	Type of Policy: Hospital Wide
	POLICY TITLE: Version 1.1 Baricitinib (Olumiant) Emergency Use Authorization
	Effective Date: 11/23/2020

PURPOSE:
To outline the mandated requirements in accordance with the Food and Drug Administration (FDA) issued Emergency Use Authorization (EUA), on 11/19/20, for the use of baricitinib in combination with (+) remdesivir for the treatment of COVID-19.

BACKGROUND:
Baricitinib is a Janus kinase (JAK) inhibitor. JAKs are intracellular enzymes which transmit signals arising from cytokine or growth factor-receptor interactions on the cellular membrane to influence cellular processes of hematopoiesis and immune cell function. Baricitinib (Olumiant) is approved by the FDA for the treatment of adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more tumor necrosis factor antagonist therapies[1]. Baricitinib has not been approved by the FDA for the treatment of COVID-19[1]. Based on the totality of evidence, baricitinib + remdesivir, may be effective in treating COVID-19 in hospitalized adults and pediatric patients ≥2 years requiring supplemental oxygen, invasive mechanical ventilation, or ECMO, when used under the conditions described in the EUA. The known and potential benefits of baricitinib + remdesivir to treat COVID-19 in such patients outweigh the known and potential risks. Currently, no adequate, approved, and available alternative to the emergency use of baricitinib + remdesivir is available[1].

PROCEDURE:

I. <u>EUA Approved Patients:</u> Suspected or confirmed COVID-19 in patients who are:
- **a)** Hospitalized **AND**
- **b)** Adults or pediatric patients ≥ 2 years of age **AND**
- **c)** Require supplemental oxygen, invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO)

At CHKD, Barcitinib is reserved for patients who meet the stated EUA criteria and have a contraindication to corticosteroid treatment. Corticosteroids should be 1st line and baricitinib used in lieu of steroids.[2]

II. <u>Scope of Authorization</u>:
- The baricitinib covered by this authorization will be used only by healthcare providers, in combination with remdesivir, to treat suspected or confirmed COVID-19 in hospitalized adults and pediatric patients ≥ 2 years of age requiring supplemental oxygen, invasive mechanical ventilation, or ECMO
- The use of baricitinib covered by this authorization must be in accordance with the dosing regimens as detailed in the authorized Fact Sheets

III. <u>Product Description</u>:
- Baricitinib is a film-coated, immediate-release tablet. Tablets are to be taken orally or can be crushed, dispersed in water, and given via a gastrostomy tube (G-tube)
- Lilly's website at: www.baricitinibemergencyuse.com
- The authorized baricitinib includes commercially available Olumiant (baricitinib) supplied in 30 count bottles as follows:
  - **a)** OLUMIANT (baricitinib) 1 mg (NDC 0002-4732-30)
  - **b)** OLUMIANT (baricitinib) 2 mg (NDC 0002-4182-30)

  Store at 20° to 25°C (68° to 77°F) with excursions permitted to 15° to 30°C (59° to 86°F)

IV. Prescribing Information:

<table>
<tr><th>Criteria</th><th>Description</th></tr>
<tr><td>Dosing</td><td>
<table>
<tr><th>Age</th><th>Dose</th></tr>
<tr><td>≥ 2-8 years</td><td>2 mg once daily</td></tr>
<tr><td>≥ 9 years</td><td>4 mg once daily</td></tr>
</table>
</td></tr>
<tr><td colspan="2">Dose Adjustments</td></tr>
<tr><td>Renal</td><td>
<table>
<tr><th>eGFR*</th><th>Recommendation</th></tr>
<tr><td>≥ 60</td><td>≥ 2-8 years: No adjustment
≥ 9 years: No adjustment</td></tr>
<tr><td>30 to < 60</td><td>≥ 2-8 years: 1 mg once daily
≥ 9 years: 2 mg once daily</td></tr>
<tr><td>15 to < 30</td><td>≥ 2-8 years: Not recommended
≥ 9 years: 1 mg once daily</td></tr>
<tr><td>< 15</td><td>≥ 2-8 years: Not recommended
≥ 9 years: Not recommended</td></tr>
</table>
*(mL/min/1.73m^2)
</td></tr>
<tr><td>Hepatic</td><td>If ↑ ALT or AST and/or drug-induced liver injury is suspected, hold therapy until diagnosis of liver injury is excluded
In patients with severe hepatic impairment consider use based on risk vs benefit</td></tr>
<tr><td>ALC</td><td>
<table>
<tr><th>Cells/µL</th><th>Recommendation</th></tr>
<tr><td>≥ 200</td><td>No change</td></tr>
<tr><td>< 200</td><td>Consider holding until ≥ 200</td></tr>
</table>
</td></tr>
<tr><td>ANC</td><td>
<table>
<tr><th>Cells/µL</th><th>Recommendation</th></tr>
<tr><td>≥ 500</td><td>No change</td></tr>
<tr><td>< 500</td><td>Consider holding until ≥ 500</td></tr>
</table>
</td></tr>
<tr><td>Duration</td><td>Optimal duration is unknown
The recommended total treatment duration is 14 days or until hospital discharge, whichever comes first</td></tr>
<tr><td>Administration</td><td>Given orally once daily with or without food
If unable to swallow whole tablets may give via:
▪ Oral dispersion, Gastrostomy tube (G tube), Nasogastric tube (NG tube)</td></tr>
<tr><td>Preparation
Alt Administration</td><td>
<table>
<tr><th>Route</th><th>Dispersion (mL)</th><th>Container Rinse (mL)</th><th>Administration</th></tr>
<tr><td>Oral Dispersion</td><td>10 mL</td><td>10 mL</td><td>Place tablets in container with RT water, gently swirl and use immediately
Rinse container to ensure all contents are administered</td></tr>
<tr><td>G-Tube</td><td>15 mL</td><td>15 mL</td><td>Place tablets in container with RT water, gently swirl, when dispersed ensure free passage through syringe tip, withdraw contents into syringe and administer via G-tube. Rinse container with RT water, withdraw into syringe, and give via G-tube</td></tr>
<tr><td>NG-Tube</td><td>30 mL</td><td>15 mL</td><td>Place tablets in container with RT water, gently swirl, when dispersed ensure free passage through syringe tip, withdraw contents into syringe and administer via G-tube. Rinse container with RT water, withdraw into syringe, and give via G-tube. To avoid clogging, the syringe can be held horizontally and shake during administration</td></tr>
</table>
Intact tablets are not hazardous. Tablets may be crushed. Unknown if powder or crushed tablets are a reproductive hazard to the preparer
Use proper control measures (e.g. ventilated enclosure) or personal protective equipment
</td></tr>
</table>

