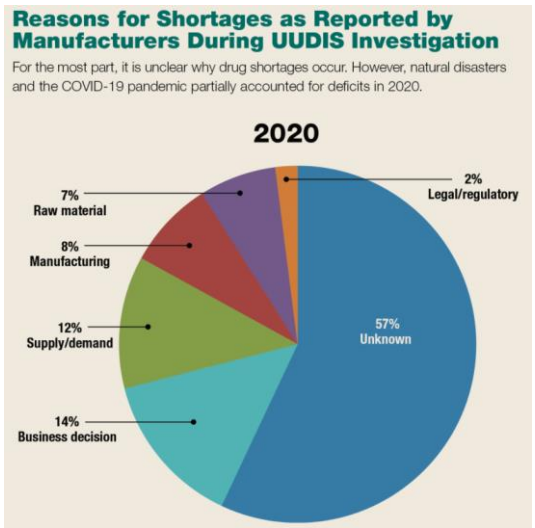
Objective 1: Identify current trends in drug shortages and what may be causing them



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Objective 1: Identify current trends in drug shortages and what may be causing them

More to think about:

- Consumers aren't choosing the products –prescribers are, so supply/demand cannot be predicted
- Unlikely that another supplier can step in when there's a problem
- Shortages don't impact profits –consumers feel effects
- Average duration of a shortage is 286 days
- 64% of shortages are repeat shortages

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Objective 1: Identify current trends in drug shortages and what may be causing them

Of Interest: Generic Injectables

- 71% of products in market are manufactured by just 3 companies
- >33% of products are made by just 1 or 2 manufacturers
- Single lines for multiple products
- Making just enough in time
- Complex when something needs fixed

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Objective 1: Identify current trends in drug shortages and what may be causing them

Of Interest: Generic Injectables

- In Feb 2017 FDA found significant violations in a Pfizer plant in Kansas
- In June 2017 it cut back production at this facility to make significant upgrades
- West-Ward and Fresenius Kabi become flooded with backorders as they cannot keep up with the increase in demand

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Objective 1: Identify current trends in drug shortages and what may be causing them

To make things more complicated:

- The DEA has limits (quotas) on the amount of controlled substances a manufacturer can produce in a year
- The DEA and FDA do not agree on basic terms that impact quantifying drug shortages
- The DEA reportedly does not reply timely to quota adjustment requests and therefore supplies cannot be obtained in time to account for changes in demand
- In response to the opioid crisis, the DEA reduced by 25% approved opioid manufacturing in 2017 and 20% more in 2018.

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Objective 1: Identify current trends in drug shortages and what may be causing them

What you can do:

- BE PREPARED!
- Actively participate as part of the interdisciplinary team
- Visit the FDA website or follow/like/connect with them on Twitter, Facebook, and/or LinkedIn
- Visit the ASHP website where you can search for drugs on shortage
- Check your email! Newsletters and alerts are sent by many organizations when shortages are known.
- Set Google alerts for news stories about manufacturers/drugs

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Objective 1: Identify current trends in drug shortages and what may be causing them

Current shortages of note:

- We will discuss at end!!

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Objective 2: Discuss patient safety concerns as a result of drug shortages

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Objective 2: Discuss patient safety concerns as a result of drug shortages

Basic medications going short supply:

1. Dextrose
2. Diazepam
3. Epinephrine
4. Fentanyl
5. Lorazepam
6. Morphine
7. Ondansetron
8. Nalbuphine
9. Naloxone
10. Promethazine
11. Saline
12. Lactate ringers
13. Dextrose
14. Water

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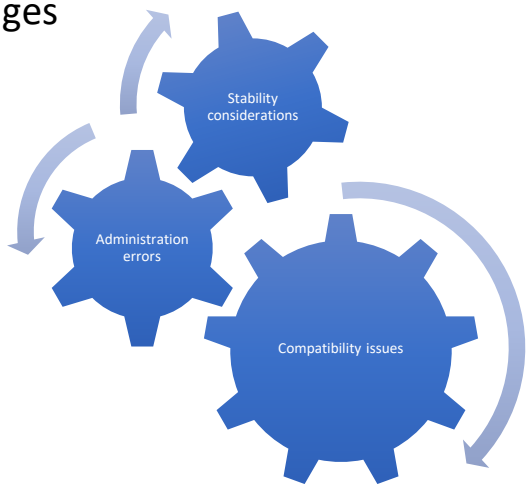
Objective 2: Discuss patient safety concerns as a result of drug shortages



