Updates to COVID Treatment Pathway

8-20-21

- Added REGEN-COV Treatment/Prophylaxis algorithm (see pg. 1 of document)
- Added Baricitinib to treatment page (see pg. 4 of document)
- Updated REGEN-COV dosing for COVID+/direct exposure/high risk for ongoing exposure (see pgs. 1 & 4 of document

9-15-21

- Removed obesity from anticoagulation treatment portion of the pathway. Obesity will remain a risk factor for prophylaxis.

Last updated
8-20-21

Management of COVID-19 Patients
REGEN-COV (casirivimab and imdevimab)

Arkansas Children's
HOSPITALS · RESEARCH · FOUNDATION

Inclusion Criteria:
Patients 12 years of age and older weighing ≥40 kg
AND
Are at *risk of progressing to severe COVID-19 and/or hospitalization

Exclusion Criteria:
- Hospitalization due to COVID-19
- Patients who require oxygen therapy due to COVID-19
- Increased oxygen requirement due to COVID-19 in those patients who are on oxygen at baseline for non-COVID related disease process

*Risk Factors

- Obesity or overweight (e.g. BMI >25 kg/m² or age 12-17 BMI ≥85th% for age/ gender
- Pregnancy
- Chronic kidney disease
- Diabetes
- Immunosuppressive disease/treatment
- Cardiovascular disease (including congenital)
- Hypertension
- Chronic lung disease (e.g. moderate – severe asthma, CF, Pulmonary hypertension, interstitial lung disease
- Sickle cell disease
- Neurodevelopmental disorders (e.g. cerebral palsy)
- Medically complex (e.g. genetic/metabolic/severe congenital anomalies
- Technology dependent (e.g. tracheostomy, gastrostomy, positive pressure ventilation)

See all risk factors at:
https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html

!
REGEN-COV restricted to Infectious Disease

Is the patient either outpatient COVID + or inpatient COVID + (not primary diagnosis), in direct exposure, or lives in high transmission area
AND
- Not fully vaccinated or
- Fully vaccinated immunocompromised patients or
- Fully vaccinated patients on immunosuppressant medications

NO →
- Patient does not qualify for REGEN-COV
- See pg. 3 for COVID+ treatment

YES (COVID +/Direct Exposure to COVID)

COVID +/Direct Exposure to COVID

Onset of symptoms within the last 7 days
OR
Direct exposure within the last 7 days

YES

For administration of REGEN-COV:
- Order Ambulatory Referral for Infectious Disease (501) 364-1416 during normal business hours
- Outside of business hours, call (501) 364-1416 and leave a message with patient's name and MRN for follow-up on the next business day.

NO
- Patient does not qualify for REGEN-COV
- See pg. 3 for COVID+ treatment

YES (Patient lives in high transmission area)

Patient lives in high transmission area

For administration of REGEN-COV:
- Order Ambulatory Referral for Infectious Disease (501) 364-1416 during normal business hours
- Outside of business hours, call (501) 364-1416 and leave a message with patient's name and MRN for follow-up on the next business day.

See pg. 2 for more REGEN-COV information

REGEN-COV (casirivimab and imdevimab)

- REGEN-COV (casirivimab and imdevimab) is a monoclonal antibody that has received FDA emergency use authorization for treatment of mild to moderate COVID 19 in patients 12 year of age and older and weighing at least 40 kg who are at risk for progressing to severe COVID 19 and/or hospitalization:
    - Older age (for example, age ≥65 years of age)
    - Obesity or being overweight (for example, BMI >25 kg/m2 , or if age 12-17, have BMI ≥85th percentile for their age and gender based on CDC growth charts, https://www.cdc.gov/growthcharts/clinical_charts.htm)
    - Pregnancy
    - Chronic kidney disease
    - Diabetes
    - Immunosuppressive disease or immunosuppressive treatment
    - Cardiovascular disease (including congenital heart disease) or hypertension
    - Chronic lung diseases (for example, chronic obstructive pulmonary disease, asthma [moderate-to-severe], interstitial lung disease, cystic fibrosis and pulmonary hypertension)
    - Sickle cell disease
    - Neurodevelopmental disorders (for example, cerebral palsy) or other conditions that confer medical complexity (for example, genetic or metabolic syndromes and severe congenital anomalies)
    - Having a medical-related technological dependence (for example, tracheostomy, gastrostomy, or positive pressure ventilation (not related to COVID 19))
    - EUA is not restricted to the above medical conditions or risk factors. The following website share details about risk for COVID disease progression: https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html
    - It is not authorized of use in patients
        - Who are hospitalized due to COVID-19
        - Who require oxygen therapy due to COVID-19
        - Who require an increase in baseline oxygen flow rate due to COVID-19
        - Those on chronic oxygen therapy due to underlying COVID-19 related comorbidity
    - REGEN-COV (casirivimab and imdevimab) use will be restricted to Infectious Disease
- Administration
    - Dosage: 600 mg casirivimab/600 mg imdevimab IV as a one-time infusion
    - Must be administered within 7 days of symptom onset
- **Scheduling/Clinic Visits**
    - Patients will be required to be seen either via in person or telemedicine visit by an ACH Infectious Disease provider**. Please contact ID Section during normal business hours at 501-364-1416 to schedule a visit.**
    - Patients will be scheduled through the Infusion Center with medications administered by Infusion Center staff
    - Location – Infusion Center