Stability	Dispersed tablets are stable in water for up to 4 hours
Pregnancy	Use only if the potential benefit justifies the potential risk for the mother and the fetus Limited human data on use in pregnant women
Monitoring	Baseline and daily CMP and CBC
Drug Interactions	Strong OAT3 Inhibitors: ↑ baricitinib when given with strong OAT3 inhibitors In patients on strong OAT3 inhibitors: ↓ dose as follows: ▪ If 4 mg once daily, reduce dose to 2 mg once daily ▪ If 2 mg once daily, reduce dose to 1 mg once daily ▪ If 1 mg once daily, consider discontinuing strong inhibitor Baricitinib has not been studied in combination with other JAK inhibitors or with biologic DMARDs
Adverse Events (AEs)	Serious Infections-Avoid if known active tuberculosis, Consider if the benefits vs. risks in patients with active serious infections other than COVID-19 Thrombosis -Prophylaxis for VTE is recommended unless contraindicated. Abnormal Lab Values- (LFTs, CBC, BUN/Scr) at baseline & daily, careful attention in patients with abnormal baseline values Vaccinations-Avoid use of live vaccines with baricitinib Hypersensitivity-If a serious hypersensitivity occurs, discontinue baricitinib while evaluating the potential causes of the reaction
Warnings*	No known contraindications for baricitinib Serious venous thrombosis-including pulmonary embolism, and serious infections have been observed in patients with COVID-19 on therapy and are known adverse drug reactions of baricitinib

ALC: Absolute Lymphocyte Count, ANC: Absolute Neutrophil Count, RT: Room Temperature, OAT3: organic anion transporter 3

V. Requirements for Healthcare Providers: (MUST *complete each step of the below*)

Step	Criteria	Description
1	**Confirm EUA Criteria**	Suspected or confirmed COVID-19 + meets criteria for remdesivir use **AND** **a)** Hospitalized **AND** **b)** Adults or pediatric patients ≥ 2 years of age **AND** **c)** Require supplemental oxygen, invasive mechanical ventilation, or ECMO
2	**Monitoring**	**1.** Evaluate baseline renal function, LFTs, and CBC to confirm eligibility and dose **prior** to the 1st dose **2.** Monitor daily LFTs, CBC, renal function **3.** Follow dosage adjustments, stated in section IV., for patients with lab abnormalities **4.** Baricitinib is **NOT** recommended for: **a)** Patients on dialysis, ESRD, or AKI **b)** Patients with known active tuberculosis
3	**Obtain ID Approval**	At CHKD, Baricitinib is ***restricted to ID***, Contact ASAP if use is anticipated The ID physician will notify: ▪ Sarah Parsons Pharm. D., BCPPS (Simon 6491, 8-5492) 07:30-16:00, M-F Pharmacy MEDS on call Pharm. D. (Simon 7337) after hours, holidays, and weekends
4	**Education**	Counsel patient or parent/caregiver, information consistent with the "Fact Sheet for Patients, Parents and Caregivers" Available at: https://www.lilly.com/news/media/media-kits/baricitinib-covid19 This education **MUST** include: **1.** Baricitinib is authorized for the unapproved use under this EUA in combination with remdesivir for treating COVID-19 in hospitalized adults and pediatric patients ≥2 years requiring supplemental oxygen, invasive mechanical ventilation, or ECMO **2.** The patient or parent/caregiver has the option to accept or refuse baricitinib **3.** Known and potential risks and benefits of baricitinib, and the extent to which such potential risks and benefits are unknown **4.** Information on available alternative treatments and the risks and benefits of those alternatives, including clinical trials *If providing this information delays therapy to a degree that would endanger the life of a patient, the information must be provided to the patients as soon as practicable after baricitinib is administered*
5	**Documentation**	**Must be completed on each patient prior to receiving barcitinib** Document in the EMR that the patient/caregiver has been: **a)** Given the "Fact Sheet for Patients, Parents and Caregivers" **b)** Informed of alternatives to receiving authorized baricitinib **c)** Informed that baricitinib is an unapproved drug that is authorized for use under this Emergency Use Authorization

