University HOSPITAL
Newark, NJ

Pharmacy News

Third Quarter 2021
Vol. XIV, Issue 3

Special Points of Interest:

- P&T Update-Formulary Additions/Deletions
- Policy and Procedure Update
- Clinical Trials at University Hospital
- Teprotumumab (Tepezza®): An Eye-Opening Novel Therapy
- Cardiovascular Benefits with Low Dose Colchicine Use
- Guidelines for Naloxone Use
- Naloxone: Adult Dosing and Administration

P&T Update

Formulary Additions

1. ***Daratumumab (Darzalex™)***
   INDICATIONS: Daratumumab is indicated for the treatment of patients with multiple myeloma – Approved for Formulary Addition with Restriction for use to Oncology Service

2. ***Diclofenac 1% Gel***
   Multi-modal pain management is a medication therapy model that utilizes different medication classes that act upon different target sites to provide greater pain relief compared to monotherapy. – Approved for Formulary Addition

3. ***Tenecteplase (TNKase™)***
   INDICATIONS: Tenecteplase is indicated for the treatment of ST-Elevation Myocardial Infarction, and has off-label indications for ischemic stroke and pulmonary embolism. – Approved for formulary addition

4. ***Doyxlamine (UnisomeTM***
   INDICATIONS: Doxylamine is approved for insomnia and when used in combination with pyridoxine (Vitamin B6) is indicated for nausea and vomiting in pregnant women. – Approved for formulary addition

Formulary Deletions

1. ***Biotin 300mcg***
   Manufacturer discontinued - Approved

Line Extension

1. ***Fentanyl***
   Fentanyl 10 mcg/mL Syringe
   Request for fentanyl 10 mcg/mL syringe formulary line extension for the FICN – Approved

Policies & Procedures/Floor stocks

1. Low-Dose Ketamine IVPB for Treatment of Pain in the Emergency Department and ED Observation Unit (New)

PURPOSE:
To provide standardization for administration of low dose ketamine (also known as sub-dissociative dose ketamine) for analgesia in adult patients in the Emergency Department, including the ED Observation Unit (EDOU). – Approved

Medication/Clinical Guidelines

1. Sedation of Agitated Patient in the Emergency Department (Update)
   Committee members presented updates to this guideline – Approved

2. Bamlanivimab & Etesevimab Emergency Department Workflow (Update)
   Committee members presented updates to this guideline – Approved

Continued on Page 2

P&T Update

Continued from Page 1

Medication/Clinical Guidelines

3. 707-700-105A – Intravenous Medication Administration Guidelines
   Policy outlines the recommendations regarding intravenous push, intravenous infusion, and central line infusion routes of administration for various medications. – Approved

4. Sepsis Management: A Team Effort 2021
   Outlines core fundamentals of sepsis and septic shock, pathophysiology, assessment tools, sepsis protocol, treatment modalities, and other related sepsis tools. - Informational

Miscellaneous

Alaris Drug Library Update (06/17/21)
Updates to hypertonic saline, and additions for daratumumab, fentanyl 10mcg/1mL syringe. – Approved

Milrinone as Compared with Dobutamine in the Treatment of Cardiogenic Shock

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Cardiogenic shock (CS) is a heart condition in which the heart is unable to pump an adequate amount of blood to meet tissues and organs' need.[1] This cardiac failure results in organ hypoperfusion and ultimately in end-organ damage. During cardiogenic shock, peripheral vasoconstriction occurs, and cardiac output decreases. Because of this decompensation, CS triggers a sequence of compensatory mechanisms such as changes in heart rate, pulmonary and systemic vascular resistance, and myocardial contractility.[1]

The clinical manifestations of CS are hypotension, altered mental status, arrhythmias, dyspnea, and peripheral edema.[2] Patients with cardiogenic shock most commonly present with cool extremities and signs of pulmonary congestion. The pharmacologic treatment used in this condition consists of inotropes and vasopressors, to enhance contractility and modulating vascular tone. According to the guidelines, Norepinephrine is associated with fewer arrhythmias and can be considered the vasopressor of choice in many patients with CS; however, the optimal first-line inotrope medication remains unclear.[2]

