Pharmacy & Therapeutics Committee Meeting

Zoom Virtual Meeting

August 19, 2021 7:00 a.m.

Next Meeting Date: October 7, 2021 at 7:00 a.m.

PHARMACY AND THERAPEUTICS COMMITTEE

DATE: June 10, 2021 CALLED TO ORDER: 7:00 a.m.
LOCATION: Private Dining Room + Zoom conference call ADJOURNED: 7:36 a.m.

Physician Member Attendance:		Non-Physician Member Attendance:				Guests:
X	**Nathan Chamberlain, MD- Chairman**		Karen Babb, PharmD- Manager		Shannon Harris, RN-Infection Prevention	Sierra Detwiler, PharmD
	Mark Anderson, MD- Infectious Disease		Jamie Barrie, PharmD- Manager, Hixson	X	**Rhonda Hatfield, RN-CNO**	La'Travia Howard, PharmD
X	**Justin Blinn, MD- Anesthesiology**	X	**Patrick Ellis, PharmD-Director**		Kevin Hopkins, RT- Director of Resp Therapy	Andrea Wilkinson, PharmD
X	**David Dodson, MD- Hospitalist**	X	**Rodney Elliott- Purchasing**	X	**Rachel Kile, PharmD-Clinical Manager**	
	F. Lee Hamilton MD- Hospitalist	X	**Karen Frank, RN-Quality**	X	**Daniel Marsh, PharmD- Operations Manager**	
	William Haren, MD- Psychiatry	X	**Susan Fuchs, RD-Nutrition**		Carey Smith, RPh- Manager, Georgia	
	Matthew Kodsi, MD-Quality		Lori Hammon, RN-Quality			
	Aditya Mandawat, MD- Interventional Cardiology					
	Chad Paxson, MD- Intensivist/Pulmonology/ICU					
	Vimal Ramjee, MD- Cardiology					
	James Wahl, MD- Hospitalist, GA					
X	**Richard Yap, MD- Hospitalist**					

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 April 2021 minutes were approved as submitted.	Approved	Complete
CommonSpirit Health System P&T Committee	**May 2021 Decision Brief:** The medication decisions that were approved at the CommonSpirit Health System P&T committee meeting were reviewed. All new system formulary medications or changes were either consistent with existing CHI Memorial formulary decisions or are described in the "Therapeutic Interchanges and Formulary Changes" section of the minutes below, or will be reviewed at an upcoming P&T committee meeting.	Approved	Complete
Formulary Decisions & Therapeutic Interchanges	1. **Alteplase (Activase®):** This committee previously approved replacing Activase® (alteplase) with TNKase® (tenecteplase) for the treatment of acute ischemic stroke at CHI Memorial hospitals. It was recommended to revise the formulary status for Activase® 50 mg or 100 mg vials to the following restricted indications: 1. Pulmonary embolism, and 2. Acute ischemic stroke when alteplase is required for clinical trial participation only. The EHR build, including order set(s), will reflect the above formulary recommendations. 2. **Erythropoietin agents - Therapeutic Interchange:** It was recommended to approve a pharmacist-driven automatic therapeutic interchange from darbepoetin alfa (Aranesp®) to epoetin alfa-epbx (Retacrit®), or to the most cost effective epoetin alfa biosimilar agent on formulary. Inpatient orders for darbepoetin alfa for interchange to the epoetin alfa biosimilar should be limited to those scenarios in which the administration of the medication cannot be deferred to post-discharge.	Approved Approved Approved	Complete Complete Complete

	3. **Annual Formulary List Review:** The committee reviewed the formulary list for all CHI Memorial facilities.		
Protocols & Orders	1. **Order sets with Opioid Analgesics for Mild Pain:** Rachel reviewed a summary of current order sets which include opioids for mild pain. Tramadol is the most common, and it was recommended to remove tramadol from order sets which also have acetaminophen as a mild pain option currently available, with exceptions for the following order sets in which Rachel will work with physician champions to form a plan: Standard Post Anesthesia, Colorectal Surgery Post-Op, and Orthopedic Surgery Post-Op. Lortab solution will be changed to acetaminophen solution for the Bariatric Surgery Pre Op order set, with prior approval by Dr. Jamie Ponce. **2. Cardiac Arrest Post Cardiac Surgery Protocol:** This new policy was reviewed. It was developed at the request of cardiothoracic surgeons with the goal of providing an evidence-based resuscitation protocol to meet the needs of patients immediately after cardiac surgery (within the first 24 hours post-op in the CVICU). Specific to medication use during ventricular fibrillation (VF) or pulseless ventricular tachycardia (pVT) arrest, this policy approves of CVICU nurses placing and order for amiodarone 300 mg IV push only after 3 attempts to defibrillate when VF or pVT persists, 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. **3. Neostigmine IV Order Panel:** Rachel reviewed a neostigmine IV ordering panel for EHR build which was shared from another CHI Epic hospital. The orders ensure adequate patient monitoring for the administration of neostigmine IV route for use outside of the OR (floors, ICU) for colonic pseudo-obstruction. Atropine PRN, cardiac monitoring for 1 hour, and patient monitoring instructions for nursing are included. It was recommended to approve the order panel build for with restrictions to inpatient units with telemetry monitoring and neostigmine administration limited to an ACLS certified RN.	Approved Approved Approved	Complete Complete Complete
Medication Safety	1. **ADR Summary:** Rachel reviewed the adverse drug reaction summaries for Jan-Mar 2021 and no new trends were observed.	Informational	Complete
Miscellaneous	1. **Blue Top Tube Lab Shortage:** Due to a shortage of citrate for lab testing, blue top lab tubes are on a nationwide shortage and it is impacting our facilities. Blue top tubes are used for coagulation tests such as aPTT, PT/INR, D-dimer, fibrinogen, and TEG. The committee discussed options for temporarily reducing orders of laboratory tests required for drug monitoring to conserve supply. It was recommended to temporarily authorize a modification to the Anticoagulation Monitoring policy to allow pharmacists to order an INR for patients on warfarin as often as every 72 hours, when clinically appropriate, instead of daily.	Approved	Complete

There being no further business, the meeting was adjourned at 7:36 a.m. The next P&T meeting is **TBD 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

CSH SYSTEM PHARMACY AND THERAPEUTICS COMMITTEE DECISION BRIEF

July 2021 Decisions

NOTE: Local/divisional P&T committees may implement more restrictive statuses

Medication Name	Medication Used For	Formulary Decision			Comments/Restrictions/Therapeutic Interchange	Timeline to Implementation
		Formulary Unrestricted	NonFormulary	Formulary Restricted		
Aminolevulinic acid	Diagnostic agent used for visualization of high-grade glioma fluorescence-guided surgical resections			GLEOLAN	Inpatient: Restricted to hospitals that are confirmed to have the appropriate microscope and filters and to neurosurgeons who have completed the training program provided by the distributor NX Development Corp. The dispensing pharmacist must confirm that the requesting neurosurgeon is an Approved User prior to Gleolan being dispensed. Outpatient: Restricted to FDA-approved indications or payer-approved off-label indications subsequent to insurance approval or prior authorization. Outpatients must be admitted to the hospital prior to surgery in order to receive preoperative treatment.	Within 90 days of decision
Artesunate	Antimalarial agent			ARTESUNATE	• Severe malaria per CDC guidelines • Recommended to maintain as non-formulary in hospitals that did not have a malaria case in the previous year	Within 60 days of decision

Medication Name	Medication Used For	Formulary Decision			Comments/Restrictions/Therapeutic Interchange	Timeline to Implementation
		Formulary Unrestricted	NonFormulary	Formulary Restricted		
Cholestyramine	Dyslipidemia and diarrhea	CHOLESTYRAMINE/ASPARTAME				Within 60 days of decision
		CHOLESTYRAM				
		CHOLESTYRAMN				
		CHOLESTYR				
		CHOLESTYR REG				
		CHOLESTYRAMIN				
		CHOLESTYR LT				
		QUESTRAN REG				
		PREVALITE				
Copper CU 64 dotatate	Neuro-endocrine tumor imaging			DETECTNET	Outpatient Imaging for Somatostatin Receptor expressing neuro-endocrine tumors, Only adult patients	Within 90 days of decision
Gallium GA 68 dotatate				NETSPOT	Outpatient Imaging for Somatostatin Receptor expressing neuro-endocrine tumors, Adults and Pediatrics	
Indium IN 111 pentetate disodium				INDIUM IN-111 DTPA	Imaging for Somatostatin Receptor expressing neuro-endocrine tumors at facilities without PET capability	
Alogliptin	Antidiabetic agent	ALOGLIPTIN			DPP4 Interchange	Within 90 days of decision
		NESINA				
Linagliptin			TRADJENTA			
Saxagliptin			ONGLYZA			
			ONGLYZA 5MG			
			ONGLYZA TAB			
Sitagliptin			JANUVIA			
			JANUVIA UD			

Medication Name	Medication Used For	Formulary Decision			Comments/Restrictions/Therapeutic Interchange	Timeline to Implementation
		Formulary Unrestricted	NonFormulary	Formulary Restricted		
Diatrizoate	Ionic contrast media	CYSTOGRAFIN				Within 90 days of decision
		GASTROGRAFIN				
			MD-GASTRO			
Iothalamate meglumine			CONRAY			
			CYSTO-CONRAY			
Isoflurane	Inhaled anesthetic	FORANE				Within 90 days of decision
		ISOFLURANE				
Leuprolide acetate	Gonadotropin releasing hormone antineoplastic agent			ELIGARD, LEUPROLIDE AND LEUPROLIDE 2W	• Restricted to advanced prostate cancer • Outpatient setting subsequent to insurance approval or prior authorization.	Within 90 days of decision
				LUPRON DEPOT, 3 and 4 MO	• Restricted to non-prostate indications (ex: premenopausal hormone receptor positive breast cancer, endometriosis, fibroids, etc.) • Outpatient setting subsequent to insurance approval or prior authorization.	
Iodixanol	Non-ionic contrast media			VISIPAQUE	Patients intolerant of LOMC	Within 90 days of decision
Iohexol			OMNIPAQUE			
			ULTRAVIST			
			OPTIRAY			
Iopamidol		ISOVUE				
Iopromide			ULTRAVIST			
Ioversol			OPTIRAY			

