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Formulary Update

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Rozanolixizumab for Generalized Myasthenia Gravis

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Background: Generalized myasthenia gravis (gMG) is a rare, autoimmune disease characterized by immunoglobulin G (IgG) antibody-mediated inhibition of conduction at the neural synapse, impairing neuromuscular function.[1] Patients with gMG are either anti-acetylcholine receptor (AChR) antibody positive and/or anti-muscle-specific tyrosine kinase (MuSK) antibody positive.[2] Major symptoms of gMG include fatigue and severe muscle weakness which may lead to serious complications including myasthenia crisis.[2,3] While conventional treatment options for gMG such as acetylcholinesterase inhibitors (e.g., pyridostigmine), corticosteroids, and non-steroidal immunosuppressants may be somewhat effective, long-term use of these treatments could result in serious adverse effects. Plasma exchange (PLEX) and intravenous immunoglobulin (IVIg) are employed short-term for gMG exacerbations, but lack feasibility for chronic use. Therefore, new targeted therapies focused on reducing the pathogenic IgG circulation were created to treat this often debilitating disease. Efgartigimod alfa (Vyvgart®) intravenous injection and its subcutaneous counterpart, efgartigimod alfa and hyaluronidase (Vyvgart® Hytrulo), approved by the Food and Drug Administration (FDA) in 2021 and 2023, respectively, are targeted therapies indicated for adult patients who are anti-AChR antibody positive.[4,5] Rozanolixizumab-noli (Rystiggo®; UCB, Inc), approved by the FDA in June 2023, is the first agent indicated for the treating of both anti-AChR and anti-MuSK antibody positive gMG.[6]

Mechanism of Action: Rozanolixizumab is a recombinant, humanized IgG4 monoclonal antibody that lowers pathogenic IgG by binding to the neonatal Fc receptor (FcRn), enabling IgG to be degraded by lysosomal breakdown.[6] Lowering circulating serum IgG inhibits the immune response against the neuromuscular synapse, thus improving neuromuscular function.

Clinical Trials: MycarinG was a phase 3, double-blind, placebo-controlled trial evaluating the safety and efficacy of rozanolixizumab in gMG.[7] A total of two-hundred patients at least 18 years of age with gMG with AChR or MuSK autoantibodies were enrolled. Participants had a Myasthenia Gravis Activities of Daily Living (MG-ADL) score of at least 3 without ocular symptoms and a minimum Quantitative Myasthenia Gravis (QMG) score of 11. The MG-ADL survey is an 8-item patient-reported outcome measure that assesses symptoms and functional activities of daily living with scores ranging from 0 to 24, while the QMG is a 13-item direct physician assessment tool that assesses disease severity based on impairments of body function and structures with scores ranging from 0 to 39. Higher scores for these assessment tools corre-

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spond to greater disease severity. Study participants were stratified by gMG autoantibody type and randomized in a 1:1:1 ratio to the following intervention groups for weekly subcutaneous infusions over a 6-week period: rozanolixizumab 7 mg/kg (n=66), rozanolixizumab 10 mg/kg (n=67), or placebo (n=67). The primary efficacy endpoint assessed the change in MG-ADL from baseline to day 43 of therapy. The greatest reduction in MG-ADL occurred within rozanolixizumab treatment groups, with a least-squares mean change of –3.37 in the 7 mg/kg group and –3.40 in the 10 mg/kg group, contrasted to –0.78 in the placebo group. The least squares mean difference from placebo was –2.59 in the rozanolixizumab 7 mg/kg group (95% CI, -4.09 to –1.25, p<0.0001) and –2.62 in the rozanolixizumab 10 mg/kg treatment group (95% CI, -3.99 to –1.16, p<0.0001). Treatment-emergent adverse events (TEAEs) occurred in 83% of the rozanolixizumab 10 mg/kg group, 81% in the rozanolixizumab 7 mg/kg group, and 67% in the placebo group. Headache was the most frequently reported TEAE, followed by diarrhea and pyrexia. Based on the results of this study, the authors concluded that rozanolixizumab represents another potential targeted treatment option for gMG. A pooled analysis of MycarinG and two open-label extension studies, MG0004 and MG0007, assessed the long-term efficacy and safety of rozanolixizumab.[8] Patients enrolled in MG0004 received weekly subcutaneous infusions for up to 52 weeks, while those in MG0007 received additional infusions based on symptom worsening following one dose cycle of six weekly infusions. The pooled findings showed MG-Composite (MGC) scores improved across all rozanolixizumab cycles, noting a median of four treatment cycles were reported for patients requiring rozanolixizumab therapy beyond 1 year. A total of 89.9% of patients who received rozanolixizumab reported at least one TEAE, with most being mild-moderate in severity. The investigators found that rozanolixizumab was generally well-tolerated and efficacious throughout each 6-week infusion cycle.

