1. COVID-19 Treatment
   a. Adult Treatment Algorithm
   b. Pediatric Treatment Algorithm
   c. Ambulatory Pharmacy Treatment Guide

2. COVID-19 Testing
   a. FAQs

3. COVID-19 Specific Medications
   a. Hydroxychloroquine
      i. Crushing Tablets/Oral Suspension
      ii. Mitigation of Drug-Induced Malignant Arrhythmias
   b. Tocilizumab
   c. JAK Inhibitors
   d. Clinical Trial Contact Information (Remdesivir, Sarulimab, Convalescent Plasma)
   e. COVID-19 Convalescent Plasma
   f. Documentation of Convalescent Plasma
   g. Review of Emergency Use Authorization (EUA) for Baricitinib

4. COVID-19 Potential Interacting Therapies
   a. Nonsteroidal Anti-Inflammatory Drugs (NSAIDS)
   b. Renin-Angiotensin-Aldosterone System (RAAS) Inhibitors

5. Pharmacologic Therapy Optimization
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   b. Medication Consolidation Strategies
   c. Insulin Infusion
      i. COVID Insulin Infusion Protocol for Adult Patients
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   e. COVID i-Vent Monitoring
   f. COVID Drug Monitoring Standing Order
   g. Anticoagulation My List
   h. Anticoagulation Order Panel
      i. Anticoagulation Recommendations for COVID-19 Patients Receiving Convalescent Plasma
   j. Addition of Aspirin Therapy for COVID-19 Patients
   k. Sedatives and Paralytics Titration Goals and Parameters

6. Respiratory Therapy
   a. Metered Dose Inhaler Use and Stewardship
   b. Nebulized Prostacyclin Medications
   c. Nebulizer Treatment in COVID Positive and Negative Patients
   d. Standing Order for Epinephrine Conversion as First-line for Respiratory Distress Hypersensitivity

Continued on Page 2
7. Drug Shortages
   a. Sedatives, Analgesics, and Paralytics Alternatives
      i. Phenobarbital for Alcohol Withdrawal Syndrome Dosing Guidelines
      ii. Treatment of Alcohol Withdrawal during Benzodiazepine Shortage
      iii. Ketamine for Analgesia and Sedation Criteria for Use Guidance
      iv. Enteral Clonidine for Dexmedetomidine Transition
   b. Lorazepam Infusion
   c. Neuromuscular Blocking Agents
   d. Metered Dose Inhalers

8. Operations
   a. Medication Storage and Relabeling of Patient Own Medications (POM)
   b. Albuterol MDI Recycling Program
   c. Pharmacologic Formulation Optimization
For the most up-to-date treatment algorithm please use the link below and refer to the “Medication” section under the “Inpatient - Clinical Resources”.

COVID-19 Adult Treatment Algorithm and Appendices

Includes:

i. Clinical Trials
ii. Remdesivir, Tocilizumab, and Convalescent Plasma Exclusion Criteria
iii. Acute Respiratory Failure MICU/SDU Triage Guidelines
iv. Anticoagulation Dosing Guidelines
v. Medications
## Pediatric Treatment Algorithm

<table>
<thead>
<tr>
<th>Link</th>
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</table>
| For the most up-to-date treatment algorithm please use the link below and refer to the “Pediatrics” section under the “Inpatient - Clinical Resources”.  

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mechanism</th>
<th>Rationale of possible efficacy</th>
<th>Recommendation and Rationale</th>
</tr>
</thead>
</table>
| Vitamin D2 (ergocalciferol)/ Vitamin D3 (cholecalciferol) | Immune system modulation<sup>1</sup> | • Lower viral replication<sup>2</sup>  
• Reduce mortality<sup>2</sup>  
• Vitamin D deficiency linked with cytokine storm biomarkers<sup>3-5</sup> | • There is insufficient evidence to recommend for or against vitamin D for prevention of COVID-19  
• Patients who require vitamin D replacement can continue or be initiated as appropriate  
• There are no completed randomized clinical trials evaluating usage of Vitamin D for COVID-19. There are ongoing clinical trials assessing potential benefit.<sup>6, 7</sup>  
• Some recently published retrospective observational studies concluded that patients with COVID-19 had lower levels of vitamin D.<sup>21, 22</sup> While these patients may need vitamin D replacement regardless of COVID-19 prevention, further clinical trials are necessary to connect its relationship with COVID-19.  
• There is conflicting evidence regarding the benefits of Vitamin D in preventing other respiratory viral infections, such as influenza. In these studies, several studies using lower doses of Vitamin D support its benefit in preventing respiratory tract infections<sup>8, 9, 10</sup>, while another showed opposite effects in pediatric patients<sup>11</sup>, and other studies showed mixed results.<sup>12</sup> |
| HMG-CoA reductase inhibitors (statins) | HMG-CoA reductase inhibition<sup>13</sup> | • Inhibition of MYD88 pathway related to immunity<sup>14-16</sup>  
• Lower incidence of viral pneumonia<sup>17-19</sup> | • There is insufficient evidence to recommend statins for prevention of COVID-19  
• Patients who require statins for non-COVID indications should be continued or initiated  
• No published peer review studies in medical literature were found to support the usage of statins based solely on COVID positive status. Further studies are necessary to connect its relationship with COVID-19.  
• Current NIH COVID-19 guidance does not recommend to use statins to treat COVID.<sup>13</sup> |
| Dextromethorphan | Antitussive<sup>20</sup> | Promotes viral activity<sup>20</sup> | • Appropriate to use as an antitussive agent in COVID-19 patients.  
• No published peer review studies in medical literature were found to support dextromethorphan worsening COVID-19 infections. Further studies are necessary to connect its relationship with COVID-19.  
• Theoretical adverse effects of dextromethorphan in COVID-19 is based on the proteins involved with viral infection and replication of viral activity<sup>20</sup> |
| Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) | COX-1/2 inhibition | Potential increase ACE2 expression and worsen COVID-19 infection | • Appropriate to use in COVID-19 patients  
• Considerations for NSAID prescribing should always include evaluation of inherent NSAID side effects (i.e. risk of renal dysfunction), regardless of COVID-19 diagnosis  
• No published peer reviewed studies support NSAIDs worsening COVID-19 infections.  
• European Medicines Agency (EMA) and the Food and Drug Administration (FDA) issued statements that there is no scientific evidence connecting NSAID use and worsening COVID-19 symptoms<sup>23, 24</sup> |
| Renin-Angiotensin-Aldosterone System (RAAS) Inhibitors | ACE inhibition and ARB antagonist | Potential increase ACE2 expression and worsen COVID-19 infection | • RAAS antagonists should be continued for patients currently prescribed such agents for indications for which these agents are known to be beneficial, such as heart failure, hypertension, or ischemic heart disease.  
• In the event patients with cardiovascular disease are diagnosed with COVID-19, individualized treatment decisions should be made according to each patient’s hemodynamic status and clinical presentation. |
### References:

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3166406/

2. Grant WB, et al. Evidence that Vitamin D Supplementation Could Reduce Risk of Influenza and COVID-19 Infections and Deaths. nutrients. 2020  


5. Xiaohua Chen, Binghong Zhao, Yueming Qu, Yurou Chen, Jie Xiong, Yong Feng, Dong Men, Qianchuan Huang, Ling Li, Bo Yang, Jinya Ding, Feng Li, Detectable serum SARS-CoV-2 viral load (RNAemia) is closely correlated with drastically elevated interleukin 6 (IL-6) level in critically ill COVID-19 patients, Clinical Infectious Diseases, ciaa449, https://doi.org/10.1093/cid/ciaa449


14. Yuan, Shu. “Statins May Decrease the Fatality Rate of Middle East Respiratory Syndrome Infection.” mBio vol. 6,4 e01120. 11 Aug. 2015, doi:10.1128/mBio.01120-15

Prepared By:
YNHHS Pharmacy Drug Use Policy Action Team

Reviewed By:
Ambulatory SIM Clinical Steering
### COVID-19 Testing FAQs

<table>
<thead>
<tr>
<th><strong>Why does the nasal swab have to go so deep? If the COVID virus is so contagious, shouldn't a regular nasal swab be enough? Are false negatives related to swab location?</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>The gold standard for viral diagnostics of upper respiratory tract infections has traditionally been a nasopharyngeal swab.</td>
</tr>
<tr>
<td>For many respiratory viruses, the anterior nares or mid nasal swabs often is not comparable to a nasopharyngeal swab specimen in terms of sensitivity. For example, in SARS CoV-1, the nasopharyngeal swab specimen was often negative but the sputum or a BAL specimen was positive when the patient had pneumonia later in the course of the disease process.</td>
</tr>
<tr>
<td>In COVID 19 (SARS CoV-2), the distribution of virus along the naso-respiratory epithelium can vary by patient as well as by the date from the initial infection. So, there have been rare patients who have severe COVID 19 pneumonia but have a negative nasopharyngeal swab but sputum or an endotracheal specimen were positive for SARS CoV-2.</td>
</tr>
<tr>
<td>In COVID 19, the maximal sensitivity in using the CDC’s PCR assay was combining a nasopharyngeal swab with an oropharyngeal swab. The CDC assay can detect a few 10 copies/ml of the virus which is quite good. The CDC has been able to validate that a nasopharyngeal swab alone has comparable sensitivity to the combined nasopharyngeal and oropharyngeal swabs with their PCR assay.</td>
</tr>
<tr>
<td>So, all subsequent COVID 19 testing by PCR is compared to nasopharyngeal swab testing. Unpublished data from the Cleveland Clinic revealed that the Cepheid SARS CoV-2 PCR test (the more rapid test across YNHHS) has a sensitivity of 98% compared to the CDC PCR assay.</td>
</tr>
<tr>
<td>Using a just a nasal swab can lower the sensitivity of a SARS CoV-2 PCR test but is easier to perform, so lab companies have created such tests as the Abbott ID Now COVID-19 test which is FDA approved. This is the test that CVS drive-through testing is using. So this is the trade-off can occur with a decrease in sensitivity but ease of obtaining swabs (increasing through-put).</td>
</tr>
</tbody>
</table>
**Situation**

There are questions if hydroxychloroquine tablets can be crushed. In addition, there are questions if a hydroxychloroquine oral suspension should be used for adult patients with enteral feeding tubes.

**Background**

Hydroxychloroquine tablets are currently utilized for treatment of COVID-19 patients. Some patients are unable to swallow or have enteral feeding tubes and need to have the tablets crushed. However, per the prescribing information for hydroxychloroquine, the manufacturer recommends that the tablets should not be crushed.1

This recommendation is based on the tablet having a bitter taste if the tablet is chewed or crushed and taken by mouth.2 Therefore, many generic manufacturers (including many of the manufacturers that supply YNHHS hydroxychloroquine) produce film coated tablets to mask the bitter taste even for swallowing the tablet whole. However, if crushing the tablet and administering hydroxychloroquine via an enteral feeding tube, the bitter taste side effect is avoided.

In addition, the film coating with hydroxychloroquine can delay time to dissolution of the crushed powder compared to non-film coated tablets. Dissolution time can potentially take longer than 5 minutes.3 Administering hydroxychloroquine before it has dissolved can potentially clog an enteral feeding tube. However, one study concluded that hydroxychloroquine can be administered via an enteral feeding tube, if appropriate dissolution time is allowed.4 Therefore, based on these characteristics, other institutions have recommended crushing hydroxychloroquine tablets when needed.5,6

There is an established oral suspension compounding recipe for hydroxychloroquine that is located on the YNHHS Pharmacy Sharepoint web site and available in Epic. However, at this time, it is reserved for pediatric patients, as broad expansion to adult patients would increase pharmacy compounding workload and potentially waste tablets if there is un-used oral suspension.

**Assessment**

Hydroxychloroquine tablets may be crushed. However, the dissolution time may take longer than 5 minutes compared to other drugs.

**Recommendation**

Hydroxychloroquine tablets can be crushed when administration of the whole tablet is not feasible, such as administration into an enteral feeding tube.

If it is crushed and administered into an enteral feeding tube, it is recommended to instruct the nurse to crush the tablet into a powder AND that potentially greater than 5 minutes is needed for the crushed tablet to dissolve. The hydroxychloroquine oral suspension is currently reserved for pediatric patients.

**References**

Situation

Treatment of COVID-19 with hydroxychloroquine and/or other medications such as antimicrobials and antivirals may result in prolongation of the QT interval which in turn may increase the risk of Torsades de Pointes (TdP) and cardiac arrest.

Background

Prolongation of the QT interval can result in increasing risk for the development of malignant cardiac arrhythmias including TdP and cardiac arrest. An increase in the QT interval correlates with increased risk of developing TdP (data shown below from sotalol FDA label).

### Relationship Between QTc Interval Prolongation And Torsade de Pointes

<table>
<thead>
<tr>
<th>On-Therapy QTc Interval (msec)</th>
<th>Incidence of Torsade de Pointes</th>
<th>Change from QTc Interval from Baseline (msec)</th>
<th>Incidence of Torsade de Pointes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 500</td>
<td>1.3% (1787)</td>
<td>Less than 65</td>
<td>1.6% (1516)</td>
</tr>
<tr>
<td>500-525</td>
<td>3.4% (236)</td>
<td>65-80</td>
<td>3.2% (158)</td>
</tr>
<tr>
<td>525-550</td>
<td>5.6% (125)</td>
<td>80-100</td>
<td>4.1% (146)</td>
</tr>
<tr>
<td>&gt;550</td>
<td>10.8% (157)</td>
<td>100-130</td>
<td>5.2% (115)</td>
</tr>
</tbody>
</table>

Hydroxychloroquine and/or other medications such as antimicrobials which are increasingly being used to treat patients with COVID-19 are known to cause prolongation of the QT interval, but their individual risk of TdP is low. Accordingly, these medications have been prescribed in the outpatient setting with no requirement for cardiac monitoring. However when QT-prolonging medications are used in combination, there is a possibility of a synergistic effect on the QT interval. There is little published data regarding the pro-arrhythmic risk of combined use of these agents in COVID-19 patients.

Assessment

Pro-arrhythmic risk of medications would usually be mitigated by use of telemetry, but we need to prepare for the possibility that the number of treated COVID-19 patients may exceed our telemetry resources. Thus delineation of care pathways that minimize this possible risk of COVID-19 treatment in the setting of limited telemetry monitoring is needed. Recognizing that the situation is very fluid, the recommendations below are subject to further modification at any time.

Recommendation

All COVID-19 patients should have the following:

- When ordering an EKG for a COVID 19 patient to monitor their QTc, select the diagnosis “COVID 19” to alert cardiology to expedite the formal reading of the EKG.
- Daily monitoring of electrolytes; maintain K > 4.0 and Mg > 2.0.
- All unnecessary QT prolonging drugs should be avoided or switched to alternatives whenever possible.

See [Adult Treatment Algorithm](#) - Mitigation of Drug-Induced Malignant Arrhythmias for further guidance.
**Situation**
The chimeric antigen receptor T cell (CAR-T) program has been active at Yale New Haven Hospital for around a year. In order to treat critical COVID-19 patients, there will now be a supply of one of the rescue medications, tocilizumab, available for non-oncology inpatients.

**Background**
CAR-T are infused after receiving a lymphodepleting regimen and then monitored for adverse effects particularly Cytokine Release Syndrome (CRS) and Cytokine Related Encephalopathy Syndrome (CRES).

Treatment of CRS and CRES can consist of tocilizumab and/or steroids. Due to the reversal effect that these products have on CAR-T, tocilizumab and steroids need to be approved by an approved CAR-T provider prior to ordering these medications.

**Assessment**
Given the strict restriction for tocilizumab and steroids, the pharmacist will need to confirm that the patient meets the criteria prior to verification.