Medication Name	Medication Used For	Formulary Decision			Comments/Restrictions/Therapeutic Interchange	Timeline to Implementation
		Formulary Unrestricted	NonFormulary	Formulary Restricted		
Polidocanol	Varicose vein sclerosing agent			VARITHENA	Restricted to outpatient procedures with confirmed payer approval. Treatment of superficial venous insufficiency, varicose veins, and incompetent tributaries and perforators in the legs. It is for symptomatic venous insufficiency and associated varicose veins. It can be used stand alone or in combination with other venous procedures.	Within 90 days of decision
Osilodrostat	Cushing's disease		ISTURISA			Within 60 days of decision
Lansoprazole	Decreasing gastric acid secretion			FIRST LANSOPRAZOLE SUSPENSION	• Acute upper GI bleeding • Active Helicobacter pylori infection • Erosive esophagitis • Gastric or duodenal ulcer • GERD refractory to H2 blockers • Stress ulcer prophylaxis in the ICU* • Zollinger Ellison syndrome • Gastric outlet obstruction • Patient receiving Dual antiplatelet therapy (DAPT)	Within 90 days of decision
Omeprazole				FIRST OMEPRAZOLE SUSPENSION		

Medication Name	Medication Used For	Formulary Decision			Comments/Restrictions/Therapeutic Interchange	Timeline to Implementation
		Formulary Unrestricted	NonFormulary	Formulary Restricted		
Pantoprazole sodium				PANTOPRAZOLE TABLETS AND INJECTION	*Require an indication for stress ulcer prophylaxis: • Mechanical ventilation >48 hrs • Spinal or head injury with low GCS • Coagulopathy at risk of GI bleed (INR>1.5, PTT>2x, PLT<50k) • Major trauma • Multiple organ failure • Thermal burn injury of body >35%BSA • Septic shock on vasopressors • >/=2 of the following risk factors: sepsis, ICU stay of more than one-week, occult bleeding lasting six days or more, and use of high-dose corticosteroids (>50 mg per day of solumedrol or the equivalent) • Partial hepatectomy or perioperative solid organ transplant • History of GI bleed within 1 year • Acute pancreatitis in pediatric patients	
Olanzapine	Antipsychotic agent			OLANZAPINE ODT	• Patients who have problems swallowing medications or	Within 90 days of decision
Risperidone				RISPERIDONE		

Medication Name	Medication Used For	Formulary Decision			Comments/Restrictions/Therapeutic Interchange	Timeline to Implementation
		Formulary Unrestricted	NonFormulary	Formulary Restricted		
				ODT	who have adherence issues • Continuation from home	
Antivenin, crotalidae	Snake Antivenom	ANAVIP				Within 90 days of decision
			CROFAB			
Teprotumumab-TRBW	Insulin like growth factor monoclonal antibody agent used for thyroid eye disease			TEPEZZA	Outpatient setting for FDA-approved indications or payer-approved off-label indications subsequent to insurance approval or prior authorization	Within 60 days of decision
Vericiguat	Soluble guanlylate cyclase stimulator used for heart failure		VERQUVO			Within 60 days of decision

SPECIALTY MEDICATIONS

Drug Name	Active Ingredient	Approval Date	FDA-approved use on approval date*	Recommendation
Truseltiq	infigratinib	5/28/2021	To treat adults with cholangiocarcinoma whose disease meets certain criteria	NonFormulary
Lumakras	sotorasib	5/28/2021	To treat adults with non-small cell lung cancer whose disease meets certain criteria	NonFormulary
Rybrevant	amivantamab-vmjw	5/21/2021	To treat adults with subset of non-small cell lung cancer	NonFormulary
Empaveli	pegcetacoplan	5/14/2021	To treat adult patients with paroxysmal nocturnal hemoglobinuria	NonFormulary
Zynlonta	loncastuximab tesirine-lpyl	4/23/2021	To treat certain types of relapsed or refractory large B-cell lymphoma	NonFormulary
Ponvory	ponesimod	3/18/2021	To treat patients with relapsing forms of multiple sclerosis	NonFormulary
Fotivda	tivozanib	3/10/2021	To treat patients with renal cell carcinoma	NonFormulary
Pepaxto	melphalan flufenamide	2/26/2021	For the treatment of certain patients with relapsed or refractory multiple myeloma	NonFormulary
Nulibry	fosdenopterin	2/26/2021	To treat patients with molybdenum cofactor deficiency Type A	NonFormulary
Amondys 45	casimersen	2/25/2021	For the treatment of Duchenne muscular dystrophy	NonFormulary

THERAPEUTIC INTERCHANGES

DPP4 Inhibitors

Order	Interchange to
Linagliptin 5 mg Daily	**Alogliptin** 25 mg Daily
Saxagliptin 2.5 mg Daily 5 mg Daily	**Alogliptin** 25 mg Daily
Sitagliptin 100 mg Daily	**Alogliptin** 25 mg Daily
Sitagliptin 50 mg Daily	**Alogliptin** 12.5 mg Daily
Sitagliptin 25 mg Daily	**Alogliptin** 6.5 mg Daily

The pharmacy will adjust dose for renal function if required. Guidance is provided below:

Agent	Usual Dose CrCl ≥ 60 ml/min	Dosage for Renal Insufficiency CrCl ≥ 30 to < 60 ml/min	Dosage for Renal Insufficiency: CrCl ≥ 15 to < 30 ml/min or ESRD (CrCl <15 mL/min or requiring hemodialysis)
Alogliptin	25 mg Daily	12.5 mg Daily	6.5 mg Daily (Without regard to dialysis timing)

FORMULARY UPDATE

THERAPEUTIC CLASS: Non-Ionic X-Ray Contrast Media

BACKGROUND/RATIONALE:

During the July meeting, the CommonSpirit Health System P&T Committee voted in favor of removing Omnipaque from formulary and approved Isovue as the formulary, unrestricted non-ionic contrast media agent. Visipaque is on formulary, but with restrictions for use limited to patients intolerant of low-osmolar contrast.

X-Ray contrast products for general radiography, interventional procedures, computed tomography (CT) and cardiovascular procedures are divided into two molecular types: ionic and non-ionic. Non-ionic contrasts currently purchased by the CHI Memorial include Isovue, Omnipaque, and Visipaque. Isovue and Omnipaque are low osmolar (LOMC). Visipaque is the only available iso-osmolar (IOMC) agent.

Omnipaque-300 is currently only used in surgery at all 3 facilities. It is also used intrathecally. Isovue 300 is already on formulary and is utilized widely across facilities.

WARNINGS/PRECAUTIONS

- Black box warning for Isovue, Visipaque:
  - Not for intrathecal use. Inadvertent intrathecal administration may cause death, convulsions/seizures, cerebral hemorrhage, coma, paralysis, arachnoiditis, acute renal failure, cardiac arrest, rhabdomyolysis, hyperthermia, and brain edema
- Isovue-M: Administer with caution in patients with increased intracranial pressure or suspicion of intracranial tumor, abscess or hematoma, those with a history of convulsive disorder, severe cardiovascular disease, chronic alcoholism, or multiple sclerosis, and elderly patient

DOSING

- The maximum recommended total dose of iodine for adults is 80 grams
- Dosing of non-ionic contrast is individualized with the volume and concentration of contrast to be used determined by procedure. Doses are adjusted based on factors such as age, body weight, size of the vessel and the rate of blood flow within the vessel.

PHARMACOKINETICS

ISOVUE	OMNIPAQUE	VISIPAQUE
The elimination serum or plasma half-life is approximately two hours; the half-life is not dose dependent.	First-order terminal elimination half-life was 12.6 hrs and total body clearance was 131 (98-165) mL/min. Clearance was not dose dependent.	In doses of 0.3 to 1.2 Gram Iodine/kg body weight, the elimination half-life was 2.1 hr. (± 0.1). Renal clearance was 110 ± 14 mL/min, equivalent to glomerular filtration (108 mL/min).

PRODUCT DATA

Product	Generic name (Concentration in mg/ml)	Iodine (mg/ml)	Viscosity 25°C (cp or mPa.s.)	Viscosity 37°C (cp or mPa.s.)	Osmolality (mOsm/kg H20)
Isovue 300	iopamidol (612)	300	8.8	4.7	616
Omnipaque 300	iohexol (647)	300	11.8	6.3	672
Visipaque 270	iodixanol (550)	270	12.7	6.3	290
Visipaque 320	iodixanol (652)	320	26.6	11.8	290

	Isovue	Omnipaque	Visipaque
Storage	20-25° C (68-77° F)	20°-25°C (68°- 77°F), may be stored in a contrast media warmer for up to one month at 37°C (98.6°F).	20°-25°C (68°- 77°F), may be stored in a contrast media warmer for up to one month at 37°C (98.6°F).
Stability PBP once punctured	10 hrs	8 hrs	8 hrs
Stability once IBP punctured (room temp)	10 hrs	8 hrs	8 hrs

INDICATIONS - ADULT

Intra-arterial Use Adult							
	Cerebral Arteriography	**Peripheral Arteriography**	**Visceral/Renal Arteriography**	**Coronary Arteriography**	**Aortography**	**Left Ventriculography**	**IA-DSA ***
Isovue 300	✓	✓					
Omnipaque 300	✓				✓		
Visipaque 270							✓
Visipaque 320	✓	✓	✓			✓	✓

**IA-DSA - Intra-arterial digital subtraction angiography*

Intrathecal Adult				
	Myelography	**Myelography - CT**	**Cisternography - CT**	**Ventriculography-CT**
Isovue-M 300	✓	✓	✓	✓
Omnipaque 300	✓	✓	✓	✓

Black Box Warning: Except for Isovue-M and Omnipaque listed above, non-ionic contrast is not to be administered via the intrathecal route.

Intravenous Adult					
	CT Head/Body	**Venography**	**IV Excretory Urography**	**IV-DSA***	**CCTA***
Isovue 300	✓		✓		
Omnipaque 300	✓	✓	✓		
Omnipaque 350	✓		✓	✓	
Visipaque 270	✓	✓	✓		
Visipaque 320	✓		✓		✓

PHARMACOECONOMICS/COST:

Product (Drug, Strength, Form)	Price
Omnipaque 300, 50 ml vial x 10	$338.03
Isovue 300, 50 ml vial x 10	$36.12
Isovue M 300, 15 ml vial x 10	$167.98

Omnipaque 6 month Utilization (Jan-June 2021)	Anticipated 12 month Cost Savings with Isovue
1,247 vials dispensed	**$75,316**

RECOMMENDATION/DISCUSSION:

It is recommended to align with the CommonSpirit Health System P&T decision to remove Omnipaque 300 from formulary and replace it with Isovue 300.

Isovue M-300 should be added for intrathecal use only.

Visipaque should be limited to patients intolerant of low-osmolar contrast media.