COVID-19 Treatment Pathway

Arkansas Children's
HOSPITALS · RESEARCH · FOUNDATION

Referring Hospitals -
if you need to transfer a child:
Contact Angel One
for transfer to Arkansas Children's Hospital
1-800-ACH-HELP

!
Special Respiratory Enhanced Contact Isolation

COVID-19 (+) or suspected acute COVID infection

Consider MIS-C throughout evaluation

Mild/Moderate

- No new O2 requirement
- No respiratory distress

- Supportive care
- ID consult for consideration of REGEN-COV (casirivimab and imdevimab) based on high risk criteria (see pg. 1)

Severe

- New O2 requirement
- Increased O2 from baseline
- Not rapidly progressing

- Steroids*
- Consider remdesivir
- ID consult
- Consider addition of tocilizumab or baricitinib for rapidly increasing oxygen needs
- Consider anticoagulation – see guideline (pg. 5&6)
- Consider CRP/Procalcitonin

Critical

- Rapidly progressing O2 requirement
- Requires intubation or non-invasive ventilation in PICU
- Shock or organ failure

- Steroids*
- Tocilizumab
- ID consult
- Consider anticoagulation – see guideline (pg. 5&6)
- Consider CRP/Procalcitonin

Clinical judgement for transfer of patients to AC Little Rock:

- Current ID recommendation - transfer of all adolescent patients with new O2 requirement or increasing O2 requirement, rapidly progressing O2 requirement, or respiratory distress
- Shock, ARDS, or organ failure

!
High suspicion for bacterial infection:
Sepsis Pathway – ED/Inpatient
Sepsis Pathway – PICU

***Refer to the following page for details regarding eligibility, treatment, and dosing**

COVID-19 Treatment Agents

Medication (recommended or authorized)	Recommended Dose and Comments
Corticosteroids	Dexamethasone **0.15** mg/kg (max **6** mg) IV or PO once daily (preferred) OR Equivalent dose of substitute – methylprednisolone **0.8** mg/kg (max **32** mg) IV once daily **Duration** 10 days or until discharge
Remdesivir (Veklury®) *ID Consult Required*	3.5-40 kg: **5** mg/kg IV on day 1 then **2.5** mg/kg IV once daily on day 2 – 5 (or 10) ≥ 40 kg: **200** mg IV on day 1 then **100** mg IV once daily on day 2 – 5 (or 10) **Duration:** 5 or 10 days **Indication:** Hospitalized patients confirmed COVID (+) requiring supplemental oxygen **Exclusion:** Renal impairment – Age > 28 days with eGFR < 30 mL/min Age 7-28 days with Cr > 1 mg/dL Hepatic impairment – ALT > 5x upper limit of normal
REGEN-COV (casirivimab and imdevimab) - SARS-CoV-2 Monoclonal antibody *ID Consult Required*	**Treatment or Post-Exposure Prophylaxis – Call ID for procedure – 501-364-1416** 600 mg/600 mg IV x1 (no additional doses) **Ongoing High Risk Exposure** 600 mg/600 mg IV x1, followed by 300 mg/300 mg IV every 4 weeks for duration of ongoing exposure See inclusion/exclusion criteria on pg. 2 **Patients receiving SARS-CoV-2 monoclonal antibodies cannot receive SARS-CoV-2 vaccination for 3 months
Tocilizumab - IL-6 receptor antagonist	Required testing before dose: • T-Spot • Consider Hep B titers based on risk factors Dosing <30 kg: 12 mg/kg x1 ≥30 kg: 8 mg/kgx1 (max 800 mg)
Baricitinib -Janus Kinase Inhibitor	For children 2 - <9 years of age 2 mg once daily for 14 days For children 9 years of age and older 4 mg once daily for 14 days

<u>Not</u> recommended for treatment of COVID-19

- **Hydroxychloroquine**
- **Azithromycin**
- **Lopinavir-ritonavir**
- **Ivermectin**

Anticoagulation Guidelines for Acute COVID-19

Guidelines are derived from adult guidelines and various adaptations from pediatric hospitals.