Safety: The most common adverse effects of rozanolixizumab with an incidence of ≥ 5% included headache, infection, diarrhea, pyrexia, hypersensitivity reactions, nausea, administration site reactions, abdominal pain, and arthralgia.[6] Rozanolixizumab may rarely cause aseptic meningitis. Administration of live or live-attenuated vaccination is not recommended due to a diminished immune response via serum IgG reduction during rozanolixizumab therapy.

Dosing and Administration: Rozanolixizumab is administered undiluted via subcutaneous infusion at 20 mL/hour once weekly for 6 weeks.[6] Dosing is weight-based and listed in Table 1.

Table 1: Rozanolixizumab Dosing[6]

Body Weight	Dose (mg)	Infusion Volume (mL)
< 50 kg	420 mg	3 mL
50 kg to < 100 kg	560 mg	4 mL
≥ 100 kg	840 mg	6 mL

Any missed doses of rozanolixizumab may be administered up to 4 days after the initially scheduled dose.

Cost and Availability: Rozanolixizumab (NDC: 50474-980-79) is available in preservative-free, single-use 280 mg/2 mL vials with an average wholesale price of approximately $7260 per vial.[6,9] The cost for a patient who weighs 100 kg, requiring a total of 18 vials for a 6-week course of therapy, would be $130,680. Rozanolixizumab should be stored in the original carton and protected from light until administration.[6] Vials may be stored at room temperature (up to 77°F [25° C]) for up to 30 days, but should not be returned to refrigeration following storage at room temperature.

Formulary Status: Rozanolixizumab has been added to the CCHS Formulary restricted to the Department of Neurology for outpatient use only in patients with refractory gMG positive for anti-acetylcholine receptor (AChR) or anti-muscle specific tyrosine kinase (MuSK) antibodies.

References:

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Additions to the Adult CCHS Formulary			
Drug	**Pharmacologic Class**	**Formulary Use**	**Restrictions/Comments**
ADAMST13 Recombinant-krhn (Adzynma®) Intravenous Injection	Blood Factor	Congenital TTP	Restricted to the Department of Hematology/Oncology for congenital TTP for outpatient use only
Aminolevulinic Acid Topical Products (Levulan® Kerastick® 20% Topical Solution) (Ameluz® Topical Gel 10%)	Photosensitizing Agent	Actinic Keratosis	Restricted to the Department of Dermatology for outpatient use only
Clozapine Orally-Disintegrating Tablets (Fazaclo®)	Antipsychotic	Psychiatric Disorders	Restricted to the Department of Psychiatry for use in patients with a documented suspicion of cheeking or oral access issues limiting the use of tablets. Continuation of therapy is not restricted.
Melphalan with Hepatic Delivery System (Hepzato Kit™) Intra-arterial Infusion	Chemotherapy Agent	Uveal Melanoma With Unresectable Hepatic Metastases	Restricted to the Department of Hematology/Oncology for Main Campus use only
Milrinone Inhalation	PDE-3 Inhibitor	Severe PAH Complicated CAD Surgery with Right Ventricular Failure	Restricted for use in ICUs and ORs meeting parameters outlined in the Respiratory Therapy Inhaled Milrinone Administration in the Adult Patient SOP.
Mirikizumab-mrkz (Omvoh™) Intravenous Injection	Monoclonal Antibody	Ulcerative Colitis	Restricted to the Department of Gastroenterology for outpatient use only. Note: Mirikizumab-mrkz subcutaneous injection will remain non-formulary
Nadofaragene firadenovec-vncg (Adstiladrin®) Intravesical Instillation	Gene Therapy	BCG-Resistant Non-Muscle Invasive Bladder Cancer	Restricted to the Department of Urology for outpatient use only
Pegfilgrastim-cbqv (Udenyca® On-Body) Subcutaneous Injection	Colony Stimulating Factor	Prevention of Chemotherapy-Induced Neutopenia	Restricted to the Department of Hematology/Oncology for outpatient use only
Rezafungin (Rezzayo®) Intravenous Injection	Antifungal Agent	Candidemia and Invasive Candidiasis	Restricted to the Department of Infectious Diseases for outpatient use only