The EHR and order sets will be updated to reflect these recommendations.

FORMULARY UPDATE

THERAPEUTIC CLASS: Snake antivenom

GENERIC NAME: Crotalidae immune Fab (equine) F(ab')

PROPRIETARY NAME: Anavip®

BACKGROUND/RATIONALE:
For patients that incur venomous snakebites, two antigen-binding (FAB) antivenoms are available in North America: CroFab, crotalidae polyvalent immune Fab (ovine) FabAV and Anavip, crotalidae immune Fab (equine) F(ab')2 . Crofab is the current formulary product for CHI Memorial. The FDA recently expanded the indication for Anavip to include all North American Pit Vipers from the original indication for treatment of rattlesnake envenomations only.

CroFab: Dosage is titrated to clinical effect and does not need to be adjusted for age, weight, or hepatic/renal dysfunction. Studies have shown most copperhead snakebite patients respond well to an initial 4-vial dose and maintenance dosing may not be necessary. The elimination half-life of CroFab is approximately 15 hours which may be shorter than that of the venom. Recurrent or late venom effects may occur as a result of continued circulating venom. Due to this issue, it is recommended patients platelet count, prothrombin time and fibrinogen levels be reevaluated at days 2-3 post snakebite and days 5-7 after administration of the last CroFab dose.

Anavip: FDA approved for pediatric and adult management of envenomation of all North American Pit Vipers. Patients should be observed for signs of continued venom toxicity for a period of eighteen hours once initial control is obtained. Due to the long elimination half-life of 133 hours, no scheduled maintenance dose is recommended.

	Anavip®	**CroFab®**	**Advantage**
Indications	North American rattlesnakes and Pit Vipers	Polyvalent: rattlesnake, copperhead, cottonmouth	
Source	Venom from eastern diamondback rattlesnakes, western diamondback rattlesnakes, Mojave rattlesnakes, and cottonmouth snakes, manufactured in sheep	Venom from South American rattlesnakes and fer-de-lance snakes, manufactured from horse serum	
Kinetics	Prolonged action; reduced late coagulopathy from venom (7.8% overall; 5.3% in Anavip + placebo group)	Shorter acting; higher prevalence of late coagulopathy from venom (29.7%)	Anavip
Dose:	Initial Dose: 10 vials in 250ml 0.9% NaCl at 25-50ml/hr x 10 minutes, then 250ml/hr Repeat initial dose every hour until initial control achieved Maintenance: 4 vials as needed during 18hr observation period	Initial Dose: 4 to 12 vials in 250ml 0.9% NaCl, at 25-50ml/hr x 10 minutes, then 250ml/hr Repeat initial dose every 2 hours until initial control achieved Maintenance: 2 vials every 6 hours x 3 doses	Anavip; Late coagulopathy may require further administration of CroFab; unclear if more Anavip is necessary or not. See below for average number of vials administered in phase III trial.

PHARMACOECONOMICS/COST:

Product (Drug, Strength, Form)	Price
CroFab – crotalidae immune Fab (Ovin) 2 vials per package	$3,581
Anavip - crotalidae immune F(ab')2 (equine) 1 vial each	$1,138

Product (Drug, Strength, Form)	Cost/Defined Course of Therapy
CroFab initial dose 4-12 vials (repeat q2h until control achieved)	$7,162-$21,486
CroFab maintenance 2 vials q6h x 3	$10,743
Anavip initial dose 10 vials (repeat q1hr until control achieved)	$11,380
Anavip maintenance 4 vials (if needed)	$4,552

RECOMMENDATION/DISCUSSION:
With the expanded FDA indication, last month the CommonSpirit Health approved a single antivenom to formulary, Anavip. Based on the lower cost of initial therapy for more severe envenomations, it is recommended to convert use of CroFab to Anavip, and remove Crofab from formulary. Additionally, the longer half-life of Anavip may reduce the need for late coagulopathy treatment, and Anavip is available to purchase via consignment.

FORMULARY REVIEW

GENERIC NAME: Eptinezumab

PROPRIETARY NAME: *Vyepti®*

INDICATIONS:

FDA Approved
Migraine prophylaxis: Preventive treatment of migraine in adults

THERAPEUTIC CATEGORY: Monoclonal Antibody; Calcitonin Gene-Related Peptide (CGRP) Receptor Antagonist; Antimigraine Agent

PHARMACOKINETICS:

	Eptinezumab
Absorption	100% bioavailability
Distribution	$V_{central}$: ~3.7 L
Metabolism	Expected to be degraded by proteolytic enzymes into small peptides and amino acids
Elimination	T ½ ~27 days

SPECIAL POPULATIONS:

	Eptinezumab
Pregnancy	No adequate data on developmental risks associated with the use of eptinezumab in pregnant women
Lactation	No data on the presence of eptinezumab in human milk, the effects on the breastfed infant, or the effects on milk production.
Pediatrics	Safety and efficacy not established
Geriatrics	No sufficient numbers of patients aged 65 and over to determine whether they respond differently from younger patients.
Hepatic Impairment	There are no dosage adjustments provided in the manufacturer's labeling; however, hepatic impairment is not expected to alter pharmacokinetics.
Renal Impairment	There are no dosage adjustments provided in the manufacturer's labeling; however, renal impairment is not expected to alter pharmacokinetics.

CLINICAL STUDIES:

PROMISE-1 (NCT02559895)	
METHODS	
Study Design	This was a randomized, double-blind, multicenter, placebo-controlled phase 3 trial performed at 84 sites in the USA and the Republic of Georgia from 30 September 2015 to 14 December 2017 conducted to evaluate the efficacy, safety, and pharmacokinetics of eptinezumab administered intravenously in patients with episodic migraine.
Patient Enrollment Inclusion	● Diagnosis of migraine at ≤ 50 years of age (ICHD-II, 2004 Section 1) ● History of migraine ≥ 12 months with o ≤ 14 headache days of which at least 4 have to be migraine days (migraine days count as headache days) in each 28-day period in the 3 months prior to screening o During the 28 days following the screening visit, the subject experiences ≤ 14 headache days of which at least 4 have to be migraine days (migraine days count as headache days) as recorded in the eDiary ● No use of any botulinum toxin for migraine or for any other medical/cosmetic reasons requiring injections in the head, face, or neck 4 months prior to screening and during the 28-day period prior to randomization ● Headache eDiary was completed on at least 25 of the 28 days prior to randomization
Patient Enrollment Exclusion	● Confounding pain syndromes, e.g. fibromyalgia, complex regional pain syndrome or any pain syndrome that requires regular analgesia ● Psychiatric conditions that are uncontrolled and untreated, including conditions that are not controlled for a minimum of 6 months prior to screening ● History or diagnosis of complicated migraine (ICHD- II, 2004 Section 1), chronic tension-type headache, hypnic headache, cluster headache, hemicrania continua, new daily persistent headache, migraine with brainstem aura, sporadic and familial hemiplegic migraine

	● Unable to differentiate migraine from other headaches ● Have any clinically significant concurrent medical condition ● Receipt of any monoclonal antibody treatment within 6 months of screening (within or outside a clinical trial) ● Previously dosed with ALD403 or any monoclonal antibody targeting the CGRP pathway
Baseline Characteristics	● Mean age: 40 years ● 84% female ● 84% White, 12% Black ● 18% percent of patients identified as Hispanic/Latino ● Mean baseline migraine days/month = 9 days ● Mean headache days/month = 10 days ● Mean triptan/ergotamine days (over 28- day screen period per eDiary) = 2 days o 98.8% reported using at least one concomitant medication during the study o Concomitant medication use was well balanced across treatment groups
Treatment Plan	Participants were randomly assigned to receive eptinezumab 30 mg, 100 mg, 300 mg, or placebo by IV infusion every 12 weeks, in a 1:1:1:1 ratio. Randomization was stratified by the number of migraine days recorded during the screening period (≤9 days vs. >9 days). During the study, patients could use concurrent acute migraine medications (e.g. triptans, ergotamine derivatives). Total study duration was 60 weeks, with 12 scheduled visits (screening, day 0 [randomization] weeks 4, 8, 12, 16, 20, 24, 28, 36, 48, and 56. The 56 weeks were divided into two periods: fully blind primary efficacy and safety period (through week 24) and a long-term safety period (through week 56). Patients used an eDiary to document headaches and migraines for 4 weeks after screening to confirm eligibility and to establish baseline values. Patients received up to four treatments of eptinezumab or placebo (administered IV day 0, week 12, week 24, and week 36). ● Placebo (n = 222) ● Eptinezumab 30 mg (n = 219) ● Eptinezumab 100 mg (n = 223) ● Eptinezumab 300 mg (n = 224)
RESULTS	
Primary Endpoint	● Eptinezumab 100 and 300 mg significantly reduced MMDs over weeks 1–12 relative to placebo (primary endpoint; mean change from baseline − 3.9 ($p = 0.0182$) and − 4.3 ($p < 0.0001$) vs − 3.2; baseline mean MMD ≈ 8.7)
Secondary Endpoint	● Eptinezumab 100 and 300 mg over weeks 1-4 compared to placebo, significantly had ≥ 75% reduction from baseline in MMDs [31% ($p = 0.01$) and 32% ($p < 0.01$) vs 20%]. Over weeks 1–12, Eptinezumab 300 compared to placebo had ≥ 75% reduction (30% vs 16%; $p = 0.0007$) and ≥ 50% reduction (56% vs 37%; $p = 0.0001$) from baseline in MMDs.
Adverse Events	● No dose-related trends in TEAE incidence were observed ● The most commonly reported adverse events among treated patients were o Upper respiratory infection (10%) o Nasopharyngitis (7%) o Sinusitis (4%) ● 7 (1%) of patients who received eptinezumab had the study drug withdrawn due to hypersensitivity. All incidences were mild to moderate: o Eptinezumab 30 mg = 2% o Eptinezumab 100 mg = ≤ 1% o Eptinezumab 300 mg = ≤ 1%
Promise-2 (NCT02974153)	
METHODS	
Study Design	This was a randomized, double-blind, multicenter, placebo-controlled, parallel-group, phase 3 efficacy and safety study was performed at 128 sites in 13 countries (United States, Spain, Ukraine, Russian Federation, United Kingdom, Republic of Georgia, Hungary, Italy, Slovakia, Germany, Czech Republic, Denmark, and Belgium) from November 30, 2016, to April 20, 2018.
Patient Enrollment Inclusion	● Males and females between 18 and 65 years of age, inclusive, who were diagnosed with migraines at ≤ 50 years of age, and have a history of chronic migraine for ≥ 12 months before screening.