**Recommendation**
- For Oncology patients, please change the dispense logic upon order verification to the NP8 pharmacy from the hours of 6a-11p. The new default dispense location will be the Central IV room to accommodate the expected volume of COVID-19 patients.
- Tocilizumab has a 2 hour window to complete the infusion from the time the order is placed to the time the drug has completed the infusion. This timeline gives pharmacy one hour to review, verify, compound and hand deliver this medication to the nurse.
- Prior to the infusion of the CAR-T cells, 2 vials of tocilizumab will be stocked for each patient. Supply of tocilizumab will be stocked in both central and in Smilow NP8 pharmacy.
- If a STAT order for tocilizumab is placed during the day the CAR-T pharmacist will be responsible for verification and communication to production. If after 4:30 pm, please page the pharmacy oncology on-call pager to review and verify the order.
- During these hours 0600 to 2200 weekdays and 0700 to 1630 weekends – tocilizumab will be made in Smilow NP8 pharmacy
  - During these hours 2200 to 0600 weekdays and 1630 to 0700 weekends – tocilizumab will be made in Central pharmacy.
- Pharmacist will verify the dose then call the IV room or Smilow NP8 pharmacy to communicate that tocilizumab is a STAT mediation and is to hand delivered to the nurse.
- **Tocilizumab is not classified as a hazardous medication. Therefore, tocilizumab can be made in a non-chemotherapy hood and any nurse can administer the drug. Tocilizumab does not need to be primed and is light-sensitive (needs to be delivered in an amber bag).**
- Tocilizumab will be reassessed prior to each dose, during the day the CAR-T pharmacist will confirm with the Smilow NP8 pharmacy that the next dose is wanted prior to manufacturing. Clinical evening pharmacist will confirm if evening and overnight doses will be needed. If the overnight dose cannot be assessed prior to completion of the shift the clinical evening pharmacist and Smilow operations pharmacist will contact central IV room to make overnight dose.
- When tocilizumab is approved overnight, the CAR-T pharmacist or the on-call oncology pharmacy resident will contact Smilow NP8 pharmacy in the morning to have the upcoming tocilizumab dispensing location changed from Central to Smilow NP8 pharmacy.
## JAK Inhibitors

<table>
<thead>
<tr>
<th><strong>Situation</strong></th>
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<tbody>
<tr>
<td>There is interest in using JAK inhibitors as an alternative therapy for treating COVID-19</td>
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<table>
<thead>
<tr>
<th><strong>Background</strong></th>
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</table>
| Due to a potential benefit of interrupting viral passage into cells and helping with inflammation, JAK inhibitors (baricitinib, ruxolitinib, tofacitinib, and upadacitinib) have been considered as a potential therapy option for COVID-19.  

These medications have significant adverse effects including pancytopenias which put patients at risk for infections or worsening infections.  

Currently, the data supporting the use of these medications is limited to theoretical benefit, but several of these medications are actively being used in clinical trials in other countries to assess efficacy in this patient population.  

Procurement of these medications is challenging given these agents are non-formulary across YNHHS and many drug companies have limited distribution to specialty pharmacies for their approved indications, which does not include COVID-19. |

<table>
<thead>
<tr>
<th><strong>Assessment</strong></th>
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</thead>
<tbody>
<tr>
<td>It is unclear at this time whether or not these medications provide benefit due to no clinical data supporting their use and there is an increased risk with utilizing these medications and limited ability to obtain the medications.</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th><strong>Recommendation</strong></th>
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<tbody>
<tr>
<td>At this time, JAK inhibitors are not recommended at YNHHS for the treatment of COVID-19 due to our inability of obtaining the medication, insufficient data on use and potential side effect risk. If new data becomes available these recommendations may change and that will be communicated to staff accordingly. If there is any persistence from teams to acquire these medications please escalate them to either the antimicrobial stewardship team at YNHH, infectious disease pharmacists, and/or clinical managers as appropriate.</td>
</tr>
</tbody>
</table>

See [Adult Treatment Algorithm - Medications](#) for further guidance.
### Clinical Trial Contact Information (Remdesivir, Sarilumab, Convalescent Plasma)

<table>
<thead>
<tr>
<th>Remdesivir</th>
<th>Sarilumab</th>
</tr>
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<tbody>
<tr>
<td>PI: Onyema Ogbuagu (<a href="mailto:Onyema.Ogbuagu@yale.edu">Onyema.Ogbuagu@yale.edu</a>) and study coordinator: Laurie Andrews (<a href="mailto:laurie.andrews@yale.edu">laurie.andrews@yale.edu</a>) or MHB</td>
<td></td>
</tr>
<tr>
<td><strong>Remdesivir Supply Communication</strong></td>
<td></td>
</tr>
<tr>
<td>Sarilumab</td>
<td></td>
</tr>
<tr>
<td>PI : Geoffrey Chupp (<a href="mailto:Geoffrey.Chupp@yale.edu">Geoffrey.Chupp@yale.edu</a>) or MHB</td>
<td></td>
</tr>
<tr>
<td><strong>Convalescent Plasma</strong></td>
<td></td>
</tr>
<tr>
<td>PI : Mahalia Desruisseaux (<a href="mailto:Mahalia.desruisseaux@yale.edu">Mahalia.desruisseaux@yale.edu</a>) or MHB</td>
<td></td>
</tr>
<tr>
<td><strong>Other Resources</strong></td>
<td></td>
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<tr>
<td>You may also contact the YNH IDS department (203) 688-4872 with additional questions.</td>
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</table>
**COVID-19 Convalescent Plasma (CCP)**

<table>
<thead>
<tr>
<th>Situation</th>
<th>There is a need to update the recommendations for the use of COVID-19 convalescent plasma (CCP) in patients with COVID-19 at YNHHS.</th>
</tr>
</thead>
</table>
| Background| On August 23, the FDA issued an Emergency Use Authorization for CCP as a potential COVID–19 treatment. This recommendation was based on observational data obtained from the Mayo Expanded Access Program, from which it was concluded that CCP potentially confers benefit when used early in the disease course of COVID-19.  

CCP remains an investigational treatment, as emphasized in the EUA announcement. There have not been any robust randomized placebo-controlled studies demonstrating benefit of CCP. Two studies were ended early due to decreased number of patients with COVID-19 and the presence of adequate titers of anti-SARS-CoV-2 in patients with COVID-19 at baseline. In addition, CCP remains a scarce resource and will be for the foreseeable future. |
| Assessment| There is a need to obtain robust data on the efficacy of CCP and to prioritize patients who might gain benefit from receiving this investigational treatment as well as to optimize the ordering of convalescent plasma for COVID-19 patients. |
| Recommendation| Based on input from the Ad hoc COVID-19 Treatment Team YNHHS Antimicrobial Subcommittee, and the YNHH Blood Bank Team for CCP, the following procedures for CCP should be followed. |

1. **YNHH, York Street Campus Only at this time:**  
   Patients who are being considered for CCP, should be reviewed for enrollment in the randomized clinical trial for CCP (https://www.ynhhs.org/patient-care/covid-19/for-employees/for-employees.aspx)  
   Exclusion Criteria include:  
   A) Patients beyond 3 days of hospitalization  
   B) Patients who are mechanically ventilated despite meeting criterion 1.  

2. **For GH, BH, LMH, WH, YNHH-SRC, and YNHH-YSC Campus (who do not meet criteria for the above CCP RCT):**  
   For patients who do not meet criteria for enrollment in the randomized clinical trials (i.e. patients on mechanical ventilation or patients beyond 3 days of hospitalization) or for patients hospitalized in a hospital where the RCT cannot be implemented, it should be realized that CCP remains an investigational treatment.  

   1. If CCP is being considered, the patient must meet the following 2 criteria:  
      * Patient has a confirmed positive SARS-CoV-2 PCR result  
      * Patient has been admitted for ≤ 6 days  
      * Patient requires > 3 liters of oxygen supplementation  

   2. Patients who meet these any of the following criteria should be excluded:  
      A: History of anaphylaxis to blood products or history of IgA deficiency  
      B. D-dimer > 10  
      C. Evidence or suspicion of thrombosis  
      D. Active bleed or high risk for bleeding  

   3. Any patient who receives this investigational therapy should receive, at minimum, intermediate dose prophylaxis anticoagulation with enoxaparin for 72 hours, regardless of d-dimer. After 72 hours, the
need for intermediate dose prophylaxis can be re-assessed based on d-dimer level and risk for thrombosis.

4. To order CCP outside of the clinical trial, effective 11/18/2020, use the following order in EPIC entitled: “Evaluation for COVID-19 Convalescent Plasma (CCP)”: The above order will trigger a pharmacist review for the CCP to determine if the patient meets YNHHS Criteria for use.

NOTE: Since CCP must be ordered from a regional blood center by the blood bank, the consult for CCP will be evaluated from 7AM to 4PM during the business hours of regional blood centers.

References

https://www.fda.gov/media/141478/download
Documentation of Convalescent Plasma

On the summary page under oncology click “blood product summary”

Click on “blood products” it will drop down to show document with “transfuse plasma” if it has been given.

This can further be confirmed by referring to the media tab and looking for the consent for convalescent plasma.
Situation

Background
The baricitinib EUA was granted based on data from a recent double-blind, placebo-randomized controlled trial (ACTT-2) from which the FDA concluded the known and potential benefits of baricitinib in combination with remdesivir outweighed the known and potential risks for the treatment of COVID-19.

The primary endpoint of the ACTT-2 trial revealed that baricitinib, in combination with remdesivir, reduced the time to recovery by 1 day within 29 days after initiating treatment compared to patients who received a placebo with remdesivir (7 vs. 8 days respectively, p=0.047; 95% CI 1.00-1.1).

However, the mortality rate by day 29 was 4.7% (24/515) baricitinib + remdesivir versus 7.1% (37/518) for placebo + remdesivir (p NS; 95% CI -5.8%. 0.5%).

While ACTT-2 was already underway, data from the RECOVERY trial revealed a mortality benefit for dexamethasone therapy in moderate to severe COVID-19 that in turn has guided our current COVID-19 treatment algorithm.

The safety and efficacy of baricitinib in combination with dexamethasone, the only medication shown to have an effect on mortality for COVID-19, has not been established though an increased risk of infection could be possible. Additionally, baricitinib has a risk for thrombosis which dexamethasone does not have.

Assessment
Based on current information, the YNHHS COVID-19 Treatment Team met to review the data behind the FDA’s EUA for baricitinib.

Recommendation
Given the data that is currently available, it is recommended to not make changes to the YNHHS COVID-19 Adult Treatment Algorithm at this time. Dexamethasone will continue to be recommended with remdesivir as the therapy for COVID-19 inpatients who have a RA O2 sat of < 95% and require supplemental oxygen.

Baricitinib will not be added to the YNHHS COVID-19 Adult Treatment Guideline at this time. As additional data become available, the use baricitinib may be re-evaluated as we have done with all of our COVID-19 therapies to date.

References
### Nonsteroidal Anti-Inflammatory Drugs (NSAIDS)

<table>
<thead>
<tr>
<th>Situation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confusion exists regarding the usage of NSAIDs in suspected or confirmed COVID-19 patients.</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Background</th>
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</thead>
<tbody>
<tr>
<td>There has been controversial guidance to avoid ibuprofen in patients with COVID-19. On 3/14/20, France’s minister of health advised to avoid NSAIDs because it may worsen the effects of the COVID-19. This statement was made due to studies that suggest ibuprofen increases ACE2 expression, which allows COVID-19 to enter the cells in our lungs, in addition to a letter published in the Lancet on March 11, 2020.(^2,^3,^6) However, there is no specific clinical data that supports NSAIDs worsen the COVID-19 infection.</td>
</tr>
</tbody>
</table>

While NSAIDs, in general, should be used with caution in patients with renal dysfunction or at high risk of renal dysfunction, there is no specific clinical data that supports NSAIDs should be avoided in COVID-19 patients due to an increased risk of worsening renal function. On 3/18/20, the World Health Organization (WHO) stated they do not recommend against the use of ibuprofen in COVID-19 patients.\(^5\) In addition, the European Medicines Agency (EMA) recommended continuing NSAIDs following package insert guidance as there was no connection between ibuprofen and COVID-19.\(^4\) The Food and Drug Administration also issued a statement that they are not aware of any scientific evidence connecting NSAID use and worsening COVID-19 symptoms.\(^7\)

<table>
<thead>
<tr>
<th>Assessment</th>
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</thead>
<tbody>
<tr>
<td>Without strong evidence linking NSAIDs to adverse clinical outcomes in patients with suspected or confirmed COVID19, it is recommended to follow guidance from WHO and EMA and not discontinue NSAIDs in these patients based primarily on a COVID-19 diagnosis. Considerations for NSAID prescribing should include the inherent adverse effects of NSAIDs such as the risk for renal dysfunction.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Recommendation</th>
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<tbody>
<tr>
<td><strong>There is no specific contraindication or precaution to using NSAIDs in COVID-19 patients.</strong> Considerations for NSAID prescribing should always include the inherent adverse effects of NSAIDs such as the risk for renal dysfunction regardless of a COVID-19 diagnosis.</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>References</th>
</tr>
</thead>
</table>
## Situation
New data and recommendations from governing cardiology societies have changed perspective regarding use of RAAS antagonists in patients with COVID-19.

## Background
Concern has arisen regarding the potential effects of ACE and/or ARB use in the setting of suspected or confirmed COVID-19.

An SBAR released on March 14th outlined recommendations in response to these concerns. On March 17th, a joint statement from the Heart Failure Society of America (HFSA), the American College of Cardiology (ACC), and the American Heart Association (AHA) was released specifically addressing this topic.

The [Statement](#) acknowledges uncertainty regarding the potential effects of ACE and/or ARB use in the setting of COVID-19, and that recommendations are shifting in response to emerging data.

## Assessment
The joint recommendation from the cardiology societies supersedes the notice sent out by the Office of the Chief Clinical Officer on March 14.

The summary statement for these recommendations is as follows: Do not add or remove any RAAS-related treatments, beyond actions based on standard clinical practice.

## Recommendation
- The recommendations in the prior SBAR on this topic released on March 14th, 2020 to hold RAAS antagonists in the setting of COVID-19 are out of date and should not be followed.
- **RAAS antagonists should be continued for patients currently prescribed such agents for indications for which these agents are known to be beneficial, such as heart failure, hypertension, or ischemic heart disease.**
- **In the event patients with cardiovascular disease are diagnosed with COVID19, individualized treatment decisions should be made according to each patient's hemodynamic status and clinical presentation.**
## Situation

There is a need to concentrate fluids whenever possible in COVID-19 positive patients.

## Background

The leading cause of mortality from COVID-19 is respiratory failure from Acute Respiratory Distress Syndrome (ARDS), an inflammatory form of lung injury that results in respiratory failure with hypoxemia.

Fluid overload in ARDS has been associated with worse patient outcomes, so a fluid-conservative approach should be utilized when clinically appropriate (absence of shock, no evidence of tissue hypoperfusion). Pharmacists have advanced knowledge of formulary medications that have the ability to be concentrated.

## Assessment

In order to ensure that each patient’s fluids are optimized, pharmacists should assess the IV medications in COVID-19 patients.

## Recommendation

Some strategies for pharmacists to evaluate IV medications (IVP, IVPB, continuous infusions) are the following:

- Determine if patient meets criteria for IV to enteral
- Ensure unnecessary fluids are discontinued
- Concentrate continuous fluids when possible
  - Must contact provider to discuss any changes
  - Should contact RN to determine if they have central line access to run concentrated fluid (if central line required)
  - Most commonly, vasopressor infusions may be concentrated
    - If the IV room has multiple requests in a short period of time for additional vasopressor bags, please assess rate of therapy and determine if bag can be concentrated
    - If upon order verification you see orders for second, third, and fourth-line vasopressors at once, it is likely that vasopressors should be concentrated
  - Many continuous infusions have standard concentrations that cannot be concentrated further. In these cases, we do not recommend entering custom orders due to safety concerns unless the benefit outweighs risks, which should be discussed with a manager or ICU pharmacist
    - Anticoagulation infusions
    - Insulin infusions
    - Antimicrobials mixed in standard fluid concentrations
Medication Administration Consolidation

Situation
There is a need to evaluate clustering administration of medications in order to limit health care worker exposure to COVID-19 and reduce the need and waste of PPE.

Background
It is imperative to conserve PPE at Yale New Haven Health System, given the likelihood of a national shortage with PPE related to a surge in COVID-19 patients. In addition, it is crucial to minimize exposure of healthcare workers to COVID-19 patients. Many medications are scheduled at various times throughout the day, potentially resulting in multiple interactions between health care practitioners and patients.

Assessment
In an effort to reduce the use of PPE, medication administration times can be consolidated and re-scheduled in Epic upon pharmacist review and verification of: (1) appropriateness of schedule, (2) drug-drug and drug-food interactions and (3) timing regarding meals.

Recommendation
For patients with confirmed COVID-19, consider consolidating medications to recommended COVID-19 administration times, as outlined below. Pharmacists will evaluate consolidation of medication administration times during order verification and during clinical patient review based on the recommended frequencies below. In addition, pharmacy will evaluate medication necessity to further minimize the number of medications administered. If the nurse or prescriber identifies additional opportunities for administration time adjustments to improve consolidation, they should utilize their judgement and call pharmacy for any assistance retiming medications.

*These frequencies refer to frequencies that have the word, “scheduled” in the Epic order and automatically default to routine scheduled times.
†If medication deemed urgent, include a “Now” dose, then if possible, adjust to a COVID-19 administration time

Medications Administration Consolidation Tips

Epic optimization
1. Rescheduling administration times in Epic
2. Document consolidation IVENTS

Targeted drug interventions:
3. COVID Administration times
4. Common daily interventions

Communication
5. Tips for Nursing to Adjust MAR
6. Mobile Heartbeat Nursing Broadcast
Epic Optimization:

1. The best way to consolidate dose administrations is by proactively changing dosing times upon order verification.

Reschedule active orders

1. Active orders can be rescheduled by finding the medication tab and selecting Adjust times after choosing the desired medication.