TTP=Thrombotic thrombocytopenic purpura PDE-3=Phosphodiesterase-3 PAH=Pulmonary arterial hypertension
CAD=Cardiac assist device ICUs=Intensive care units ORs=Operating rooms SOP=Standard operating procedure BCG=Bacillus calmette-guerin

Additions to the Adult CCHS Formulary			
Drug	**Pharmacologic Class**	**Formulary Use**	**Restrictions/Comments**
Sodium Zirconium Cyclosilicate (Lokelma®) Oral Powder for Suspension	Potassium Binder	Hyperkalemia	No Restrictions
Toripalimab-tpzi (Loqtorzi®) Intravenous Injection	Monoclonal Antibody	Nasopharyngeal Carcinoma	Restricted to the Department of Hemaology/Oncology for outpatient use only

Changes to Restrictions of Medications on the Adult CCHS Formulary			
Drug	**Pharmacologic Class**	**Formulary Use**	**Changes to Restrictions/ Comments**
Anakinra (Kineret®) Subcutaneous/ Intravenous Injection	Interleukin-1 Receptor Antagonist	Refractory HLH	Modified restrictions to: 1) Management of CRS and neurotoxicity in patients receiving CAR-T therapy for inpatient or outpatient use.* 2) The Department of Hematology/ Oncology for management of HLH
Esketamine (Spravato®) Intranasal Solution	Antidepressant	TRD	Modified restrictions to include the Department of Psychiatry for the management of TRD in the outpatient setting at Lutheran and Marymount Hospital.
Fosaprepitant (Emend®) Intravenous Injection	Antiemetic	PONV Chemotherapy-Induced NV	Modified restrictions to: Restricted to the Department of Anesthesiology for the treatment of PONV
Hypertonic Saline 23.4% Intravenous Injection	Electrolyte	Refractory Intracranial Hypertension Traumatic Brain Injury	Modified restrictions to allow for peripheral administration for emergent use prior to obtaining central line venous catheter access
Ketamine (Ketalar®) Intravenous Injection	General Anesthetic Analgesic	Analgesia	Modified restrictions to include Palliative and Support Care and Chronic Pain Management for non-ICU units meeting the monitoring parameters in the Subanesthetic Ketamine Infusion SOP.
Lacosamide (Vimpat®) Intravenous Injection	Anti-Epileptic Agent	Seizures Trigeminal Neuralgia	Modified restrictions to include the Departments of Neurology and Neurosurgery for trigeminal neuralgia
Ziprasidone (Geodon®) Intramuscular Injection	Antipsychotic Agent	Psychiatric Disorders	All restrictions were removed to allow ordering by any provider specialty

*May be ordered by Emergency Medicine Staff Physicians, Hematology/Oncology Staff Physicians, Intensivists, Hematology/Oncology or ICU Fellows, Advanced Practice Practitioners, or Hospitalists in consultation with a Hematology/Oncology Staff Physician.

HLH=Hemophagocytic lymphohistiocytosis CRS=Cytokine release syndrome CAR-T=Chimeric antigen receptor-T TRD=Treatment-resistant depression PONV=Postoperative nausea and vomiting NV=Nausea and vomiting ICU=Intensive care unit SOP=Standard Operating Procedure

Product Standardizations to the Adult CCHS Formulary			
Drug	**Pharmacologic Class**	**Formulary Use**	**Details**
Angiotensin-Converting Enzyme Inhibitors	Antihypertensive	Hypertension CHF	A therapeutic interchange has been created for ACE-Is. Details are in Lexicomp.
Leuprolide Injection (Eligard®) (Lupron® Depot)	Gonadotropin-Releasing Hormone Agonist	Prostate Cancer	Pharmacists will be able to interchange Eligard® for Lupron® Depot for the indication of advanced prostate cancer based on the patient's insurance.
Levonorgestrel Intrauterine Device Standardization	Progestin	Abnormal Uterine Bleeding Contraceptive	Inpatient use of Liletta® is restricted to the immediate postpartum period. If restriction criteria are not met, then use is restricted to outpatient use only. Liletta® is available outpatient for patients needing to pay out-of-pocket. Mirena®, Kyleena®, and Skyla® are restricted to outpatient use only.
Sulfonylureas	Antidiabetic Agents	Type II Diabetes	The following modifications were made to the current sulfonylurea therapeutic interchange: 1. Discontinued sulfonylurea agents were removed (chlorpropamide, tolazamide, tolbutamide). 2. Glipizide ER will be interchanged with Glipizide IR 3. Glimepiride will not be included in the interchange Details are in Lexicomp.