	● During the 28-day screening period, subjects must adequately complete the headache eDiary and must have headaches occurring on ≥ 15 to ≤ 26 days of which at least 8 must be migraine days. ● Headache eDiary was completed on at least 24 of the 28 days prior to randomization. ● Patients using barbiturates or prescription opioids ≤4 days/month were eligible for participation if use was stable for ≥2 months before screening (restriction was maintained through week 24 of study) ● Other medications for the treatment of acute migraine such as triptans, nonsteroidal anti-inflammatory drugs, and simple analgesics were not restricted
Patient Enrollment Exclusion	● Confounding and clinically significant pain syndromes (e.g. fibromyalgia, chronic low back pain, complex regional pain syndrome) ● Psychiatric conditions that are uncontrolled and/or untreated, including conditions that are not controlled for a minimum of 6 months prior to screening. Patients with a lifetime history of psychosis, mania, or dementia are excluded ● Any use of botulinum toxin for migraine or for any other medical/cosmetic reasons requiring injections within 4 months prior to screening and during the screening period ● History or diagnosis of complicated migraine (ICHD-III beta version, 20134), chronic tension-type headache, hypnic headache, cluster headache, hemicrania continua, new daily persistent headache, or sporadic and familial hemiplegic migraine ● Receipt of any monoclonal antibody treatment (within or outside a clinical trial) within 6 months before screening ● Previously dosed with ALD403 or any monoclonal antibody targeting the CGRP pathway
Baseline Characteristics	● Mean age: 41 years ● 88% female ● 91% White, 8% Black ● 8% percent of patients identified as Hispanic/Latino ● Mean duration of chronic migraine, year = 12 ● Mean migraine days/month = 16 ● Mean headache days/month = 20 days ● Mean triptan/ergotamine days) = 7 days
Treatment Plan	Participants were randomly assigned to receive eptinezumab 100 mg, 300 mg, or placebo by IV infusion every 12 weeks, in a 1:1:1 ratio. Randomization was stratified by the number of migraine days recorded during the screening period (≤17 days vs >17 days). Preventive medication uses during the 3 months before screening (use vs no use). Total study duration was 32 weeks, with 10 scheduled visits (screening, day 0, and weeks 2, 4, 8, 12, 16, 20, 24, and 32). Patients used and eDiary to document headaches and migraines for 4 weeks after screening to confirm eligibility and to establish baseline values. Patients received up to 2 treatment of either eptinezumab or placebo (day 0 and week 12). ● Placebo (n = 366) ● Eptinezumab 100 mg (n = 356) ● Eptinezumab 300 mg (n = 350)
RESULTS	
Primary Endpoint	● Subjects in both 100 mg and 300 mg of eptinezumab showed statistically significant reductions in MMDs during weeks 1 to 12 ($p < 0.0001$) o Eptinezumab 100: MMDs decreased from 16.1 to 8.5 days o Eptinezumab 300: MMDs decreased from 16.2 to 10.5 days
Secondary Endpoint	● Eptinezumab 100 and 300 mg over weeks 1-12 compared to placebo significantly had ≥ 75% reduction from baseline in MMDs o Eptinezumab 100 = 27% ($p = 0.0001$) o Eptinezumab 300 = 33% ($p < 0.0001$) o Placebo = 15%. ● Both groups achieved a ≥ 50% significant reduction in monthly migraines compared to placebo o Eptinezumab 100 = 58% o Eptinezumab 300 = 61% o Placebo = 39%. ● Day 1 post infusion significantly decreased in eptinezumab 100 and 300 mg compared to placebo

	o Eptinezumab 100 = 51% o Eptinezumab 300 = 52% o Placebo = 27%
Adverse Events	● No dose-related trends in TEAE incidence were observed ● Most frequently reported study-drug-related TEAEs were o Nausea (3%)) o Fatigue (2%) o The remaining study-drug-related TEAEs were reported in <1% ● 6 (2%) patients who received eptinezumab 300 mg had the study drug withdrawn due to hypersensitivity. All incidences were mild to moderate

COMPARATIVE EFFICACY: Currently there are no head-to-head trials comparing erenumab, fremanezumab, galcanezumab, or eptinezumab and there are no clinically relevant differences in efficacy, based on indirect comparisons.

WARNING AND PRECAUTIONS: Hypersensitivity reactions, including angioedema, urticaria, facial flushing, and rash have occurred; and consider discontinuing therapy if hypersensitivity occurs.

CONTRAINDICATIONS: Serious hypersensitivity (eg, angioedema) to eptinezumab or any component of the formulation or to any of the excipients. Reactions have included angioedema.

ADVERSE REACTIONS:

Adverse Reaction	Eptinezumab 300 mg
Bronchitis	7/128 (5.47%)
Influenza	8/128 (6.25%)
Nasopharyngitis	18/128 (14.06%)
Sinusitis	10/128 (7.81%)
Upper respiratory tract infection	10/128 (7.81%)
Migraine	7/128 (5.47%)

CLINICALLY SIGNIFICANT DRUG INTERACTIONS: None

DOSING AND ADMINISTRATION:

Adult Dosing/Indication and Administration

- 100 mg Intravenous (IV) infusion every 3 months administered for preventive treatment of migraines.
- 300 mg intravenous (IV) infusion every 3 months (some patients may benefit from a 300 mg dose of IV eptinezumab and there are no clinical characteristics to prospectively identify those patients most likely to respond to therapy)

RECOMMENDED MONITORING: Monitoring of adverse events such as hypersensitivity and angioedema

PHARMACOECONOMICS/COST:

Product (Drug, Strength, Form)	Price
VYEPTI 100mg-mL SDV ASD	**$1,532.28**
AIMOVIG 140 MG PFS 1 ML	$616.42
AIMOVIG 70 MG-ML Auto INJ	$616.42
AJOVY 225 MG AUTO INJ 1.5 ML	$591.06
AJOVY 225 MG PFS 1.5 ML	$591.06
EMGALITY 300 MG/3ML PFS	$1464.20
EMGALITY 120 MG PFP	$585.68
EMGALITY 120 MG PFS 1	$585.68

Product (Drug, Strength, Form)	Cost/Year
VYEPTI 100mg-mL SDV ASD	$5,980.00 (100 mg) -$17,940 (300 mg)
AIMOVIG 70 MG-ML Auto INJ or AIMOVIG 140 MG PFS 1 ML	$7,057.32
AJOVY 225 MG AUTO INJ 1.5 ML	$6,740.40
EMGALITY 120 MG PFP	$7,307.04

CONCLUSION & RECOMMENDATION:
Eptinezumab (Vyepti) is the first intravenous monoclonal antibody inhibitor of CGRP approved by the FDA, and the fourth drug in this class to be approved. Currently there are no head-to-head trials comparing erenumab, fremanezumab, galcanezumab, or eptinezumab. There does not appear to be clinically relevant differences in efficacy, based on indirect comparisons. All CGRP receptor antagonists except eptinezumab can be self-administered, whereas eptinezumab requires healthcare provider administration.

It is recommended to add eptinezumab to formulary, with restrictions to the outpatient setting for FDA-approved indications or payor-approved off-label indications 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?	N/A	N/A
Special storage (e.g. refrigeration, protect from light, controlled substance)?	Store at room temperature, 20°C to 25°C (68°F to 77°F). Do not freeze.	Follow package insert recommendations.
Pharmacist/Technician Education?	Pharmacists should be educated on appropriate clinical utilization and dispensing.	Provide staff education
Ordering & Prescribing		
Restriction to particular specialty, indication, or particular patient population?	Preventive treatment of migraine in adults.	Provider education needed
Dosing Issues (e.g. renal, hepatic dosage adjustment, max dose warnings)?	N/A	N/A
Drug Interactions?	Eptinezumab is not metabolized by cytochrome P450 enzymes; therefore, interactions with concomitant medications that are substrates, inducers, or inhibitors of cytochrome P450 enzymes are unlikely.	N/A
Pregnancy?	There are no adequate data on developmental risks associated with the use of VYEPTI in pregnant women.	Advise patients to notify their healthcare provider if they become pregnant during treatment or plan to become pregnant. Benefits of treatment should outweigh any potential risks to the patient.
Absolute Contraindications?	Contraindicated in patients with serious hypersensitivity to eptinezumab or to any of the excipients.	Inform patients that hypersensitivity reactions, including angioedema, urticaria, facial flushing, and rash, can occur. Advise patients to contact their healthcare provider immediately if signs or symptoms of hypersensitivity reactions occur.
Requires Order Set, Protocol, concomitant therapy with another drug?	N/A	N/A
LASA* nomenclature issues?	N/A	N/A
Prescriber education?	Prescribers should be educated on appropriate clinical utilization.	Provide staff education
Processing, Preparing, & Dispensing		
High-risk drug double check?	N/A	N/A
Drug Interaction check in place?	N/A	N/A
LASA* computer warnings?	N/A	N/A
Administration Notes for MAR (e.g. handling precautions, surrounding food or other drugs)?	No other medications should be administered through the infusion set or mixed with VYEPTI. VYEPTI is for intravenous infusion only. Use an intravenous infusion set with a 0.2 micron or 0.22 micron in-line or add-on sterile filter. After the infusion is complete, flush the line	Create an administration note

	with 20 mL of 0.9% Sodium Chloride Injection, USP.	
Packaging/Labeling (e.g. prepacking)?	N/A	N/A
Dispensing (e.g. auxiliary labeling, light protection, refrigeration)?	No other medications should be administered through the infusion set or mixed with VYEPTI. VYEPTI is for intravenous infusion only. Use an intravenous infusion set with a 0.2 micron or 0.22 micron in-line or add-on sterile filter. VYEPTI requires dilution prior to administration. Dilute only in 100 mL 0.9% Sodium Chloride Injection, USP. The infusion bags must be made of polyvinyl chloride (PVC), polyethylene (PE), or polyolefin (PO). Use appropriate aseptic technique when preparing VYEPTI solution for intravenous infusion. VYEPTI single-dose vials contain no preservative; discard unused portion remaining in the vial.	Provide staff education
Documentation required (e.g. double check, worksheet)?	N/A	N/A
Pharmacist/Technician Education?	Pharmacists should be educated on appropriate clinical utilization and dispensing.	Provide staff education

Administration		
Handling precautions, high-risk double check, administration with/without food, interactions, incompatibilities, or other administration information?	No other medications should be administered through the infusion set or mixed with VYEPTI. VYEPTI is for intravenous infusion only.	Create an administration note
Special delivery system (e.g. pump)?	N/A	N/A
Documentation required? (e. g. double check)	N/A	N/A
Nurse education?	No other medications should be administered through the infusion set or mixed with VYEPTI. VYEPTI is for intravenous infusion only.	Provide staff education
Monitoring		
Interactions, adverse effects, efficacy, changes in renal function, or similar?	A complete list of adverse effects can be found in the package insert.	Patients should be monitored for adverse effects and efficacy.
Follow-up laboratory tests?	N/A	N/A
Education?	Pharmacists and providers should be educated on appropriate clinical utilization.	Provide staff education

FORMULARY UPDATE

THERAPEUTIC CLASS: Angiotensin II Receptor Antagonists; Neprilysin Inhibitor

GENERIC NAME: Sacubitril/valsartan

PROPRIETARY NAME: Entresto®

BACKGROUND/RATIONALE:

Sacubitril/valsartan was approved to CHI Memorial formulary several years ago, with formulary use criteria. The label for sacubitril/valsartan was recently updated to allow use in heart failure regardless of ejection fraction (EF) based on the PARAGON-HF trial results. PARAGON-HF, was a multicenter, randomized, double-blind trial comparing sacubitril/valsartan and valsartan in 4,796 adult patients with symptomatic heart failure with left ventricular ejection fraction ≥ 45%. The study demonstrated a numerical reduction in the rate of the composite endpoint of total heart failure hospitalizations and CV death.