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Objective 2: Discuss patient safety concerns as a result of drug shortages

Safety concerns:

1. Same med, different strength
2. Same med, different packaging
3. Imported med
4. No med

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Objective 2: Discuss patient safety concerns as a result of drug shortages

Other safety concerns:

1. Frustrated members of interdisciplinary team
2. More time spent looking for alternatives means less time focusing on direct patient care
3. Delayed treatments/time to comfort
4. Less effective medications being utilized?
5. Using SDV multiple times
6. Using non-sterile products to make sterile products hastily
7. Using expired drugs
8. Rationing drugs

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Objective 2: Discuss patient safety concerns as a result of drug shortages

ISMP Survey (2017)

- 21% of respondents were aware of at least 1 drug error that occurred as a result of drug shortages
- Over 100 errors were described
- 67% were wrong dose or concentration
- People that were NOT aware of errors said that they very well could just not have been reported

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Objective 2: Discuss patient safety concerns as a result of drug shortages

ISMP Survey (2017)

1 mL **LOR**azepam vials (2 mg per mL) were not available; pharmacy received 10 mL vials (2 mg per mL), which entered into stocks as 10 x 1 mL vials.
1 mL vials of morphine 10 mg dispensed when 2 mg vials were unavailable; 10 mg IV administered in error.
HYDROmorphone 1 mg administered instead of 0.5 mg because the 0.5 mg syringes were unavailable.
Ordered **HYDRO**morphone prefilled syringes from a different manufacturer; nurse gave the medication orally because the syringe looked like an oral syringe, although it was clearly labeled for IV use.
Selected an ampul of **SUF**entanil instead of fenta**NYL** and administered it during a fenta**NYL** shortage.
A patient received no treatment when a drug known to be unavailable was ordered verbally, and the nurse did not notify the pharmacy about the order or request an alternative.

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Objective 3: Review suggestions of strategies to mitigate shortages

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Objective 3: Review suggestions of strategies to mitigate shortages

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Objective 3: Review suggestions of strategies to mitigate shortages

Pharmacists

- Proactively manage inventory
  - Don't wait for meds to go on backorder whenever possible!
- Inform providers proactively
- Be involved with the development of protocols for if a drug is not available
- Place extra labeling on meds that may be different than normal stock
- Assist with the ethical distribution of meds on backorder
- Educate patient/caregivers about changes in medications

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Objective 3: Review suggestions of strategies to mitigate shortages

Nurses/Medical Director/Prescribers

- Ethically distribute drugs that are on backorder
- Stay on top of communication surrounding potential and current shortages
- Utilize the PO route if patient has a functioning gut
  - Especially important since so many meds that go on shortage are injectable
- Engage the pharmacy department when creating protocols for shortages
- Educate patient/caregivers about changes in medications
- Analyze recommendations from pharmacy critically
- "MASTER" medication therapy

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Objective 3: Review suggestions of strategies to mitigate shortages

MASTER: Rules for rational drug therapy

- Minimize the # of drugs used by maximizing multiple uses*
- Alternatives should be considered
- Start low, go slow!
- Titrate to effect
- Educate patient/caregiver(s)
- Review regularly

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Objective 4: Evaluate alternative medications that could be utilized when others are on shortage

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Objective 4: Evaluate alternative medications that could be utilized when others are on shortage

One drug for multiple symptoms = ”portmanteau” drug

- Minimize risk of DDI
- Maximize symptom management
- Promote compliance
- Minimize risk of drug errors
- Reduce pill burden

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Objective 4: Evaluate alternative medications that could be utilized when others are on shortage

Additional ”portmanteau” drug benefits

- Favorable adverse effects –use to benefit!
- Multiple ROA
- Easy dosing schedules
- Cost effective

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Objective 4: Evaluate alternative medications that could be utilized when others are on shortage

”Portmanteau” example: Steroids

- Appetite induction, mood elevation, pain (bone mets), energy, inflammation (airway inflammation = sob!)
- PO/SQ/IV/PR/SL
- Injectables, tablets, oral solutions
- Flexibility based on patient parameters: CHF? Dex!
- $1 or less PPD
- Benefits > risk in majority of cases

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Objective 4: Evaluate alternative medications that could be utilized when others are on shortage

"Portmanteau" example: Mirtazapine (Remeron)

- Appetite induction, mood elevation, restfulness
- PO/SL
- Tablets, ODTs
- Sedation maxes out at doses of 15mg/day
- Less than $1 PPD