CHF=Congestive heart failure ACE-Is= Angiotensin converting enzyme-inhibitors ER=Extended-release IR=Immediate-release

Process Changes to the Adult CCHS Formulary			
Process	**Pharmacologic Class**	**Formulary Use**	**Details**
Adult (18+) Infectious Diseases Sexually Transmitted Infections Prophylaxis and Treatment Standard Operating Procedure for Pharmacist Consult Agreements*	Anti-infectives	Sexually Transmitted Infections	Various updates to this SOP were approved.
Aminoglycoside Dosing Service Standard Operating Procedure	Aminoglycosides	Various Infections	Establishment of this dosing service for adult patients was approved.
Guideline for Dosing of Anti-Malarial Agents	Anti-Malarial Agents	Malaria	Guideline for dosing antimalarial agents was added to the CCHS Antimicrobial Use Guidelines for adult dosing and was excluded from the Medication Dose Optimization Service.
Guideline for Dosing Mycobacterial Infections	Antimycobacterial Agents	Mycobacterial Infections	An antimycobacterial dosing table was added to the CCHS Antimicrobial Use Guidelines for adult dosing and included in the Medication Dose Optimization Service.
Hypertonic Sodium Chloride Guideline Update	Electrolyte	Hyponatremia	The guideline includes details about safe peripheral administration of 23.4% hypertonic sodium chloride.
Infliximab (Renflexis®)	TNF Inhibitor	Various Indications	Infliximab doses ≥ 300 mg will be automatically rounded by Pharmacy to the nearest 100 mg vial size. Doses less than 300 mg will not be automatically rounded. 1. Doses ≤ 50 mg will be rounded down to the nearest 100 mg (e.g., 750 mg = 700 mg) 2. Doses > 50 mg will be rounded up to the nearest 100 mg (e.g., 351 mg =400 mg)**+

*Formerly known as Infectious Diseases Sexually Transmitted Infections Prophylaxis and Treatment Services Standard Operating Procedure
**This includes all infliximab doses for adult patients, both inpatient and outpatient, and for all indications (both oncology and non-oncology).
+Dose rounding is automated within the electronic order entry system without prior authorization of the ordering physician.
SOP=Standard Operating Procedure TNF=Tumor necrosis factor

Process Changes to the Adult CCHS Formulary			
Process	**Pharmacologic Class**	**Formulary Use**	**Details**
Sugammadex (Bridion®)	Selective Relaxant Agent	Reversal of rocuronium- or vecuronium-induced blockade	Dose rounding will be allowed up to the nearest 50 mg 1. Dose 301 mg rounded to 350 mg
Travel Medicine Standard Operating Procedure for Pharmacist Consult Agreement	Various Medications	Various Indications	Updates to SOP were approved.

SOP=Standard operating procedure

Removals from the Adult CCHS Formulary			
Drug	**Pharmacologic Class**	**Formulary Use**	**Details**
Conivaptan (Vaprisol®)	Vasopressin Antagonist	Hyponatremia	Medication was removed due to shortages and price increase. Tolvaptan can be considered as an alternative.
Copanlisib (Aliqopa™) Intravenous Injection	Antineoplastic Agent	Relapsed/Refractory Follicular Lymphoma	The drug was pulled from the market due to toxicities and therefore, removed from the CCHS Formulary.
Diazepam Rectal Gel	Antiepileptic	Seizures	Removed due to low usage

Removals from the Pediatric CCHS Formulary			
Drug	**Pharmacologic Class**	**Formulary Use**	**Details**
Diazepam Rectal Gel	Antiepileptic	Seizures	Removed due to low usage
Phenylephrine 0.125% Nasal Drops	Decongestant	Nasal Congestion	Manufacturers discontinued product