The CommonSpirit Health System P&T Committee also voted to allow use without restriction to a reduced EF value.

CURRENT CHI MEMORIAL FORMULARY USE CRITERIA:

- Patient has not taken an ACE inhibitor in the last 36 hours
- Patient has a blood pressure sufficiently high enough to support Entresto initiation
- **Patient has hemodynamically stable NYHA Class II to IV HF with reduced EF (≤ 40%)**
- Patient does not have a history of hereditary angioedema or history of angioedema related to previous ACE inhibitor or ARB therapy

RECOMMENDATION/DISCUSSION:

It is recommended to revise the current use criteria for sacubitril/valsartan by removing the existing criterion limiting use to EF ≤40%. This order question will be removed from the order in Epic. This recommendation was approved by Cardiology.

FORMULARY REVIEW

GENERIC NAME: Polidocanol injectable foam

PROPRIETARY NAME: *Varithena®*

INDICATIONS:

FDA Approved
Treatment of incompetent great saphenous veins (GSV), accessory saphenous veins, and visible varicosities of the great saphenous vein system above and below the knee

THERAPEUTIC CATEGORY: Non-ionic surfactant sclerosing agent

PHARMACOKINETICS:

Absorption	Tmax within 25 min (1st dose) within 5 min (2nd dose)
Distribution	Vd: 35 to 82 L
Metabolism	-
Excretion	0.2 to 0.4 L/min
Elimination Half-Life	102 to 153 minutes

SPECIAL POPULATIONS:

Pregnancy	Inconclusive - Do not use
Lactation	Inconclusive – Do not use
Pediatrics	Not established
Geriatrics	No clinically important differences in safety or efficacy were observed between older and younger patients
Hepatic Impairment	None
Renal Impairment	None

CLINICAL STUDIES:

Study Name 1: VANISH-1	
METHODS	
Study Design	Multicenter, parallel group, single-blinded study
Patient Enrollment Inclusion	● 279 patients were tested ● 275 patients completed the study to week 8 ● Males and females ● Ages 18-75 ● Saphenofemoral junction (SFJ) incompetence ● Reflux of > 0.5 seconds on duplex ultrasonography of the GSV or accessory saphenous veins ● Visible varicosities with symptoms
Patient Enrollment Exclusion	● Small saphenous and deep vein incompetence ● History of DVT, PE, or stroke ● Inability to comply with post-treatment compression or walk unaided
Baseline Characteristics	● 75% females ● Average age of 48 ● More than 90% Caucasian
Treatment Plan	Patients were split into five groups: ● Placebo ● PEM 0.5% ● PEM 1% ● PEM 2%

	All patients were blinded to their treatment. A maximum volume of 15 mL of study drug in 5 mL aliquots was allowed regardless of treatment assignment. The vein to be treated was cannulated at the mid-thigh under ultrasound guidance. Up to 5 mL of the drug was injected proximally under ultrasound guidance to a 0.5 cm distal to the SFJ. Additionally, study drug was injected to fill both the GSV from the mid-thigh catheter and visible varicose tributaries. The treated leg was wrapped in bandage in compression pads over the treated venous segments. An over-stocking thigh length 30 to 40 mmHg compression stocking with waist band was placed over the dressing. Compression bandages and stockings were worn continuously for 48 hours. The compression stocking alone was worn for an additional 12 days. Patients were encouraged to walk for at least 5 minutes during each waking hour for the week following treatment.
RESULTS	
Outcomes Summary	The adjusted mean changes from baseline to week 8 in VVSymQ score ● Placebo: -2.13 ● PEM 0.125%: -4.63 ● PEM 0.5%: -5.68 ● PEM 1%: -4.87 ● PEM 2%: -5.78 ● Pooled PEM (0.5%, 1%, 2%): -5.44
Primary Endpoint	● At week 8 pooled PEM (0.5%, 1%, and 2%) patients were significantly superior to placebo. p <0.0001 ● VVSymQ scores decreased significantly with a p <0.0001 from baseline to week 8 for all PEM individual doses
Secondary Endpoint	Mean changes from baseline to week 8 in IPR-V3 and PA-V3 scores were significantly greater in the pooled PEM group compared with the placebo group (p <0.0001)
Adverse Events	The most common adverse events included pain in extremity (21.1%), superficial thrombophlebitis (10.5%), infusion site thrombosis (9.1%), injection site hematoma (8%), limb discomfort (6.9%), limb venous thrombosis (5.5%), injection site pain (5.5%), and deep vein thrombosis (3.3%).

WARNING AND PRECAUTIONS:
- Anaphylaxis (must be prepared to treat)
- Tissue ischemia and necrosis: Do not inject intra-arterially
- Venous thrombosis

CONTRAINDICATIONS: Known allergy to polidocanol

ADVERSE REACTIONS:

Adverse Reactions	Intervention Group (N=149)	Placebo or Standard of Care Group (N=151)
Dermatologic	Contusion/injection site hematoma (15.4%)	Contusion/injection site hematoma (6.0%)
Cardiovascular	Infusion site thrombosis (16.1%), Venous thrombosis limb (8.1%), Deep vein thrombosis (4.7%), Thrombophlebitis superficial (5.4%)	Infusion site thrombosis (0%), venous thrombosis limb (0%), Deep vein thrombosis (0%), Thrombophlebitis superficial (1.3%)
Neuromuscular & Skeletal	Pain in extremity (16.8%), Limb discomfort (12.1%), tenderness/injection site pain (10.7%)	Pain in extremity (9.3%), Limb discomfort (3.3%), tenderness/injection site pain (3.3%)

CLINICALLY SIGNIFICANT DRUG INTERACTIONS: None

DOSING AND ADMINISTRATION:
Adult Dosing/Indication and Administration
- Intravenous injectable foam using ultrasound guidance. It is administered via a single cannula into the lumen of the target incompetent trunk veins or by direct injection into varicosities. 5 mL per injection and no more than 15 mL per session.
- Activate Varithena™ using the Varithena™ Oxygen Canister and Polidocanol Canister. Transfer Unit is in place, foam can be generated and transferred to a syringe. Discard the syringe contents if there are any visible bubbles. Administer the injectable foam within 75 seconds of extraction from the canister to maintain injectable foam properties
- Inject slowly (approximately 1 mL/second in the GSV and 0.5 mL/second in accessory veins) while monitoring using ultrasound. Confirm venospasm of the treated vein using ultrasound.
- Treatment sessions should be separated by a minimum of 5 days.
- Physicians who are administering Varithena™ must be experienced with different venous procedures and possess a working knowledge of the use of a duplex ultrasound in venous disease and be trained in administration.

RECOMMENDED MONITORING:

- Monitor the injection of Varithena™ foam by ultrasound, confirming venospasm of the treated vein.
- Monitor patients for at least 10 minutes after administration for signs or symptoms of severe allergic reactions (anaphylaxis).
- Monitor patients walking for 10 to 20 minutes after treatment.
- Monitor for signs of venous thrombosis after treatment with Varithena™ foam.

PHARMACOECONOMICS/COST:

Product (Drug, Strength, Form)	Price
Varithena™ (polidocanol) injectable foam 1% (180mg/18mL) vial	$3,834

CONCLUSION & RECOMMENDATION:

Varicose veins are dilated, elongated, and tortuous subcutaneous veins that are >/ 3 mm in diameter. They are present in about 10-30% of the population and are more common in the elderly. Treatment options range from sclerotherapy, laser treatment, ligation, stripping, etc. Polidocanol injectable foam 1% has CPT reimbursement codes allowable when used for medical need.

Varithena was approved to the CommonSpirit Health System formulary last month. Since it is currently being used by our vascular surgeons for outpatients, it is recommended to approve Varithena to formulary with the following restrictions:

- **Restricted to outpatient procedures with confirmed payer approval, and**
- **Treatment of superficial symptomatic venous insufficiency, varicose veins, and incompetent tributaries and perforators in the legs.**

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?	N/A	N/A
Special storage (e.g. refrigeration, protect from light, controlled substance)?	Store canisters at room temperature. Do not refrigerate or freeze. Store in a well-ventilated area, protect from sources of heat and strong light. Store activated canisters upright with the transfer unit attached and use within 30 days of activation.	N/A
Pharmacist/Technician Education?	N/A	N/A
Ordering & Prescribing		
Restriction to particular specialty, indication, or patient population?	Not approved/studied in children	N/A
Dosing Issues (e.g. renal, hepatic dosage adjustment, max dose warnings)?	None	N/A
Drug Interactions?	None	N/A
Pregnancy?	No well controlled studies in pregnant women	N/A
Absolute Contraindications?	A known allergy to Varithena™	Avoid if you developed an allergic reaction during a past administration
Requires Order Set, Protocol, concomitant therapy with another drug?	N/A	N/A
LASA* nomenclature issues?	N/A	N/A
Prescriber education?	Physicians must be experienced with venous procedures, possess a detailed working knowledge of the use of the duplex ultrasound in venous disease and be trained in the administration of Varithena™	N/A
Processing, Preparing, & Dispensing		
High-risk drug double check?	N/A	N/A