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Objective 4: Evaluate alternative medications that could be utilized when others are on shortage

"Portmanteau" example: Gabapentin (Neurontin)

- Pain, seizures, insomnia
- PO/SL
- Tablets, capsules, oral solution
- Needs renally dosed –lower doses/longer intervals
- Less than $1 PPD (solution a bit more $)

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Objective 4: Evaluate alternative medications that could be utilized when others are on shortage

"Portmanteau" example: Haloperidol (Haldol)

- Agitation, nausea, vomiting
- PO/SL/IV/SQ/IM/PR
- Tablets, oral solution, injectable
- Currently on shortage
- Less than $1 PPD

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Objective 4: Evaluate alternative medications that could be utilized when others are on shortage

"Portmanteau" example: Lorazepam (Ativan)

- Anxiety, nausea, vomiting, seizures, dyspnea
- PO/SL/IV/SQ/IM/PR
- Tablets, oral solution, injectable
- Less than $1 PPD PO, $2-3 PPD injectable
- Caution: anxiety≠agitation/delirium.

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Objective 4: Evaluate alternative medications that could be utilized when others are on shortage

"Portmanteau" example: Olanzapine (Zyprexa)

- Agitation, nausea, vomiting, appetite induction
- PO/SL/PR –avoid inj due to $$
- Tablets, ODTs
- Intractable/refractory N/V –included in NCCN guidelines!
- Less than $1 PPD for IR. $2-3/PPD for ODT

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Objective 4: Evaluate alternative medications that could be utilized when others are on shortage

"Portmanteau" example: Metoclopramide (Reglan)

- Gastroparesis, nausea, vomiting, bloating, abdominal pain
- PO/SL/IV/SQ(?)/TP(?)
- Tablets, inj, gel (?)
- Do not use if patient using haloperidol –tardive dyskinesia
- Less than $1 PPD for tabs. $2-3/dose for inj

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Objective 4: Evaluate alternative medications that could be utilized when others are on shortage

"Portmanteau" example: SNRI's (Cymbalta/Effexor)

- Depression, pain
- PO
- Capsules/tablets
- $1-2 PPD for generic options

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Objective 4: Evaluate alternative medications that could be utilized when others are on shortage

"Portmanteau" example: TCA's (Elavil/Pamelor)

- Depression, pain, insomnia
- PO
- Tablets
- Avoid amitriptyline
- Less than $1 PPD for tabs

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Objective 4: Evaluate alternative medications that could be utilized when others are on shortage

”Portmanteau” example: Modafinil (Provigil)

- Chronic fatigue, narcolepsy, depression, sleep apnea daytime fatigue
- PO
- Tablets
- Approx $3/tab for #15 200mg tabs
- Favorable side effect profile, low abuse potential

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Objective 4: Evaluate alternative medications that could be utilized when others are on shortage

”Portmanteau”

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Objective 4: Evaluate alternative medications that could be utilized when others are on shortage

Other useful meds: Systemic lidocaine

- Refractory neuropathic pain
- Non-selective sodium channel blocker
- Caution ADRs:
  - Cardiac
  - CNS (dose related)
  - Respiratory toxicity
- Mexiletine?? 150mg PO TID. $100/15ds

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Objective 4: Evaluate alternative medications that could be utilized when others are on shortage

Other useful meds: Methadone

- Mu agonist
- Slow onset of action, long duration of action (inherent)
- PO, (IV&SQ = $$)
- Blunted euphoria,
- Methadone safe use protocol
- No DATA waiver ("X" number) needed for PAIN indication
- PO $1 PPD
- **Low dose, qday dosing can reduce IV/SQ opioid requirements even if total conversion is not realistic!**

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Objective 4: Evaluate alternative medications that could be utilized when others are on shortage

Other useful meds: Methadone

- Three Qs: Smoker status? Adipose tissue? Cardiac status
  - Smoking increases the metabolism of methadone!
  - Methadone is stored in adipose tissue –increased t½!
  - Methadone should be used with caution in those with documented hx of arrhythmia. QT prolongation seen with TDD >100mg.

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Objective 4: Evaluate alternative medications that could be utilized when others are on shortage

Other useful meds: Methadone

- MUST be dosed appropriately for safe use!