2. Adjust the medication administration time according to COVID consolidation times.

Updated 11/25/2020
2. Document your administration consolidations in IVENTS. This can serve as useful data for the future and promote new ideas for consolidation.

Directions

1. Select **COVID-19 Intervention/Optimization** IVENT type

2. Select Subtype **cluster medication administration times** (option to select clustering labs as well)

3. Record a **brief** summary of either time or therapy adjustment for consolidation

4. **Close** the IVENT
**Targeted Drug Therapy Interventions:**

3. Follow the recommended COVID-19 administration times when clinically appropriate (SBAR 3/31/20)

<table>
<thead>
<tr>
<th>Frequency/ Specific Medication</th>
<th>Standard Administration Times</th>
<th>COVID-19 Administration Times</th>
</tr>
</thead>
<tbody>
<tr>
<td>Every 4 hours</td>
<td>No set standard time</td>
<td>Consider changing to 0100/0500/0900/1300/1700/2100</td>
</tr>
<tr>
<td>Every 4 hours scheduled*</td>
<td>0000/0400/0800/1200/1600/2000</td>
<td>0100/0500/0900/1300/1700/2100</td>
</tr>
<tr>
<td>Every 6 hours</td>
<td>No set standard time</td>
<td>Consider changing to 0900/1500/2100/0300</td>
</tr>
<tr>
<td>Every 6 hours scheduled*</td>
<td>0000/0600/1200/1800</td>
<td>0900/1500/2100/0300</td>
</tr>
<tr>
<td>Every 8 hours</td>
<td>No set standard time</td>
<td>Consider changing to 0500/1300/2100 (same as TID)</td>
</tr>
<tr>
<td>Every 8 hours scheduled*</td>
<td>0600/1400/2200</td>
<td>0500/1300/2100</td>
</tr>
<tr>
<td>Every 12 hours</td>
<td>No set standard time</td>
<td>Consider changing to 0900/2100 (same as BID)</td>
</tr>
<tr>
<td>Every 12 hours scheduled*</td>
<td>0800/2000</td>
<td>0900/2100 (same as BID)</td>
</tr>
<tr>
<td>Every 24 hours</td>
<td>No set standard time</td>
<td>Consider changing to one of the every 6 hours times: 0900/1500/2100/0300</td>
</tr>
<tr>
<td>TID</td>
<td>0900/1400/2100</td>
<td>0500/1300/2100 (same as every 8 hours)</td>
</tr>
<tr>
<td>QID</td>
<td>0800/1200/1800/2100</td>
<td>0900/1300/1700/2100 (can usually be coordinated around meals)</td>
</tr>
<tr>
<td>Levothyroxine oral</td>
<td>0600</td>
<td>0500</td>
</tr>
<tr>
<td>Warfarin</td>
<td>1800</td>
<td>2100</td>
</tr>
<tr>
<td>Gentamycin IV, high-dose only at BH</td>
<td>2000</td>
<td>2100</td>
</tr>
</tbody>
</table>

*These frequencies refer to frequencies that have the word, “scheduled” in the Epic order and automatically default to routine scheduled times.

*If medication deemed urgent, include a “Now” dose, then if possible, adjust to a COVID-19 administration time*

Updated 4/24/202
4. The following examples can be common consolidation interventions

*Individual patient evaluations on efficacy, adverse reactions, and indication should be carefully performed before any changes are made to medication regimens or administration.*

**Bowel Regimen**

Patients may be ordered scheduled senna BID or docusate TID. Instead, consider recommending once daily polyethylene glycol as first line therapy and align with COVID administration times.

*May be difficult with patients requiring combination therapy or failing first line therapy. While polyethylene glycol 17g daily is standard dosing, patients requiring 17g BID can be considered for a once daily dosing of 34g. Data shows that 34 g once daily is still effective, but increases chances of adverse effects (DiPalma 1999).*

**Endocrine**

Change Levothyroxine preset administration time from 0600 to 0500 (or 0900) to align with COVID administration times.

*0500 time is preferable over 0900 as levothyroxine should be taken 30-60min before or 3-4 hours after a meal. Calcium or iron containing products should not be consumed within 4 hours of medication administration, as the absorption can be severely affected. A 0900 administration time can be a risk due to breakfast.*

**GERD/Stress ulcer prophylaxis**

Consider recommending use of pantoprazole once daily over famotidine twice daily

*Clinical decision should be made pending C. difficile risk evaluation*

**Critical Care**

Utilize our drug monitoring standing order protocol to optimize infusion bag size and concentration

### Pharmacist COVID Drug Monitoring Standing Order Protocol

<table>
<thead>
<tr>
<th>Concentrating infusion OR changing to a larger bag size for the following drugs:</th>
<th>The pharmacist can concentrate/make into larger bag the listed infusions provided the patient has met the following criteria:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Midazolam, lorazepam, cisatracurium, rocuronium, dopamine, norepinephrine, epinephrine, and phenylephrine</td>
<td>• Infusion rate necessitates changing the bag more frequently than q6hrs AND the infusion rate has not been down-trending in the last 6 hours</td>
</tr>
<tr>
<td></td>
<td>• VASOPRESSORS ONLY: patient has a documented central line and pharmacist has confirmed that a lumen is available for vasopressor use</td>
</tr>
<tr>
<td></td>
<td>Exclusion: The pharmacist will not change infusions to a more diluted concentration as that would require evaluation of the patient’s volume status</td>
</tr>
</tbody>
</table>

<p>|  | 1. Pharmacist can enter the order as a “Standing order: cosign required” after consideration of inclusion/exclusion criteria in previous column |
|  | 2. Pharmacist will ensure that the dosing range (e.g., titratable vs non-titratable), fluid type (D5W vs NS), dosing weight, indication, and titration parameters (e.g., MAP goals, RASS goals, etc) remain the same between orders |
|  | 3. Pharmacist will communicate to the RN that the concentration/bag size have been changed and that the RN will need to change to correct concentration on the smart pump and replace the existing tubing (for changes in concentration only) |</p>
<table>
<thead>
<tr>
<th>Analgesia</th>
</tr>
</thead>
<tbody>
<tr>
<td>For patients ordered for scheduled acetaminophen 650mg q6 hours, consider increasing the dose to 975mg at a reduced frequency of every 8 hours</td>
</tr>
<tr>
<td>Evaluate pain scores and if patients are on other drugs that require q4-6 hour dosing before making this change</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dietary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reach out to dietary for consolidating products such as <em>Prosource</em> (<strong>enteral feeds</strong>). Although not a medication, these items can be adjusted on the MAR and total daily needs can be achieved at less frequent feedings.</td>
</tr>
</tbody>
</table>
Communication:

5. Encourage and educate nursing staff on their ability to adjust medication administration times on the MAR.

Nurses and Respiratory Therapists have the ability to reschedule medications on the MAR. The entire schedule can be adjusted or the due time for a specific dose can be adjusted.

A. Rescheduling Frequencies:

- Click the medication's row on the MAR or the Show all Details button to expand the order details (Do not select on the medication name hyperlink)

- Click Adjust times

For specified frequencies (Every 4 hours scheduled etc.), the Existing Times column displays a list of the current scheduled times and you can enter new times for any or all of them. If you adjust the first scheduled time for the medication, the start time is adjusted, but the start date does not change.

1. Change scheduled times by entering new times in the ‘Adjust Times’ columns for the doses you wish to change (This will adjust the time for all subsequent days) and press Enter. Review the ‘Current Schedule’ and the ‘Adjusted Schedule’.
   A. View Recent schedule
   B. View Adjusted Schedule

2. Enter a “Reason for reschedule”
3. Select “Accept”
B. Change a Due time for a single dose:

**Scenario:** Your patient is off the unit for a scheduled dose due at 0900. You want to change the due time for this one dose to 1000.

You have the ability to adjust the due time for the one dose.

4. Click on the 0900 time tab (in this example, I receive a Patient not scanned warning because the patient is off the unit and cannot be scanned).

5. Change the Action from **Given** to **Due**. Click **Accept**.

6. Adjust the administration Due time to 1000. Enter a comment, if desired.

7. An Administration warning will pop up. Click **Move** (You are not adding a dose, but moving a dose).

8. This one dose will appear on the MAR with the new due time.
6. Send broadcast messages to nursing staff at the beginning of the shift to spread awareness of medication consolidation and offer assistance if needed (YNH, GH, BH).

- 1. Select broadcasts
- 2. Change to Groups
- 3. Select RN Only
- 4. Select New Broadcast
- 5. Change to Unit only
- 6. Select covering units
# Insulin Infusions

## Situation
It was identified that there is potential to conserve personal protective equipment (PPE) by minimizing patient room entrance to monitor blood sugars.

## Background
Due to the COVID-19 Pandemic PPE supply continues to be a significant concern. Insulin, especially when given as a continuous infusion, requires frequent blood glucose (BG) monitoring.

## Assessment
In order to preserve PPE supplies, Endocrinology was consulted for guidance.

## Recommendation
Best practice advisories (BPAs) were developed by our Endocrinology team and will fire for COVID positive and rule out patients when the provider orders an ICU or non-ICU insulin infusion:

### ICU Insulin Infusion:
For COVID-19 positive or person under investigation (PUI) patients:
- Consider a trial of subcutaneous (SC) regular insulin sliding scale every 6hrs (or insulin lispro every 4-6 hrs), with a rapid transition to daily insulin glargine (Lantus®) within 24 hrs if appropriate and the actual or anticipated short-acting insulin total daily dose is >10 units per day.
- Reserve insulin drips for patients with persistent BGs >300 mg/dl in the following circumstances:
  - BGs not decreasing adequately despite attempts at SC insulin, non-dextrose-containing IV fluids and temporary caloric restriction, with aggressive titrations over at least 6-12 hrs.
  - Concomitant diabetic ketoacidosis (DKA) (using YNHHS DKA Guidelines) or hyperosmolar hyperglycemic state (HHS).
  - Type 1 diabetes with very labile ICU control.

### Non-ICU insulin infusion:
For COVID-19 positive or person under investigation (PUI) patients:
- Consider a trial of subcutaneous (SC) regular insulin sliding scale every 6hrs (or insulin lispro every 4-6 hrs), with a rapid transition to daily insulin glargine (Lantus®) within 24 hrs if appropriate and the actual or anticipated short-acting insulin total daily dose is >10 units per day.
- Reserve insulin drips for patients with persistent blood glucose (BGs) >350 mg/dl in the following circumstances:
  - BGs not decreasing adequately despite attempts at SC insulin with aggressive titrations over at least 24 to 48 hrs.
  - Concomitant diabetic ketoacidosis (DKA) (using YNHHS DKA Guidelines) or hyperosmolar hyperglycemic state (HHS).
  - If the patient is eating and clinically stable, CONSIDER metformin 500-1000 mg by mouth twice daily (renal function should be adequate, no acidosis, and no upcoming radiographic studies) AND/OR linagliptin 5 mg by mouth daily, either in combination with or in lieu of insulin. Watch for hypoglycemia when adding any oral agent to insulin.
COVID Insulin Infusion Protocol for Adult Patients

**Situation**

There is need to provide insulin infusions to markedly hyperglycemic COVID+ and PUI patients while also minimizing room entry for staff safety and conserving PPE.

**Background**

The current Yale New Haven Health Insulin Infusion Protocol (IIP) has been in use since 2011. This protocol targets a blood glucose of 120 to 160 mg/dL and requires frequent blood glucose determinations, every 1 hour, for safe implementation.

**Assessment**

There is opportunity to adapt the current Yale New Haven Health IIP for intravenous insulin delivery needs in COVID+ and PUI patients with a somewhat higher blood glucose range and less frequent blood glucose determinations.

**Recommendation**

Effective April 23rd, 2020 an alternate IIP will be available for use in COVID+ and PUI patients. Key differences to the COVID IIP from the current (non-COVID) IIP are as follows:

1. Higher blood glucose target range of 150 to 199 mg/dL
2. Blood glucose checks every 2 hours with the possibility of every 3 to 4 hours in very stable patients
   a. It is imperative that for any adjustments to the infusion rate are based off HOURLY rate of change from the prior blood glucose (BG) level
   b. EXAMPLE: BG at 2pm was 150 mg/dL and the next BG at 4pm is 120 mg/dL. The total BG change over 2 hours is a decrease of 30 mg/dL, however, the hourly rate of BG change for calculating the insulin rate adjustment is a decrease of 15 mg/dL/hour
3. Multiple changes in the adjustment values within the Adjusting Infusion Rate section of the protocol. Closely review the COVID Insulin Infusion Protocol for Adult Patients (Nurse-Driven) for these variations.
4. Two new panels with associated nursing and hypoglycemia management orders have been created for the COVID IIP. The protocol should be employed with COVID+/PUI patients with severe persistent hyperglycemia not responding to aggressive titration of SC insulin dosing:
   a. One for use in critical care units (ALL hospitals in health system) if BG ≥ 200 mg/dL
   b. A second for use in non-critical care units (ONLY at Yale New Haven Hospital) if BG 300-350 mg/dL
COVID Monitoring My List

**Situation**
Updates are needed to the COVID-19 My List to standardize pharmacist monitoring alerts with the most recent COVID-19 treatment algorithm.

**Background**
COVID-19 positive patients require close monitoring of their medications, especially as many medication therapies being used in this patient population are high-risk medications. A COVID-19 My List was created in April to provide optimal monitoring for COVID-19 positive patients and provided actionable alerts to the pharmacist. At the time, hydroxychloroquine was the main therapy recommended in the COVID-19 treatment algorithm. However, due to evolving literature, remdesivir has now replaced hydroxychloroquine in the COVID-19 treatment algorithm.

**Assessment**
In order to optimize clinical monitoring for COVID positive patients, the My List COVID-19 alerts should be revised to reflect our standard medication therapy used for treatment.

**Recommendation**
Effective June 11th, 2020, the following changes will be made to the COVID-19 My List:

<table>
<thead>
<tr>
<th>Alerts Added</th>
<th>Alerts Removed</th>
<th>No Changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Patient on remdesivir therapy with no ALT obtained in the previous 24 hours</td>
<td>- Hydroxychloroquine expiring within 24 hours (only maintenance dose)</td>
<td>- Triglycerides &gt; 600 AND on propofol infusion (most recent value only)</td>
</tr>
<tr>
<td>- Patient on remdesivir therapy and ALT is greater than or equal to 5 times the upper limit of normal from the previous 24 hours</td>
<td>- QTC &gt; 500 (past 24 hours) + hydroxychloroquine</td>
<td>- On propofol infusion AND no triglycerides in the past 72 hours</td>
</tr>
<tr>
<td></td>
<td>- On lorazepam infusion AND no serum osmolality in 24 hours</td>
<td>- On lorazepam infusion AND no serum osmolality in 24 hours</td>
</tr>
</tbody>
</table>
COVID i-Vent Monitoring

**Situation**
There is not an easy way to track the number of pharmacist interventions/workload for COVID-19 positive patients.

**Background**
Pharmacists commonly use the Epic My List or i-Vents to document interventions and/or to monitor patient’s medication therapy. During to the COVID-19 pandemic, there is a crucial need to closely track pharmacist interventions to recognize trends and optimize decision support tools where needed.

**Assessment**
In order to optimize pharmacist intervention monitoring for COVID-19 positive patients, a new i-Vent type has been requested for pharmacist documentation.

**Recommendation**
It is recommended to create a COVID-19-specific pharmacist i-Vent type and associated subtypes that allow for documentation in this specific patient population. This will allow for easier data monitoring/abstraction and assessment of pharmacist workload as it relates to the care of COVID-19 patients.

For interventions made via the MyList, we can continue documenting in the MyList per our current guidelines, and pharmacists would not have to open an i-Vent in addition unless therapy was changed requiring one to capture that intervention. The proposed i-Vent is as follows with those subtypes marked by an asterisk (*) to auto-populate selection text within the documentation section:

<table>
<thead>
<tr>
<th>Type</th>
<th>Subtype</th>
<th>Auto-Populated Documentation Text</th>
</tr>
</thead>
<tbody>
<tr>
<td>COVID-19 Intervention/Optimization</td>
<td>Add ECG</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Add laboratory value*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Add new drug: stress ulcer prophylaxis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Add new drug: ventilator-acquired pneumonia prophylaxis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Add patient height</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Add patient weight</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Change drug/dose/formulation/frequency/route*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cluster laboratory data</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cluster medication administration times</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Concentrate infusion</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Drug information</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Drug monitoring</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Emergency department</td>
<td></td>
</tr>
<tr>
<td></td>
<td>MDI stewardship</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Optimize anticoagulation*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Optimize blood glucose management</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Optimize sedation/analgesia*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Add CRP</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Add CBC</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Add metabolic panel</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Add D-dimer</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Add PT/PTT</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Add fibrinogen</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Add procalcitonin</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Add magnesium level</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Add triglyceride level</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Add lipase</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Add osmolality</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Based on clinical response</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Based on weight</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Based on indication</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Due to shortage</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Adjust based on D-Dimer</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Adjust based on weight</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Adjust based on renal function</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Typical use (dose adjustments, etc.)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Adjusting antibiotic selection based on frequency of dosing</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Changing formulations based on access type</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Therapy that should be held</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Discontinue therapy</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Change monitoring parameters</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• (RASS, BIS)</td>
<td></td>
</tr>
</tbody>
</table>
# COVID Drug Monitoring Standing Order

## Purpose
The pharmacist may initiate standing orders for COVID positive patients or COVID PUI to reduce entry into patient’s rooms, and ensure appropriate drug monitoring.