Drug Interaction check in place?	N/A	N/A
LASA* computer warnings?	N/A	N/A
Administration Notes for MAR (e.g. handling precautions, surrounding food or other drugs)?	Use within 30 days of activation, ensure physician is educated in administration	N/A
Packaging/Labeling (e.g. prepacking)?	N/A	N/A
Dispensing (e.g. auxiliary labeling, light protection, refrigeration)?	Protect from sources of heat and light	N/A
Documentation required (e.g. double check, worksheet)?	N/A	N/A
Pharmacist/Technician Education?	N/A	N/A
Administration		
Handling precautions, high-risk double check, administration with/without food, interactions, incompatibilities, or other administration information?	Varithena™ comes as a Tyvek pouch containing two sterile, connected 303 mL aluminum alloy canisters: one containing Polidocanol Solution, 180mg/18 mL, under CO2 atmosphere, the second containing pressurized oxygen at approximately 5.4 bar absolute. The connector joins the two canisters and allows activation of the product. Once activated, Varithena™ injectable foam delivers a 1% solution.	N/A
Special delivery system (e.g. pump)?	Injection	N/A
Documentation required? (e. g. double check)	N/A	N/A
Nurse education?	Know proper administration	-
Monitoring		
Interactions, adverse effects, efficacy, changes in renal function, or similar?	Monitor for anaphylaxis	Avoid administering if history of an allergy to Varithena™
Follow-up laboratory tests?	Monitor the injection of polidocanol foam by ultrasound, confirming venospasm of the treated vein	N/A
Education?	N/A	N/A

FORMULARY REVIEW

GENERIC NAME: Venetoclax

PROPRIETARY NAME: *Venclexta®*

INDICATIONS:

FDA Approved
● ***Chronic lymphocytic leukemia (CLL)***
● ***Small lymphocytic lymphoma (SLL)***
● ***Acute myelogenous leukemia (AML)***

THERAPEUTIC CATEGORY: Antineoplastic Agent; Antineoplastic Agent, BCL-2 Inhibitor

PHARMACOKINETICS:

Absorption	--
Distribution	256 to 321 L
Metabolism	Hepatic, predominantly via CYP3A; the major metabolite is M27 (has BCL-2 inhibitory activity)
Elimination	Half-life: ~26 hours

SPECIAL POPULATIONS:

Pregnancy	Based on the mechanism of action and data from animal reproduction studies, venetoclax is expected to cause fetal harm if administered during pregnancy. Pregnancy Testing is recommended prior to initiation.
Lactation	It is not known if venetoclax is present in breast milk. Due to the potential for serious adverse reactions in the breastfed infant, breastfeeding is not recommended by the manufacturer during treatment and for 1 week after the last venetoclax dose.
Pediatrics	The safety and effectiveness of VENCLEXTA have not been established in pediatric patients.
Geriatrics	No dosage adjustments necessary
Hepatic Impairment	Severe impairment (Child-Pugh class C): Reduce the daily venetoclax dose by 50%
Renal Impairment	No dosage adjustments necessary

CLINICAL STUDIES:

Azacitidine and Venetoclax in Previously Untreated Acute Myeloid Leukemia	
METHODS	
Study Design	Phase 1b study
Patient Inclusion	Key eligibility criteria included an age of 18 years or older and a confirmed diagnosis of previously untreated AML according to World Health Organization criteria.
Patient Exclusion	Patients were considered to be ineligible for standard induction therapy if they were 75 years of age or older or if they had at least one of the following coexisting conditions precluding intensive chemotherapy: a history of congestive heart failure for which treatment was warranted or an ejection fraction of 50% or less or chronic stable angina, a diffusing capacity of the lung for carbon monoxide of 65% or less or a forced expiratory volume in 1 second of 65% or less, and an Eastern Cooperative Oncology Group performance-status score of 2 or 3 (on a 5-point scale, with higher numbers indicating greater disability). Previous receipt of any hypomethylating agent, venetoclax, or chemotherapy for myelodysplastic syndrome was exclusionary. Patients with a favorable cytogenetic risk according to the AML National Comprehensive Cancer Network (NCCN) guidelines.
Treatment Plan	Venetoclax was administered orally, once daily, with food. For mitigation of the tumor lysis syndrome during cycle 1, the dose of venetoclax was 100 mg on day 1 and 200 mg on day 2; on day 3, the target dose of 400 mg was reached and continued until day 28. In all subsequent 28-day cycles, the dose of venetoclax was initiated at 400 mg daily. Patients in the control group received an oral venetoclax placebo according to the same schedule. Patients in both groups received azacitidine at a dose of 75 mg per square meter of body-surface area, subcutaneously or intravenously, on days 1 through 7 every 28-day cycle.
RESULTS	
Primary Endpoint	The median overall survival was 14.7 months (95% confidence interval [CI], 11.9 to 18.7) in the azacitidine–venetoclax group and 9.6 months (95% CI, 7.4 to 12.7) in the control group (hazard ratio for death, 0.66; 95% CI, 0.52 to 0.85; P<0.001).

Secondary Endpoint	The incidence of complete remission was higher with azacitidine–venetoclax than with the control regimen (36.7% vs. 17.9%; P<0.001), as was the composite complete remission (complete remission or complete remission with incomplete hematologic recovery) (66.4% vs. 28.3%; P<0.001).
Adverse Events	Key adverse events included nausea of any grade (in 44% of the patients in the azacitidine–venetoclax group and 35% of those in the control group) and grade 3 or higher thrombocytopenia (in 45% and 38%, respectively), neutropenia (in 42% and 28%), and febrile neutropenia (in 42% and 19%). Infections of any grade occurred in 84% of the patients in the azacitidine–venetoclax group and 67% of those in the control group, and serious adverse events occurred in 83% and 73%, respectively.
Venetoclax plus obinutuzumab versus chlorambucil plus obinutuzumab for previously untreated chronic lymphocytic leukaemia (CLL14)	
METHODS	
Study Design	Multicenter, open-label, randomised, phase 3 trial
Patient Inclusion	- Documented previously untreated CLL - CLL requiring treatment according to IWCLL criteria - Total Cumulative Illness Rating Scale (CIRS score) greater than (>) 6 - Adequate marrow function independent of growth factor or transfusion within 2 weeks - Adequate liver function - Life expectancy > 6 months - Agreement to use highly effective contraceptive methods per protocol
Patient Exclusion	- Transformation of CLL to aggressive Non-Hodgkin's lymphoma - Known central nervous system involvement - History of confirmed progressive multifocal leukoencephalopathy (PML) - An individual organ/ system impairment score of 4 as assessed by the CIRS definition limiting the ability to receive the treatment regimen of this trial with the exception of eyes, ears, nose, throat organ system - Participants with uncontrolled autoimmune hemolytic anemia or immune thrombocytopenia - Inadequate renal function - History of prior malignancy, except for conditions as listed in the protocol if participants have recovered from the acute side effects incurred as a result of previous therapy - Use of investigational agents or concurrent anti-cancer treatment within the last 4 weeks of registration - Participants with active bacterial, viral, or fungal infection requiring systemic treatment within the last two months prior to registration - History of severe allergic or anaphylactic reactions to humanized or murine monoclonal antibodies or known sensitivity or allergy to murine products - Hypersensitivity to chlorambucil, obinutuzumab, or venetoclax or to any of the excipients - Pregnant women and nursing mothers - Positive test results for chronic hepatitis B virus (HBV) or for hepatitis C - Participants with human immunodeficiency virus (HIV) or human T-cell leukemia virus-1 (HTLV-1) - Requires the use of warfarin, marcumar, or phenprocoumon - Received agents known to be strong and moderate Cytochrome P450 3A inhibitors or inducers within 7 days prior to the first dose of study drug
Treatment Plan	The treatment duration in both groups consisted of 12 cycles lasting 28 days each; no crossover was allowed. Obinutuzumab was administered intravenously for 6 cycles starting with 100 mg on day 1 and 900 mg on day 2 (or 1000 mg on day 1), 1000 mg on day 8 and 1000 mg on day 15 of cycle 1, and subsequently 1000 mg on day 1 of cycles 2 through 6. Chlorambucil was administered orally at 0.5 mg per kilogram of body weight on days 1 and 15 of each cycle until completion of 12 cycles. The daily oral venetoclax regimen was initiated on day 22 of cycle 1, starting with a 5-week dose ramp-up (1 week each of 20, 50, 100, and 200 mg, then 400 mg daily for 1 week), thereafter continuing at 400 mg daily until completion of cycle 12.
RESULTS	
Outcomes Summary	After a median follow-up of 28.1 months, 30 primary end-point events (disease progression or death) had occurred in the venetoclax–obinutuzumab group and 77 had occurred in the chlorambucil–obinutuzumab group (hazard ratio, 0.35; 95% confidence interval [CI], 0.23 to 0.53;

	P<0.001). The Kaplan–Meier estimate of the percentage of patients with progression-free survival at 24 months was significantly higher in the venetoclax–obinutuzumab group than in the chlorambucil–obinutuzumab group: 88.2% (95% CI, 83.7 to 92.6) as compared with 64.1% (95% CI, 57.4 to 70.8). This benefit was also observed in patients with TP53 deletion, mutation, or both and in patients with unmutated immunoglobulin heavy-chain genes.
Adverse Events	Grade 3 or 4 neutropenia occurred in 52.8% of patients in the venetoclax–obinutuzumab group and in 48.1% of patients in the chlorambucil–obinutuzumab group, and grade 3 or 4 infections occurred in 17.5% and 15.0%, respectively. All-cause mortality was 9.3% in the venetoclax–obinutuzumab group and 7.9% in the chlorambucil–obinutuzumab group. These differences were not significant.

COMPARATIVE EFFICACY: This is the first and only approved BCL-2 Inhibitor.

WARNING AND PRECAUTIONS:

- Bone marrow suppression
- Infection
- Tumor lysis syndrome
- Hepatic impairment
- Multiple myeloma
- Renal impairment
- Immunizations

CONTRAINDICATIONS: Concomitant use with strong CYP3A inhibitors at initiation and during ramp-up phase in patients with CLL or SLL due to the potential for increased risk of tumor lysis syndrome.