Pharmacologic thromboprophylaxis should be considered in all pediatric and adolescent patients admitted to Arkansas Children's Hospital unless contraindicated (active bleeding, thrombocytopenia, recent or upcoming surgical intervention, etc.)

Anticoagulation

Inclusion Criteria:

All hospitalized patients who have been diagnosed with COVID-19 who meet one or ore of the following criteria of high-risk*:

- Any patient admitted to intensive care unit
- Patients admitted with suspected MIS-C
- Patients with active cancer, autoimmune disorders, decreased mobility, sickle cell disease, central line, diabetes, personal or family history of thrombosis, inherited thrombophilia, estrogen therapy
- Elevated D-dimer that is ≥5 times the upper limit normal or with evidence of inflammation (elevated CRP, etc.)

Special Considerations

- MIS-C/Kawasaki patients – if Cardiology recommends aspirin therapy (due to concern for abnormal coronary arteries or persistently diminished systolic function), carefully review clinical indication for additional prophylactic Lovenox. May not be required unless high risk for VTE based on above criteria. Concomitant use of low dose aspirin (<5 mg/kg/day) with prophylactic anticoagulation likely does not confer a high risk of bleeding in the absence of other bleeding risk factors.
- Daily assessment for signs/symptoms of DVT or PE with impaging (US or CTA chest) if VTE suspected.

Labs to be drawn at admission or upon consult:

- CBC, PT/PTT, D-dimer, fibrinogen, CRP, BUN, creatinine

Repeat every 2-3 days as clinically indicated and prior to discharge:

- CBC, D-dimer, fibrinogen, creatinine and inflammatory markers

D-dimer ≥ 5 times upper limit normal/ high risk* factor

Signs/symptoms or very high risk of thrombosis

Treatment Considerations:

If D-dimer ≥ 5 times upper limit normal or other high risk* factor present and no contraindications to anticoagulation:

- Start enoxaparin (e.g. Lovenox) 0.5 mg/kg/dose SQ q12h (prophylaxis dose)
- At least weekly anti-Xa testing while critically ill with goal anti-Xa 0.2-0.5 (follow ACH Anticoagulation guidelines)

!

Direct Oral Anticoagulants not preferred inpatient (can interact with medications used to treat COVID-19)

Treatment Considerations:

If signs/symptoms of microvascular thrombosis, or very high risk of thrombosis based on clinical impression (obesity, active cancer, sickle cell disease, or history of thrombosis):

- Consider increase in enoxaparin (e.g. Lovenox) to 1 mg/kg/dose SQ q12h (treatment dose)
- Target low molecular weight anti-Xa 0.5-1
- If contraindicated to anticoagulation (bleeding, thrombocytopenia, surgery):
  - -Strongly consider mecahnical thromboprophylaxis (SCD)
- If CrCl <30 or very high risk of bleeding, utilize unfractionated heparin instead of enoxaparin (follow ACH Anticoagulation guidelines)

Hematology Follow-Up:

- Assess patient for ongoing risk of thrombosis
- If ready for discharge, it is likely the patient no longer has risk factors for VTE
- If high risk (active cancer, SCD, thrombophillia, or history of thrombosis), discuss with Hematology the need for anticoagulation upon discharge
- No need to trend D-dimer or inflammatory markers after discharge
- If discharged home on Lovenox, follow up with Hematology within 2 weeks.

See pg. 6 for Anticoagulation Guidelines

Anticoagulation Guidelines for Acute COVID-19

Guidelines are derived from adult guidelines and various adaptations from pediatric hospitals.

Pharmacologic thromboprophylaxis should be considered in all pediatric and adolescent patients admitted to Arkansas Children's Hospital unless contraindicated (active bleeding, thrombocytopenia, recent or upcoming surgical intervention, etc)

Target population to be considered for VTE prophylaxis:

- All hospitalized patients who have been diagnosed with COVID-19 who meet one or more of the following criteria of high-risk*:
  - Any patient admitted to intensive care unit
  - Patients admitted with suspected MIS-C
  - Patients with active cancer, autoimmune disorders, decreased mobility, sickle cell disease, obesity, central line, diabetes, personal or family history of thrombosis, inherited thrombophilia, estrogen therapy.
  - Elevated D-dimer that is ≥ 5 times the upper limit normal or with evidence of inflammation (elevated CRP, etc.).