A recent article comparing the efficacy and safety of milrinone and dobutamine in patients with cardiogenic shock was published aiming to address an important knowledge gap in the management of CS.[3] Dobutamine is an inotropic drug that acts on alpha-1, beta-1, and beta-2 adrenergic receptors. This agent has a stronger effect on beta-2 (vasodilation) than on alpha-1 (vasoconstriction), therefore it produces systemic vasodilation.[3,4] The expected hemodynamic effects are an increase in contractility and cardiac output and a decrease in systemic vascular resistance. Milrinone is another inotropic agent that causes vasodilation in both arteries and veins by inhibiting the enzyme phosphodiesterase III.[3,5] When milrinone is administered, the hemodynamic effects are similar to dobutamine causing an increase in contractility and cardiac output and a decrease in systemic vascular resistance.

This study, by Mathew, et al[1,3] was done to address the knowledge gap in the selection of inotropic agents in cardiogenic shock. The study was a double-blinded, randomized clinical trial, in which 192 patients with cardiogenic shock were enrolled from a single cardiac institute between September 2017 and May 2020 and were randomized to receive inotropic support with either dobutamine or milrinone. Patients were eligible for enrollment if they were >18 years of age, admitted to a cardiac ICU, and met the Society for

Cardiovascular Angiography and Interventions (SCAI) definition for cardiogenic shock stage B, C, D, or E; all inclusion and exclusion criteria are shown in Table 1. Baseline characteristics were similar in both groups except in the coexisting conditions for invasive mechanical ventilation, previous myocardial infarction, previous percutaneous coronary intervention, and vasopressor of use before randomization, that were higher in the milrinone group. Although these differences were observed, this did not have an impact on the outcome measured. Participants were assigned in a 1:1 ratio to receive either milrinone or dobutamine. Both milrinone and dobutamine doses were determined with a standardized dosing scale that ranged from stage 1 to stage 5. The doses corresponding to each stage are outlined in Table 2.

The primary endpoint measured was the composite of in-hospital death from any cause: resuscitated cardiac arrest, receipt of a cardiac transplant or mechanical circulatory support, nonfatal myocardial infarction, transient ischemic attack, or stroke diagnosed by neurologist, and initiation of renal replacement therapy. The secondary endpoints were all the individual components of the primary composite outcome.[3]

Table 1. Inclusion and exclusion criteria of participants[3]

Inclusion Criteria	Exclusion Criteria
Aged 18 years or older and had one of the following indications: • Clinical diagnosis of cardiogenic shock and SBP <90 mmHg with end-organ dysfunction. • Clinical evidence of systemic and/or pulmonary congestion despite use of vasodilators and/or diuretics • Acute coronary syndrome complicated by cardiogenic shock with hemodynamic reduction in cardiac index • A clinically determined need to augment cardiac output in addition to ongoing vasopressor therapy • A treating team's clinical assessment that inotropic therapy is required for developing cardiogenic shock without current evidence of hypoperfusion.	• Presented with an out-of-hospital cardiac arrest • Pregnant • Had milrinone or dobutamine initiated prior to randomization • Treating physician was of the opinion that the patient was not eligible for the study • Patient was participating in another interventional trial • Inability to obtain written informed consent from the patient or substitute.

Table 2. Standardized dosing scale of milrinone and dobutamine[3]

Stages	Milrinone	Dobutamine
Stage 1	0.125 µg/kg/min	2.5 µg/kg/min
Stage 2	0.250 µg/kg/min	5.0 µg/kg/min
Stage 3	0.375 µg/kg/min	7.5 µg/kg/min
Stage 4	0.500 µg/kg/min	10.0 µg/kg/min
Stage 5	>0.500 µg/kg/min	>10.0 µg/kg/min

Continued on Page 4

Milrinone as Compared with Dobutamine in the Treatment of Cardiogenic Shock

Continued from Page 3

In patients requiring inotropic support for treatment of cardiogenic shock, there was no difference between milrinone and dobutamine with respect to the primary composite outcome or length of time until the occurrence of the primary composite outcome. The secondary outcomes were also similar in both groups, and no significant advantage of milrinone was found over dobutamine. In previous trials comparing milrinone and dobutamine in patients with low cardiac output and/or cardiogenic shock, dobutamine was associated with more arrhythmias, while milrinone was associated with more hypotension.[6,7] In this study, however, additional safety outcome measures such as heart rate, MAP, vasoactive-inotropic score, lactate levels, creatine level, or hourly urine output showed no significant difference.