## Order Type
Standing Order with Authentication.

## Population
Adult patients with confirmed or suspected COVID-19.

## Procedure
When a patient is assessed by the pharmacist for appropriate drug monitoring and drug concentration, based on this assessment, the role the pharmacist orders:

<table>
<thead>
<tr>
<th>ACTION</th>
<th>DESCRIPTION/CONDITION</th>
<th>RECOMMENDATION</th>
</tr>
</thead>
</table>
| **Height and Weight (NUR463)** | Pharmacist can place this order if the patient is on a medication which requires either parameter for drug dosing | 1. Pharmacist is to confirm that this order is not already in place  
2. Pharmacist can enter the order as a "Standing order: cosign required" |
| **Triglycerides (LAB134) & Lipase (LAB99)** | Pharmacist can order these labs if the patient is on a propofol drip and no triglycerides/lipases have been ordered. | 1. Pharmacist can enter the order as a "Standing order: cosign required" IF they are adding the lab unto an existing specimen or clustering the lab with existing lab draws  
2. If TG <600, the pharmacist can order baseline and standing q72h levels. If TG >600, the pharmacist should order TG to be drawn every 24 hours  
3. Any abnormal level will be discussed with the LIP |
| **Osmolality (LAB107)** | Pharmacist can place this order if the patient is on a lorazepam infusion and no serum osmolality has been ordered. | 1. Pharmacist can enter the order as a "Standing order: cosign required" IF they are adding the lab unto an existing specimen or clustering the lab with existing lab draws  
2. The pharmacist should order serum osmolality to be drawn every 24 hours  
3. The serum osmolality must be drawn at the same time as the BMP  
4. Any abnormal level will be discussed with the LIP |
| **Magnesium (LAB103)** | Pharmacist can place this order if the patient is on hydroxychloroquine and no magnesium has been ordered in last 24 hours | 1. Pharmacist can enter the order as a "Standing order: cosign required" IF they are adding the lab unto an existing specimen or clustering the lab with existing lab draws  
2. The pharmacist should order magnesium to be drawn every 24 hours  
3. Any abnormal level will be discussed with the LIP |
| **D-Dimer [LAB313]** | Pharmacist can place this order for patients with confirmed COVID-19 in whom no d-dimer lab has been ordered in 24 hours | 1. Pharmacist can enter the order as a "Standing order: cosign required" IF they are adding the lab unto an existing specimen or clustering the lab with existing lab draws  
2. Any abnormal level will be discussed with the LIP |
| **Concentrating infusion OR changing to a larger bag size for the following drugs:** | | 1. Pharmacist can enter the order as a "Standing order: cosign required" after consideration of inclusion/exclusion criteria in previous column  
2. Pharmacist will ensure that the dosing range (e.g., titratable vs non-titratable), fluid type (DSW vs NS), dosing weight, indication, and titration parameters (e.g., MAP goals, RASS goals, etc) remain the same between orders  
3. Pharmacist will communicate to the RN that the concentration/bag size have been changed and that the RN will need to change to correct concentration on the smart pump and replace the existing tubing (for changes in concentration only) |

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Updated 11/25/2020
| Liver Function Tests [LAB3218] | Pharmacist can place this order if the patient is on remdesivir and no liver function tests or comprehensive metabolic panel has been ordered in last 24 hours | 1. The pharmacist should order liver function tests to be drawn at baseline and every 24 hours  
2. Pharmacist can enter the order as a “Standing order: cosign required” IF they are adding the lab unto an existing specimen or clustering the lab with existing lab draws  
   Any abnormal level (i.e. AST/ALT ≥ 5 times ULN) will be discussed with the LIP |

**Documentation**

A standing order is placed by the pharmacist. Assessment for the standing order is documented by the pharmacist. The standing order is authenticated by a provider involved in the care of the patient.
Anticoagulation My List

<table>
<thead>
<tr>
<th>Situation</th>
</tr>
</thead>
<tbody>
<tr>
<td>The COVID-19 anticoagulation dosing guidelines were recently incorporated into the “Anticoagulation and Scoring” pharmacist My List.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Background</th>
</tr>
</thead>
<tbody>
<tr>
<td>COVID-19 positive patients may be at a higher risk of developing thrombotic complications. Due to high-risk nature of this condition, hematology created enoxaparin dosing guidelines to ensure that patients receive adequate dosing based on their risk factors. The following was previously incorporated into My List column:</td>
</tr>
</tbody>
</table>

1. If a D-Dimer is > 10 mg/L from within the past 24 hours, the pharmacist will receive an alert to review these patients and assess if they require a weight-based prophylactic dose of enoxaparin
2. If a patient’s creatinine clearance is < 30 mL/min and/or they are on RRT, the pharmacist will receive an alert to trigger an assessment and discussion with the primary team/hematology about what drug/dosing strategy should be used and to order an anti-Xa level if warranted

Since the creation of these alerts in the My List column, the anticoagulation guidelines have been further updated.

<table>
<thead>
<tr>
<th>Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Due to the changes to the anticoagulation guideline recommendations for the treatment of COVID-19 positive patients, further decision support is needed in the My List columns to prevent excessive flagging of alerts to pharmacists.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effective immediately, the “Anticoagulation and Scoring” My List rules have been updated.</td>
</tr>
</tbody>
</table>

- The alerts will NOT flag for patients on heparin infusions, bivalirudin infusions, and warfarin therapy
- The alerts will NOT flag for patients on DOACs as long as they are dosed appropriately
- The alerts will NOT flag for SQ heparin as long as it is dosed correctly based on BMI

1. If D-Dimer > 5, patient is COVID positive, and BMI > 40 or < 40, column will only alert if the enoxaparin dose is outside of the recommended dosing for COVID-19 positive patients
   a. **NOTE** This alert is based on the reason for use from the new enoxaparin order panel. If enoxaparin is ordered outside of this order panel, the column will flag an alert. The pharmacist should direct the provider to reorder through the enoxaparin order panel, which in turn will resolve the alert.
2. All patients who are COVID positive and are listed as being pregnant in the header will fire daily for pharmacist review

See [Adult Treatment Algorithm](#) - Anticoagulation Dosing Guidelines for further guidance.
Anticoagulation Order Panel

Situation
Anticoagulation dosing guidelines for VTE prophylaxis and treatment were added to the COVID Treatment Algorithm on 4/3/20.

Background
There is a growing literature about the coagulopathy of patients with COVID-19 infection. The general hematologic picture is that many patients with COVID-19 infection have some component of a coagulopathy that appears to be a consumptive coagulopathy consistent with disseminated intravascular coagulation (DIC), but with a prothrombotic phenotype. There are some laboratory and phenotypic differences from how we otherwise often think about DIC in sepsis. The international hematology community is uncertain how to most appropriately manage coagulopathy in COVID-19 infection except that it appears to have a prothrombotic phenotype that warrants vigilance in the absence of data to support standard intervention.

ASH and ISTH have issued interim guidance supporting baseline VTE prophylaxis with Enoxaparin. Based on the recommendations from our hematology service, YNHHS has added VTE prophylaxis dosing guidelines in COVID-19 patients that is extrapolated from the current available minimal evidence and surveying other hospitals across the nation.

Assessment
Additional provider order guidance and decision support is needed in order to facilitate order entry of the anticoagulation dosing guidelines for VTE prophylaxis and treatment in COVID-19 patients.

Recommendation
Effective immediately, Epic order screens have been updated to include a new order panel for decision support. See Adult Treatment Algorithm - Anticoagulation Dosing Guidelines for further guidance.

Appendix 1: Clinical Pearls for Anticoagulation in COVID-19 Patients
- If d-dimer decreases, after increasing to intermediate-dose VTE ppx, should we decrease anticoagulation dose accordingly?
  - At this time, we don’t know if a downtrending d-dimer warrants decreasing/dose adjusting back down to baseline VTE ppx dosing.
  - From a clinical assessment standpoint, would suggest keeping a patient on intermediate-dose and not dose adjusting based on d-dimer changes because the risk of VTE may still be present, unless patient is bleeding, platelet drop, or other clinical factors that would warrant easing up on the anticoagulation
- When should we escalate to VTE treatment (therapeutic anticoagulation)?
  - Confirmed VTE or high clinical suspicion
  - VTE can be confirmed by checking US, sudden changes in O2 sat not explained by other clinical finding of CXR finding, or if asymmetric UE/LE edema
- What if a patient is already on anticoagulation chronic therapy?
  - If a patient is already on anticoagulation for VTE or atrial fibrillation, therapeutic doses of anticoagulant therapy should continue but may need to be held if platelets < 50 or fibrinogen < 1.0 g/L (American Society of Hematology)
  - At this time, YNHHS hematology service is recommending to continue with enoxaparin with most patients in the event a procedure or surgery is needed (more so with hemodynamically unstable or critically ill patients). This is because reversing enoxaparin is less complex than if the patient were continued on DOACs.
- Duration of VTE ppx therapy: Is there guidance on how long a patient would stay on VTE prophylaxis or intermediate-dose VTE prophylaxis?
  - At this time, we don’t have enough information to recommend a duration of therapy but would assess all clinical factors.
- Discharge: What do we do at discharge?
  - The current recommendations from our hematology service specifies for inpatient use. We’re assuming that an infected patient with COVID-19 is sickest while inpatient thus at increased risk of clotting.
- VTE prophylaxis in COVID is evolving daily – more information will be provided as we learn more
**Situation**
There is a need to update the recommendations for anticoagulation in COVID-19 patients receiving convalescent plasma via expanded access.

**Background**
Convalescent plasma is an investigational therapy for the treatment of COVID-19 that is being utilized across YNHHS. Data on COVID-19 patients that have received convalescent plasma across the health system has been recently reviewed. Two thrombotic events have been identified in patients who received convalescent plasma at YNHHS. Both patients were receiving standard dose venous thromboembolism (VTE) prophylaxis.

**Assessment**
Although it is an unknown whether the thrombotic events were due to convalescent plasma, there is a need to re-assess the anticoagulation recommendations in these patients.

**Recommendation**
Based on recommendations from hematology, the ad hoc COVID-19 treatment team, and the primary investigators of convalescent plasma it is recommended that any patient receiving this investigational therapy receive, at minimum, intermediate dose prophylaxis anticoagulation regardless of d-dimer for 72 hours. After 72 hours the need for intermediate dose prophylaxis can be re-assessed based on d-dimer level and risk for VTE.

These recommendations will be incorporated into the next edition of the COVID-19 treatment algorithm and will be recommended by the study team when starting a patient on convalescent plasma therapy.
**Addition of Aspirin Therapy for COVID-19 Patients**

<table>
<thead>
<tr>
<th>Situation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Some hospitalized COVID patients have evidence of microthrombotic events associated with endothelial disruption which may be mediated in part by platelet over-activation.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Background</th>
</tr>
</thead>
<tbody>
<tr>
<td>COVID illness may predispose patients to arterial and venous micro/macro thrombotic disease.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial analysis of thromboelastography in COVID positive patients reveals a hypercoagulopathy state that is dissimilar to disseminated intravascular coagulation. Markers of platelet hyperfunction and excess von Willebrand factor indicative of endothelial cell activation have raised the question as to whether the addition of platelet inhibitors to the current anticoagulation pathways for COVID patients would be appropriate.</td>
</tr>
</tbody>
</table>

An in-house analysis has suggested that the addition of aspirin does not significantly increase bleeding risk although its efficacy is unclear. Given its low-risk safety profile, it is reasonable to consider adding aspirin as an antiplatelet agent to treatment of hospitalized COVID patients.

<table>
<thead>
<tr>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>All COVID positive patients should receive aspirin 81 mg daily unless contraindicated while hospitalized. Refer to the <a href="#">YNHHS Treatment Algorithm</a> for details.</td>
</tr>
</tbody>
</table>
Sedatives and Paralytics Titration Goals and Parameters

**Situation**
There is a need to update the titration parameters and titration goals of sedatives and paralytics on 4/29/20.

**Background**
The COVID-19 pandemic resulted in a surge in critically ill patients. Several of these patients require deep levels of sedation and paralysis to optimize their respiratory status. Bispectral index (BIS) monitors are usually used to monitor patient’s level of sedation while receiving continuous infusion of neuromuscular blocking agents. Additionally, a peripheral nerve stimulator (PNS) is used to assess the level of paralysis. Currently, there is a shortage in BIS monitors and PNS stimulators to meet the patient care demands.

**Assessment**
In the setting of this shortage there is a need to provide guidance to nursing on monitoring patients’ level of sedation and paralysis when BIS monitors and PNS stimulators are not available.

**Recommendation**
In order to provide guidance to nursing on monitoring patients’ level of sedation and paralysis during the shortage in BIS monitors and PNS stimulators, Epic records for sedatives and paralytics will be updated as follows:

- Continuous infusion sedatives (ketamine, propofol, lorazepam, midazolam)
  - Administration instructions will be updated to include “If paralytic infusion is initiated, contact provider to adjust sedative titration goal parameter to option: BIS 40-60 (if available) or absence of signs of under-sedation (HR > 15% baseline, HTN, tearing, diaphoresis)”.
  - Titration goal parameters will be updated to include “BIS 40-60 (if available) or absence of signs of under-sedation (HR > 15% baseline, HTN, tearing, diaphoresis)”.

- Continuous infusion neuromuscular blocking agents (cisatracurium, vecuronium, rocuronium)
  - Update titration goal parameters to “Maintain 1-2 twitches with train-of-four or patient RR matches vent set RR”.

Updated 11/25/2020
# Metered Dose Inhaler Use (MDI) and Stewardship

## Situation
To limit the spread of the novel coronavirus (COVID-19) from person-to-person, infection control precautions are needed, which includes limiting the use of nebulized medications. With increasing presentations of respiratory symptoms, metered dose inhalers (MDIs) also need to be conserved.

## Background
Respiratory treatments are considered to be a potential factor for the nosocomial transmission of COVID-19 due to aerosolization of droplet nuclei. Larger aerosol particles may stimulate both patients' and bystanders' cough which may increase the risk of transmission. For this reason, nebulization use should be avoided in COVID-19 positive patients or COVID-19 rule out (R/O) patients.

## Assessment
In order to preserve MDI supplies, additional precautions are warranted.

## Recommendation
- In response to outbreak, for COVID-19 positive or COVID-19 R/O patients only, all required nebulized therapy should be changed to MDI products only to reduce the risk of transmission.
- Currently, all emergency department patients are receiving MDI therapy if they are not in a negative pressure room at some delivery networks.
  - Please ensure the MDI travels with the patient to their new location in the hospital so supply is not wasted
  - Follow infection prevention guidelines for handling of MDIs in these situations
  - Ensure that we are not dispensing a second inhaler when patient arrives to floor or ICU
- Best Practice Alerts (BPAs) have been created and trigger for patients that are COVID-19 positive or COVID-19 R/O for the most common nebulized medications advising prescribers to use MDI therapy instead of
  - Albuterol nebs
  - Albuterol/ipratropium nebs
  - Ipratropium nebs
  - Budesonide nebs (currently in process)
- Nebulizers may have to be used in certain clinical scenarios when patients are COVID-19 positive or COVID-19 R/O. If a nebulization must be used, the patient should be in a negative pressure room as that may lower the risk of nosocomial transmission.
  - When a patient is in respiratory distress
  - When a patient has FAILED MDI therapy
  - Remain in respiratory distress after MDI therapy (such as therapy at home)
  - Unable to use MDI therapy with spacer
  - When a patient has acute bronchospasm (asthma, COPD exacerbations)
- Epic ordering screens for nebulized hypertonic saline 3% have been turned off as this medication may induce a cough and will be restricted to pharmacist-entry only.
- We are already experiencing supply issues with MDIs. To conserve MDIs for patients that are COVID-19 positive or COVID-19 R/O please adhere to the following:
  - Fluticasone (Flovent®) inhalers are restricted to use in pediatric patients < 5 years old.
  - Ipratropium HFA screens will be turned off for adults and restricted to pharmacist-entry only for patients with acute bronchospasm if albuterol therapy has failed after the first dose.
Nebulized Prostacyclin Medications

**Situation**
In an effort to limit the potential spread of COVID-19, the institution is working towards limiting the use of nebulized medications and/or implementing safeguards where appropriate.