Additions to the Pediatric CCHS Formulary			
Drug	**Pharmacologic Class**	**Formulary Use**	**Restrictions/Comments**
Exagamglogene Autotemcel (Casgey™) Intravenous Injection	Gene Therapy	Beta-thalassemia Sickle Cell Disease	Restricted to Staff Physicians from the Department of Pediatric Bone Marrow Transplant and only after prior authorization or covered approval has been obtained from the patient's insurance company in conjunction with the manufacturer.
Lovotibeglogene Autotemcel (Lyfgenia™) Intravenous Injection	Gene Therapy	Sickle Cell Disease	Restricted to Staff Physicians from the Department of Pediatric Bone Marrow Transplant and only after prior authorization or covered approval has been obtained from the patient's insurance company in conjunction with the manufacturer.
Mirikizumab-mrkz (Omvoh™) Intravenous Injection	Monoclonal Antibody	Ulcerative Colitis	Restricted to the Department of Pediatric Gastroenterology for outpatient use only. Note: Mirikizumab-mrkz subcutaneous injection will remain non-formulary
Phenylephrine 0.25% Nasal Spray	Decongestant	Nasal Congestion	Phenylephrine 0.25% nasal spray will only be allowable for pediatric patients aged ≥ 35 weeks actual or corrected to < 6 years of age.
Rezafungin (Rezzayo®) Intravenous Injection	Antifungal Agent	Candidemia and Invasive Candidiasis	Restricted to the Department of Pediatric Infectious Diseases for outpatient use only
Trabectedin (Yondelis®) Intravenous Injection	Antineoplastic Agent	Unresectable or Metastatic Liposarcoma or Leiomyosarcoma	Restricted to the Department of Pediatric Hematology/Oncology

Product Standardizations to the Pediatric CCHS Formulary			
Drug	**Pharmacologic Class**	**Formulary Use**	**Details**
Nasal Decongestant Spray Therapeutic Interchange	Decongestants	Nasal Congestion	Due to the discontinuation of phenylephrine 0.125% nasal drops, the existing nasal decongestant spray automatic interchange was updated. Details are in Lexicomp.

Changes to Restrictions of the Pediatric CCHS Formulary			
Drug	**Pharmacologic Class**	**Formulary Use**	**Changes**
Bevacizumab (Avastin®) Intravenous Injection	Monoclonal Antibody	Recurrent/Refractory Primary CNS Tumor Refractory Solid Tumor	Modified restrictions to include the Department of Pediatric Hematology/Oncology for outpatient use only
Epoprostenol (Veletri®) Intravenous Injection	Prostaglandin	Anticoagulant	Modified restrictions to include use as an anticoagulant during CRRT restricted to Staff Physicians from Pediatric Nephrology or Staff Physicians from the Pediatric ICU
Epoprostenol (Veletri®) Injection	Prostaglandin	PAH	Modified restrictions when used for **PAH** to include the Pediatric Pulmonary Hypertension Nurse Practitioner*
Iloprost (Ventavis®) Inhalation	Prostaglandin	PAH	Modified restrictions to include the Pediatric Pulmonary Hypertensin Nurse Practitioner*

*Nurse practitioner will be permitted to order for initiation and continuation, including dose titrations.
CNS=Central nervous system CRRT=Continuous renal replacement therapy ICU=Intensive care unit PAH=Pulmonary arterial hypertension

Process Changes to the Pediatric CCHS Formulary			
Process	**Pharmacologic Class**	**Formulary Use**	**Details**
Aminoglycoside Dosing Service Standard Operating Procedure	Aminoglycosides	Various Infections	Establishment of this dosing service for pediatric patients was approved.
Infliximab (Remicade®)	Monoclonal Antibody	UC CD	All doses of infliximab ordered in mg/kg DOWN by no more than 10% may be rounded to the nearest vial size. Doses exceeding the 10% margin or entered as flat doses will NOT be rounded.*+ Example: A dose for 330 mg will automatically be rounded down to 300 mg. A dose for 331 mg will not be automatically rounded up or down. **Please note: The pediatric dose rounding scheme is different from the adult dose rounding scheme.**

*This includes all infliximab doses for pediatric patients, both inpatient and outpatient for all indications (both oncology and non-oncology).
+Dose rounding is automated within the electronic order entry system without prior authorization of the ordering physician.
UC=Ulcerative colitis CD=Crohn's disease