Pharmacy & Therapeutics Committee Meeting

Private Dining Room

April 15, 2021 7:00 a.m.

Next Meeting Date: TBD at 7:00 a.m. in the Private Dining

PHARMACY AND THERAPEUTICS COMMITTEE

DATE: February 11, 2021 CALLED TO ORDER: 7:02 a.m.
LOCATION: Private Dining Room + Zoom conference call ADJOURNED: 8:00 a.m.

Members Present:		**Members Absent**:	**Guests**:
Nathan Chamberlain, MD David Dodson, MD Mark Anderson, MD F. Lee Hamilton MD Chad Paxson, MD Matthew Kodsi, MD Richard Yap, MD Allen Atchley, MD	Karen Frank, RN-Quality Patrick Ellis, PharmD Rachel Kile, PharmD Karen Babb, PharmD Carey Smith, RPh Susan Fuchs, RD Kevin Hopkins, RT Daniel Marsh, PharmD Lori Hammon, RN-Quality Shannon Harris, RN	Vimal Ramjee, MD Rhonda Hatfield, RN-CNO Rodney Elliott	Kristen Liveris, PharmD La'Travia Howard, PharmD Andrea Wilkinson, PharmD

This meeting will be convened under the protection of the Tennessee Statute 63-6-219 and the Health Care Quality Improvement Act of 1986, Public Law 99-660. All information, case reviews, meeting minutes, statistics and correspondence are confidential and protected. Included in that protection are those that are involved in the review of the information. Any discussion of this information outside the realm of Peer Review constitutes a breach and violates the protection of the persons involved in the breach.

AGENDA ITEM	FINDINGS OR CONCLUSION	ACTION, RESPONSIBILITY	STATUS
Minutes	The December 2020 minutes were approved as submitted.	Approved	Complete
Formulary Decisions & Therapeutic Interchanges	1. **CommonSpirit Health Formulary Alignment:** The February 2021 System P&T committee reviewed additional medications for formulary alignment opportunities across the entire system. The below medications represent formulary variances from the current CHI Memorial formulary: a. *Cardiology*-The following medications were recommended for *non-formulary* status and the recommendations were previously approved by Cardiology: i. Benazepril: Add to our current ACE-I therapeutic interchange table substituted to the clinically appropriate lisinopril dose. Benazepril will be replaced on cardiology order sets with alternative ACE inhibitor formulary options. ii. Simvastatin: Add to the current statin therapeutic interchange table substituted to the clinically appropriate atorvastatin or pravastatin dose. iii. Gemfibrozil: Use is ~100 doses per month, driven by home medication continuation. Compared to gemfibrozil, fenofibrate has shown significantly greater clinically efficacy and has less drug interactions. A therapeutic interchange to fenofibrate 67 mg daily was approved.	Approved	Complete
	2. **Empagliflozin (Jardiance®) use criteria:** The February 2021 CommonSpirit Health System P&T committee meeting voted to remove all existing ordering restrictions for empagliflozin. Our P&T committee had a robust discussion on how to ensure new medication orders are safely initiated and subsequently monitored. The committee approved modifying the current restriction criteria to allow for new inpatient starts, with clinical criteria requirements. The clinical criteria will be built into the EHR.	Approved	Complete

AGENDA ITEM	FINDINGS OR CONCLUSION	ACTION, RESPONSIBILITY	STATUS
Medication Use	1. **Pharmacist-driven 4T score calculation for streamlining HIT lab tests:** Andrea Wilkinson, pharmacy resident, presented her MUE results which demonstrated that by calculating a 4T score for all orders, pharmacists played a role in decreasing heparin antibody tests being performed in patients unlikely to have HIT (low 4T scores). Additional pharmacist education on the 4T score calculation will be provided, as there is opportunity to improve calculation accuracy because 78% of the orders sent to lab still resulted in negative heparin antibody tests. The committee discussed upcoming plans to send all HIT Ab and SRA tests to Erlanger (instead of Quest) for faster result turnaround time.	Informational	Complete
	2. **Collagenase (Santyl®) ointment:** Rachel shared MUE results on inpatient collagenase ointment utilization. From May through December 2020, Santyl dispensed from the inpatient pharmacy had a total drug cost of ~$43,000. Based on the MUE results, it was recommended to adopt the CHI approved restriction criteria for use, which will be built into the EHR. This recommendation was previously reviewed and supported by Dr. John Gwin.	Approved	Complete
	3. **Tocilizumab (Actemra®) for Inpatient Treatment of COVID-19:** A P&T subcommittee convened earlier in the week to review available clinical data on tocilizumab (Actemra®) in COVID-19 and determine criteria for appropriate use. Rachel reviewed the locally designated restriction criteria finalized by the subcommittee, which will be updated as needed based on available data.	Approved	Complete
Protocols & Orders	1. **Respiratory Distress Orders Policy (Protocol):** Kevin Hopkins presented changes to the policy which will allow oxygen, bronchodilators, and arterial blood gas orders to be placed by respiratory therapists, per protocol, with physician co-signature required in the EHR. This policy will be added to the list of protocols reviewed annually per TJC requirements.	Approved	Complete
Policies	1. **Titrating Medications:** This policy was updated to include dosing (titrating) instructions for nitroglycerin infusions on cardiac telemetry floors. No other changes to this policy.	Approved	Complete
	2. **Look-Alike Sound-Alike Medications:** This policy was reviewed and no changes were needed.	Approved	Complete
Nutrition	1. **Nutrition Care Manual:** Susan Fuchs reviewed the changes made for the November 2020 update. The manual can be found on the Mnet under “Clinical Tools”.	Approved	Complete
	2. **Enteral Policy:** Susan reviewed policy changes which included verbiage update to reflect the EHR transition, in addition to RD managed enteral nutrition ordering workflow(s).	Approved	Complete

There being no further business, the meeting was adjourned at 8:00 a.m. The next P&T meeting is **April 15, 2021 at 7:00 a.m.**

Respectfully submitted,
Patrick N. Ellis, PharmD, Director of Pharmacy
Rachel Kile, PharmD, Pharmacy Clinical Manager

Approved by,
Nathan Chamberlain, MD, Chairman

COMMONSPIRIT HEALTH FORMULARY ALIGNMENT

BACKGROUND:
The February & March 2021 CommonSpirit Health System P&T committees reviewed additional medications for formulary alignment opportunities across the entire system. The below medications represent formulary variances from the current CHI Memorial formulary. As per the system formulary process, local P&T's may approve the below with no changes or approve with more restrictions. Additionally, sites may request an exception or appeal to any formulary decision with accompanying clinical documentation supporting the appeal.

The formulary variances are detailed below:

BiDil (isosorbide dinitrate 20 mg plus hydralazine 37.5 mg)

- Recommendation/Discussion:

  BiDil was removed from national formulary. The cost of BiDil is >6x that of the individual components ($3.57 vs $0.58). Local use of BiDil is ~70 doses/month between both GW and HX. Use is split between home medication continuation vs. new inpatient orders.

  It is recommended to remove BiDil from local formulary and approve a therapeutic interchange to the individual components during inpatient admission. This recommendation was approved by Cardiology.

Ordered	Provided
BiDil 20-37.5 mg	Isosorbide dinitrate 20 mg + hydralazine 20 mg (1 ½ tabs)

Demeclocycline 150 mg tab

- Recommendation/Discussion:

  Demeclocycline was removed from formulary on the recommendation of the national oncology pharmacy clinical council. Utilization is very low; only 4 doses have been administered since November 2019.

  It is recommended to remove from formulary and allow patients to utilize their own supply.

FORMULARY REVIEW

GENERIC NAME: Droperidol

INDICATIONS:

FDA Approved
• Prevention and/or treatment of nausea and vomiting associated with surgical and diagnostic procedures
Non-FDA Approved
• Treatment of acute undifferentiated agitation (AUA) • Emergent treatment of nausea and vomiting not associated with surgical or diagnostic procedures • Treatment of acute migraine

THERAPEUTIC CATEGORY:
First generation (typical) antipsychotic; butyrophenone
Anti-emetic; dopamine D2 receptor antagonist

PHARMACOKINETICS:

	Droperidol
Absorption	Rapid absorption after IM administration
Distribution	Crosses blood-brain barrier Vd ~1.5 L/kg (adults) and ~0.6 L/kg (children)
Metabolism	Hepatic, not significantly metabolized by CYP450 enzymes
Elimination	75% in the urine, <1% as unchanged drug 22% in feces, 11% as unchanged drug
Onset	Within 3-10 minutes following IV or IM administration Reaches peak effect approximately 30 minutes after administration
Duration	2-4 hours, may extend up to 12 hours

SPECIAL POPULATIONS:

	Droperidol
Pregnancy	There are no adequate and well-controlled studies in pregnant women. Droperidol should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.
Lactation	It is not known whether droperidol is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when droperidol is administered to a nursing mother.
Pediatrics	Droperidol is approved for use in patients two years of age and older. The safety of droperidol in children younger than two years of age has not been established.
Geriatrics	No specific dosing recommendations per manufacturer's labeling; initial dose of droperidol should be appropriately reduced in the elderly.
Hepatic Impairment	No specific dosing recommendations per manufacturer's labeling; administer with caution to patients with severe hepatic impairment
Renal Impairment	No specific dosing recommendations per manufacturer's labeling; administer with caution to patients with severe renal impairment

CLINICAL STUDIES BY INDICATION[5-10]

Nausea and Vomiting

Braude D, et al. Antiemetics in the ED[5]	
METHODS	
Study Design	Single center, randomized, double-blind, placebo-controlled trial
Patient Enrollment Inclusion	• Adults of 18-65 years of age • Primary or secondary complaint of nausea and/or vomiting • Baseline nausea rated at least 40 mm on a 100-mm visual analog scale (VAS)
Patient Enrollment Exclusion	• Mild symptoms (nausea and/or vomiting rated <40 mm on a VAS) • Hypotension (systolic blood pressure < 90 mm Hg) • Greater than 1 liter of intravenous fluids administered before study enrollment • **Use of commonly accepted antiemetic within the previous 24 hours**

- Known or suspected congestive heart failure
- Pregnancy
- Their primary ED physician did not wish the patient enrolled
- A reported allergy to any study medication

Baseline Characteristics

	Total	Droperidol	Metoclopramide	Prochlorperazine	Saline Placebo
N	97	22	25	24	26
Characteristics					
Male*	42 (43.3)	7 (31.8)	8 (32.0)	17 (70.8)	10 (38.5)
Female	55 (56.7)	15 (68.2)	17 (68.0)	7 (29.2)	16 (61.5)
Age	37.5 +/- 11.8 (19-63)	16.6 +/- 12.6 (19-60)	38.9 +/- 11.5 (22-63)	36.1 +/- 11.0 (19-55)	38.2 +/- 12.5 (29-58)
IV fluid before randomization (mL)	83.5 +/- 218.3	115.9 +/- 265.2	56.0 +/- 172.2	50.0 +/- 143.7	113.5 +/- 269.7
Mean baseline scores					
Nausea	69.6 +/- 17.6	69.8 +/- 16.3	65.4 +/- 17.5	72.2 +/- 18.1	70.7 +/- 18.8
Anxiety	56.8 +/- 26.7	56.2 +/- 23.9	52.6 +/- 23.1	60.2 +/- 31.1	58.2 +/- 28.7
Sedation	40.9 +/- 27.2	36.2 +/- 27.7	45.1 +/- 28.2	41.2 +/- 24.7	40.2 +/- 28.8
*unequal distribution of sex by treatment group (p = 0.017)					