Overall, based on this study, there was no significant difference in primary or secondary outcomes. Clinically, the selection of milrinone versus dobutamine to treat cardiogenic shock can be based more on the pharmacokinetic profile. These medications have different pharmacological properties and therefore they should be chosen based on patient-specific factors, the onset of action, half-life, and elimination. Dobutamine has a rapid onset of action and shorter half-life as compared to milrinone, which may be the preferred agent in the emergency department setting, while milrinone's PK properties may be more desirable for the outpatient setting.[8,9]

References

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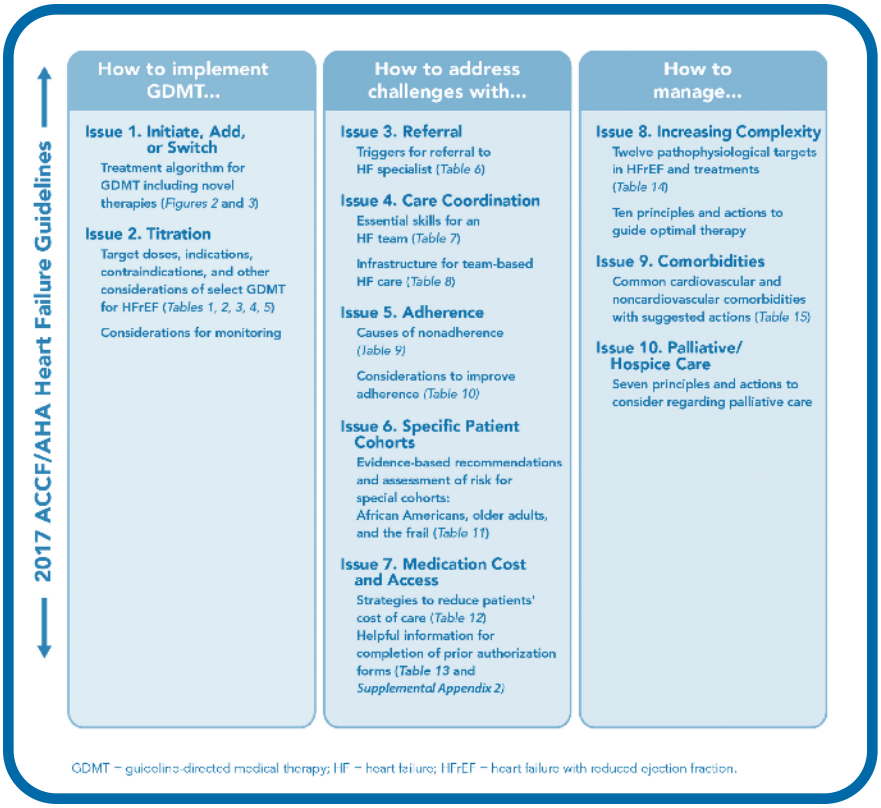
Examining the 2021 update to the ACC Expert Decision Pathway for HFrEF Treatment Optimization

Heart Failure is a chronic condition that causes reduced blood flow from the heart, depriving the body of oxygen and nutrients needed for proper function. Approximately 6.2 million persons ≥20 years of age in the United States have HF, with approximately 1 million new HF cases diagnosed annually, and the prevalence continues to rise. Heart Failure can be broken down into 2 categories; systolic dysfunction or Heart Failure with reduced ejection fraction (HFrEF) or diastolic dysfunction, also known as Heart Failure with preserved ejection fraction (HFpEF). Patients with more progressive stages of HFrEF, specifically Stage C, NYHA Class II-IV, are at an increased risk for hospitalizations, worsening symptoms and increasing mortality rates. In February 2021, an update to the 2017 American College of Cardiology (ACC) Expert Consensus Decision Pathway for Optimization of Heart Failure Treatment was published. This guideline focused on 10 Pivotal issues in the management of HFrEF, which consists of: There are several key points to emphasize from the 2021 update, specifically the initiation of novel therapies. For patients with newly diagnosed Stage C HFrEF, initiating guideline-recommended beta-blockers or angiotensin-converting enzyme inhibitor (ACEI)/angiotensin receptor blocker (ARB)/angiotensin receptor-neprilysin inhibitor (ARNI) can be done in any order. However, when choosing between an ARNI (Entresto®), ACEI or ARB, ARNI is now the preferred agent when there are no contraindications and is financially feasible. Based on the findings from recent clinical trials, the direct initiation of ARNI without prior exposure to an ACEI or ARB or in patients with de novo HFrEF can be done in a safe and effective matter. As a result, directly initiating therapy with ARNI is now being recommended.