6	**Tracking & Reporting**	The prescribing healthcare provider/designee are responsible for **MANDATORY** reporting which includes: **a)** Responding to mandatory requests from the FDA about AEs and medication errors following administration **b)** Reporting of all medication errors and *serious adverse*◊ events within 7 calendar days from the onset of the event ▪ Reports must include unique identifiers and the words "Baricitinib treatment under Emergency Use Authorization (EUA)" in the description section of the report." **c)** As soon as possible post event, submit a Verge and contact Elizabeth Rogers Pharm. D.,(8-5285) and Sarah Parsons Pharm. D.(8-5492) **d)** Complete and submit AE reports to FDA MedWatch using one of the following methods: **1)** Online:www.fda.gov/medwatch/report.htm **2)** Postage-paid Form FDA 3500 (available at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM163919.pdf) and returning by mail (MedWatch, 5600 Fishers Lane, Rockville, MD 20852-9787) **3)** Fax (1-800-FDA-0178) **4)** Call 1-800-FDA-1088 to request a reporting form ▪ Submitted reports should include in the field name, "Describe Event, Problem, or Product Use/Medication Error" the statement "Baricitinib treatment under Emergency Use Authorization (EUA) **e)** Report adverse events or medication errors to Lilly at: 1-855-LillyC19 (1-855-545-5921) **AND** provide a copy of all FDA MedWatch forms to: Eli Lilly and Company, Global Patient Safety Fax: 1-317-277-0853 E-mail: mailindata_gsmtindy@lilly.com
7	**Require Record Maintenance**	Healthcare facilities **MUST** **1.** Maintain records regarding the dispensed authorized baricitinib including: **a)** Product specific information including: lot numbers, quantity, receiving site, receipt date, product storage **b)** Patient specific information including: ▪ Patient name ▪ Disease manifestation ▪ Number of doses administered per patient ▪ Other drugs administered **2.** Ensure that any records associated with this EUA are maintained until notified by Lilly and/or FDA. Such records will be made available to Lilly, HHS, and FDA for inspection upon request

◊ Serious AEs: death; a life-threatening adverse event; inpatient hospitalization or prolongation of existing hospitalization; a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions; a congenital anomaly/birth defect; a medical or surgical intervention to prevent death, a life-threatening event, hospitalization, disability, or congenital anomaly

RESOURCES:

Lilly: 1-855-LillyC19 (1-855-545-5921)

For additional information visit: www.baricitinibemergencyuse.com

a) Fact Sheet for Health Care Providers: http://pi.lilly.com/eua/baricitinib-eua-factsheet-hcp.pdf
b) Fact Sheet for Patients, Parents and Parent/Caregivers:
   - http://pi.lilly.com/eua/baricitinib-eua-factsheet-patient.pdf (English)
   - http://pi.lilly.com/eua/span/baricitinib-eua-factsheet-patient-span.pdf (Spanish)
c) FDA Letter of Authorization: http://pi.lilly.com/eua/baricitinib-eua-fda-authorization-letter.pdf

RELATED DOCUMENTS: CHKD Treatment Guideline for COVID-19 in Children: Version 3.1 December 15, 2020

REFERENCES:

1. Baricitinib [EUA Fact Sheet]. Copyright © 2020, Eli Lilly and Company. All rights reserved, issued 11/19/2020
2. NIH COVID-19 Treatment Guidelines Panel's Statement on the Emergency Use Authorization of Baricitinib for the Treatment of COVID-19. Available at https://www.covid19treatmentguidelines.nih.gov/statement-on-baricitinib-eua/. Updated: December 14, 2020. Accessed (12/15/2020)

INDIVIDUALS REVIEWING:
Reviewer: Brittany Asaban, Pharm. D., BCPS, Chris Foley, MD., FAAP
Policy Owner **Sarah Parsons, Pharm D, BCPPS,** Pharmacy Specialist, Gen Peds/CF/ID
Laura Sass, MD, Pediatric Infectious Disease

This policy is in effect for Children's Hospital of The King's Daughters Health System (CHKDHS) to include the following subsidiaries: Children's Hospital of The King's Daughters, Incorporated (CHKD), Children's Medical Group, Inc., and CMG of North Carolina, Inc. (CMG), and Children's Surgical Specialty Group, Inc. (CSSG).