Treatment Plan

- IM injection of **1.25 mg droperidol**, 10 mg metoclopramide, 10 mg prochlorperazine, or saline
- 30 minutes after administration, rated nausea, sedation and anxiety on a 100-mm VAS scale; patients were asked if they were satisfied with nausea treatment received and if further medication was needed
- During the 30-minute study period, intravenous fluid administration was controlled and drugs with antiemetic properties were withheld. All other aspects of treatment continued at the discretion of the treating physician

RESULTS

Primary Endpoint

Droperidol was significantly better than metoclopramide or prochlorperazine in comparison to placebo in reducing nausea at 30 minutes (Dunnett multiple comparisons procedure, P = 0.04)

Change from Baseline in VAS Scores for Nausea, mean +/- SD			
Droperidol	Metoclopramide	Prochlorperazine	Placebo
– 54.5 mm +/- 18.4	– 40.2 mm +/- 23.8	– 40.5 mm +/- 24.1	– 38.7 mm +/- 21.1

Secondary Endpoint

- No significant differences between groups at 30 minutes with respect to subjective anxiety (P = 0.70) or sedation (P = 0.17)
- No significant differences between groups in persistent nausea (P = 0.12) or need for a rescue medication (P = 0.23)

Secondary Outcomes				
	Droperidol	Metoclopramide	Prochlorperazine	Placebo
Change in VAS score at 30 min, mean +/- SD				
Anxiety	– 23.8 +/- 25.4	– 25.4 +/- 24.3	– 21.9 +/- 38.0	– 31.7 +/- 31.6
Sedation	13.5 +/- 32.2	0.4 +/- 30.1	5.1 +/- 26.5	– 4.8 +/- 25.0
Characteristics, n (%)				
Liked the study medication	20 (95.2)	21 (84.0)	20 (83.3)	22 (95.7)
Required rescue medication	1 (4.5)	1 (4.0)	6 (25.0)	4 (15.4)

Adverse Events

- Adverse effects data were available for 72 (74%) subjects
- No significant difference in akathisia between groups (P = 0.51, Fisher exact test)
- **Droperidol was noted to cause significantly more self-reported anxiety or restlessness (droperidol, 71.4%, vs all others, 23.5%)**
- Only 1 patient, who had received droperidol, developed a dystonic reaction

Limitations

- Adverse events not reported in detail
- **No discussion of cardiovascular events or EKG monitoring**

<table>
<tr><td></td><td>• Did not compare to current standard therapy for nausea/vomiting</td></tr>
<tr><td>Author's Conclusion</td><td>• When administered intravenously to adult patients with moderate to severe nausea, 1.25 mg of droperidol was more effective than 10 mg of metoclopramide or 10 mg of prochlorperazine but caused more extrapyramidal symptoms
• 10 mg of metoclopramide and 10 mg of prochlorperazine were not more effective than saline placebo
• All patients improve over time and/or with intravenous hydration</td></tr>
<tr><td colspan="2"></td></tr>
<tr><td colspan="2">Fortney JT, et al. Ondansetron versus droperidol for elective outpatient surgery[6]</td></tr>
<tr><td colspan="2">METHODS</td></tr>
<tr><td>Study Design</td><td>Two identical, multi-center, randomized, double-blind, placebo-controlled studies</td></tr>
<tr><td>Patient Enrollment Inclusion</td><td>• ASA physical status I or II
• Between the ages of 18 and 65 years
• History of motion sickness or PONV after general anesthesia
• Scheduled for general anesthesia for outpatient procedures planned to last no longer than 2 hours, limited to procedures with high emetogenic potential (laparoscopic, genitourinary, lower extremity orthopedics, umbilical or ventral herniorrhaphies, partial mastectomies, or lumpectomies)</td></tr>
<tr><td>Patient Enrollment Exclusion</td><td>• Major organ disease
• ASA physical status >II
• Weight >100% over IBW
• Pregnancy or breastfeeding
• History of alcohol or drug abuse
• Receipt of an investigational drug within 30 days of the study
• Receipt of an antiemetic agent within 24 hours of the study
• Known hypersensitivity to 5-HT3 antagonists</td></tr>
<tr><td>Baseline Characteristics</td><td>
<table>
<tr><td></td><td>Placebo</td><td>Droperidol 0.625mg</td><td>Droperidol 1.25mg</td><td>Ondansetron 4mg</td></tr>
<tr><td>Patients (n)</td><td>518</td><td>518</td><td>510</td><td>515</td></tr>
<tr><td>Age</td><td>35 +/- 10</td><td>35 +/- 9</td><td>35 +/- 9</td><td>36 +/- 10</td></tr>
<tr><td>Weight (kg)</td><td>71 +/- 17</td><td>71 +/- 17</td><td>72 +/- 17</td><td>70 +/- 16</td></tr>
<tr><td>Women, n (%)</td><td>449 (87)</td><td>450 (87)</td><td>462 (91)</td><td>456 (89)</td></tr>
<tr><td>History of motion sickness, n (%)</td><td>316 (61)</td><td>309 (60)</td><td>330 (65)</td><td>319 (62)</td></tr>
<tr><td>History of PONV, n (%)</td><td>445 (86)</td><td>442 (85)</td><td>450 (88)</td><td>436 (85)</td></tr>
</table>
</td></tr>
<tr><td>Treatment Plan</td><td>• Ondansetron 4 mg, droperidol 0.625mg, droperidol 1.25mg, or placebo administered IV 20 minutes before anesthesia induction
• Baseline vital signs and nausea assessment using verbal rating score of 1-10
• Nausea assessments every 30 minutes from time of patient consciousness after surgery through 2 hours post-operation
• Rescue antiemetics given for intractable nausea for at least 15 minutes, if 3 emetic episodes within 15 minutes, or at patient request</td></tr>
<tr><td colspan="2">RESULTS</td></tr>
<tr><td>Outcomes</td><td>• The number of patients experiencing complete response within 2 hour period was significantly higher in droperidol and ondansetron groups than placebo
• Incidence of complete response at 2 hours was similar between the ondansetron and droperidol 0.625mg groups, but significantly higher in the droperidol 1.25mg group
• The proportion of patients receiving opioid analgesics were significantly lower in both droperidol groups than ondansetron or placebo
• The number of patients experiencing complete response at 24 hours was higher in all of the treatment groups compared to placebo, and was significantly greater in the droperidol 1.25mg group compared to ondansetron group</td></tr>
<tr><td>Adverse Events</td><td>• No significant differences among treatment groups with respect to the incidence of hypotension, sedation, or agitation
• Significantly lower incidence of headache in droperidol groups compared to ondansetron group</td></tr>
<tr><td>Limitations</td><td>• Did not assess higher ondansetron dose of 8 mg or repeated dosing
• High percentage of female patients
• Significantly different opioid use between treatment groups</td></tr>
<tr><td>Author's Conclusion</td><td>Droperidol 1.25 mg IV was more effective in reducing the incidence of emesis in the first 2 hours and the first 24 hours postoperatively than either ondansetron 4 mg or droperidol 0.625 mg. No increased incidence of</td></tr>
</table>

	adverse event in the droperidol groups compared to ondansetron. All three antiemetic treatments were superior to placebo in terms of patient satisfaction.

Headache and Migraine

Silberstein SD, et al. Acute migraine treatment with droperidol: a randomized, double-blind, placebo-controlled trial[7]

METHODS

Study Design

Randomized, double-blind, placebo-controlled, dose-ranging, multicenter study

Patient Enrollment Inclusion

- Patients 18 to 65 years of age who met the International Headache Society diagnostic criteria for migraine with or without aura
- **Minimum 1-year documented history of migraine, with a frequency of two to six moderate or severe migraine attacks per month, over the previous 6 months**

Patient Enrollment Exclusion

- Pregnant, lactating, or of childbearing potential and not practicing adequate contraception
- History of drug abuse
- Frequent tension-type headaches (>10 days/month)
- Inability to distinguish between tension-type or migraine headache
- Active overuse of medication intended for the acute treatment of headache
- Pheochromocytoma
- Coexisting condition that might expose the patient to a disproportionately increased risk of a significant adverse event (seizure disorder, PD, use of lithium or monoamine oxidase inhibitors, or a history of myocardial infarction, hypertension, unstable angina, silent ischemia, significant syncope, Printzmetal angina, clinically significant EKG abnormality, stroke, TIA, or congestive heart failure)
- **Already received other medication for headache (analgesics, triptans, ergotamines, opioids)**

Baseline Characteristics

	Placebo	**0.1 mg**	**2.75 mg**	**5.5 mg**	**8.25 mg**
Demographic Characteristics of Patient History					
N	61	63	61	59	61
Sex (% Female)	85	81	80	81	77
Age	41 +/- 9.7	42 +/- 10.5	41 +/- 9.1	41 +/- 10.8	42 +/- 10.0
Duration of illness (years)	21 +/- 10.7	21 +/- 11.5	20 +/- 13.6	19 +/- 11.0	20 +/- 11.9
Median attacks/ month	4	4	4	4	4
Symptoms present during attack (%)					
Aura	36	41	39	49	41
Nausea	92	94	90	92	98
Vomiting	48	46	38	47	43
Photophobia	98	97	98	98	100
Phonophobia	95	98	95	98	98
Demographic Characteristics of Acute Attack					
Mean duration of headache (hrs)	3.7	3.6	3.1	3.6	3.5
Severity (moderate/ severe)	56/44	60/44	70/30	59/41	64/36
Symptoms present during attack (%)					
Aura	23	25	26	29	23
Nausea	78	68	72	73	69
Vomiting	10	10	7	15	5
Photophobia	93	97	98	95	93
Phonophobia	79	87	84	92	84

Treatment Plan

- Droperidol 0.1, 2.75, 5.5, or 8.25 mg IM or matching placebo, injected into deltoid, thigh, or buttock
- All patients remained in the clinic for a minimum of 30 minutes following treatment or until reaching pain-free status at any time after 30 minutes
- Patients not achieving headache relief by 2 hours were given alternative rescue medication including, but not limited to, opioids, triptans, or ergotamine. If rescue medication was administered at 2 hours, the patient remained in the clinic for 2 additional hours.
- One week following treatment, patients returned for a final evaluation of pain recurrence, medication use, associated symptoms, adverse events, physical examination, and laboratory studies

RESULTS

Primary Endpoint

- Significantly more patients treated with droperidol 2.75 mg, 5.5 mg, and 8.25 mg achieved a pain-free response at 2 hours after treatment compared with placebo