Another significant update to the 2021 guidelines is the inclusion of Sodium-Glucose Cotransporter-2 Inhibitors (SGLT2I) as part of the treatment pathway for patients with newly diagnosed Stage C HFrEF. SGLT2 inhibitors have demonstrated considerable cardiovascular risk reduction benefits in patients with Type 2 Diabetes. However, it was not until the DAPA-HF study, published November 2017, that an SGLT2 inhibitor was shown to reduce the risk of worsening HF or death from CV causes in patients with or without Type 2 diabetes. During this study, there was a 30% decrease in the risk of experiencing a first episode of worsening HF and an 18% decrease in the risk of cardiovascular death. As a result, Dapagliflozin (Farxiga®) became the first SGLT2 inhibitor approved for the treatment of HFrEF (NYHA class II-IV). In August 2021, a second SGLT2 inhibitor, Empagliflozin (Jardiance®) received approval for the treatment of HFrEF. This approval was based on the results of the EMPEROR-Reduced trial. Given these results and recent FDA approvals, the use of an SGLT2 inhibitor is now recommended as part of guideline directed medical therapy for patients with HFrEF Stage C whose eGFR is > 30mL/min.



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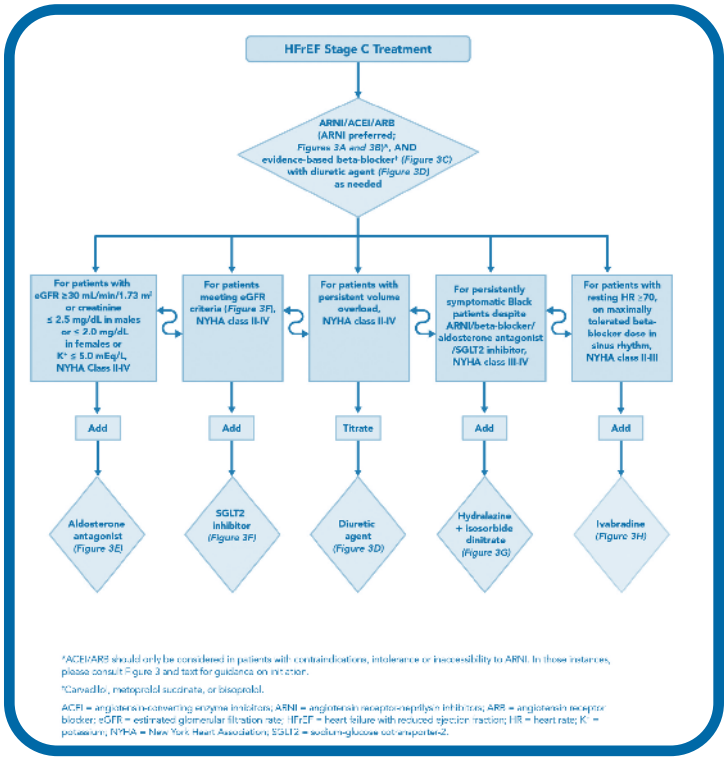
Examining the 2021 update to the ACC Expert Decision Pathway for HFrEF Treatment Optimization

Continued from Page 5

inclusion to the hospital's formulary, there has been a gradual usage increase for both medications. Our Healthy Heart Team in the Ambulatory Care Center has helped oversee the continuation of therapy established for patients who have been hospitalized, as well as initiate therapy in those that are naïve to treatment. As guidelines are updated and novel therapies emerge, University Hospital will continue to remain at the forefront of heart failure care.



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Casirivimab/Imdevimab for Emergency Department Use

See full EAU prescribing information https://www.fda.gov/media/145611/download

Mechanism of Action:
- Neutralizing monoclonal antibodies that binds to the SARS-CoV-2 – they bind to the spike protein and blocks attachment to the human ACE2 receptor

Indication – see algorithm on page 8
- The US FDA has issued an Emergency Use Authorization (EUA) to permit the emergency use of the unapproved products casirivimab/imdevimab treatment of mild to moderate COVID19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization

Dosing – 600 mg casirivimab/600 mg imdevimab given as a single infusion over at least 20 minutes x one
- No dosage adjustment recommended in pregnant or lactating women and in patients with renal impairment
- Primary endpoint of COVID-19-related hospitalization or all-cause death through Day 29 occurred in 7 (1.0%) subjects treated with 600 mg casirivimab and 600 mg imdevimab compared to 24 (3%) subjects randomized to placebo, demonstrating a 70% reduction in COVID-19-related hospitalization or all-cause death compared to placebo (p=0.0024)

Ordering in Epic:
- Medication is generally used in ED only
- If ordered by any other service, please reach out to infectious disease/antimicrobial stewardship to confirm appropriateness

Administration Instructions for Nursing:
- Product is preservative-free and should be administered **immediately**. Store no more than 4 hours at room temperature
- Medication will be delivered from pharmacy as an IVPB with a 0.2 micron filter. This will be provided with every dispensed dose. Prime the infusion with Alaris pump tubing and attach the filter prior to administration.
- Administer the infusion solution via an infusion pump over at least 20 minutes
- Flush line with at least **25 mL 0.9% sodium chloride** when the infusion is complete

Monitoring:
- Patient must be monitored during the 20-minute infusion and for **60 minutes after the infusion**
  - **Hypersensitivity including anaphylaxis**
    - If signs or symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue administration and initiate appropriate medications and/or supportive therapy
  - **Infusion related reactions**
    - Signs and symptoms of infusion related reaction: fever, chills, nausea, headache, bronchospasm, hypotension, angioedema, throat irritation, rash including urticaria, pruritus, myalgia, dizziness
    - If signs or symptoms of an infusion reaction occur, consider stopping the infusion and administer appropriate medications and/or supportive care

- All medication errors and serious adverse events potentially related to casirivimab/imdevimab treatment must be reported by the prescriber within 7 days of onset to FDA MedWatch at www.fda.gov/medwatch/report.htm