Laboratory monitoring:

- Labs to be drawn at admission or upon consult:
  - CBC, PT/PTT, D-dimer, fibrinogen, CRP, BUN, Creatinine
  - Repeat CBC, D-dimer, fibrinogen, creatinine and inflammatory markers every 2-3 days as clinically indicated and prior to discharge.

Treatment considerations:

- If **D-dimer ≥ 5 times upper limit normal or other high-risk* feature** present and no contraindication to anticoagulation:
  - **Start enoxaparin (e.g. Lovenox) 0.5mg/kg/dose SQ q12h (prophylaxis dose)**
  - At least weekly anti-Xa testing while critically ill with goal anti-Xa 0.2-0.5 (follow ACH Anticoagulation guidelines)
- If **signs/symptoms of microvascular thrombosis, or very high risk** of thrombosis based on clinical impression (e.g. active cancer, sickle cell disease, diabetes, or history of thrombosis)
  - Consider **increase in enoxaparin (e.g. Lovenox) to 1mg/kg/dose SQ q12h (treatment dose)**
  - Target low molecular weight anti-Xa 0.5-1
- If contraindication to anticoagulation (bleeding, thrombocytopenia, surgery)
  - Mechanical thromboprophylaxis should be strongly considered (SCD)
- If CrCl <30 or very high risk of bleeding, utilize unfractionated heparin instead of enoxaparin (follow ACH Anticoagulation Guidelines)

Special considerations:

- MIS-C/Kawasaki patients – If cardiology recommends aspirin therapy (due to concern for abnormal coronary arteries or persistently diminished systolic function), carefully review clinical indication for additional prophylactic Lovenox. May not be required unless high risk for VTE based on above criteria. Concomitant use of low dose aspirin (<5 mg/ kg/day) with prophylactic anticoagulation likely does not confer a high risk of bleeding in the absence of other bleeding risk factors.
- Direct Oral Anticoagulants (DOAC) are not preferred inpatient as they can interact with medications (antivirals) used to treat COVID-19.
- Daily assessment for signs/symptoms of DVT or PE with imaging (US or CTA chest) if VTE suspected.

Hematology follow-up:

- Assess patient for ongoing risk of thrombosis. If ready for discharge, it is likely patient no longer has risk factors for VTE.
- If high risk (active cancer, sickle cell disease, thrombophillia or history of thrombosis), discuss with Hematology the need for anticoagulation upon discharge.
- No need to trend D-dimer or inflammatory markers after discharge.
- If discharged home on Lovenox, follow up with Hematology within 2 weeks.

References

Massgeneral.org/news/coronavirus/treatment-guidelines.

American Society of Hematology. https://www.hematology.org/covid19/covid-19-and-coagulopathy. http://www.hematology.orgcovidcovid-and-coagulopathy.

Loi, M., Branchford, B., Kim, J., Self, C. & Nuss, R. COVID-19 anticoagulation recommendations in children. *Pediatric Blood & Cancer* **67**, e28485 (2020).

ASPHO Summer Virtual Learning Series. "Clinical aspects of evaluating and treating COVID-19 patients in pediatric hematology/oncology". Aspho.org/meetings/summer-virtual-learning-series.

"COVID-19 and venous thromboembolism prophylaxis: recommendations in children and adolescents." Texas Children's Hospital Supportive Care Practice Standard (S-20200011).

Goldenberg NA, Sochet A, Albisetti M, et al; the Pediatric/Neonatal Hemostasis and Thrombosis Subcommittee of the ISTH SSC. Consensus-based clinical recommendations and research priorities for anticoagulant thromboprophylaxis in children hospitalized for COVID-19–related illness. *J Thromb Haemost*. 2020;18:3099–3105.

https://doi.org/10.1111/jth.15073

Contributing Members

Dr. Jessica Snowden, Infectious Disease
Dr. Holly Maples, Antimicrobial Stewardship
Caleb McMinn, Antimicrobial Stewardship
Dr. Rebecca Latch, Hospital Medicine
Dr. Kendall Stanford, Emergency Medicine
Dr. Sanjiv Pasala, Intensive Care Medicine
Blair Langston, RN Pediatric Intensive Care Unit
Emma Rhoads, RN Quality and Patient Safety
Dr. Melissa Magill, Hospital Medicine/Emergency Medicine ACNW
Dr. Abdallah Dalabih, Clinical Effectiveness & Outcomes
Dr. Jared Capouya, Quality and Safety Division
Emily Rader, RN Clinical Effectiveness & Outcomes