TDD Morphine	Methadone conversion ratio
<30mg	2:1
30-99mg	4:1
100-299mg	8:1
300-499mg	10:1
500-999mg	15:1
>1000mg	20:1

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Objective 4: Evaluate alternative medications that could be utilized when others are on shortage

Other useful meds: Buprenorphine

- Buccal film (2015), transdermal patches, SQ injection, (tabs)
- Antagonist at high doses –use lower doses for mod-severe pain
- Partial agonist at mu –analgesia, sedation, resp depression, euphoria
- Antagonist at kappa –antidepressant effect?
- No DATA waiver ("X" number) needed for PAIN indication
- Schedule III, NOT 2
- Butrans = $8 PPD, Belbuca = $12-15/day

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Objective 4: Evaluate alternative medications that could be utilized when others are on shortage

Other useful meds: Buprenorphine

Initiating Butrans therapy in opioid-experienced patients

CURRENT THERAPY	CURRENT DAILY DOSE*	BUTRANS RECOMMENDED STARTING DOSE†
Tramadol	<300 mg	5 mcg/hour
	300-400 mg‡	10 mcg/hour
Codeine	<90 mg	5 mcg/hour
	90-250 mg	10 mcg/hour
	>250 mg	Butrans may not be appropriate
Morphine	<30 mg	5 mcg/hour
	30-80 mg	10 mcg/hour
	>80 mg	Butrans may not be appropriate
Hydrocodone	<15 mg	5 mcg/hour
	15-40 mg	10 mcg/hour
	>40 mg	Butrans may not be appropriate
Oxycodone	<15 mg	5 mcg/hour
	15-40 mg	10 mcg/hour
	>40 mg	Butrans may not be appropriate

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Objective 4: Evaluate alternative medications that could be utilized when others are on shortage

Other useful meds: Buprenorphine

Previous Daily Dose of Opioid Analgesic (prior to taper)	BELBUCA® STARTING DOSE	TITRATION: INCREASE DOSE AS NEEDED*					
		1	2	3	4	5	6
<30 mg oral MME	75 mcg† once daily or q12h	150 mcg	300 mcg	450 mcg	600 mcg	750 mcg	900 mcg
30 – 89 mg oral MME	150 mcg q12h	300 mcg	450 mcg	600 mcg	750 mcg	900 mcg	
90 –160 mg oral MME	300 mcg q12h	450 mcg	600 mcg	750 mcg	900 mcg		

For patients previously taking oral MME >160 mg, consider an alternative analgesic.[10]

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Objective 4: Evaluate alternative medications that could be utilized when others are on shortage

Other useful meds: Ketamine

- Solution for injection, compounded oral suspension, intranasal?
- Blocks NMDA receptors, resensitizes mu opioid receptors –opioid sparing!
- Single doses effective for cancer patients receiving morphine? 0.25-0.5mg/kg IV x1
- Minimal respiratory depression, does have cardiac side effects
- Quick onset
- Daily-QID, duration of analgesia 1h-24h
- PO short term efficacy?
- Portmanteau –antidepressant!
- Schedule 3, NOT 2

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Objective 4: Evaluate alternative medications that could be utilized when others are on shortage

Other useful meds: Ketamine

Contents lists available at ScienceDirect

European Journal of Pain

journal homepage: www.EuropeanJournalPain.com

Review

Use of oral ketamine in chronic pain management: A review

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Objective 4: Evaluate alternative medications that could be utilized when others are on shortage

Other useful meds: Ketamine

REGIONAL ANESTHESIA AND ACUTE PAIN

SPECIAL ARTICLE

OPEN

Consensus Guidelines on the Use of Intravenous Ketamine Infusions for Acute Pain Management From the American Society of Regional Anesthesia and Pain Medicine, the American Academy of Pain Medicine, and the American Society of Anesthesiologists

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Regional Anesthesia and Pain Medicine • Volume 43, Number 5, July 2018

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Objective 4: Evaluate alternative medications that could be utilized when others are on shortage

Drugs on Backorder RIGHT NOW:

- Ciprofloxacin 500mg tabs -some manufacturers d/c the line which resulted in increased demand of others who expect resolution Jan 2022. Intermittent. Use 2-250mg tabs but know that one line of ciprofloxacin 250mg tabs has also been cut.
- Oxycodone 10mg tabs -supplier allocation. Regional. Use 2-5mg tabs or ½ of a 20mg tab. PILL COUNTS!
- Hydrocodone/Homatropine Syrup -Nov 2021 resolution? Tabs available. Depending on indication you can use Hydrocodone/Chlorpheniramine Suspension or Hydrocodone/APAP solution.

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Objective 4: Evaluate alternative medications that could be utilized when others are on shortage

Drugs on Backorder RIGHT NOW:

- Temazepam 15mg caps: manufacturer d/c line. Other NDCs available. Caution 7.5mg caps are $$$. Consider alt benzo. Buprop 75mg tab
- Haloperidol sol for inj: intermittently available. Q4 2021 resolution expected. Olanzapine, chlorpromazine, haloperidol deconate
- Neomycin 500mg tablets: Hi-Tech d/c this item, 3 other manufacturers cant keep up with demand. ETA of resolution TBD/small allocation mid-September.
- Lorazepam 2mg/ml soln for inj: SOME manufacturers (not all, but remember supply/demand!). Resolution ETA mid-Oct 2021.

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Objective 4: Evaluate alternative medications that could be utilized when others are on shortage

Drugs on Backorder RIGHT NOW:

- **Hydromorphone 2mg/ml soln for inj:**

Vendor	PFIZER INC INJECTABLE
Expected Resolution	SPLR BACKORDER NEXT RELEASE TBD
Notes	PRODUCT IS ON A LONG TERM BACKORDER STATUS. FULL RECOVERY TBD

Vendor	PFIZER INC INJECTABLE
Expected Resolution	LATE PO PENDING SUPPLIER COMMUNICATION

Vendor	PFIZER INC INJECTABLE
Expected Resolution	SPLR ALLOCATION NEXT RELEASE MID NOV 2021
Notes	VENDOR EXPERIENCING DELAYS IN PRODUCTION. FULL RECOVERY MID NOV 2021

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Objective 4: Evaluate alternative medications that could be utilized when others are on shortage

Drugs on Backorder RIGHT NOW:

- **Morphine Sulfate Soln for inj:**

Vendor	PFIZER INC INJECTABLE
Expected Resolution	SPLR BACKORDER NEXT RELEASE MID NOV 2021
Notes	MANUFACTURER IS OUT OF STOCK. FULL RECOVERY MID DEC 2021
Last Updated	Mon Oct 04 00:00:00 PDT 2021

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Objective 5: Apply knowledge gained to patient case

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Objective 5: Apply knowledge to case example

1/3: GS is a 67yom with NSC lung cancer with mets. His PPS is 50% though his appetite has sharply declined as he is becoming more symptomatic. He was in the hospice IPU as GIP previously for severe unrelieved pain that is exacerbating SOB and agitation, and he is now being readmitted. His family is distraught seeing him in pain and wants him to be able to remain at home after this admission. Rates pain 9/10 laying in bed and says it is all over but points to chest/ribs.

Comorbidities: BPH (no catheter), depression, HTN (controlled), CKD3

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Objective 5: Apply knowledge to case example

2/3: Current Meds:

- Lisinopril 20mg PO qam
- Fentanyl patch 25mcg/hr TP q72h
- Tamsulosin 0.4mg PO qpm
- Tramadol 50mg PO TID PRN pain (hardly takes –'doesn't work')
- Hydrocodone-APAP 10-325mg PO q4h PRN pain (takes 4-5x/day)
- Senna S 8.6-50mg PO 1-2 tabs BID PRN constipation
- Lorazepam 1mg PO BID and q6h PRN anxiety/agitation/SOB
- Ipratropium-albuterol Nebs QID PRN SOB

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Objective 5: Apply knowledge to case example

3/3: Family is requesting a 'pain pump' as he was receiving injectable pain medication during his last hospital admission prior to the hospice referral.

THOUGHTS?

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Objective 5: Apply knowledge to case example

Things to keep in mind:

- In a hydromorphone backorder, opioid infusion options become morphine or fentanyl. Patient has CKD3 and a PPS of 50% -avoid morphine due to accumulation of metabolites in renal impairment.
- Patient already on a fentanyl patch that is under-dosed. Using 10mg hydrocodone tablets 4-5x/day = 40-50mg hydrocodone/24h and still reporting pain. Consider increasing fentanyl patch to 50mcg/hr TP q72h. Discuss dose increase with family as alternative to infusion.
- Keep hydrocodone for BTP. D/C tramadol.

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Objective 5: Apply knowledge to case example

Things to keep in mind:

- Consider initiating dexamethasone for bone pain 4mg qam. Addition of dexamethasone may help SOB also.
- Patient has a PMH of depression but is not taking anything for management. Discuss addition of mirtazapine 15mg qHS for mood/appetite/sleep.
- Determine if haloperidol should be initiated which may manage the agitation more appropriately than lorazepam. Lorazepam should be reserved for true anxiety/SOB exacerbations.

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THANKS!

Do you have any questions?

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