	Placebo	0.1 mg	2.75 mg	5.5 mg	8.25 mg
2-hour headache response, recurrence within 24 hours (%)	43	49	30	27	39
2-hour headache response, no recurrence within 48 hours (%)	16	27	49	37	31

Secondary Endpoint

- Treatment with droperidol 8.25 mg was associated with a significant improvement in 30-minute headache response, while 2.75 mg demonstrated significant improvement over placebo 1 hr after treatment and 5.5 mg demonstrated significant improvement over placebo 1.5 hrs after treatment
- The median time to no pain was 12 hours for droperidol 0.1 mg, 1.5 hours for droperidol 2.75 mg, 4 hours for droperidol 5.5 mg, and 2 hours for droperidol 8.25 mg
- Significantly more patients who received droperidol 2.75 mg reported relief of associated symptoms (nausea, vomiting, photophobia, and phonophobia) compared with placebo. This effect was most pronounced with a significantly large reduction in nausea. Specifically, droperidol 2.75 mg was significantly ($p = 0.05$) more effective in reducing nausea at the 1, 1.5, 3, and 4 hours after treatment assessments. The 2.75-mg dose also yielded significantly greater relief of phonophobia (1.5, 4, and 12 hours; $p = 0.05$), and photophobia (1.5, 2, and 4 hours). Droperidol 8.25 mg was significantly more effective than placebo in relieving associated symptoms at 4, 12, 24, and 48 hours

Adverse Events

- Most adverse events were of mild or moderate intensity
- Anxiety, akathisia, and somnolence (considered by the investigators to be possibly or probably related to study medication) were rated as severe in 30% of patients who experienced those symptoms
- Above the 0.1 mg dose of droperidol, the incidence of severe events did not appear to be dose related
- No cardiovascular adverse events were reported
- Most common adverse events reported included asthenia, akathisia, somnolence, and anxiety without a clear dose-response relationship

Limitations

- Compared to placebo, not compared to standard treatment
- **High placebo headache response rate (57%)**
- Results for primary outcome were not fully reported

Author's Conclusion

- Therapeutic benefit was evident at doses ≥2.75 mg; however, more adverse events were associated with higher doses, suggesting that the optimal dose may be about 2.75 mg IM
- Treatment with droperidol appears to be very effective in reducing both the nausea and vomiting associated with migraine
- **Droperidol should be considered in the patient who does not respond to treatment with dihydroergotamine or triptans, in patients for whom ergotamines and triptans are contraindicated, or in patients who do not tolerate or are unable to take other pain medications such as opiates and barbiturates**

Richman PB, et al. Intramuscular droperidol for the treatment of acute migraine headache[8]

METHODS

Study Design

Randomized controlled trial, double-blind

Patient Enrollment Inclusion

Patients meeting IHS criteria for migraine with or without aura

Patient Enrollment Exclusion

- Use of phenothiazine or narcotic medications within 24 hours of presentation
- Pregnancy

Baseline Characteristics

	Droperidol	Meperidine	p-value
N	15	14	
Age	30.7 +/- 8.9	32.7 +/- 9.9	0.59
Female sex	73%	71%	0.91
Mean headache duration (hours)	24.7 +/- 28.3	18.3 +/- 25.8	0.55
Mean initial VAS score	88	77	0.03

Treatment Plan	• **Droperidol 2.5 mg IM or meperidine 1.5 mg/kg IM**
RESULTS	
Outcomes	

	Droperidol	Meperidine	p-value
Mean change in VAS score	47	37	0.33
Average Likert score	1.1	1.9	0.85
Percentage of patients who did not want rescue medication	67%	57%	0.61

Adverse Events	• Sedation occurred in 6.7% of patients given droperidol and 14.3% of patients given meperidine • **Akathisia occurred in 13.3% of patients given droperidol**
Limitations	• Small study • Low dose of droperidol compared to other studies for treatment of migraine
Author's Conclusion	Intramuscular droperidol was similar in efficacy to meperidine with a low incidence of side effects

Miner JR, et al. Droperidol vs prochlorperazine for benign headaches in the emergency department[9]

METHODS	
Study Design	Randomized, single-blind clinical trial
Patient Enrollment Inclusion	• Between 18 and 60 years of age • Presence of benign headache defined by examining physician to be without identifiable etiology from history, physical examination, laboratory analysis, or imaging studies
Patient Enrollment Exclusion	• Pregnant or breastfeeding • History of neuroleptic malignant syndrome, hypotension, cardiac arrhythmia, hepatic or renal dysfunction, or a suspicion of a malignant headache
Baseline Characteristics	

	Droperidol (N = 82)	Prochlorperazine (N = 86)	p-value
Age	31.7 +/- 8.23	33.9 +/- 12.1	0.19
Gender – female, n (%)	42 (51.2%)	45 (52.3%)	0.47
Previously diagnosed migraine, n (%)	23 (28.0%)	24 (27.9%)	0.37
Prior use of analgesics at home, n (%)	34 (41.5%)	29 (33.7%)	0.14
Baseline pain score	79.8 mm	74.3 mm	0.08
IM administration, n (%)	49 (59.8%)	57 (66.3%)	0.12

Treatment Plan	• Droperidol 5 mg IM or 2.5 mg IV, or prochlorperazine 10 mg IM or IV • Assessment of pain using VAS at baseline, 30 minutes, and 60 minutes • Assessment for side effects at 30 minutes, 60 minutes, and 24 hours • Rescue medication given at 60 minutes if insufficient pain relief
RESULTS	
Outcomes	

	Droperidol (n = 82)	Prochlorperazine (n = 86)	p-value
30-minute VAS (95% CI)	33.1 mm (26.4, 39.7)	40.6 mm (37.9, 47.3)	0.03
Change in VAS from baseline at 30 minutes (95% CI)	60.7% (53.4, 67.9)	48.7% (41.3, 56.1)	0.011
60-minute VAS (95% CI)	16.3 mm (10.7, 21.8)	28.9 mm (21.9, 35.9)	0.007
Change in VAS from baseline at 60 minutes (95% CI)	81.4% (76.1, 86.8)	66.9% (59.9, 73.9)	0.001
Number (%) of patients with >50% change in VAS at 30 minutes	50 (60.9%)	38 (44.2%)	0.09
Number (%) of patients with >50% change in VAS at 60 minutes	74 (90.2%)	59 (68.6%)	0.017
Rescue medications given	13 (15.9%)	18 (20.9%)	0.012

Adverse Events	• 13 (15.2%) of patients receiving droperidol and 8 (9.6%) of patients receiving prochlorperazine experienced adverse effects (p-value 0.19) • One patient in the droperidol group experienced dystonia, which was successfully treated with no further events

	• 5 (6.1%) of patients receiving droperidol and 7 (8.1%) of patients receiving prochlorperazine experienced akathisia • 7 (8.5%) of patients receiving droperidol and 1 (1.2%) of patients receiving prochlorperazine experienced decreased levels of consciousness requiring additional observation time in the ED • No patients experienced hypotension
Limitations	• Investigators were not blinded to study drug • Patients were able to see their previous VAS scores when reporting their pain • Lack of randomization of route of administration (determined by provider prior to enrollment) • No EKG monitoring performed
Author's Conclusion	Droperidol was superior to prochlorperazine for treating headache pain at the doses used in this study

Agitation

Matrel M, et al. Management of acute undifferentiated agitation (AUA) in the Emergency Department[10]

METHODS

Study Design: Randomized, double-blind trial of agitated ED patients requiring emergent sedation

Patient Enrollment Inclusion: Patients presenting to the ED with **AUA requiring emergent sedation**, as determined by the treating physician

Patient Enrollment Exclusion:
- Known pregnancy
- Age younger than 18 years
- Prisoner status

Baseline Characteristics

	Droperidol	Ziprasidone	Midazolam	p-value
N	50	46	48	
Age, mean +/- SD	36.9 +/- 10.9	36.8 +/- 10.8	36.9 +/- 10.9	
Number of men	33	32	33	0.92
Initial clinical assessment of agitation				
Alcohol intoxication	**46**	**43**	**46**	0.73
Illicit substance intoxication	4	5	8	0.40
Head injury	7	9	14	0.03
Psychiatric etiology	2	8	4	0.08
Delirium	0	1	0	0.34
Seizure	0	0	1	0.37

Treatment Plan:
- A convenience sample of patients was randomized to receive droperidol 5 mg, ziprasidone 20 mg, or midazolam 5 mg IM
- The AMS scores, SaO_2 data, and $ETCO_2$ data were then recorded when agitation was controlled at 15, 30, 45, 60, 90, and 120 minutes
- The need for additional sedatives, respiratory depression requiring intervention, endotracheal intubation, cardiac dysrhythmias, and other complications were monitored
- Final diagnosis, disposition, and total time to discharge after sedative administration were recorded

RESULTS

Primary Endpoint:
- More patients remained agitated at 15 minutes in the ziprasidone group (28 of 46) than in the droperidol (20 of 50) and midazolam (15 of 48) groups (p = 0.01)
- No difference in the number of patients who remained agitated at the 30-minute interval (ziprasidone, 14 of 46; droperidol, 6 of 50; midazolam, 11 of 48; p = 0.08)
- More patients remained agitated at 45 minutes in the midazolam group (14 of 48) than in the droperidol (9 of 50) and ziprasidone (9 of 46) groups (p = 0.03)

Secondary Endpoint

	Droperidol	Ziprasidone	Midazolam	p-value
Rescue medications required				**0.05**
Total number of patients, n (%)	5 (10)	9 (19.6)	24 (50)	
Total number of doses	6	11	30	
Respiratory Depression				

	Occurrence, n %	20 (40)	26 (56.5)	24 (50)	0.26
	Requiring supplemental oxygen, n (%)	4 (8)	7 (15.2)	10 (20.8)	0.20
	Requiring intubation	0	0	0	
Adverse Events	• No cardiac dysrhythmias were identified • One patient receiving droperidol, four patients receiving ziprasidone, and one patient receiving midazolam (and subsequently droperidol rescue sedation) developed akathisia • No additional complications or adverse events were seen				
Limitations	• Endpoints not clearly stated • Adverse events not reported in detail • High proportion of patients enrolled with acute alcohol intoxication (performance of the medications may vary in patients with different causes of AUA) • Higher percent of patients in midazolam group with head injury (statistically significant)				
Author's Conclusion	• Droperidol, ziprasidone, and midazolam are effective in the management of AUA in the ED • More patients remained agitated at 15 minutes with ziprasidone relative to the other agents, and patients receiving midazolam more frequently required additional sedation.				

COMPARATIVE EFFICACY[11]

Droperidol is effective for the treatment of nausea and vomiting, and for treatment of acute migraine. Studies comparing droperidol to 5-HT3 receptor antagonists for nausea and vomiting are limited to the peri-operative setting, but show droperidol 1.25 mg to be more effective than ondansetron 4 mg. Compared to prochlorperazine and metoclopramide, droperidol has demonstrated superior efficacy in treatment of nausea and vomiting in the emergency setting. Droperidol has been demonstrated to be more effective than placebo and prochlorperazine, and similar in efficacy to meperidine, for treatment of acute migraine.