**Background**
Expert consensus guidelines have identified the nebulization/aerosolization of medications as high-risk factors for nosocomial transmission of infection. Actions are being put into place in order to limit this nosocomial spread of COVID-19 such as switching nebulizer treatments to meter-dose inhalers and limiting the frequency of visits that Respiratory therapy into COVID-19 positive patient rooms to no more than every 8 hours. In addition, the pulmonary arterial hypertension patient population is at higher risk of serious illness from COVID-19 and faces unique medication challenges due to the administration of their nebulized medications.

**Assessment**
Use of nebulized medications in patients with COVID-19 can increase the risk of disease transmission by generating aerosol particles which can carry viruses/bacteria and disperse them into the environment.

**Recommendation**
In response to the COVID-19 outbreak, the following changes are recommended for all patients on nebulized/aerosolized prostacyclin medications who are COVID-19 positive or COVID-19 Person Under Investigation (COVIDPUI):

<table>
<thead>
<tr>
<th>Medication</th>
<th>Concern</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AEROSOLIZED epoprostenol</strong></td>
<td>Respiratory would need to change filter between the Aerogen pump &amp; the ventilator q4h* which exposes RT to infection.</td>
<td>• In COVID (+) or COVID R/O patients, this therapy will be allowed ONLY in those who are mechanically ventilated. • At this time, no other restrictions will be placed on the therapy but this recommendation is subject to change if there is increased demand that cannot be met with supply.</td>
</tr>
<tr>
<td></td>
<td>There is concern that we may experience a shortage of pumps &amp; Aerogen devices should we see a surge in patient volumes.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>*q4h filter changes applies to YSC and SRC only. BH changes the filter q24h.</td>
<td></td>
</tr>
</tbody>
</table>

**The section BELOW applies to ANY patient located within the MICUs at YSC, SRC, and BH**

*NOTE: aerosolized epoprostenol is NOT exclusive to PAH patients. This therapy is available for any patient with refractory hypoxemic respiratory failure.*

**The section BELOW applies to PULMONARY ARTERIAL HYPERTENSION (PAH) patients ONLY**

*NOTE: PAH patients are geographically restricted to YSC only*

<table>
<thead>
<tr>
<th>Self-Administered Therapy</th>
<th>Treprostinil (Tyvaso™) OR iloprost (Ventavis™) administered via patient’s own nebulizer device</th>
<th>Patients who leave their respective nebulization devices at home typically receive these medications in-house as nebulizations administered by RT which increases risk of transmitting infection</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>There is limited potential for aerosolization of the respective medication into the environment</td>
<td>In order to receive their respective nebulized treprostinil or iloprost the patient MUST meet the following criteria: • Be located in a negative pressure room • The medication must be given via a filtered nebulizer.</td>
</tr>
</tbody>
</table>

*NOTE: when starting the nebulization, the provider/RT must leave the room immediately after starting therapy and should avoid returning until one hour after the nebulization is complete.*
Adult Respiratory Care Practice Guidelines for COVID-19
POSITIVE or PUI patients

These practice guidelines were structured in order to optimize the safety practices around respiratory treatments and devices in COVID POSITIVE or Persons Under Investigation (PUI) patients.

Clustered Care
• All care should be coordinated with nursing; including treatments, therapies and ventilator-patient assessments.

Transport through the hospital
• Patients on nasal cannula must wear a face mask covering their nose and mouth.
• Prior to transport on HFNC, nasal prongs should be checked for good fit and minimal leak. Face mask should be worn by the patient over the HFNC.
• Patients on NIV must be transitioned to High Flow Nasal Cannula (HFNC), 100% NRB or be intubated for transport.
• An HME filter can be placed on the tracheostomy tube directly, allowing for venturi masks during transport or ambulation.

Nebulized Medication
• MDI treatments are preferred. May use higher doses (i.e. 6-12 puffs) with spacer.
• Intubated patients may receive small volume nebulizers (SVN) and nebulized epoprostenol via Aerogen delivery system.
• Non-intubated patients should avoid use of SVN (bronchodilators, corticosteroids). Permissible when strongly clinically necessary or patient fails MDI. These may be administered via filtered nebulizer and should be self-administered when patient is compliant. HCP should maintain arms length when initiating nebulizer and minimize time in the room during administration.

Oxygen Nasal Cannula or Oxymizer
• Nasal Cannula / Oxymizer flows should be limited to 5 LPM or less. Avoid using aerosol/Venturi masks.
• Patients requiring higher FiO2 should be transitioned to an alternate oxygen (100% NRB, HFNC, NIV, intubate).
• Patients that desaturate with movement may benefit from pre-oxygenation with 100% NRB PRN for 5-10 minutes before movement. Order 100% NRB PRN pre-oxygenate for activity.

THE FOLLOWING are HIGH RISK AEROSOL GENERATING PROCEDURES (HR-AGP).
The following precautions should be taken in order to minimize the risk of HCP transmission.
• Please refer to accompanying chart for recommended location and PPE for respective AGP.

High Flow Nasal Cannula (HFNC)
• Maximum setting is 50LPM and 100% FiO2.
• Patients that desaturate with movement may benefit from pre-oxygenation with 100% NRB PRN for 5-10 minutes before movement. Order 100% NRB PRN pre-oxygenate for activity. Continuous use of 100% NRB simultaneously with HFNC 100% 50LPM is an indication to evaluate for intubation.
• Nasal prongs must be well seated in the nares with minimal leak. If more than minimal leaking occurs, must use alternate oxygen (100% NRB, or intubate).

Non-Invasive Ventilation (NIV=BIPAP or CPAP)
• Discouraged unless clinically necessary due to risk for HCP.
• Acute Hypercarbic Respiratory Failure - if PCO2 > 65 or >10 mmHg from baseline, consider intubation
• Acute Hypoxemic Respiratory Failure – Mild to Moderate ARDS with PaO2/FiO2 >150, otherwise consider intubation
• Maximum Settings: IPAP 12 cm H2O and EPAP 8 cm H2O.
• All patients on BIPAP are required to have an ABG AND CLINICAL ASSESSMENT within 2 hrs to determine either continuance of NIV or advancement to Intubation.
• Continuance of NIV is defined by Sat >93% and improved RR or pH and decreased work of breathing.

1 Face Mask refers to PPE
Rev 4/23/2020

Updated 11/25/2020
● Chronic Respiratory Failure on NIV at home.
   ● If COVID Positive / PUI initiate NIV at home settings only until test results. If pt fails home settings, intubate.
● Obstructive Sleep Apnea/Obesity Hypoventilation Syndrome on NIV QHS
   ● ABG on admission.
      ● If PCO2 <45, 2L NC can be given QHS and ABG will be done in the morning.
      ● If PCO2 >45, NIV QHS can be ordered at no more than maximum settings (see above).
● All NIV will be set up with a filtered circuit on the expire valve.
● Good mask seal must be ensured. Leaks >20% should be reported to respiratory supervisor and provider.

Suctioning and Physiotherapy
● Chest PT is restricted to patients with strong clinical necessity. HCP should maintain airms length when administering and minimize time in the room afterwards.
● Nasotracheal/open suctioning should be avoided. Failure to manage secretions is reason for intubation.

Tracheostomy tube
● Chronic respiratory failure on a home ventilator. Most home ventilators do NOT allow for filters on the exhale valve resulting in large exposure to aerosolized virus. All patients are preferentially placed on hospital ventilators (with filter).
● An HME filter can be placed on the tracheostomy tube directly, allowing for venturi masks during transport or ambulation.
● A closed T-piece system can be attached to the tracheostomy tube to provide aerosol oxygenation/humidification with an in-line suction catheter and appropriate filters.
● Suctioning should be done in-line. Open suctioning results in aerosolization of virus.
● A speaking valve (PMV) on the tracheostomy tube is aerosolizing. It should be covered with a paper mask.

Exubation
● Do NOT stand directly in front of the patient. Position yourself optimally to avoid path of coughing.
● Immediately after disposing of dirty materials the outside gloves should be removed, inside out.
● Patients transitioning to comfort measure may be extubated. The order in which life sustaining measures are discontinued (vasopressors, hemodialysis, mechanical ventilation, etc) is left to the discretion of the attending provider.

References:


Please contact Respiratory Care or ICU leadership with any questions related to these practice guidelines.

Face Mask refers to PPE
Rev 4/23/2020

Updated 11/25/2020
# COVID-19 Guidelines for Aerosol Generating Procedures for COVID POSITIVE / PUI patients

<table>
<thead>
<tr>
<th>Aerosol Generating Procedures (AGP) for COVID POSITIVE/PUI</th>
<th>Regular Pressure with COVID Isolation</th>
<th>Staff PPE</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasal Cannula</td>
<td>Permitted*</td>
<td>Respirator, face shield/goggles, isolation gown and gloves</td>
<td>*If not in negative pressure room, ask pt to wear face mask when HCP in the room</td>
</tr>
<tr>
<td>Nebulized Medications (use limited to clinical necessity)</td>
<td>Permitted*</td>
<td>Isolation gown and gloves</td>
<td>*Door is closed. PUI always in room by themselves (see neb notes)</td>
</tr>
<tr>
<td>Sputum induction</td>
<td>Yes</td>
<td>AVOID</td>
<td></td>
</tr>
<tr>
<td>High Flow Nasal Cannula</td>
<td>Yes</td>
<td>Permitted*</td>
<td>Respirator, face shield/goggles, isolation gown and gloves</td>
</tr>
<tr>
<td>High Flow Mask</td>
<td>Yes</td>
<td>AVOID</td>
<td></td>
</tr>
<tr>
<td>Non-Invasive Ventilation (BiPAP/CPAP)</td>
<td>Strongly recommended</td>
<td>Respirator, face shield/goggles, isolation gown and gloves</td>
<td>Discouraged unless clinically necessary</td>
</tr>
<tr>
<td>Nasopharyngeal Specimen collection, Aspiration, Washing</td>
<td>Recommended if available</td>
<td>Not recommended</td>
<td></td>
</tr>
<tr>
<td>Feeding Tube Placement</td>
<td>Recommended if available</td>
<td>Permitted</td>
<td></td>
</tr>
<tr>
<td>Open Suctioning</td>
<td>Recommended if available</td>
<td>Permitted</td>
<td></td>
</tr>
<tr>
<td>CPR</td>
<td>Recommended if available</td>
<td>Permitted</td>
<td></td>
</tr>
<tr>
<td>Bag Mask Ventilation</td>
<td>Recommended if available</td>
<td>Permitted</td>
<td></td>
</tr>
<tr>
<td>Intubation</td>
<td>Recommended if available</td>
<td>Permitted</td>
<td>Procedure gown, double gloves, bouffant/balsacava, footcover</td>
</tr>
<tr>
<td>Exubilation</td>
<td>Recommended if available</td>
<td>Permitted</td>
<td></td>
</tr>
<tr>
<td>Bronchoscopy</td>
<td>Yes</td>
<td>AVOID</td>
<td></td>
</tr>
<tr>
<td>GI tract Endoscopy</td>
<td>Strongly Recommended if available</td>
<td>Not recommended</td>
<td>Respirator, face shield/goggles, bouffant/balsacava, procedure gown, double gloves and footcover</td>
</tr>
<tr>
<td>Chronic Tracheostomy</td>
<td>Recommended if available</td>
<td>Permitted*</td>
<td>Respirator, face shield/goggles, isolation gown and gloves</td>
</tr>
<tr>
<td>Chest Physiotherapy</td>
<td>Strongly Recommended if available</td>
<td>Not recommended</td>
<td>*RT to place closed filtered system</td>
</tr>
</tbody>
</table>

1 High Risk 2 Isolation gown = semi-fluid resistant 3 Procedure gown = fluid resistant 4 PPE Face Mask

* Note: if SLO pt is in a shared room and must receive rab-emergently - Draw the curtain and isolate as much as possible.

* Face Mask refers to PPE

Rev 4/23/2020

Updated 11/25/2020
Adult Respiratory Care Practice Guidelines for COVID-19 NEGATIVE or NOT SUSPECTED patients

These guidelines were structured to give health care providers (HCP) guidance for safe practices when administering respiratory treatments or devices in patients not known to be infected with COVID-19.

COVID-19 STATUS
• COVID-19 testing is recommended within 24hrs of INITIATION of the following devices, assuming that a new requirement signals a change in respiratory status that may be consistent with COVID-19 infection.
• Recommend COVID-19 testing only once for intermittent or repeated treatments/devices upon INITIATION of that treatment/device.

Nebulized Medications
• A curtain can be drawn between 2 patients sharing a room in order to create space for respiratory distancing.
• MDI shortages currently dictate that nebulized bronchodilators, anticholinergics and inhaled corticosteroids be used in patients not known to be infected with COVID-19. Nevertheless, these medications should be limited to patients with clinical necessity, as in bronchospasm from asthma or COPD.
• Nebulized bronchodilators and anticholinergics should not be ordered for asymptomatic patients.

Oxygen Nasal Cannula
• Patients wearing nasal cannula are asked to wear a face mask¹ when HCP are present.
• HCP should maintain arms length whenever possible.
• A curtain can be drawn between 2 patients sharing a room in order to create space for respiratory distancing.

High Flow Nasal Cannula (HFNC)
• Nasal prongs should be placed, evaluated for good fit and face mask¹ placed prior to starting flow.
• Nasal prongs must be well seated in the nares with minimal leak.
• Patients wearing HFNC are asked to wear a face mask¹ when HCP are present.
• HCP should maintain arms length whenever possible.
• A curtain can be drawn between 2 patients sharing a room in order to create space for respiratory distancing.

Non-Invasive Ventilation (NIV=BIPAP or CPAP)
• Mask interface should be placed and evaluated for good fit prior to starting NIV machine.
• Good mask seal must be ensured. Leaks >20% should be reported to respiratory supervisor and provider.
• HCP should keep their face and body to the side of the patient’s mouth or nose to avoid direct alignment to the path of coughing.
• A curtain can be drawn between 2 patients sharing a room in order to create space for respiratory distancing.

Suctioning / Physiotherapy
• Chest PT is limited to patients with clinical necessity. HCP should maintain arms length when administering.
• Nasotracheal/open suctioning - HCP should maintain arms length when administering and keep their face and body to the side of the patient’s mouth or nose to avoid direct alignment to the path of coughing.

Tracheostomy tube
• Chronic respiratory failure on a home ventilator. All patients are preferentially placed on hospital ventilators (with filter on exhale port).
• Standard humidification delivery system should be maintained (per institution).
• An HME filter can be placed on the tracheostomy tube directly, allowing for venturi masks during transport.
• During suctioning, HCP should maintain arms length when administering and keep their face and body to the side of the patient’s mouth and trach to avoid direct alignment to the path of coughing.

¹ Face Mask refers to PPE

Updated 11/25/2020
Exubation

- Do NOT stand directly in front of the patient. Position yourself optimally to avoid path of coughing.
- Immediately after disposing of dirty materials the outside gloves should be removed, inside out.
- Patients transitioning to comfort measure may be exubated. The order in which life sustaining measures are discontinued (vasopressors, hemodialysis, mechanical ventilation, etc) is left to the discretion of the attending provider.

References:


Please contact Respiratory Care or Infection Prevention leadership with any questions related to these practice guidelines.
## Aerosol Generating Procedures (AGP) for Covid NEGATIVE/ NOT SUSPECTED Patients

AGP should not be withheld or delayed by COVID testing. Protective measures have been provided to optimize safety during testing period.