ADVERSE REACTIONS:

Adverse Reactions		**Any grade % (N=240)**	**Grade 3 or 4 % (N=240)**
Blood and lymphatic system disorders	Neutropenia	45	41
	Anemia	29	18
	Thrombocytopenia	22	15
	Febrile neutropenia	5	5
Gastrointestinal disorders	Diarrhea	35	<1
	Nausea	33	<1
	Vomiting	15	<1
	Constipation	14	0
General disorders and administration site conditions	Fatigue	21	2
	Pyrexia	16	<1
	Peripheral edema	11	<1
Infections and infestations	Upper respiratory tract infection	22	1
	Pneumonia	8	5
Metabolic and nutrition disorders	Hypokalemia	12	4
Musculoskeletal and connective tissue disorders	Back pain	10	<1
Nervous system disorders	Headache	15	<1
Respiratory, thoracic, and mediastinal disorders	Cough	13	0

CLINICALLY SIGNIFICANT DRUG INTERACTIONS:

Interacting Drug	**Effect**
Strong CYP3A Inhibitors	Concomitant use of VENCLEXTA with strong CYP3A inhibitors at initiation and during ramp-up phase is contraindicated.
Moderate CYP3A Inhibitors and P-gp Inhibitors	Avoid concomitant use of moderate CYP3A inhibitors or P-gp inhibitors. Avoid grapefruit products, Seville oranges, and starfruit during treatment with VENCLEXTA, as they contain inhibitors of CYP3A.
CYP3A Inducers	Avoid concomitant use of VENCLEXTA with strong CYP3A inducers or moderate CYP3A inducers.
Warfarin	In a drug-drug interaction study in healthy subjects, administration of a single dose of venetoclax with warfarin resulted in an 18% to 28% increase in Cmax. Monitor INR closely.

DOSING AND ADMINISTRATION:

Adult Dosing/Indication and Administration

- **AML**, newly diagnosed: 100 mg on day 1; 200 mg on day 2; 400 mg on day 3; and 400 mg once daily on day 4 and beyond.
    - Venetoclax in combination with azacitidine or decitabine: Day 4 and beyond: 400 mg once daily until disease progression or unacceptable toxicity (DiNardo 2019; DiNardo 2020).
    - Venetoclax in combination with low-dose cytarabine: Day 4 and beyond: 600 mg once daily until disease progression or unacceptable toxicity (Wei 2019; Wei 2020).
- **CLL/SLL**: 20 mg orally once daily for 7 days. Dose is increased once weekly over 5 weeks as follows: week 2, 50 mg/day; week 3, 100 mg/day; week 4, 200 mg/day; and week 5 and beyond, 400 mg/day. Continue therapy until disease progression.
    - Monotherapy: Week 5 and thereafter: 400 mg once daily; continue until disease progression or unacceptable toxicity.
    - In combination with obinutuzumab: Note: Obinutuzumab begins on day 1 of cycle 1; initiate venetoclax on day 22 of cycle 1 according to the 5-week ramp-up schedule for chronic lymphocytic leukemia/small lymphocytic lymphoma above; ramp-up will be completed at the end of cycle 2. Cycle 3 (day 1 and beyond): 400 mg once daily until the end of cycle 12. Each cycle is 28 days (Fischer 2019).
    - In combination with rituximab: Week 5 and thereafter: 400 mg once daily; continue venetoclax until disease progression or unacceptable toxicity, for up to 24 months from day 1 (cycle 1) of rituximab; begin rituximab after receiving venetoclax at the 400 mg once daily dose for 7 days (Kater 2020; Seymour 2018).

DOSING ADJUSTMENTS:

Hepatic Impairment

- Mild or moderate impairment (Child-Pugh classes A or B): No dosage adjustment necessary.
- Severe impairment (Child-Pugh class C): Reduce the daily venetoclax dose by 50%.

Renal Impairment

- No dosage adjustment necessary

Toxicity

- Dose adjustment necessary for toxicity:
    - Tumor lysis syndrome
    - Hematologic toxicity: Grade 3 neutropenia with infection or fever or grade 4 hematologic toxicities (except lymphopenia)

RECOMMENDED MONITORING:

- CBC with differential
- Blood chemistries (potassium, uric acid, phosphorus, calcium, and creatinine)
- Pregnancy status
- Tumor burden via radiographic evaluation for TLS risk evaluation
- Signs/symptoms of infection
- Hepatic impairment
- Hepatitis B screening

PHARMACOECONOMICS/COST:

Product (Drug, Strength, Form)	Cost/Product	Cost/Cycle
VENCLEXTA 1 X 100 MG TAB	$107.56	$11,508.92 for C1 AML $12,046.72 for C2 and beyond

CONCLUSION & RECOMMENDATION:

Venetoclax is a B-cell lymphoma-2 (BCL-2) protein inhibitor that has demonstrated cytotoxic activity in tumor cells that overexpress BCL-2. It is indicated as a single agent or in combination with obinutuzumab or rituximab for the treatment of CLL or SLL. Venetoclax is also indicated in combination with azacitidine, decitabine, or low-dose cytarabine for the treatment of newly-diagnosed AML in adults who are ≥75 years or who have comorbidities that make them ineligible for intensive induction chemotherapy.

Venetoclax was recently added to the CommonSpirit Health System formulary, with use restrictions.

It is recommended to add venetoclax (Venclexta) to the inpatient formulary with use restrictions in alignment with CommonSpirit Health system formulary, as follows:

- Restricted to hematology oncology service for CLL, SLL, or AML
- First cycle or for admitted patients and next cycle is needed (unable to defer to outpatient administration or obtain from specialty pharmacy)
    - For continuation of therapy, patient's own medication supply must be utilized if on therapy prior to hospitalization

FAILURE, MODE AND EFFECTS ANALYSIS (FMEA):

Medication Management Step	Identified Risk	Steps for Prevention
Selection & Procurement		
Therapeutic interchange?	No	
Special Ordering Requirements?	No	
Storage		
LASA* separation of stock?	No	
Special storage (e.g. refrigeration, protect from light, controlled substance)?	Yes	Hazardous storage in outpatient infusion center
Pharmacist/Technician Education?	Yes	Wear gloves when dispensing and checking the medication.
Ordering & Prescribing		
Restriction to particular specialty, indication, or particular patient population?	Yes	Medication should be ordered only by hematologist or oncologist for patients with approved indication of leukemia (AML or CLL) or lymphoma.
Dosing Issues (e.g. renal, hepatic dosage adjustment, max dose warnings)?	Yes	Dose adjustment is recommended for hepatic impairment.
Drug Interactions?	Yes	Most significant interaction is with CYP3A inhibitors and inducers. Alerts should be created to ensure adjustment of dose for interaction.
Pregnancy?	Yes	Due to teratogenic effects, there should be an alert to ensure that the patient is not pregnant. When ordering the medication, one of the criteria should be to ensure that patients are utilizing adequate contraception during treatment.
Absolute Contraindications?	Yes	Concomitant use with strong CYP3A inhibitors at initiation and during ramp-up phase in patients with chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) due to the potential for increased risk of tumor lysis syndrome
Requires Order Set, Protocol, concomitant therapy with another drug?	Yes	It can be added to existing protocols in combination with either hypomethylating agent, cytarabine, obinutuzumab, or rituximab.
LASA* nomenclature issues?	No	
Prescriber education?	No	
Processing, Preparing, & Dispensing		
High-risk drug double check?	Yes	There should be a double-check as the product is a hazardous drug
Drug Interaction check in place?	Yes	Cross-reference with drug interactions listed in Clinical Pharmacology
LASA* computer warnings?	No	
Administration Notes for MAR (e.g. handling precautions, surrounding food or other drugs)?	Yes	Cytotoxic agent. Handle with precaution. Administer with food.
Packaging/Labeling (e.g. prepacking)?	No	
Dispensing (e.g. auxiliary labeling, light protection, refrigeration)?	No	
Documentation required (e.g. double check, worksheet)?	Yes	There should be documentation of a double check by at least 2 pharmacists. There should also be documentation of delivery of medication.
Pharmacist/Technician Education?	Yes	There should be a double-check as the product is a hazardous drug
Administration		
Handling precautions, high-risk double check, administration with/without food, interactions, incompatibilities, or other administration information?	Yes	Nurses should be double-gloved to protect themselves.
Special delivery system (e.g. pump)?	No	

Documentation required? (e. g. double check)	Yes	Since chemotherapy is considered to be high-risk, there should be a double check as well as documentation from the pharmacist before dispensing and from the RN before administration.
Nurse education?	Yes	Provide medication guide to nurses for additional information on administration
Monitoring		
Interactions, adverse effects, efficacy, changes in renal function, or similar?	Yes	TLS labs including electrolytes, serum creatinine and hepatic function tests are recommended to be monitored.
Follow-up laboratory tests?	Yes	TLS labs including electrolytes, serum creatinine and hepatic function tests are recommended to be monitored.
Education?	Yes	TLS labs including electrolytes, serum creatinine and hepatic function tests are recommended to be monitored.

FORMULARY INTERCHANGE

THERAPEUTIC CLASS: Triple combination containing an inhaled corticosteroid (ICS), a long-acting muscarinic antagonist (LAMA), and a long-acting beta-2 adrenergic agonist (LABA)

GENERIC NAME: Budesonide, glycopyrrolate, and formoterol

PROPRIETARY NAME: Breztri®

BACKGROUND/RATIONALE:

Breztri® is indicated for the maintenance treatment of chronic obstructive pulmonary disease. The GOLD guidelines recommend this triple combination should be reserved for consideration at follow-up in patients who are taking a LABA/LAMA combination and who develop further exacerbation.

Another triple combination ICS, LAMA, plus LABA is Trelegy® (fluticasone, umeclidinium, vilanterol). Currently, home medication orders for Trelegy® for continuation during hospitalization are approved to automatically interchange as follows:

ORDERED	SUBSTITUTION
Vilanterol/umeclidinium/fluticasone (Trelegy Ellipta®) 25 mcg/62.5 mcg/ 100 mcg – 1 inhalation daily	Tiotropium/olodaterol (Stiolto Respimat®) 5 mcg/5 mcg (2 puffs) via oral inhalation once daily **PLUS** Mometasone HFA (Asmanex) 200mcg /inhalation - 2 inhalations BID
Note: When tiotropium (component of Stiolto Respimat®) is ordered for a patient currently on ipratropium (Atrovent®), the Atrovent® will automatically be discontinued per protocol.	

RECOMMENDATION/DISCUSSION:

It is recommended to approve an automatic therapeutic interchange for all Breztri® orders to the formulary products Stiolto Respimat® and Asmanex®, as stated in the table below. This is in alignment with the current automatic therapeutic interchange from Trelegy® to Stiolto Respimat® and Asmanex®.

Ordered	Substitution
Breztri Aerosphere® (Budesonide 160 mg, glycopyrrolate 9 mcg, and formoterol 4.8 mcg) 2 actuations BID	Tiotropium/olodaterol (**Stiolto Respimat®**) 5 mcg/5 mcg (2 puffs) via oral inhalation once daily **PLUS** Mometasone HFA (Asmanex) 200mcg /inhalation - 2 inhalations BID
Note: When tiotropium (component of Stiolto Respimat®) is ordered for a patient currently on ipratropium (Atrovent®), the Atrovent® will automatically be discontinued per protocol.	