Droperidol carries a black box warning for QTc prolongation; however, this is a dose-related effect and there is insufficient evidence to endorse this risk at the lower doses used for headaches or nausea and vomiting. A 2004 review of literature and 270 MedWatch reports submitted between November 1997 and January 2002 reported the true incidence of cardiovascular adverse effects to account for only 33 unique cases, all of which had confounding factors, such as a *significant cardiac history or a more likely cause of the adverse effect*. Two studies were cited in the FDA report on the basis of the black box warning for droperidol, and these studies were conducted using doses ranging from 0.1 mg/kg up to 0.25 mg/kg, which are significantly higher doses than the doses commonly used in practice. Based on the evidence from clinical studies and the detailed review of cardiovascular adverse event reports, caution should be used in patients known to be at a high risk for arrhythmias.

Although generally well-tolerated, *droperidol is associated with decreased level of consciousness prolonging ED observation time and extrapyramidal effects which may require additional treatment*. Given the risk of these adverse effects, droperidol should not be utilized first-line for patients with nausea and vomiting or migraine headaches, but may be considered as a suitable alternative medication for patients who have not responded to initial treatment or for whom first-line agents cannot be used.

BLACK BOX WARNINGS

- Cases of QT prolongation and/or torsade de pointes have been reported in patients receiving droperidol at doses at or below recommended doses. Some cases have occurred in patients with no known risk factors for QT prolongation and some cases have been fatal.

CONTRAINDICATIONS

- Known or suspected QT prolongation, including congenital long QT syndrome
- Known hypersensitivity to the drug
- Not recommended for any use other than for the treatment of perioperative nausea and vomiting in patients for whom other treatments are ineffective or inappropriate

WARNING AND PRECAUTIONS

- Droperidol should be administered with extreme caution in the presence of risk factors for development of prolonged QT syndrome, such as: 1) clinically significant bradycardia, 2) any clinically significant cardiac disease, 3) treatment with Class I and Class III antiarrhythmics, 4) treatment with monoamine oxidase inhibitors, 5) concomitant treatment with other drug products known to prolong the QT interval & 6) electrolyte imbalance, in particular hypokalemia and hypomagnesemia, or concomitant treatment with drugs that may cause electrolyte imbalance.
- Fluids and other countermeasures to manage hypotension should be readily available
- Droperidol can also alter circulation and may decrease pulmonary arterial pressure. Vital signs and ECG should be monitored routinely.

- Droperidol should be administered with caution to patients with liver and kidney dysfunction.
- In patients with diagnosed/suspected pheochromocytoma, severe hypertension and tachycardia have been observed after the administration of droperidol.

ADVERSE REACTIONS

Adverse Reactions	Droperidol
Cardiovascular	Cardiac arrest, hypotension, tachycardia, ventricular tachycardia, QTc prolongation (dose dependent)
Central Nervous System	Anxiety, chills, dizziness, drowsiness, extrapyramidal symptoms (e.g. akathisia, dystonia), hallucinations, neuroleptic malignant syndrome (rare)
Respiratory	Bronchospasm, laryngospasm
Systemic	Anaphylaxis, shivering

CLINICALLY SIGNIFICANT DRUG INTERACTIONS[3]

- No significant pharmacokinetic drug interactions
- Pharmacodynamic interactions:

Cardiovascular	• Combined risk for arrhythmia with proarrhythmic agents or QTc-prolonging agents • Increased risk for cardiovascular adverse events with agents that induce or exacerbate hypokalemia or hypomagnesemia
CNS	• Combined risk for seizure with medications that lower seizure threshold • Additive toxicity from anticholinergic effects when used with other anticholinergic agents • Additive CNS depression when used with other CNS depressants • Reduced therapeutic effects of dopaminergic medications, such as amphetamines and anti-Parkinson agents

DOSING AND ADMINISTRATION[3, 12]

Adult Dosing/Indication and Administration

- Nausea and vomiting: 2.5 mg IM or slow IV initial dose, additional 1.25 mg doses may be given
- Migraine (unlabeled): No labeled dosing; doses ranging 2.5 mg – 8.25 mg have demonstrated efficacy in clinical studies, although more frequent adverse effects have been reported with doses at the higher end of this range
- Agitation (unlabeled):
    - IM: 5-10 mg, wait at least 10-30 minutes before providing additional medication if needed
    - IV: 2.5-10 mg, may repeat every 5 minutes until sedation achieved, maximum dose 20 mg per episode

Pediatric Dosing/Indication and Administration

- Nausea and vomiting (2-12 years of age): 0.1 mg/kg IM or slow IV

RECOMMENDED MONITORING:

- 12-lead ECG prior to administration unless benefit from immediate treatment outweighs risk of arrhythmias
- Continuous 12-lead ECG monitoring for 2-3 hours after administration
- Observe for extrapyramidal side effects (akathisia, etc.)
- Observe mental status

PHARMACOECONOMICS/COST:

Product (Drug, Strength, Form)	Cost per 5 mg vial
Droperidol 5 mg/2 mL vial (2.5 mg/mL)	$6.64

CONCLUSION & RECOMMENDATION:

Droperidol was approved for formulary use, with restrictions, by the CHI System P&T committee last year following the reintroduction of droperidol to the market in February 2019. Given the safety profile and extended history of droperidol use prior to the product unavailability, it is recommended that droperidol should be added to the formulary with more restrictive criteria than the CommonSpirit Health approved restrictions (highlighted in yellow). These restrictions will be built into the EHR:

- ***Maximum* single dose = 2.5 mg**
- **Indications:**
  - **Prevention and/or treatment of nausea and vomiting associated with surgical and diagnostic procedures**
  - **Prior to using droperidol for off-label indications (such as nausea and vomiting, migraine and agitation), other treatments should be utilized, as clinically appropriate**
  - **When used for agitation:**
    - **i. Utilize 2.5 mg IV or IM dose**
    - **ii. Use limited to scenarios of urgent potential harm to the patient and/or staff and other medications for agitation were attempted first (EHR documentation should reflect)**
    - **iii. Do not administer if K^+ and Mg^{++} are abnormal (if labs available)**
- **Baseline Monitoring:**
  - **Baseline SBP > 100 mmHg**
  - **Baseline electrocardiogram is recommended; use of droperidol is not recommended if there is evidence of QTc prolongation**

FAILURE, MODE AND EFFECTS ANALYSIS (FMEA)

Medication Management Step	Identified Risk	Steps for Prevention
Selection & Procurement		
Therapeutic interchange?	No	N/A
Special Ordering Requirements?	No	N/A
Storage		
LASA* separation of stock?	LASA – not on ISMP list N/A	N/A
Special storage (e.g. refrigeration, protect from light, controlled substance)?	N/A	N/A
Pharmacist/Technician Education?	N/A	N/A
Ordering & Prescribing		
Restriction to particular specialty, indication, or particular patient population?	No restriction	Yes-EHR build will reflect approved ordering restrictions
Dosing Issues (e.g. renal, hepatic dosage adjustment, max dose warnings)?	No renal adjustment, no hepatic adjustment provided	N/A
Drug Interactions?	Additive toxicity: QTc prolonging agents, proarrhythmic agents, hypokalemia- or hypomagnesemia- inducing agents, anticholinergic agents, CNS depressants	EHR warnings
Pregnancy?	Category C	
Absolute Contraindications?	Known or suspected QT prolongation, including congenital low QT syndrome; known hypersensitivity to the drug	Baseline ECG recommended
Requires Order Set, Protocol, concomitant therapy with another drug?	No order set needed	N/A
LASA* nomenclature issues?	No LASA issues	N/A
Prescriber education?	No prescriber education	N/A
Processing, Preparing, & Dispensing		
High-risk drug double check?	No; not on ISMP list	N/A
Drug Interaction check in place?	Not in place; will need to add	EHR functionality
LASA* computer warnings?	N/A	N/A
Administration Notes for MAR (e.g. handling precautions, surrounding food or other drugs)?	N/A	N/A

Medication Management Step	Identified Risk	Steps for Prevention
Packaging/Labeling (e.g. prepacking)?	N/A	N/A
Dispensing (e.g. auxiliary labeling, light protection, refrigeration)?	Protect from light	N/A
Documentation required (e.g. double check, worksheet)?	No worksheet needed	N/A
Pharmacist/Technician Education?	No pharmacist/technician education	N/A
Administration		
Handling precautions, high-risk double check, administration with/without food, interactions, incompatibilities, or other administration information?	None	N/A
Special delivery system (e.g. pump)?	None	N/A
Documentation required? (e. g. double check)	None	N/A
Nurse education?	None	N/A
Monitoring		
Interactions, adverse effects, efficacy, changes in renal function, or similar?	QTc prolongation; hypotension; extrapyramidal symptoms; neuroleptic malignant syndrome	EKG monitoring for patients at higher risk for QTc prolongation; blood pressure monitoring; observation after administration
Follow-up laboratory tests?	Potassium, magnesium	N/A
Education?	None	N/A

FORMULARY REVIEW

GENERIC NAME: Lurbinectedin

PROPRIETARY NAME: *Zepzelca®*

INDICATIONS:

FDA Approved
• Indicated for the treatment of adult patients with metastatic small cell lung cancer (SCLC) with disease progression on or after platinum-based chemotherapy*. *This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

THERAPEUTIC CATEGORY: Antineoplastic Agent, Alkylating Agent

PHARMACOKINETICS:

	ZEPZELCA (Lurbinectedin)
Distribution	Vd= 504
Metabolism	Primarily hepatic, via CYP3A4
Excretion	89% (<0.2% as unchanged drug); urine: 6% (1% as unchanged drug)
t ½ (hr)	51 hours
Protein binding (%)	~99% to both albumin and α-1-acid glycoprotein

SPECIAL POPULATIONS:

	ZEPZELCA (Lurbinectedin)
Pregnancy	Based on animal data and its mechanism of action, ZEPZELCA **can cause fetal harm when administered to a pregnant woman**. **Verify the pregnancy status of females of reproductive potential prior to initiating ZEPZELCA**. Advise female patients of reproductive potential to use effective contraception during treatment with ZEPZELCA and for 6 months after the final dose. Advise males with a female sexual partner of reproductive potential to use effective contraception during treatment with ZEPZELCA and for 4 months after the final dose.
Lactation	There are no data on the presence of lurbinectedin in human milk or its effects on the breastfed child or on milk production. Because of the potential for serious adverse reactions from ZEPZELCA in breastfed children, **advise women not to breastfeed during treatment with ZEPZELCA and for 2 weeks after the final dose**.
Pediatrics	The safety and effectiveness of ZEPZELCA in pediatric patients have not been established.
Geriatrics	Of the 105 patients with SCLC administered ZEPZELCA in clinical studies, 37 (35%) patients were 65 years of age and older, while 9 (9%) patients were 75 years of age and older. **No overall difference in effectiveness** was observed between patients aged 65 and older and younger patients. **There was a higher incidence of serious adverse reactions in patients ≥ 65 years of age than in patients < 65 years of age (49% vs. 26%, respectively)**. The serious adverse reactions most frequently reported in patients ≥ 65 years of age were related to myelosuppression and consisted of febrile neutropenia (11%), neutropenia (11%), thrombocytopenia (8%), and anemia (8%)
Hepatic Impairment	The effect of moderate or severe hepatic impairment (total bilirubin > 1.5 × ULN and any AST) on the pharmacokinetics of lurbinectedin has not been studied. No dose adjustment of ZEPZELCA is recommended for patients with mild hepatic impairment (total bilirubin ≤ ULN and AST > ULN, or total bilirubin 1.0-1.5 × ULN and any AST).
Renal Impairment	No clinically significant differences in lurbinectedin pharmacokinetics were noted based on mild to moderate renal impairment (30-89 mL/min). There are no dosage adjustments provided in the manufacturer's labeling for CrCl <30 mL/min (has not been studied).