<table>
<thead>
<tr>
<th>Device / Treatment</th>
<th>HR(^1) AGP?</th>
<th>Negative Pressure</th>
<th>Regular Pressure</th>
<th>Mask</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasal Cannula</td>
<td>No</td>
<td>No</td>
<td>In a room by themselves*</td>
<td>Face mask(^*) and standard precautions</td>
<td></td>
</tr>
<tr>
<td>High Flow Nasal Cannula</td>
<td>Yes</td>
<td>No</td>
<td></td>
<td></td>
<td>Patients are asked to wear a face mask(^*) when HCP are in the room. * If not in a room by themselves, recommend COVID testing within 24 hrs of INITIATION. Curtain should be drawn between 2 patients. * If not in a room by themselves, recommend COVID testing within 24 hrs of INITIATION for intermittent treatments/device, only one time recommended). Curtain should be drawn between 2 patients. Ask pt wear paper mask over trach when HCF in the room. * If repeated suctioning anticipated AND not in a room by themselves, pt should be COVID tested negative within 24 hrs of INITIATION and curtain drawn between 2 patients. * If pt is not in a room by themselves, draw the curtain.</td>
</tr>
<tr>
<td>Nebulized Medications (use only for strong clinical necessity)</td>
<td>No</td>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High Flow Mask</td>
<td>Yes</td>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Invasive Ventilation (BIPAP/CPAP)</td>
<td>Yes</td>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chest Physiotherapy</td>
<td>Yes</td>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic Tracheostomy</td>
<td>Yes</td>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Open Suctioning</td>
<td>Yes</td>
<td>No</td>
<td>In a room by themselves*</td>
<td>Respirator, face shield/goggles, isolation gown and gloves</td>
<td></td>
</tr>
<tr>
<td>Exstubation</td>
<td>Yes</td>
<td>No</td>
<td>In a room by themselves*</td>
<td>Respirator, face shield/goggles, isolation gown and gloves</td>
<td></td>
</tr>
<tr>
<td>Sputum Induction</td>
<td>Yes</td>
<td>Strongly Recommended</td>
<td>Not recommended</td>
<td>Respirator, face shield/goggles, isolation gown and gloves</td>
<td></td>
</tr>
<tr>
<td>Nasopharyngeal Specimen collection, Aspiration, Washing</td>
<td>Yes</td>
<td>No</td>
<td>In a room by themselves*</td>
<td>Respirator, face shield/goggles, isolation gown and gloves</td>
<td></td>
</tr>
<tr>
<td>Feeding tube placement</td>
<td>Yes</td>
<td>No</td>
<td></td>
<td></td>
<td>* If pt is not in a room by themselves, draw the curtain between 2 patients.</td>
</tr>
<tr>
<td>CPR</td>
<td>Yes</td>
<td>No</td>
<td>Isolate as much as possible</td>
<td>Respirator, face shield/goggles, bouffant/balacava, procedure gown, double gloves and footcover</td>
<td></td>
</tr>
<tr>
<td>Bag Mask Ventilation</td>
<td>Yes</td>
<td>No</td>
<td>Isolate as much as possible</td>
<td>Respirator, face shield/goggles, bouffant/balacava, procedure gown, double gloves and footcover</td>
<td></td>
</tr>
<tr>
<td>Intubation</td>
<td>Yes</td>
<td>No</td>
<td>Isolate as much as possible</td>
<td>Respirator, face shield/goggles, bouffant/balacava, procedure gown, double gloves and footcover</td>
<td></td>
</tr>
<tr>
<td>Exstubation</td>
<td>Yes</td>
<td>No</td>
<td>In a room by themselves*</td>
<td>Respirator, face shield/goggles, bouffant/balacava, procedure gown, double gloves and footcover</td>
<td></td>
</tr>
<tr>
<td>Bronchoscopy</td>
<td>Yes</td>
<td>Strongly Recommended</td>
<td>In a room by themselves*</td>
<td>Respirator, face shield/goggles, bouffant/balacava, procedure gown, double gloves and footcover</td>
<td></td>
</tr>
<tr>
<td>GI tract Endoscopy</td>
<td>Yes</td>
<td>Strongly Recommended</td>
<td>In a room by themselves*</td>
<td>Respirator, face shield/goggles, bouffant/balacava, procedure gown, double gloves and footcover</td>
<td></td>
</tr>
</tbody>
</table>

\(^1\) High Risk  \(^2\) Isolation gown = Semi-fluid resistant  \(^3\) Procedure gown = fluid resistant  \(^*\) PPE Face Mask

Updated 11/25/2020
Standing Order for Converting Epinephrine injection as First-line for Respiratory Distress during Hypersensitivity Reactions

Standing Order, YNHHS

Original Date Approved/Date Effective: May 2020 during COVID pandemic
Date Reviewed/Revised: NEW
Approved by: SIM Respiratory Care Action Team on 05/1/2020

Purpose:
During COVID-19 pandemic, pharmacists may initiate standing order for converting epinephrine injection as first-line emergency medications to manage symptoms of respiratory distress resulting from hypersensitivity reactions (HSRs) or infusion-related reactions (IRRs).

Albuterol nebulization and epinephrine injection are part of the emergency medications used to manage symptoms of respiratory distress resulting from HSRs/IRRs. Currently, the albuterol nebulization is first-line for bronchospasm, wheezing or shortness of breath, and epinephrine injection is second-line if no improvement after albuterol.

In accordance with the YNHHS COVID-19 respiratory protection policies, nebulized medication administration can increase the risk of nosocomial transmission of the virus in positive, suspected, or asymptomatic COVID patients. In addition, HSRs/IRRs can happen in shared treatment areas where PPE may not be readily available for administering albuterol nebulization. Due to these considerations, YNHH Immunology/Allergy experts recommend using epinephrine injection as first-line for symptoms of respiratory distress when HSRs/IRRs occur during COVID pandemic.

Order Type
Standing Order, co-sign required.

Population:
Patients presenting with symptoms of respiratory distress resulting from HSRs/IRRs who need immediate intervention.

Procedure:
When order is released by nurses from therapy plans, treatment plans, or apheresis plans, a best practice advisory (BPA) will fire to notify nurses:

Updated 11/25/2020
After emergency medication orders are released, pharmacists will
1) discontinue the albuterol nebulization order
2) reject/reorder to modify the epinephrine injection order PRN comment field as follows:
   • For adults:
     o Epinephrine 0.3mg (Erx 40811049), intramuscular, every 15 minutes PRN, first-line for bronchospasm, wheezing, shortness of breath, decrease peak expiratory flow or hypoxia (O2 Sat < 90%). Repeat x 1 if absence of clinical improvement. For 2 doses.
   • For Pediatrics:
     o Epinephrine weight-base dosing (Erx 40811049), intramuscular, every 15 minutes PRN, first-line for bronchospasm, wheezing, shortness of breath, decrease peak expiratory flow or hypoxia (O2 Sat < 90%). Repeat x 1 if absence of clinical improvement. For 2 doses.

Documentation:
A standing order is placed by the pharmacist. The standing order is authenticated by the provider who initiated the therapy or treatment plan or the provider who signed the order.

National Guideline/Evidence for Practice:
**Drug Shortage: Sedatives, Analgesics, and Paralytics Alternatives**

**Situation**
There is a need to provide guidance on currently available and alternative therapies for sedation, analgesia and paralysis.

**Background**
As a result of the increase in volume of COVID-19 critically ill patients, there is a nationwide shortage in commonly used sedatives, analgesics and paralytics. Several alternative medications have been acquired to meet the increased demand for these therapies. Additionally, there is an ongoing expansion of critical care units and familiarizing staff with these newly added agents is warranted.

**Assessment**
There is a need for an alternative therapy guide to familiarize clinicians with available therapies for sedation, analgesia, and paralysis.

**Recommendation**
The alternative drug therapy guide below will provide guidance to clinicians on existing and alternative therapies.

<table>
<thead>
<tr>
<th>Sedatives, Analgesics, Neuromuscular Blocking Agents – Alternative Drug Shortage Guide</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Drug supply is inconsistent and changes frequently, alternative therapies will be guided based on drug availability</strong></td>
</tr>
</tbody>
</table>

**ANALGESICS**

- **Analgesia Management** (current inventory may determine selection)
  - Preferred: Morphine, fentanyl (preferred in AKI, CKD, and RRT)
  - Alternative: Hydromorphone (continuous infusion) - pharmacist order entry (patients with high opioid requirements; receiving 10 mg IV morphine per hour for at least 2 hours)
  - Remifentanil - pharmacist order entry
  - Ketamine - pharmacist order entry (patient with adverse reaction to hydromorphone and when remifentanil not available)
  - Adjunct therapy: Enteral acetaminophen, tramadol, gabapentin, oxycodeone, methadone

**SEDATIVES**

- **Sedation Management** (optimize pain management, current inventory may determine selection)
  - Preferred: Dexmedetomidine (not for deep level of sedation)
  - Propofol
  - Alternative: Midazolam (use with caution in hepatic and renal dysfunction)
    - Ketamine - pharmacist order entry, third-line agent, restricted to the following:
      - Escalating doses or contraindication to propofol (≥65 mcg/kg/min or TG >600 mg/dl)
      - Escalating doses to midazolam/lorazepam (≥10mg/hr) or contraindication to midazolam (cirrhosis, AST/ALT >5xULN) and lorazepam (Osmol gap >10 mOsm/kg)
  - Critical shortage: Lorazepam (use with caution in hepatic and renal dysfunction)
  - Adjunct therapy: to lower sedation requirements; phenobarbital, enteral donidine, atypical antipsychotic (quetiapine, olanzapine)

**PARALYRICS**

- **Neuromuscular blocking agents continuous infusion** (adequate sedation and analgesia required prior to and during paralysis, current inventory may determine selection)
  - Preferred: Rocuronium
  - Alternative: Vecuronium

- **Neuromuscular blocking agents for rapid sequence intubation** current inventory may determine selection
  - Preferred: Succinylcholine
  - Alternative: Rocuronium

*AKI: acute kidney injury, CKD: chronic kidney disease (GFR <30 mL/min), RRT: renal replacement therapy, TG: serum triglyceride (mg/dL), ULD: upper limit of normal*
<table>
<thead>
<tr>
<th>Drug</th>
<th>Mechanism of action</th>
<th>Dosing recommendation</th>
<th>Side effects and considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine 100 mg/100 mL (1 mg/mL)</td>
<td>Opioid (mu)-receptor agonist</td>
<td>MD: 1 -10 mg/hr&lt;br&gt;Titrating by: 1 mg/hr&lt;br&gt;Frequency: No more than every 15 minutes&lt;br&gt;Maximum dose: 10 mg/hr&lt;br&gt;IV Bolus: 2-4 mg IV q 4 hr PRN or scheduled</td>
<td>Hypotension and bradycardia can occur due to histamine release.&lt;br&gt;Avoid renal dysfunction due to accumulation of active metabolite. Use with caution in hepatic dysfunction. Can cause respiratory depression, CNS depression, constipation, and ileus.</td>
</tr>
<tr>
<td>Hydromorphone 40 mg/100 mL (0.4 mg/mL)</td>
<td>Opioid (mu)-receptor agonist</td>
<td>MD: 0.2 – 5 mg/hr&lt;br&gt;Titrating by: 0.2 mg/hr&lt;br&gt;Frequency: No more than every 30 minutes&lt;br&gt;Maximum Dose: 5 mg/hr&lt;br&gt;IV Bolus: 0.5 – 1 mg IV q 2 hr PRN or scheduled</td>
<td>Hydromorphone is 5 – 7 times MORE POTENT than morphine.&lt;br&gt;Use lower doses in opioid-naive patients.&lt;br&gt;Use with caution in hepatic dysfunction. Can cause respiratory depression, CNS depression, constipation, and ileus.</td>
</tr>
<tr>
<td>Remifentanil 5000 mcg/100 mL (50 mcg/mL)</td>
<td>Inhibits alpha 2-delta subunit of voltage-gated calcium channels → reduce neuronal hyperexcitability</td>
<td>MD: 0.5 – 12.5 mcg/kg/hr&lt;br&gt;Titrating by: 1.5 mcg/kg/hr&lt;br&gt;Frequency: No more than every 5 minutes&lt;br&gt;Maximum dose: 12.5 mcg/kg/hr&lt;br&gt;Use actual body weight. Use ideal body weight (IBW) if patient's actual weight is &gt;130% of IBW&lt;br&gt;IV Bolus: 25 – 100 mcg every 30 min PRN</td>
<td>Monitor for opiate withdrawal symptoms for 24 hours after discontinuing Remifentanil. Consider x1 dose of morphine/hydromorphone injection prior to remifentanil infusion discontinuation. Can cause chest wall rigidity. Drug clearance occurs by blood and tissue esterases. Can cause respiratory depression, CNS depression, constipation, and ileus.</td>
</tr>
</tbody>
</table>

**ANALGESIA ADJUNCT THERAPY**<br>(consider adjunct therapy to lower continuous infusion analgesia requirements)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mechanism of action</th>
<th>Dosing recommendation</th>
<th>Additional Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxycodone</td>
<td>Opioid (mu)-receptor agonist</td>
<td>PO: 2.5 – 10 mg PO q 4 hr PRN or scheduled</td>
<td>Avoid in patients with seizure disorder. Associated with serotonin syndrome. Hepatically metabolized to active metabolite O-desmethyltramadol that is renally eliminated. Requires dose adjustment in renal failure.</td>
</tr>
<tr>
<td>Tramadol</td>
<td>Opioid (mu)-receptor agonist, inhibit norepinephrine and serotonin reuptake, and NMDA receptor antagonist</td>
<td>PO: 25 – 100 mg PO q 6 hr&lt;br&gt;Maximum dose: 400 mg/day</td>
<td>Preferred therapeutic option for neuropathic pain. Adjust dose based on renal function.</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>Inhibits alpha 2-delta subunit of voltage-gated calcium channels → reduce neuronal hyperexcitability</td>
<td>PO: 300 mg – 1200 mg three times daily</td>
<td></td>
</tr>
<tr>
<td>Methadone</td>
<td>Mu-receptor agonist, NMDA-receptor antagonist</td>
<td>PO: 5 – 10 mg PO q 8 – 12 hr scheduled</td>
<td>Very long half-life (up to 60 hours). Dose-dependent QTc prolongation.</td>
</tr>
</tbody>
</table>
## Sedatives

### Continuous infusion for mechanically ventilated patients, optimize pain management

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose Formulation</th>
<th>Administration</th>
<th>Adverse Effects</th>
<th>Special Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Propofol</strong></td>
<td>1000 mg in 100 mL (10 mg/mL)</td>
<td>LD: Not recommended outside RSI MD: 5-80 mcg/kg/min Start: 5 mcg/kg/min Titr: by 5 mcg/kg/min Frequency: No more than every 5 minutes Maximum Dose: 80 mcg/kg/min</td>
<td>Bolus and rapid dose titration can cause cardiac and respiratory depression. Propofol-related infusion syndrome (PRIS) at doses &gt;65 mcg/kg/min for &gt;48 hours. Tubing should be changed every 12 hours. Avoid in patient allergic to egg or soy products.</td>
<td></td>
</tr>
<tr>
<td><strong>Midazolam</strong></td>
<td>50 mg/50 mL NS (1 mg/mL)</td>
<td>LD: 0.5-1 mg MD: 0.5-20 mg/hr Start: 0.5 mg/hr Titr: by: 0.25 mg/hr Frequency: No more than every 5 minutes Maximum Dose: 20 mg/hr</td>
<td>Respiratory depression Use with caution in renal and hepatic impairment. Monitor for CYP-enzyme drug-drug interactions.</td>
<td></td>
</tr>
<tr>
<td><strong>Lorazepam</strong></td>
<td>50 mg/50 mL DSW (1 mg/mL)</td>
<td>LD: 0.5-1 mg MD: 1-20 mg/hr Start: 1 mg/hr Titr: by: 0.5 mg/hr Frequency: No more than every 15 minutes Maximum Dose: 20 mg/hr</td>
<td>Respiratory depression At high doses, propylene glycol excipient can cause hypotension, metabolic acidosis, increase in osmolarity (&gt;320 mOsm/Kg), acute tubular necrosis. Monitor arterial blood gas pH, osmolar gap, serum creatinine, and urine output. Use with caution in hepatic and renal (mild and moderate) impairment.</td>
<td></td>
</tr>
<tr>
<td><strong>Dexmedetomidine</strong></td>
<td>200 mcg/50 mL DSW (4 mcg/mL)</td>
<td>MD: 0.2-1.4 mcg/kg/hr Start: 0.2 mcg/kg/hr Titr: by: 0.1 mcg/kg/hr Frequency: No more than every 30 minutes Maximum Dose: 1.4 mcg/kg/hr</td>
<td>Dexmedetomidine doesn’t provide deep sedation (RASS &lt; -3) LD is not recommended, as IV push is associated with hypotension and bradycardia. Does not cause respiratory depression Can cause hypotension, bradycardia Caution with use in hepatic dysfunction Withdrawal symptoms can occur. Consider oral clonidine to taper off dexmedetomidine.</td>
<td></td>
</tr>
<tr>
<td><strong>Ketamine</strong></td>
<td>5000 mg in NS 500 ml (10 mg/mL)</td>
<td>LD: 1 mg/Kg MD: 0.3 - 2 mg/kg/hr Start: 0.3 mg/kg/hr Titr: by: 0.1 mg/kg/hr Frequency: No more than every 15 minutes Maximum Dose: 2 mg/kg/hr</td>
<td>Contraindicated in acute decompensated heart failure. Use with caution in cerebral vascular accident and elevated intra-cranial pressures, and pulmonary hypertension. Associated with dissociative “emergence reaction” Can cause hypersalivation, laceration, and tachycardia Monitor for CYP-enzyme drug-drug interactions</td>
<td></td>
</tr>
</tbody>
</table>
### ADJUNCT SEDATIVES
*(consider adjunct therapy to lower continuous infusion sedation requirements)*