Continued on Page 8

Casirivimab/Imdevimab for Emergency Department Use

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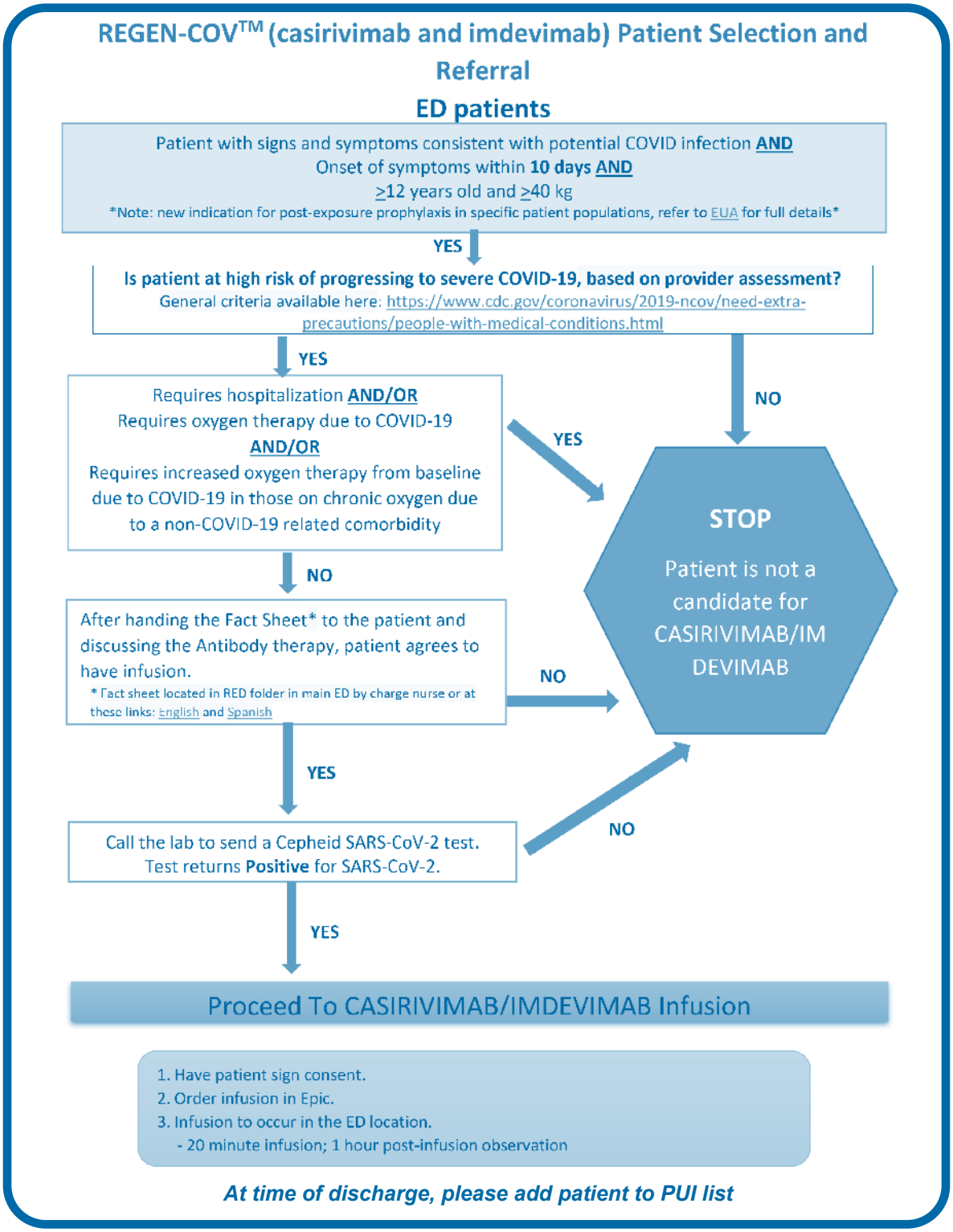

Pharmacy News

Welcome New Clinical Pharmacists

Dr. Joe Plott is the new Emergency Medicine Clinical Specialist working within the emergency department. Joe is originally from Young Harris, GA. He earned his Doctor of Pharmacy from University of Kentucky College of Pharmacy. Before coming to UH, Joe completed his PGY1 Pharmacy Residency at Oregon Health & Science University in Portland, OR and a PGY2 Pharmacy Residency in Emergency Medicine at The Ohio State University Wexner Medical Center in Columbus, OH. Outside of work Joe loves travelling, hiking, and trying out new coffee shops. Joe is excited to join our pharmacy team.

Dr. Nadeem Baalbaki was born and raised in Staten Island, New York and he completed his PharmD at Long Island University Brooklyn. He then went on to complete his PGY1 at the Bronx VA medical center and completed his PGY2 in infectious diseases at NYU Langone - Long Island. He is excited to now be a part of the UH team as one of two infectious disease pharmacists!

Welcome New Pharmacy Technicians

Nathan Chattergoon is a new Pharmacy Technician at University Hospital. He grew up in New Jersey and loves to travel to different places whenever he gets the chance! His previous job was at Walgreens, where he worked every position that there was. He started from the bottom and worked his way up. This is his first time in a hospital setting, and it is really different from retail. He is excited for his new journey and cannot wait to see where this takes him! Also, he just wants to say Thank You to those that have been so kind and so helpful while he is still learning. It truly means a lot.

Continued on Page 10

University HOSPITAL
Newark, NJ

Pharmacy News

Welcome New Pharmacy Technicians

Sabriyah Flores accomplished getting her associates in science at University of Hartford in Connecticut. After working at CVS as a Certified Pharmacy Technician for 5 years, she was promoted to Lead Tech there. She enjoys learning new things, helping others, and being around family and friends. She is excited for her new journey at University Hospital.

Welcome New Pharmacist

Dr. Michael Lim completed his Doctor of Pharmacy degree at St. John's University in Queens, New York. Prior to his recent graduation, he worked at Geriscript Pharmacy as a Pharmacy Technician. Michael is excited to exercise his clinical knowledge and critical thinking skills to provide the best patient care. He is happy to be joining the team at University Hospital.