BIOSIMILAR FORMULARY ADDITION

Per the CHI Memorial Biosimilar policy, new biosimilars that have been FDA approved for the same indications as the reference product (RP) will be automatically added to hospital formulary if the RP is currently approved as a formulary agent.

Any formulary restrictions currently in place for the RP will be applied to the biosimilar medication.

Riabni (rituximab-arrx) 12/2020 PI	**Rituxan (rituximab) 6/2021 PI**
RIABNI (rituximab-arrx) is a CD20-directed cytolytic antibody indicated for the treatment of: ● Adult patients with non-Hodgkin's Lymphoma (NHL). ○ Relapsed or refractory, low grade or follicular, CD20-positive B-cell NHL as a single agent. ○ Previously untreated follicular, CD20-positive, B-cell NHL in combination with first line chemotherapy and, in patients achieving a complete or partial response to a rituximab product in combination with chemotherapy, as single-agent maintenance therapy. ○ Non-progressing (including stable disease), low-grade, CD20-positive, B-cell NHL as a single agent after first-line cyclophosphamide, vincristine, and prednisone (CVP) chemotherapy. ○ Previously untreated diffuse large B-cell, CD20-positive NHL in combination with cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) or other anthracycline-based chemotherapy regimens. ● Adult patients with Chronic Lymphocytic Leukemia (CLL). ○ Previously untreated and previously treated CD20-positive CLL in combination with fludarabine and cyclophosphamide (FC). ● Granulomatosis with Polyangiitis (GPA) (Wegener's Granulomatosis) and Microscopic Polyangiitis (MPA) in adult patients in combination with glucocorticoids.	RITUXAN (rituximab) is a CD20-directed cytolytic antibody indicated for the treatment of: ● Adult patients with Non-Hodgkin's Lymphoma (NHL) ○ Relapsed or refractory, low grade or follicular, CD20-positive B-cell NHL as a single agent. ○ Previously untreated follicular, CD20-positive, B-cell NHL in combination with first line chemotherapy and, in patients achieving a complete or partial response to a rituximab product in combination with chemotherapy, as single-agent maintenance therapy. ○ Non-progressing (including stable disease), low-grade, CD20- positive, B-cell NHL as a single agent after first-line cyclophosphamide, vincristine, and prednisone (CVP) chemotherapy. ○ Previously untreated diffuse large B-cell, CD20-positive NHL in combination with (cyclophosphamide, doxorubicin, vincristine, and prednisone) (CHOP) or other anthracycline-based chemotherapy regimens. ● Adult patients with Chronic Lymphocytic Leukemia (CLL) ○ Previously untreated and previously treated CD20-positive CLL in combination with fludarabine and cyclophosphamide (FC). ● Rheumatoid Arthritis (RA) in combination with methotrexate in adult patients with moderately-to severely-active RA who have inadequate response to one or more TNF antagonist therapies.

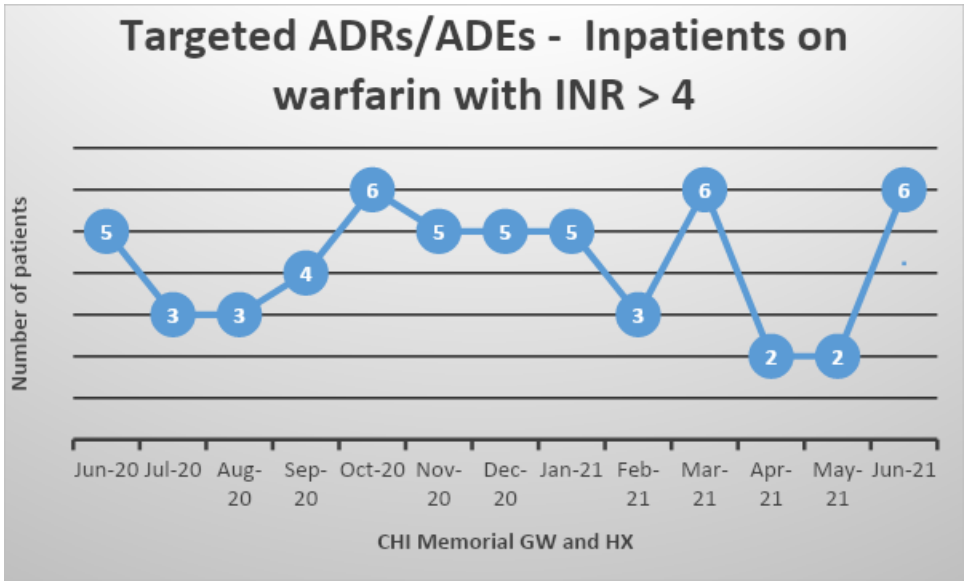
	• Granulomatosis with Polyangiitis (GPA) (Wegener's Granulomatosis) and Microscopic Polyangiitis (MPA) in adult and pediatric patients 2 years of age and older in combination with glucocorticoids • Moderate to severe Pemphigus Vulgaris (PV) in adult patients.

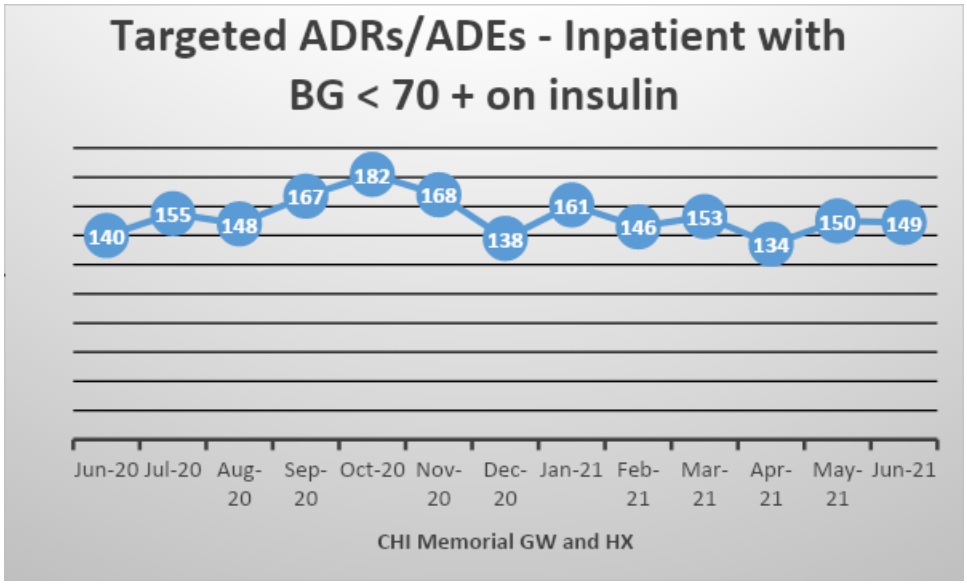
ADR Summary April - June 2021

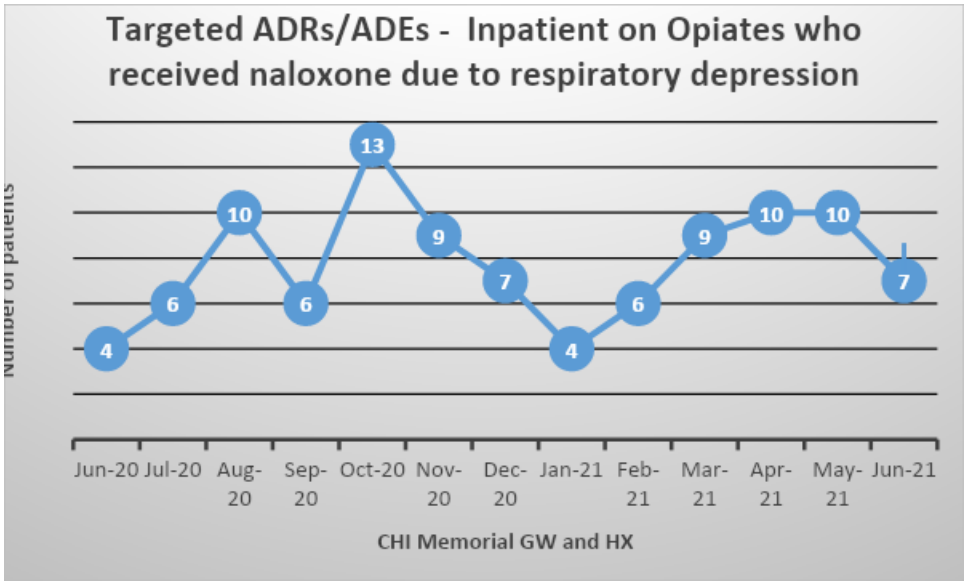
Inpatient ADRs/ADEs reported through IRIS April-June 2021							
Incident Number	Event Date	Generic	Reaction	Primary Injury	ADR Preventable?	Level of Harm	Location
210029884	4/2/2021	levophed	infiltration	Tissue Damage	Potentially Preventable	1	HX ICU
210030256	4/3/2021	Iopamidol	cardiopulmonary arrest is felt to either be hypertensive emergency causing flash pulmonary edema or reaction to the contrast administered during the CTA.	Respiratory and Cardiac changes	Not Preventable	3	ED
210043142	5/13/2021	Iopamidol	itching/hives	No apparent injury	Not Preventable	1	CT
210051158	6/7/2021	sodium ferric gluc	palpitations, elevated BP, chilly	No apparent injury	Not Preventable	1	IMCU

There were no **Inpatient** ADRs/ADEs reported through EPIC April-June 2021

Targeted Inpatient ADRs/ADEs:




Targeted ADRs/ADEs - Inpatient with BG < 70 + on insulin
140
155
148
167
182
168
138
161
146
153
134
150
149
Jun-20
Jul-20
Aug-20
Sep-20
Oct-20
Nov-20
Dec-20
Jan-21
Feb-21
Mar-21
Apr-21
May-21
Jun-21
CHI Memorial GW and HX


Targeted ADRs/ADEs - Inpatient on Opiates who received naloxone due to respiratory depression
Number of patients
4
6
10
6
13
9
7
4
6
9
10
10
7
Jun-20
Jul-20
Aug-20
Sep-20
Oct-20
Nov-20
Dec-20
Jan-21
Feb-21
Mar-21
Apr-21
May-21
Jun-21
CHI Memorial GW and HX