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose IV/IM (adjunct for sedation): 30 to 120 mg/day IV in 2 or 3 divided doses; do not exceed a rate of 60 mg/min</th>
<th>Respiratory depression</th>
<th>Additional Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenobarbital</td>
<td>Maximum 400 mg/day</td>
<td></td>
<td>May cause hypotension. IV formulation contains propylene glycol; may cause metabolic acidosis. Monitor for CYP-enzyme drug-drug interactions</td>
</tr>
<tr>
<td>Clonidine (PO)</td>
<td>Oral: 0.1-0.3 mg q 6-8 hr</td>
<td>Can cause bradycardia, hypotension, and serostomie. Can prolong effect in renal impairment. Consider to prevent dexametomidine withdrawal symptoms.</td>
<td></td>
</tr>
<tr>
<td>(PO/IV/IM)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Olanzapine</td>
<td>Affects central dopamine, muscarinic, serotonin receptors, and peripheral α-1 receptors</td>
<td>May alter cardiac conduction and prolong the QT interval Avoid concomitant use of IV benzodiazepines as they may enhance the adverse effect of benzodiazepines (cardiorespiratory depression).</td>
<td></td>
</tr>
<tr>
<td>(PO/IV/IM)</td>
<td>Use as adjunct therapy PO: 5 – 10 mg every 2 hours IV/IM: 1.25-10 mg repeat every 2-4 hours Maximum daily dose of 30 mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quetiapine (PO)</td>
<td>Affective antipsychotic</td>
<td>May alter cardiac conduction and prolong the QT interval</td>
<td></td>
</tr>
<tr>
<td>(PO)</td>
<td>PO: 50 mg BID, increase by 100 mg /day to a total dose of 400 mg /day</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### PARALYTICS
*(adequate sedation and analgesia required prior to paralysis)*

<table>
<thead>
<tr>
<th>Medication</th>
<th>Initial bolus: 0.6 – 1 mg/kg</th>
<th>MD: 5 – 12 mcg/kg/min</th>
<th>Frequency: No more than every 30 minutes</th>
<th>Maximum dose: 12 mcg/kg/min</th>
<th>Appropriate alternative to succinicholine for RSI</th>
<th>Avoid in hepatic and renal dysfunction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rocuronium</td>
<td>Inhibit acetylcholine at motor endplate</td>
<td>Titrator by: 1 mcg/kg/min</td>
<td>RSI: 1 to 1.2 mcg/kg followed by 20 ml of NS flush</td>
<td>Can cause tachycardia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vecuronium</td>
<td>Initial bolus with rocuronium MO: 0.8 – 1.2 mcg/kg/min</td>
<td>Titrator by: 0.1 mcg/kg/min</td>
<td>Frequency: No more than every 30 minutes</td>
<td>Maximum dose: 1.2 mcg/kg/min</td>
<td>Active hepatic and renal metabolites, avoid in hepatic and renal dysfunction</td>
<td></td>
</tr>
<tr>
<td>Drug</td>
<td>Initial Dosing Information</td>
<td>Adverse Effect</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>--------------</td>
<td>------------------------------------------------------------------------------------------</td>
<td>-----------------------------------------------------</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cisatracurium</td>
<td>Initial bolus with rocuronium MD: 0.5 - 10 mcg/kg/min&lt;br&gt;Titrator by: 0.5 mcg/kg/min&lt;br&gt;Frequency: No more than every 15 minutes&lt;br&gt;Maximum dose: 10 mcg/kg/min</td>
<td>Can cause bronchospasm, bradycardia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atracurium</td>
<td>Initial bolus with rocuronium MD: 5 - 20 mcg/kg/min&lt;br&gt;Titrator by: 1 mcg/kg/min&lt;br&gt;Frequency: No more than every 15 minutes&lt;br&gt;Maximum dose: 20 mcg/kg/min</td>
<td>Fast administration can cause hypotension, flushing, and bronchospasm&lt;br&gt;Tachyphylaxis can occur at high dose.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Succinylcholine</td>
<td>RSI: 1-1.5 mg/kg</td>
<td>Avoid in hyperkalemia&lt;br&gt;May cause a transient increase in intracranial pressure.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Symbols and Abbreviations:**<br>
- CYP: cytochrome<br>- SABA: gamma aminobutyric acid<br>- IV: intravenous<br>- IM: intramuscular<br>- LD: initial loading dose<br>- MD: maintenance dose<br>- NM2A: N-methyl-D-aspartate receptor<br>- PO: oral<br>- RSI: rapid sequence intubation
Phenobarbital for Alcohol Withdrawal Syndrome Dosing Guidelines

**Situation**
There is a need to provide guidance for the dosing of phenobarbital for the management of alcohol withdrawal syndrome (AWS).

**Background**
Due to the current surge in critically ill, intubated patients in the ICU, current supplies of sedatives, including benzodiazepines, are anticipated to be in critical short supply. Benzodiazepines are recommended for the treatment of AWS.\(^1\) Evidence suggests that phenobarbital is a safe and effective alternative drug therapy.\(^2\)–\(^6\)

Phenobarbital’s longer half-life, lack of cross-tolerance, reliable pharmacokinetic profile, and affinity to both gamma-aminobutyric (GABA) and glutamate receptors make it an appropriate alternative agent to benzodiazepines for the treatment of AWS in patients with active alcohol use and at high risk for AWS (such as prior symptomatic withdrawal), and for the treatment of symptomatic AWS.\(^5\)

**Assessment**
In the setting of benzodiazepines critical shortage, phenobarbital could be considered for the management of AWS. There is a need to provide guidance for the dosing of phenobarbital for management of AWS.

**Recommendation**
This phenobarbital dosing guideline provides guidance for the use of phenobarbital for the management of AWS and promote safe and appropriate use of phenobarbital in this setting. The guideline entails administering a phenobarbital loading dose (LD) followed by a maintenance phenobarbital taper in patients with AWS or at high risk for AWS.\(^5,7\) LD should be initiated in intensive care unit, emergency department, or step-down unit, with continuation of the maintenance phenobarbital taper on general patient care units.

Population: This phenobarbital dosing guideline is recommended for patients who are at risk for AWS to prevent worsening of symptoms or patients with active AWS. Patient must be in the intensive care unit, emergency department, or step-down unit to initiate phenobarbital therapy.

<table>
<thead>
<tr>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Patient with active AWS.</td>
<td>- If patient received greater than 20 mg lorazepam equivalents (approximately 100 mg of diazepam or 40 mg midazolam) in the last 8-12 hours then avoid phenobarbital and consider alternative therapy.</td>
</tr>
<tr>
<td>- Patient must be in the intensive care unit, emergency department, or step-down unit to initiate phenobarbital therapy.</td>
<td>- Patients who have started on another phenobarbital regimen for treatment of alcohol withdrawal or for other indications.</td>
</tr>
</tbody>
</table>
YNHHS Phenobarbital for Alcohol Withdrawal Guideline

Due to the risk of additive side effects, concomitant benzodiazepines are NOT recommended for the management of AWS. Discontinue any standing and PRN benzodiazepine orders.

**Phenobarbital Loading Dose**

- **Patient received benzodiazepine in last 8-12 hours?**
  - NO: 15 mg/kg Total Loading Dose (LD) given as:
    - LD part 1 (40% of total): 6 mg/kg IM/IV immediately
    - LD part 2 (50% of total): 4.5 mg/kg IM/IV given 3 hours later
    - LD part 3 (10% of total): 4.5 mg/kg IM/IV given 3 hours later
  - YES: 12 mg/kg Total Loading Dose (LD) given as:
    - LD part 1 (40% of total): 4.8 mg/kg IM/IV immediately
    - LD part 2 (50% of total): 3.6 mg/kg IM/IV given 3 hours later
    - LD part 3 (10% of total): 3.6 mg/kg IM/IV given 3 hours later

- **Less than 20 mg lorazepam equivalents?**
  - YES: If patient received greater than 20 mg lorazepam equivalents (approximately 100 mg of diazepam or 40 mg midazolam) in the last 8-12 hours then avoid phenobarbital and consider alternative therapy.
  - NO: Greater than 20 mg lorazepam equivalents?
  - YES: 20 mg lorazepam equivalent is about 100 mg of diazepam and 40 mg midazolam.

*Other dosing and administration caveats:
- Dose based on ideal body weight (IBW) unless patient actual body weight is less than IBW then use actual body weight.
- IM route is preferred to minimize side effects (drowsiness and respiratory compromise), but can be given IV.
- If given IV and patient is still symptomatic after 30 minutes, give LD part 2 or part 3 after 30 minutes.
- If total LD (15 mg/kg) was not given and there are no side effects but patient is still experiencing AWS symptoms, consider administering remainder of LD so that total of 15 mg/kg is given. See Appendix.

**Monitoring (Day 1):**
- Vital signs (blood pressure, heart rate, and respiratory status) 15 minutes after dose administration then every 2 hours for 24 hours after dose administration.
- Hold therapy if blood pressure <90/60 mm Hg, heart rate >100 bpm, respiratory rate >20 bpm, or RASS score <-2.
- CIWA (non-clinical care units) and MINDS (clinical care) can be used to assess patient’s withdrawal severity but not to determine dosing during the use of phenobarbital.
- Consider ordering serum phenobarbital level 5 hours after the LD as it might assist with further phenobarbital administration if patient experiences any phenobarbital-related adverse events. Serum concentrations greater than 30 mcg/mL have been associated with greater risk of adverse effects.

**Symptoms Worsen After Loading Dose**

The maximum peak effect of phenobarbital is at around 5 hours for IM (15 minutes for IV). If patient’s AWS symptoms worsen based on CIWA (non-clinical care units) and MINDS (clinical care) assessment 5 hours post phenobarbital total LD administration (15 mg/kg), consider alcohol withdrawal symptoms management as listed below.

**Management of alcohol withdrawal symptoms while on phenobarbital:**

**A. If continuous sedation is indicated or RASS ≤2 after receiving entire total LD:**
- Consider temazepam if clinically appropriate
- Due to the risk of additive side effects, avoid propofol or continuous benzodiazepine infusion for sedation

**B. Emergencies:**
- Agitation/anxiety: consider non-benzodiazepine alternatives
  - Quetiapine 12.5-25 mg PO every 6-12 hours as needed for agitation or anxiety
  - Haloperidol 2.5-5 mg IV every 6 hours as needed for agitation or anxiety
  - Triazolam 0.25-0.5 mg PO every 12 hours as needed for agitation or anxiety
- Tachycardia: Consider beta-blockers as clinically appropriate
- Hypertension: Consider clonidine as clinically appropriate

Updated 11/25/2020
Taper/Maintenance Dosing (Day 2 – 5)*

<table>
<thead>
<tr>
<th>Day</th>
<th>Dosing Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 2 and 3</td>
<td>Phenobarbital 64.8 mg IM/IV/PO every 12 hours for doses</td>
</tr>
<tr>
<td>Day 4 and 5</td>
<td>Phenobarbital 32.4 mg IM/IV/PO every 12 hours for doses</td>
</tr>
</tbody>
</table>

* The phenobarbital maintenance taper regimen should be started approximately 8 hours after the LD is completed (after completion of third dose of the LD).

For IM/IV administration, round up to the nearest administrable dose based on vial size, for example 32.4 mg round up to 39 mg.

Monitoring (Day 2 – 5):
- Monitor vital signs (blood pressure, heart rate, and respiratory status) every 4 hours while receiving phenobarbital maintenance taper regimen. Hold therapy if blood pressure <80/50 mm Hg, heart rate <50 bpm, respiratory rate <10 bpm, or GASS score less than 2.
- CNI (non-critical care units) and MINDS (critical care) can be used to assess patient's withdrawal severity but not to determine dosing during use of phenobarbital.
- Maintenance regimen should not be delayed in the event that phenobarbital serum level has not resulted.

Discontinuation of therapy and discharge:
- Given phenobarbital’s long half-life, discontinuation of phenobarbital taper earlier in the hospital course can occur in patients no longer experiencing withdrawal symptoms.
- A full 5-day admission to complete the detox is not always necessary.
- Patients should not be continued on phenobarbital upon discharge from the hospital including those patients who leave against medical advice (AMA).
- If patient leaves AMA, patient should be warned of a greater potential for intoxication due to higher sensitivity to alcohol after phenobarbital therapy.

Appendix:
- Phenobarbital LD can be given intramuscularly (IM) or intravenously (IV). Administration of LD via the IM route is encouraged to decrease the risk of adverse events (over-sedation and respiratory compromise). IM administration can be given in deltoid or glutus muscles. Give LD IV if platelet <50,000 per micrometer, INR >2 or if patient is therapeutically anticoagulated.
- In patients who tolerate phenobarbital LD without adverse events and did not receive the maximum LD of 15 mg/kg but are experiencing symptoms of AWS 3 hours after total LD administration, consider administering LD4 for a total of 15 mg/kg, as noted in the algorithm.
- For example: three hours after the 3rd and final loading dose, a 70 kg IDW patient begins to experience symptoms of AWS. They had received the 12 mg/kg total LD. Therefore, consider administering a one-time dose (LD4) of 3 mg/kg IV/IM (70 kg x 3 mg/kg = 210 mg IV/IM).
- Drug interactions: Phenobarbital is metabolized hepatically via cytochrome P450. Contact pharmacy for relevance of any cytochrome P450 drug-drug interactions. Avoid administering phenobarbital with clonazepam, dromedore, trazadone, nefedipine, nimodipine, ranolazine, rivaroxaban, and voriconazole.

References:
Situation
There is currently a critical shortage of the intravenous benzodiazepines (lorazepam and midazolam), therefore, there is a need to provide guidance for the treatment of Alcohol Withdrawal Syndrome (AWS).

Background
Due to the current surge in critically ill, intubated COVID-19 patients, there is increased use of continuous infusion sedation for mechanically ventilated patients, which has led to short supplies of benzodiazepines. These agents are recommended for the treatment of AWS.

Although symptom-triggered approaches are common practice, it does require frequent patient score assessment by the nurse, which may occur as often as every 15 minutes for MINDS. There is a need to limit the number of times it is required to enter COVID-19 positive patient rooms. Fixed-dose benzodiazepines in tapering doses have been found to be effective in the treatment of withdrawal symptoms, seizures, and delirium. Additionally, phenobarbital is a safe and effective alternative drug therapy to benzodiazepines for the treatment of AWS.

Assessment
In the setting of the benzodiazepine shortages, changes are needed to the current AWS protocols to conserve supply of benzodiazepines and to provide guidance to prescribers on the use of fixed-dose benzodiazepine and phenobarbital monotherapy regimens.

Recommendation
Please see the following recommendations for the treatment of AWS:

<table>
<thead>
<tr>
<th>Patient Population</th>
<th>Mild-Moderate AWS</th>
<th>Severe AWS or Intubated</th>
</tr>
</thead>
<tbody>
<tr>
<td>COVID-19 Positive</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• CIWA symptom-triggered (Refer to &quot;CIWA non-ICU&quot; order set)</td>
<td></td>
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<tr>
<td>o Diazepam PO, diazepam IV, and lorazepam PO</td>
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<tr>
<td>o For patients at high risk of withdrawal (i.e., history of DTs), may consider fixed-dose benzodiazepine therapy added to symptom-triggered regimen</td>
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<tr>
<td>OR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Phenobarbital monotherapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>COVID-19 Negative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Phenobarbital monotherapy</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patient Population</th>
<th>Mild-Moderate AWS</th>
<th>Severe AWS or Intubated</th>
</tr>
</thead>
<tbody>
<tr>
<td>COVID-19 Positive</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Fixed-dose taper, RASS based:</td>
<td></td>
<td></td>
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<tr>
<td>o Diazepam 10 mg IV q6h x 8 doses, followed by 5 mg IV q6h x 8 doses OR</td>
<td></td>
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</tr>
<tr>
<td>o Lorazepam 2 mg IV q6h x 8 doses, followed by 1 mg IV q6h x 8 doses (for patients with history of decompensated cirrhosis) OR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Phenobarbital monotherapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• YAWP Protocol (MINDS score-based):</td>
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</tr>
<tr>
<td>o Diazepam IV will be the preferred agent OR</td>
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</tr>
<tr>
<td>o Lorazepam IV (for patients with history of decompensated cirrhosis) order entry will be restricted to pharmacists</td>
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<td></td>
</tr>
<tr>
<td>o Midazolam IV will not be available due to shortage OR</td>
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<td></td>
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<tr>
<td>• Phenobarbital monotherapy</td>
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<td></td>
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</tbody>
</table>

Table 2: *Rescue/Adjunctive Therapies for Severe AWS if Patients have Worsening Symptoms Despite Fixed-Dose Benzodiazepine Therapy

<table>
<thead>
<tr>
<th>Patients on fixed-dose diazepam</th>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>• Add diazepam 10 mg IV q30 min PRN RASS &gt; +1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• If patient receives ≥3 doses in 2 hours, initiate dexmedetomidine infusion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• If patient requires dexmedetomidine infusion at a rate higher than &gt; 0.5 mcg/kg/hr, initiate benzodiazepine infusion</td>
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<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patients on fixed-dose lorazepam</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Add lorazepam 2 mg IV q30 min PRN RASS &gt; +1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• If patient receives ≥3 doses in 2 hours, initiate dexmedetomidine infusion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• If patient requires dexmedetomidine infusion at a rate higher than &gt; 0.5 mcg/kg/hr, initiate benzodiazepine infusion</td>
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<td></td>
</tr>
</tbody>
</table>
## Ketamine for Analgesia and Sedation Criteria for Use Guidance

<table>
<thead>
<tr>
<th>Situation</th>
</tr>
</thead>
<tbody>
<tr>
<td>There is a need to provide guidance on appropriate usage of ketamine for analgesia and sedation.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Background</th>
</tr>
</thead>
<tbody>
<tr>
<td>Due to the current surge in critically ill, intubated patients in the ICU, current supplies of sedatives and analgesics are in critical short supply. Ketamine is indicated as an analgesic and sedative agent for the critically-ill ventilated patients.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>To best maintain supply of all sedative and analgesic medications, guidance is needed to determine when the addition of ketamine is appropriate.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>The following criteria should be met for approval of ketamine:</td>
</tr>
</tbody>
</table>

- For analgesia: Patient has an adverse reaction to hydromorphone and fentanyl/remifentanil are unavailable or contraindicated.