CLINICAL STUDIES:

Lurbinectedin as second-line treatment for patients with small-cell lung cancer: a single-arm, open-label, phase 2 basket trial	
METHODS	
Study Design	• Multicenter, open-label, single-arm, multi-cohort, phase 2 basket trial evaluating ZEPZELCA as a single agent in patients with advanced or metastatic solid tumors
Patient Enrollment Inclusion	Adult patients aged at least 18 years with a pathologically proven diagnosis of SCLC were included if they had: • Pre-treatment with only one previous chemotherapy-containing treatment line (immunotherapy was allowed, combined with chemotherapy or alone) • Measurable disease as per the Response Criteria in Solid Tumors (RECIST; version 1.1) • Documented progression before study entry • ECOG performance status of 2 or lower • Patients had to have adequate function of the bone marrow (evaluated by laboratory tests for absolute neutrophil count, platelet count, and hemoglobin), kidneys (evaluated by serum creatinine and creatinine kinase), and liver (evaluated by total bilirubin, albumin, and aminotransferases) • The minimum interval between any previous treatment and study commencement had to be 3 weeks for chemotherapy, 4 weeks for immunotherapy or radiotherapy, and 2 weeks for any investigational or palliative therapy • Only patients with grade 1 or lower toxicities from any previous therapies, except for cases of alopecia and peripheral sensory neuropathy (both grade 2) • Women of childbearing potential had to be receiving adequate contraception during the study and for at least 3 months after study conclusion
Patient Enrollment Exclusion	• Previously received lurbinectedin or trabectedin • Previous or concurrent malignant disease unless in complete remission for more than 5 years • Known CNS involvement (screening of CNS metastases at baseline was mandatory) • Concomitant unstable or serious medical condition within the past year (history or presence of unstable angina, myocardial infarction, congestive heart failure, valvular heart disease, arrhythmia, severe dyspnea, or active infection, such as hepatitis or HIV) • Impending need for radiotherapy; or inability or restricted ability to comply with the study protocol
Treatment Plan	• All patients were treated with 3.2 mg/m² lurbinectedin administered as a 1-h intravenous infusion once every 3 weeks. Treatment was given until disease progression (defined by the RECIST criteria) or unacceptable toxicity (as per investigator decision). • Tumor assessments were conducted every 6 weeks for the first 18 weeks and every 9 weeks thereafter.
RESULTS	
Outcomes Summary	• This phase 2 trial met its primary endpoint and demonstrated that lurbinectedin was active as a second-line treatment for patients with SCLC. • Overall response assessed by the investigators was 35.2% and its lower 95% CI boundary of 26.2% met the per-protocol statistical boundaries to show anti-tumor activity
Adverse Events	• Dose administration was delayed in 23 (22%) patients • Dose was reduced in 28 (26%) because of treatment-related adverse events • Neutropenia was the most common cause of both dose delays in 13 (12%) and reductions in 17 (16%) of patients • The most common grade 3–4 adverse events and laboratory abnormalities (in ≥2% of patients) were hematological disorders, including anemia (nine [9%] patients), leukopenia (30 [29%]), neutropenia (48 [46%]), thrombocytopenia (seven [7%]), and febrile neutropenia (five [5%]); of these, only febrile neutropenia was regarded as treatment related.
Limitations	• Single-arm design with no control group • Exclusion of patients with brain metastases • Included several diseases and general, not SCLC-specific, criteria were used for patient inclusion
Author's Conclusion	• Lurbinectedin has activity in patients with relapsed SCLC and could represent a valuable potential new treatment option for a patient population with a high unmet medical need.

COMPARATIVE EFFICACY:

- ZEPZELCA (lurbinectedin) is indicated for the treatment of adult patients with metastatic small cell lung cancer (SCLC) with disease progression on or after platinum-based chemotherapy.
- After disease progression on first line treatment (cisplatin + etoposide), there are limited treatment options. Topotecan is the only other NCCN preferred regimen for SCLC patients with relapse ≤6 months after initial therapy.
- The results from the phase 2 trial above suggests higher overall response for ZEPZELCA (35.2%) than for topotecan (~16%) with a longer median duration of response and longer median overall survival. It also suggests a more favorable safety profile of ZEPZELCA than topotecan through a lower proportion of patients with hematological toxicities without the need for primary G-CSF prophylaxis.
- The only available phase 3 study evaluating cyclophosphamide–doxorubicin–vincristine (CAV) in patients with relapsed SCLC included patients with a chemotherapy free interval of longer than 60 days, whereas the ZEPZELCA trial enrolled patients with a very short chemotherapy-free interval. Indirect comparisons between the ZEPZELCA trial and the trial of favors ZEPZELCA, since ZEPZELCA resulted in a higher overall response (35.2% vs 18.3%), longer median duration of response (5.3 vs 3.8 months), and longer median overall survival (9.3 vs 6.2 months). Comparison of safety profiles is also in favor of ZEPZELCA which had a lower incidence of grade 3–4 anemia, grade 3–4 neutropenia, and febrile neutropenia than the CAV regimen.
- The NCCN Guidelines for SCLC now include ZEPZELCA as a recommended regimen for both patients who relapse six months and less after prior systemic therapy and for patients who relapse more than six months after prior systemic therapy. **For patients who relapse six months and less, ZEPZELCA is a preferred regimen.**

WARNING AND PRECAUTIONS:

- Myelosuppression
- Hepatotoxicity
- Embryo-Fetal Toxicity

CONTRAINDICATIONS: None

ADVERSE REACTIONS:

Serious adverse reactions occurred in 34% of patients who received ZEPZELCA, and dose reductions due to an adverse reaction occurred in 25% of patients.

Adverse Reactions	**ZEPZELCA (n=105)**	
	All Grades (%)	**Grades 3-4 (%)**
General Disorders		
Fatigue	77	12
Pyrexia	13	0
Chest pain	10	0
Gastrointestinal disorders		
Nausea	37	0
Constipation	31	0
Vomiting	22	0
Diarrhea	20	4
Abdominal Pain	11	1
Musculoskeletal and connective tissue disorders		
Musculoskeletal pain	33	4
Metabolism and nutrition disorders		
Decreased appetite	33	1
Respiratory, thoracic and mediastinal disorders		
Dyspnea	31	6
Cough	20	0
Infections and Infestations		
Respiratory tract infection	18	5
Pneumonia	10	7
Nervous system disorders		
Peripheral neuropathy	11	1
Headache	10	1

CLINICALLY SIGNIFICANT DRUG INTERACTIONS:

Interacting Class of Drug(s)	Effect
Strong and Moderate CYP3A Inhibitors	• Coadministration with a strong or a moderate CYP3A inhibitor increases lurbinectedin systemic exposure which may increase the incidence and severity of adverse reactions to ZEPZELCA. • Avoid coadministration of ZEPZELCA with strong or moderate CYP3A inhibitors. • If the coadministration of ZEPZELCA with a moderate CYP3A inhibitor cannot be avoided, consider dose reduction of ZEPZELCA, if clinically indicated.
Strong and Moderate CYP3A Inducers	• Coadministration with a strong CYP3A inducer decreases lurbinectedin systemic exposure which may reduce ZEPZELCA efficacy. • Avoid coadministration of ZEPZELCA with strong or moderate CYP3A inducers.

DOSING AND ADMINISTRATION:

- **Recommended dosage:** 3.2 mg/m^2 every 21 days for treatment of adult patients with metastatic SCLC with disease progression on or after platinum-based chemotherapy.
    - Continue medication until disease progression or unacceptable toxicity
- Intravenous infusion over 60 minutes
- Consider pre-medication with corticosteroids AND serotonin antagonists
    - Corticosteroids (dexamethasone 8 mg IV or equivalent)
    - Serotonin antagonist (ondansetron 8 mg IV or equivalent)

DOSING ADJUSTMENTS

Renal Impairment

- CrCl 30 to 89 mL/minute: There are no dosage adjustments provided in the manufacturer's labeling; however, no clinically significant differences in lurbinectedin pharmacokinetics were noted based on mild to moderate renal impairment.
- CrCl < 30 mL/minute: There are no dosage adjustments provided in the manufacturer's labeling (has not been studied)

Dosage Modifications for ZEPZELCA for Adverse Reactions

Adverse Reaction	Severity[a]	Dosage Modification
Neutropenia[b] *[see Warnings and Precautions (5.1)]*	Grade 4 or Any grade febrile neutropenia	• Withhold ZEPZELCA until Grade ≤ 1 • Resume ZEPZELCA at a reduced dose
Thrombocytopenia *[see Warnings and Precautions (5.1)]*	Grade 3 with bleeding or Grade 4	• Withhold ZEPZELCA until platelet ≥ 100,000/mm^3 • Resume ZEPZELCA at reduced dose
Hepatotoxicity *[see Warnings and Precautions (5.2)]* and other adverse reactions	Grade 2	• Withhold ZEPZELCA until Grade ≤ 1 • Resume ZEPZELCA at same dose
	Grade ≥ 3	• Withhold ZEPZELCA until Grade ≤ 1 • Resume ZEPZELCA at reduced dose

[a]National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) version 4.0.
[b]Patients with isolated Grade 4 neutropenia (neutrophil count less than 500 cells/mm^3) may receive G-CSF prophylaxis rather than undergo lurbinectedin dose reduction.

NOTE: Patients with isolated Grade 4 neutropenia (neutrophil count less than 500 cells/mm^3) may receive G-CSF prophylaxis rather than undergo ZEPZELCA dose reduction.

Dose Reduction for ZEPZELCA for Adverse Reaction

Dose Reduction	Total Dose
First	2.6 mg/m^2 every 21 days
Second	2 mg/m^2 every 21 days

NOTE: Permanently discontinue ZEPZELCA in patients who are unable to tolerate 2 mg/m^2 or require a dose delay greater than two weeks.

RECOMMENDED MONITORING:

- Monitor blood counts including neutrophil count and platelet count prior to each administration. For neutrophil count less than 500 cells/mm^3 or any value less than lower limit of normal, the use of G-CSF is recommended. Withhold, reduce the dose, or permanently discontinue ZEPZELCA based on severity.
- Monitor liver function tests, prior to initiating ZEPZELCA, periodically during treatment, and as clinically indicated. Withhold, reduce the dose, or permanently discontinue ZEPZELCA based on severity.
- Monitor for signs/symptoms of hepatotoxicity and nausea/vomiting.
- Evaluate pregnancy status in females of reproductive potential before each administration.

PHARMACOECONOMICS/COST:

NDC	Item Description	GPO
68727-0712-01	ZEPZELCA 4MG	$6,633.00

Product (Drug, Strength, Form)	Cost per Cycle	Cost of 4 Cycles
ZEPZELCA, 6.2 MG IV (two 4 mg vials)	$10,201.56 – 13,266	$40,806.24-53,064

**Pricing reflects costs for a patient with a BSA= 2 at full dose of 3.2 mg/m^2 every 21 days. The cost of 4 cycles was used because patients received a median of 4 cycles in the phase 2 trial.

CONCLUSION & RECOMMENDATION:

Lurbinectedin (Zepzelca®) is an alkylating drug that is FDA indicated for the treatment of adult patients with metastatic small cell lung cancer (SCLC) with disease progression on or after platinum-based chemotherapy. Pre-medications of both a corticosteroid and serotonin antagonist should be considered. A single-arm, open-label, phase 2 basket trial found that lurbinectedin was active as a second-line treatment for patients with SCLC. The NCCN included lurbinectedin into the SCLC guidelines as a preferred regimen for patients with relapse ≤6 months (with a performance status of 0-2) and as a recommended regimen in patients with relapse >6 months.

It is recommended to approve lurbinectedin to formulary with restrictions to the outpatient setting for FDA-approved indications or payer-approved off-label subsequent to insurance approval or prior authorization.

FAILURE, MODE AND EFFECTS ANALYSIS (FMEA)

Medication Management Step	Identified Risk	Steps for Prevention
Selection & Procurement		
Therapeutic interchange?	N/A	N/A
Special Ordering Requirements?	N/A	N/A
Storage		
LASA* separation of stock?	- Lurbinectedin may be confused with trabectedin. - ZEPZELCA may be confused with Zejula, Zelboraf, Zoladex, Zydelig.	- Trabectedin, Zelboraf, Zeljula, and Zydelig are not stocked the at institution - Zoladex will be stocked separately from ZEPZELCA
Special storage (e.g. refrigeration, protect from light, controlled substance)?	- Store refrigerated at 2° to 8°C (36° to 46°F)	N/A
Pharmacist/Technician Education?	- Preparation and storage - Calculation of required volume of reconstituted solution	N/A
Ordering & Prescribing		
Restriction to particular specialty, indication, or particular patient population?	- For outpatient oncology use at the infusion center	N/A

Medication Management Step	Identified Risk	Steps for Prevention
Dosing Issues (e.g. renal, hepatic dosage adjustment, max dose warnings)?	- Hepatic, neutropenia and thrombocytopenia dosing modifications - Dose reduction - Grading of toxicities	Pharmacist education
Drug Interactions?	- CYP3A4 inhibitors and inducers	EHR alerts
Pregnancy?	- May cause fetal harm	- Evaluate pregnancy status of females with reproductive potential - Counsel patients
Absolute Contraindications?	N/A	N/A
Requires Order Set, Protocol, concomitant therapy with another drug?	Administration of corticosteroid and 5HT3 antagonist	Orders for dexamethasone and ondansetron as pre-medications
LASA* nomenclature issues?	- ZEPZELCA may be confused with Zoladex	- Medications will be stored away from each other
Prescriber education?	- Dose reductions/interruptions - Toxicities	N/A
Processing, Preparing, & Dispensing		
High-risk drug double check?	In place	N/A
Drug Interaction check in place?	In place	N/A
LASA* computer warnings?	- ZEPZELCA may be confused with Zoladex	EHR alerts
Administration Notes for MAR (e.g. handling precautions, surrounding food or other drugs)?	- Administered over 60 minutes through peripheral or central line - Chemotherapy: handle with gloves and dispose of properly	- Build order comments to auto-populate when processing orders for ZEPZELCA
Packaging/Labeling (e.g. prepacking)?	N/A	N/A
Dispensing (e.g. auxiliary labeling, light protection, refrigeration)?	- Chemotherapy Caution Sticker	N/A
Documentation required (e.g. double check, worksheet)?	- In place	N/A
Pharmacist/Technician Education?	- Dose adjustments/reductions - Monitoring for toxicity	- Education session(s)
Administration		
Handling precautions, high-risk double check, administration with/without food, interactions, incompatibilities, or other administration information?	- Double check in place - Sterile water used for reconstitution - Compatible with D5W or NS as diluent - Diluent volume dependent on peripheral vs. central IV administration (peripheral=250 mL diluent, central= 100 mL diluent)	- Education session(s) - Ensure that correct diluent volume auto-populates based on route
Special delivery system (e.g. pump)?	- Administered via infusion pump over 60 minutes	N/A
Documentation required? (e. g. double check)	- In place	- In place
Nurse education?	- Administration - Monitoring parameters	- Education session(s)
Monitoring		
Interactions, adverse effects, efficacy, changes in renal function, or similar?	- CYP3A4 inducers/inhibitors - Myelosuppression - Hepatotoxicity	- Education session(s)
Follow-up laboratory tests?	- CBC, BMP, LFTs	- Education session(s)
Education?	- Interactions, adverse effects, efficacy, changes in renal function	- Education session(s)

MRSA Nasal PCR/Vancomycin Medication Use Evaluation

BACKGROUND:

IV vancomycin is frequently utilized for the empiric treatment of patients with suspected Methicillin-resistant Staphylococcus aureus (MRSA) pneumonia. The American Thoracic Society and Infectious Disease Society of America recommend using an MRSA nasal polymerase chain reaction (PCR) and sputum culture to help guide the de-escalation of empiric anti-MRSA coverage. Recent studies have found that MRSA nasal PCRs have a 95-99% negative predictive value for MRSA pneumonia.[1-5] Furthermore, studies have demonstrated the test's utility in the de-escalation of IV vancomycin without compromising clinical outcomes, particularly when combined with pharmacist-driven protocols.[6]

Based on the available clinical data, a policy was approved at the June 2020 P&T meeting allowing pharmacists to automatically order MRSA nasal PCRs when consulted for dosing IV vancomycin for the treatment of pneumonia. Pharmacists were then provided with training to order the test and make recommendations to providers to stop empiric vancomycin therapy as clinically appropriate. The purpose of this evaluation was to assess the impact of the pharmacist-driven protocol combined with antimicrobial stewardship interventions on IV vancomycin days of therapy for the management of pneumonia.

METHODS/RESULTS:

A retrospective chart review was performed in adult inpatients who were admitted from May to June 2020 (pre-intervention) and July to August 2020 (post-intervention) with a diagnosis of pneumonia and who received empiric IV vancomycin (inclusion and exclusion criteria detailed in Figure 1). A total of 113 patients were included; 51 in the pre- and 62 in the post-intervention groups (Figure 1). There was no difference in median days of IV vancomycin therapy, number of vancomycin levels drawn, length of stay, or 30-day readmission rates (Table 1).

Table 1: Primary and secondary endpoints

	Pre-intervention (n=51)		Post-intervention (n=62)	
Duration of Vancomycin (Days) *Based on days of open I-vent*	Median Mean	4 4.61	Median Mean	4 4
Duration of Vancomycin (Days) *Based on days of Vancomycin admin.*	Median Mean	4 4.67	Median Mean	4 4.17
# of levels drawn	Median Mean	1 1.43	Median Mean	1 1.18
LOS (Median Days)	Median Mean	10 12.31	Median Mean	9 11
Time to Pharmacist Intervention (Hr)*	Median Mean	N/A	Median Mean	42 56.98
30-day readmission rate	3/51	5.88%	3/62	4.84%
**Calculated based on the time from PCR result to time intervention documented*				

MRSA nasal PCR orders increased from approximately 57 to 92 percent and of the total number of PCRs ordered in the post-intervention period, protocol driven orders accounted for 30/57 (53%). The number of pharmacist interventions increased from five to 26. Despite the increase in pharmacist interventions, there were 20 missed opportunities. The five interventions in the pre-intervention group were made by antimicrobial stewardship pharmacists who were reviewing durations of therapy and respiratory cultures whereas the 26 in the post-intervention groups were all based on MRSA PCR results. Of these 26 recommendations to discontinue vancomycin, 77 percent were accepted. Three patients in the pre- and one patient in the post-intervention periods were re-escalated to IV vancomycin post-discontinuation.

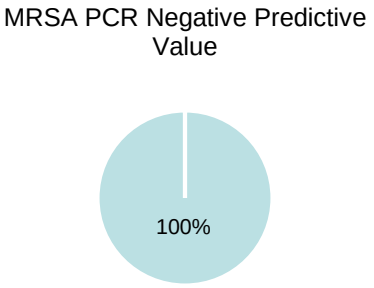
Table 2: PCR/cultures ordered and antimicrobial stewardship interventions

	Pre-intervention		Post-intervention	
% of PCRs Ordered	56.86%	29/51	91.93%	57/62
% of PCRs Ordered by MD	100%	29/29	47.37%	27/57
% of Respiratory Cultures	56.86%	29/51	52.61%	32/62
% of Interventions Made (made/opportunity)	25.00%	5/20	56.52%	26/46
% of Physician Acceptance	80.00%	4/5	76.92%	20/26
% of abx re-escalation	5.88%	3/52	1.61%	1/61
**opportunities were defined as a MRSA (-) nasal swab result* **abx re-escalation: defined as re-starting vancomycin after previously being discontinued*				

This review also found the negative predictive value of the MRSA nasal PCR to be 100% for MRSA pneumonia, which is similar to the 95-99% that has been seen in previous studies further supporting the appropriateness of de-escalation. It is important to note that the MRSA nasal PCR does not have a high positive predictive value. Therefore, if the MRSA nasal PCR detects MRSA, it does not indicate that the patient has MRSA pneumonia. The positive predictive value (PPV) found in this evaluation correlates with other studies that have found the PPV to range from 35-58%.

Table 3: Positive and negative predictive values for MRSA pneumonia

	Respiratory Culture MRSA (+) n= 6	Respiratory Culture MRSA (-) n=40	Predictive Value
MRSA Nares (+) n=9	6	3	0.66
MRSA Nares (-) n=37	0	37	1



DISCUSSION:

In conclusion, there was no difference seen in our primary outcome of median duration of IV vancomycin therapy for patients with pneumonia. However, there was an increase in MRSA nasal PCR orders, available opportunities, and pharmacists' interventions. This study identified many missed IV vancomycin de-escalation opportunities. In order to understand barriers to making recommendations, a mandatory survey was distributed to the pharmacy staff. The results of that survey will inform our pharmacist re-education strategy. Additionally, approximately 20 percent of recommendations to de-escalate IV vancomycin were rejected which indicates a need for physician re-education as well.

Finally, this review has supported previous studies by showing that the PPV of MRSA nasal PCRs should not be used for diagnostic purposes of MRSA pneumonia. However, a negative result can effectively rule it out and be used to de-escalate empiric anti-MRSA therapy in patients with pneumonia.

Moving forward, we will be holding pharmacist re-education lunch sessions with a focus on the empiric and definitive management of pneumonias, clinical data review of vancomycin de-escalation based on MRSA nasal PCRs, relevant patient cases identified from this study, and frequently asked questions from the pharmacist survey. Furthermore, we plan to develop a FAQ sheet to help support pharmacists in their recommendations by providing the data behind common questions. We also plan to attend hospitalist meetings to provide re-education and answer any questions. In conclusion, we expect that the above outlined strategies will increase the number of strong & consistent interventions from pharmacists, improve physician acceptance, and decrease the duration of vancomycin therapy for the empiric management of pneumonia. A post-education MUE will be performed to evaluate the ongoing impact of this protocol and associated interventions.

Figure 1: Inclusion and Exclusion

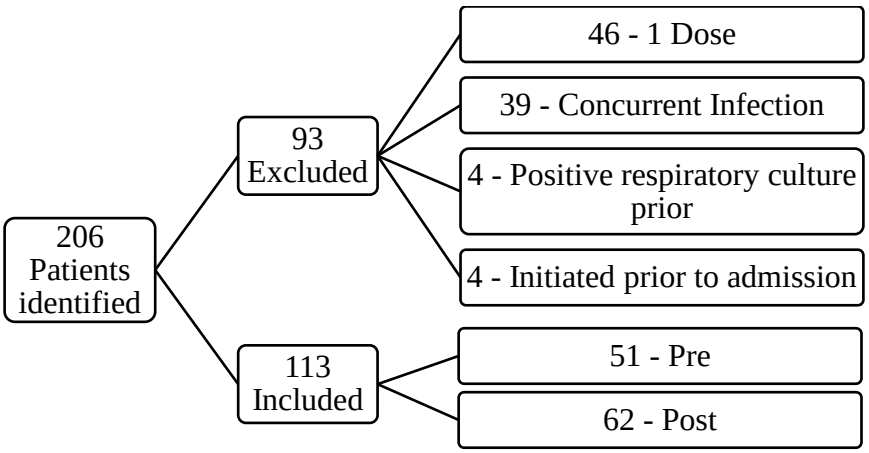


Table 4: Baseline demographics

	Pre-intervention (n=51)		Post-intervention (n=62)	
Male %	50.98%	26/51	51.61%	32/62
Female %	49.02%	25/51	48.39%	30/62
Age (mean)	Median Mean	69 69.55	Median Mean	70 67.71
% Intensive Unit (CCU/ICU/HixICU)	49.02%	25/51	41.94%	26/62
% HCAP	15.69%	8/51	16.13%	10/62
% HAP	29.41%	15/51	41.94%	26/62
% CAP	31.37%	16/51	17.74%	11/62
% Aspiration/Ventilator	23.53%	12/51	24.19%	15/62

Title:			
METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS (MRSA) NASAL PCR – PHARMACY ORDERING			
		Page 1 of 1	
Policy Number:		Date Last reviewed/Revised: 6/2020	Valid Until: 6/2023
Campus: ☒ CHI Memorial Glenwood ☒ CHI Memorial Hixson ☒ CHI Memorial Georgia ***Check all that apply***			
Department(s) Affected: Pharmacy, Clinical Staff		Review Period: every 3 years	

PURPOSE:
Intravenous (IV) vancomycin is frequently utilized for the empiric treatment of pneumonia in patients with suspected methicillin-resistant *Staphylococcus Aureus* (MRSA). The Infectious Diseases Society of America (IDSA) guidelines for pneumonia recommend empiric anti-MRSA therapy in patients with specific risk factors. When anti-MRSA coverage is initiated, it is recommended to obtain cultures and a rapid nasal PCR for de-escalation.

The MRSA rapid nasal PCR has been shown to have a high negative predictive value (95-99%) for MRSA pneumonia and has been safely used to de-escalate vancomycin therapy in studies. Several studies have also demonstrated that pharmacy managed MRSA nasal swab programs can reduce the duration of unnecessary empiric IV vancomycin therapy.

POLICY:
The policy is intended to improve the utilization of IV vancomycin for patients with pneumonia.

PROCEDURE:
1. Pharmacist performing daily IV vancomycin dosing will review patient chart for indication.
2. If IV vancomycin was ordered for the treatment of pneumonia and no MRSA nasal swab ordered, pharmacist will place order for the test. See *MEDICATION ORDERS – PHARMACIST REVIEW* policy.
3. Upon result finalization, pharmacist will discuss IV vancomycin de-escalation with the provider.

REFERENCES

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3. Kalil AC, Metersky ML, Klompas M, et al. Management of Adults With Hospital-acquired and Ventilator-associated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society [published correction appears in Clin Infect Dis. 2017 May 1;64(9):1298] [published correction appears in Clin Infect Dis. 2017 Oct 15;65(8):1435] [published correction appears in Clin Infect Dis. 2017 Nov 29;65(12):2161]. Clin Infect Dis. 2016;63(5):e61-e111.
4. Metlay JP, Waterer GW, Long AC, et al. Diagnosis and Treatment of Adults with Community-acquired Pneumonia. An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America. Am J Respir Crit Care Med. 2019;200(7):e45-e67.
5. Parente DM, Cunha CB, Mylonakis E, Timbrook TT. The Clinical Utility of Methicillin-Resistant Staphylococcus aureus (MRSA) Nasal Screening to Rule Out MRSA Pneumonia: A Diagnostic Meta-analysis With Antimicrobial Stewardship Implications. Clin Infect Dis. 2018;67(1):1-7.
6. Willis C, Allen B, Tucker C, Rottman K, Epps K. Impact of a pharmacist-driven methicillin-resistant Staphylococcus aureus surveillance protocol. Am J Health Syst Pharm. 2017;74(21):1765-1773

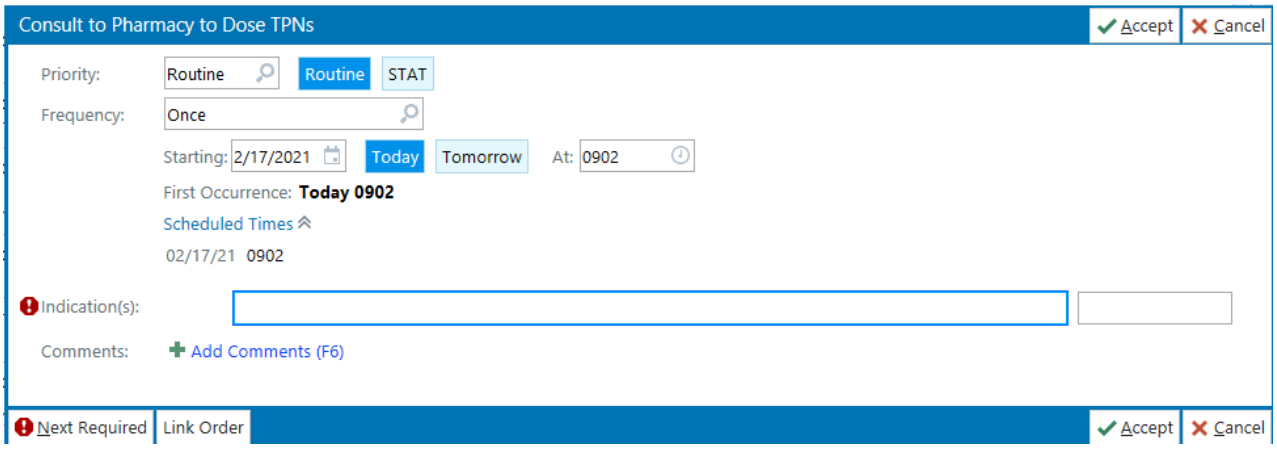
TPN MEDICATION USE EVALUATION- UPDATE

BACKGROUND/RATIONALE:
During the December 2020 P&T committee meeting, Rachel reviewed the results of a MUE performed on recent TPN utilization, with emphasis on CLABSI incidence and need for PICC lines directly due to TPN initiation.

CLABSI/PICC
Sixty percent of patients started on TPN required a PICC line to be placed directly due to TPN infusion. Approximately four percent of patients started on TPN developed a CLABSI, but none of the TPNs were ordered for an inappropriate indication at the time of initiation. None of them required a PICC line due to the TPN, but for other reasons such as vasoactive infusions.

Appropriate Use
16% of patients started on TPN did not follow ASPEN guidelines for TPN initiation criteria at the time of initiation (inappropriate). 100% of these were preventable, and 71% of these required a PICC line for TPN only. 59% were ordered by hospitalists.
39% of TPNs ordered were preventable, and the primary reason (48%) was lack of offering or patient refusal of enteral feeding, either in the days leading up to the need for TPN or at the time of the TPN order. 52% of preventable TPNs were by hospitalists and 36% by surgeons.

A separate quality review group met to review the data in detail and to develop the following recommendations:



*This is the current consult order for TPN.

Recommended TPN indication options, in alignment with ASPEN criteria, are as follows:

- High Output Fistula (greater than 500 mL/day/location)
- GI Obstruction
- Prolonged Post-Op Ileus for 7 or more days with no return of bowel function and high NG tube output (greater than 1L/day)
- Refractory inflammatory bowel disease
- Severe Pancreatitis unable to tolerate enteral support with NJ tube AND patient has been hospitalized greater than 5 days
- Short Bowel Syndrome-Bowel length 60 cm with colon in continuity; 120 cm without
- Complications from bariatric surgery
- Ischemic Bowel
- Chylous Fistula-increased output on low-fat diet or formula
- Pre-operative: Severely nutritionally-at-risk patient with nonfunctional GI tract for at least 5 days prior to surgery with duration of at least 7 days
- Well-nourished patient (not nutritionally-at-risk) and unable to tolerate at least 50% of enteral support for greater than 7 days

- Involuntary weight loss of 10% of usual body weight within 6 months or 5% within 1 month AND enteral nutrition has been attempted or is contraindicated
- BMI LESS than 18.5 AND enteral nutrition has been attempted or is contraindicated
- Nutritionally at-risk patient unable to tolerate at least 50% of enteral support for 3 to 5 days
- Intractable vomiting/diarrhea, including C. Diff, refractory to medical management
- Severe Malabsorption (disease states which impair absorption or cause loss of nutrients)
- Tube Feed Intolerance as documented by Nutrition Services
- Failed Enteral Tube Placement under IR
- Home/Chronic TPN
- If none of the above criteria are met, cancel TPN consult and place a new consult order to Nutrition Services for Tube Feeding

RECOMMENDATION/DISCUSSION:
It is recommended to modify the existing "Consult to Pharmacy to Dose TPNs" order in Epic (see image below*) to require an indication for TPN from a selection of indications which are in alignment with American Society of Parenteral and Enteral Nutrition (ASPEN) guidelines for parenteral nutrition support. The current consult order does not provide a list of options, but is a free text field for "indication".

Adverse Drug Reaction (ADR) Summary
May 2020 through July 2020

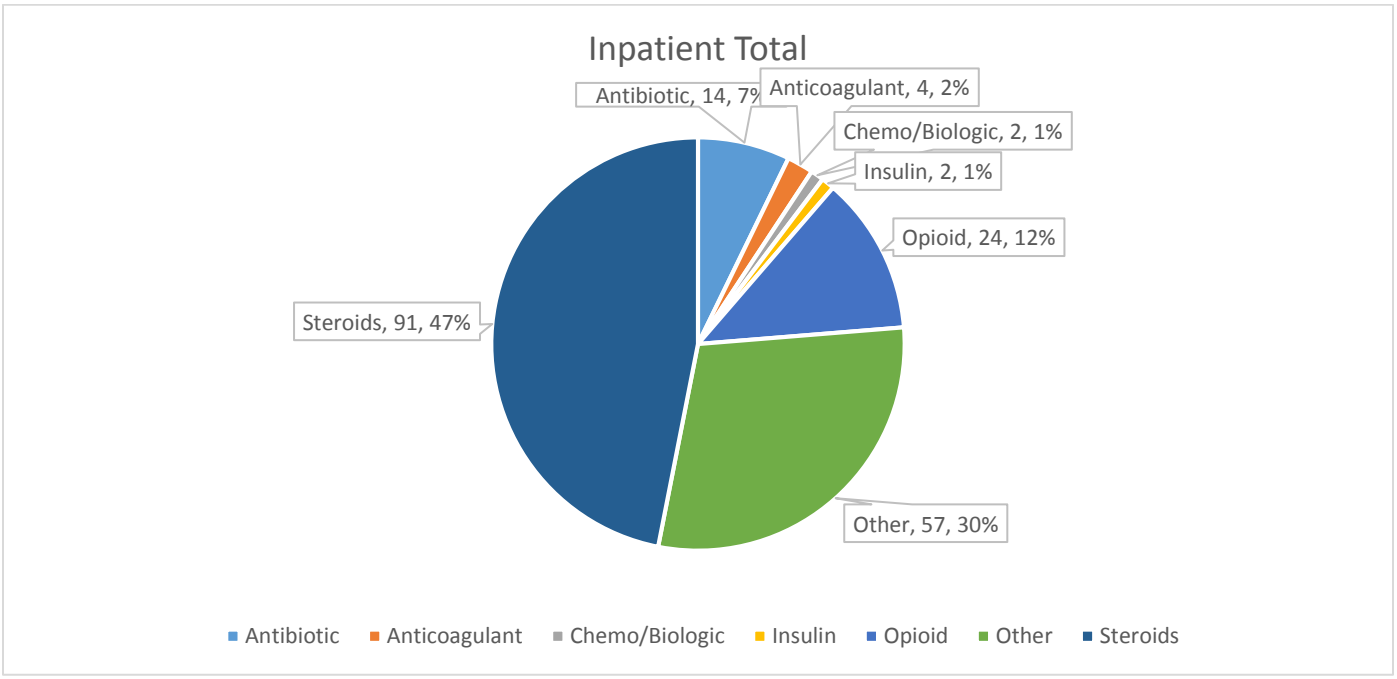
Category 1: Commonly recognized ADR's which are expected and do not result in serious medical consequences or extended hospitalization (e.g. antibiotic rash, nausea, mild hypokalemia).

Category 2: Significant ADR's which extend hospitalization and/or require extensive therapeutic measures (e.g. gastrointestinal bleed secondary to NSAIDs, Aminoglycoside nephrotoxicity.

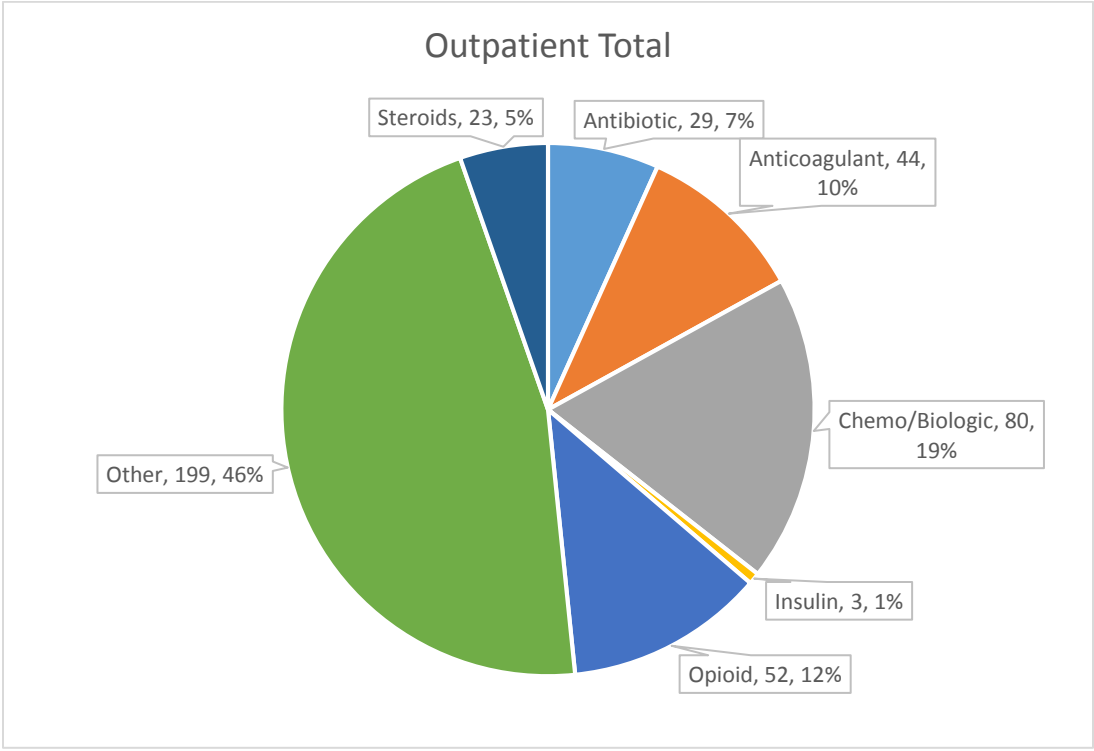
Category 3: A serious or rare ADR which has abnormal characteristics compared with published reports of the reaction (e.g. heparin induced platelet aggregation resulting in limb amputation). ADR's from this category should be reported to the manufacturer and/or the FDA (MedWatch or the Vaccine Adverse Event Reporting System).

Inpatient: 194 (31%)
Prior to hospitalization: 430 (69%)
Total: 624

Category 1: 462
Category 2: 162
Category 3: 0



Antibiotics: [N/V/D/Rash (7), AKI (1), Pancytopenia (1)]
Anticoagulants: [elevated liver enzymes (1), minor rectal bleed (1)]
Chemo/Biologic: [Diarrhea (1), mild neuropathy (1)]
Opioids: [N/V/D (2), Constipation (12), Altered Mental Status (5), Urinary Retention (1)]
Steroids: [Hyperglycemia (62), Leukocytosis (23), Altered Mental Status (3), Vaginal Candidiasis (1)]
Other: Mostly blood pressure medications associated with hypotension or bradycardia; N/V/D



Antibiotics: [N/V/D/Rash (14), AKI (1), Vasculitis (1)]
Anticoagulants: [GI Bleed (1), Hematoma (2)]
Chemo/Biologics: [Pancytopenia/Thrombocytopenia/Neutropenia (47), N/V/D (17), Other (7)]
Narcotics: [Constipation (34), Encephalopathy (3), Other (9)]
Steroids: [Hyperglycemia (7), Leukocytosis (5), Other (9)]
Other: Mostly GI/Electrolyte imbalances, hypotension, and altered mental status

POLICY

Title: **IV – CENTRAL VENOUS ACCESS DEVICE: THROMBOLYTIC DECLOTTING FOR OCCLUSION**			
		Page **1** of **1**	
Policy Number: PC-07138		Date Last reviewed/Revised: 4/21	Valid Until: 4/24
Campus: ☒ CHI Memorial Glenwood ☒ CHI Memorial Hixson ☐ CHI Memorial Georgia *Check all that apply*			
Department(s) Affected: All Clinical Areas		Review Period: every 3 years	

OUTCOME:
Restoration of the patency or function to the central venous access device, lysing the fibrin that is occluding the catheter safely by instillation of thrombolytic agent.

PERSONNEL: Credentialed IV Team and Outpatient Infusion RNs

POLICY:
Before treating a dysfunctional catheter with alteplase (Cathflo® Activase®), a tissue plasminogen activator (tPA), a thorough assessment must be performed to rule out any other causes besides thrombus formation, including catheter malposition, mechanical failure, constriction by a suture, lipid deposits, and drug precipitates.

Primary Nurse: Responsibilities when patency is in question:

1. Notify IV Team of suspected catheter occlusion or patency problems. (**Exception:** The credentialed Outpatient Infusion RN may proceed to 3. after assessment and without notifying the IV team)
2. After assessment and verification of non-patent catheter by IV Team, notify the physician and obtain an order for thrombolytic agent.
3. IV Team or Infusion Nurse will contact Pharmacist to send thrombolytic agent when ready to use it.

IV Team/Outpatient Infusion Nurse: Responsibilities prior to procedure to confirm occlusion:

1. Assess the patient's need for the procedure. **(refer to eCRS skill noted below)**

NURSING/CLINICAL PROCEDURE:
Refer to eCRS (eClinical Reference Solutions): Central Venous Access Devices: Declotting with Alteplase (Cathflo® Activase®)
eCRS is accessible from the MNET by clicking the hyperlink provided under the Clinical Tools tab. Refer to the Extended Tab for detailed version of skill

***Note**/Exception to the eCRS Skill: Memorial CHI Pharmacy & Therapeutics Committee has approved the physician ordered dose of 1 mg (off-label) for inclusion in our formulary for use in thrombolytic declotting for occlusion in central venous access devices.

The IV Team nurse will notify the primary nurse of the occlusion. The primary nurse or Infusion RN will notify the Practitioner if infection is suspected, because of the action of Alteplase in an infected catheter may disseminate the localized bacteria systemically. The primary nurse will obtain an order for the thrombolytic agent for use in declotting the catheter or device.

Administer thrombolytic as ordered. Attempts should not exceed two. If the catheter remains occluded, contact the practitioner.

The IV Team nurse will notify the primary RN of the procedure results and when the catheter may be used.

Key Contact: IV Team Coordinator; P&T Committee
Approved/Reviewed by: Director of Pharmacy; CNO; Nursing Professional Practice Council
Reference(s): eCRS Clinical Skill ; Cathflo Activase official website: http://www.cathflo.com/home/index.jsp; *Journal of Vascular and Interventional Radiology; Infusion Therapy Standards of Practice*
Joint Commission Standard: Provision of Care Chapter (PC) PC 01.01.01
Date First Effective & Revision/Review dates: 3/98 (10/03) (11/08) (04/13) (7/15) (1/19) (4/21)