- For sedation:
  1. Ketamine should be considered as a third-line agent for sedation (propofol and midazolam should be considered first) AND
  2. Patient didn’t achieve appropriate level of sedation despite propofol infusion being optimized to a rate of at least 65 mcg/kg/min or propofol use is contraindicated (TG >600 mcg/dL, pancreatitis) AND
     Patient didn’t achieve appropriate level of sedation despite benzodiazepine infusion being optimized
     - Midazolam rate of at least 10mg/hr or midazolam use is contraindicated (history of decompensated cirrhosis or AST/ALT > 5x ULN)
     - Lorazepam rate of at least 10mg/hr or lorazepam use is contraindicated (Osmol gap > 10)
  3. If patient is on an opiate infusion, titrate the patient off the opiate infusion after ketamine has been started

Guidance for transition off of Opiate infusion

- Initiate ketamine and titrate up to achieve patient comfort
- Once comfort is achieved, titrated off opiate infusion
  - Hydromorphine: decrease rate by 0.2mg/hr until off
  - Fentanyl: decrease rate by 0.25mcg/kg/hr until off
- Increase/bolus ketamine as needed while opiate infusion is being titrated off
# Enteral Clonidine for Dexmedetomidine Transition

## Situation
There is a need to provide guidance on the use of clonidine as an adjunct sedative therapy for patients receiving prolonged dexmedetomidine infusion.

## Background
The prolonged use of dexmedetomidine for sedation in critically ill patients can result in withdrawal when the infusion is abruptly discontinued. Enteral clonidine has demonstrated success in preventing withdrawal symptoms (agitation, tachycardia, and hypertension) and facilitating discontinuation of dexmedetomidine. An internal retrospective YNHHS study evaluated the efficacy and safety of clonidine for dexmedetomidine transition.

## Assessment
Due to increased volumes of critically ill patients receiving sedation with dexmedetomidine, there is a need to provide guidance on the use of clonidine for dexmedetomidine transition.

## Recommendation
- Consider enteral clonidine in patients who have been on dexmedetomidine for at least three days of therapy and/or exhibit symptoms of dexmedetomidine withdrawal with down-titration
- Initiation: 6 hours prior to dexmedetomidine down-titration/discontinuation (overlap therapy for at least 6 hours)
- Clonidine for dexmedetomidine transition medication panel
  - Current dexmedetomidine rate
    - ≥ 0.7 mcg/kg/h
      - Clonidine 0.3 mg every 6 h
    - < 0.7 mcg/kg/h
      - Clonidine 0.2 mg every 6 h
  - Taper: Decrease frequency every 48 h
    - Every 6 h → every 8 h → every 12 h → every 24 h → discontinue

## References
### Situation

There is currently a CRITICAL shortage of intravenous lorazepam for continuous infusion.

### Background

Due to the current surge in critically ill COVID-19 patients, there is increased use of continuous infusion sedation for mechanically ventilated patients. Current supplies of lorazepam for continuous infusion is in critical short supply.

### Assessment

Alternatives to lorazepam continuous infusions need to be identified to conserve its use for patients with severe liver disease or for patients who cannot utilize other available alternatives. Alcohol withdrawal syndrome (AWS) is a disease state in which alternatives to benzodiazepine infusions could be employed.

### Recommendation

Please see the following recommendations and actions for the critical shortage of lorazepam for continuous infusion. Recommendations and actions will be incorporated into Epic ordering screens and will be effective April 24th, 2020.

Please communicate this information to your colleagues and staff. Thank you for all your cooperation.

- Lorazepam for IV push will remain available for intermittent use for all indications.
- Patients requiring continuous benzodiazepine infusion should use Midazolam continuous infusion unless use is contraindicated.
- Lorazepam continuous infusion should be reserved for patients with decompensated cirrhosis, and available for pharmacist-entry only.
- Alcohol withdrawal:
  - COVID positive patients:
    - Avoid using YAWP protocol for COVID positive patients due to frequency of monitoring required
    - Enteral or IV CIWA-symptom triggered benzodiazepine or fixed-dose taper benzodiazepine (diazepam/oralzepam) for mild/moderate AWD
    - Fixed-dose taper benzodiazepine (diazepam/oralzepam) for severe AWD
    - Fixed-dose phenobarbital monotherapy for mild/moderate/severe AWD
  - COVID negative patients:
    - Enteral or IV CIWA-symptom triggered benzodiazepine or fixed-dose taper benzodiazepine (diazepam/oralzepam) for mild/moderate AWD
    - YAWP protocol (MINDS score-based) for severe AWD (diazepam)
    - Fixed-dose phenobarbital monotherapy for mild/moderate/severe AWD

See Sedatives, Analgesics, and Paralytics Alternatives for additional guidance.
# Drug Shortage: Neuromuscular Blocking Agents

## Situation
There is currently a CRITICAL shortage of cisatracurium.

## Background
Current supplies of neuromuscular blocking agent (NMBA), including cisatracurium, are in critical short supply. Cisatracurium and atracurium are intermediate-acting agents in the benzylisoquinolinium class. Both cisatracurium and atracurium are metabolized through Hoffman elimination. Metabolites of both agents produce laudanosine which is associated with neuroexcitation at higher levels. Atracurium has also been associated with hypotension due to the adverse effect of histamine release associated with faster infusion rates. One retrospective cohort analysis reviewed critically ill patients who received atracurium or cisatracurium, and found no difference in the rates of hypotension.

## Assessment
As an alternative to our currently used NMBA continuous infusion (cisatracurium) and in the setting of critical shortages, atracurium is a safe and effective alternative agent for paralyzing intubated ARDS patients.

## Recommendation
- For adult patients, rocuronium continuous infusion should be used as the first line paralytic agent. Utilize atracurium in mechanically ventilated patients during drug shortage of cisatracurium.
- Atracurium is restricted to pharmacist order entry only. Atracurium is restricted to patients with acute kidney injury, chronic kidney disease (defined as CrCl <30 mL/min), on renal replacement therapy, and/or hepatic dysfunction.

See [Sedatives, Analgesics, and Paralytics Alternatives](#) for additional guidance.

## References
# Drug Shortage: Metered Dose Inhalers

## Situation
Due to the COVID-19 pandemic YNHHS is experiencing supply issues with MDIs.

## Background
Expert consensus guidelines have identified the nebulization of medications as a risk factor for nosocomial transmission of infections and recommend preferential use of MDIs in COVID-19 patients and persons under investigation (PUI). As a result, the nationwide demand for MDIs has dramatically increased.

## Assessment
Currently, YNHHS has low supply of albuterol and ipratropium MDIs and are monitoring supply and use of all MDIs. We are receiving intermittent shipments but can change at any time.

## Recommendation
In order to preserve MDI supplies please see the below recommendations for conservation and Epic decision support that has been implemented.

To conserve MDIs for patients that are COVID-19 positive or a PUI:
- Please maximize the use of nebulizers as appropriate in patients that:
  - Are not COVID-19 positive or a PUI
  - Have tested negative for COVID-19
  - Intubated COVID-19 patients
    - Only when using the Aerogen® closed-loop system in a negative pressure room
- Please make sure MDIs are transferred with the patient per site specific policies.

### Inhaled Corticosteroid MDI Guidance (Pediatric/Newborn)

#### For PEDIATRIC patients:
- Please maximize the use of budesonide nebulizers as outlined above.
- Fluticasone HFA will be reserved for Patients <5 yrs of age or patients requiring 44 mcg inhaler. Mometasone HFA should be used for all other patients.
- For patients that can coordinate use of DPI device, please utilize DPI

#### For NEONATAL patients:
- Initiation of therapy with fluticasone MDIs for management of severe chronic lung disease (CLD)/bronchopulmonary dysplasia (BPD) will be limited to neonates and infants with an oxygen requirement while on HFOV, SIMV, NIPPV, or NCPAP
- Fluticasone HFA can be utilized for patients on NIPPV and CPAP
- Budesonide can be utilized for patients on HFOV and SIMV.
**Medication Storage and Relabeling of Patient Own Medications**

### Situation
Delivery network-specific Medication Storage Policies have been integrated in a system Medication Storage Standard Operation Procedure (SOP).

### Background
As part of the Health System wide Policy standardization project, delivery network policies and procedures have been reviewed and integrated into a system document. TJC places accountability for medication security on organizations to protect from unauthorized access, tampering, theft of diversion.

COVID-19 is presenting an opportunity to evaluate policies related to medication storage and infection control practices. Visitor restrictions are in place across Yale New Haven Health at the time of this communication.

### Assessment
Medications must be stored in a secure manner to prevent unauthorized access.

### Recommendation
The new system-wide Medication Storage SOP is attached here.

- For patients NOT on contact precautions, patient-specific multidose medications shall be stored in the secured, designated location on the patient care unit (Pyxis/Omnicell or secured cabinet).
- For patients on contact precautions, if unauthorized access cannot be ensured with the most secure manner available at the bedside, the medication must be wiped and placed in a clean plastic bag prior to returning to storage in the designated location on the patient care unit (Pyxis/Omnicell or secured cabinet).

Special note to pharmacy for relabeling of POM
- In the limited circumstances where POM has been deemed CLINICAL NECESSARY, the hospital pharmacy is unable to procure and dispense the medication in the appropriate time frame to meet the patient’s needs, AND the pharmacist is NOT on site to perform the verification process/relabeling OR the patient is COVID19+ or PUI, please complete medication verification process with bedside nurse and secure technology support, such as MHB where available. ALL efforts MUST be made to prevent unsecure transmission of PHI via images.
  - Pharmacist must use your professional judgement and clinical skills if the product is unable to be visualized such as asking clarifying questions (e.g. medication container labelling and integrity, product description and imprint, and utilize patient’s dispense history, etc).
- Coordination with central pharmacy staff will be necessary to send the label to the floor via the tube system or with a technician on the next delivery run to the floor, so that the nurse covering the patient can label the medication when s/he goes back into the room

The YNHH Patient Own Medication SOP is attached here.
**Situation**

To limit the spread of the novel coronavirus (COVID-19) from person-to-person, infection control precautions are needed, which includes limiting the use of nebulized medications. With decreased nebulization use, there is a need to conserve metered dose inhalers (MDIs).

YNHH Pharmacy Department will begin an Albuterol MDI Recycling Program in anticipation of supply constraints in the future. Front line staff need to be aware of their responsibilities and the timeline of this project.

**Background**

Albuterol MDIs are used throughout the Health System for patients that have difficulty breathing. Albuterol nebulization is also used on many patients. Nebulizer treatments should be avoided in most COVID-19 positive and COVID-19 Rule Out patients due to the risk of aerosolization and possible nosocomial transmission of the virus. Because of this, there is an increased demand for albuterol MDIs and measures must be taken to ensure there is supply available when needed.

Albuterol MDIs have traditionally been dispensed patient specifically and disposed of in a green hazardous waste bin for aerosols.

**Assessment**

An albuterol recycling program is in development that will allow the Pharmacy Department to use an albuterol canister on more than one patient after approved sterilization. This process will involve the Pharmacy Department, Emergency Department, and Sterile Processing.

The Pharmacy Department will need to collect used albuterol MDIs from the Emergency Department and from the returns that come back to central pharmacy.

**Recommendation**

Beginning on Thursday 4/23/2020, collection bins have been placed in the SRC ED and the YSC Adult ED. Other delivery networks will begin their collection process at a later date. Nursing staff have been informed to deposit any used Albuterol MDIs into these bins. Pharmacy staff will collect these albuterol MDIs every Thursday and return the bag to central pharmacy for storage.

A collection bin has also been placed in the central pharmacy on both campuses for any albuterol MDIs that are returned through other means. The bag in this bin will also be removed on Thursdays and stored securely.

For now, the pharmacy department is only collecting and storing the used Albuterol MDIs. More information on how the actuators will be delivered to Sterile Processing will be available in the future.
## Pharmacologic Formulation Optimization

<table>
<thead>
<tr>
<th>Levetiracetam Injection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levetiracetam injection orders for doses less than or equal to 1500 mg for adult patients will now be given via IV push route.</td>
</tr>
<tr>
<td>Starting on 4/6/2020, adult orders for levetiracetam for doses less than or equal to 1500mg will now be given undiluted via the IV push route. Nursing will obtain the levetiracetam 500 mg/5 mL vials from ADS. There will be no changes for adult doses greater than 1500 mg, and no changes to pediatric orders. Updates to IV push guidelines will follow.</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Oral Vancomycin</th>
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<tbody>
<tr>
<td>Vancomycin oral capsules will now be an available option for treatment of <em>C. diff</em> in adult patients able to take medications orally at all delivery networks except WH.</td>
</tr>
<tr>
<td>As of 4/17/2020, the ordering of oral vancomycin for adult patients at all delivery networks except WH will instruct providers to order capsules for patients able to take medications orally.</td>
</tr>
<tr>
<td>For adult patients with NG, OG, NG, G-tube or J-tube access Epic will instruct providers to order the solution formulation of vancomycin.</td>
</tr>
<tr>
<td>WH will continue to utilize the vancomycin solution for all patients given their ability to meet current compounding demands.</td>
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<table>
<thead>
<tr>
<th>Lacosamide Injection</th>
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<tbody>
<tr>
<td>Lacosamide IV orders for doses less than or equal to 400 mg for adult patients will now be given via IV push route.</td>
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<tr>
<td>Effective April 23, 2020, adult orders for lacosamide for doses less than or equal to 400 mg will now be given undiluted via the IV push route.</td>
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<tr>
<td>• Nursing will obtain the lacosamide 200 mg/20 mL vials from ADS.</td>
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<tr>
<td>• Lacosamide is a Schedule V controlled substance. Waste will be documented by two nurses utilizing ADS functionality.</td>
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<tr>
<td>• No changes for adult doses greater than 400 mg and no changes to pediatric orders.</td>
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<tr>
<th>Thiamine Injection</th>
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<tr>
<td>Thiamine injection is currently used for prevention and treatment of Wernicke’s Encephalopathy. It is given as a longer infusion given via IVPB in order to minimize local injection site and infusion related reactions, such as pruritus, urticaria, flushing, and injection site tenderness.</td>
</tr>
<tr>
<td>However, there is published evidence supporting administering thiamine as an IV push for doses 200 mg or less. These studies have shown thiamine given as an IV push has minimal injection site reactions and therefore, can be safely given via this route. When given as IV push, it can be given over 1-2 minutes, undiluted. It is safe to give all thiamine IV doses 200 mg or less, via IV push.</td>
</tr>
<tr>
<td>All thiamine IV orders for doses 200 mg or less will now be given as an IV push over 1-2 minutes, undiluted. It no longer needs to be compounded by Pharmacy. The 100 mg/2 mL vials will be dispensed in Pyxis. Epic orders will be limited to the Wernicke’s Encephalopathy order groups. Doses greater than 200 mg will be limited to pharmacist entry only and will be given as IVPB. The Epic screens will be updated accordingly.</td>
</tr>
</tbody>
</table>

References: