Montefiore Empiric Antimicrobial Treatment Guidelines for COVID-19 Patients with Co-infections

Version 5.23.20

These guidelines, created by the Antimicrobial Stewardship Program, Infectious Diseases, and Pharmacy are intended to help guide clinicians caring for hospitalized COVID19 patients with suspected secondary bacterial and fungal infections.

These are separate recommendations from COVID19 treatment with experimental agents/clinical trials (e.g. remdesivir, convalescent plasma, hydroxychloroquine, sarulimab, etc.) Visit http://studies.montecovid.net/ for further details.

**Please visit https://webedition.sanfordguide.com/en/montefiore or the MMC Sanford Guide smartphone app for renal dosing guidelines, campus specific restriction polices, and much more

Notes:

- Severe COVID-19 patients are at high risk of renal failure; caution with nephrotoxic regimens such as piperacillin-tazobactam/vancomycin without a clear indication
- Take an antibiotic “time-out” every 48-72 hours
  - Reassess patient’s condition
  - Switch to PO (if adequate clinical improvement, hemodynamically stable, and able to take PO) or STOP whenever possible
- Serial procalcitonin (PCT) values (e.g. x 2, 48-72 hours apart) can assist in monitoring response to treatment and guiding antibiotic de-escalation in septic patients
  - NOTE: PCT levels may be elevated in COVID19 separate from bacterial co-infection
  - Negative PCT levels may be helpful for stopping antibiotics
- Consider MRSA nasal swab to help de-escalate vancomycin IV if negative
- “De-label” penicillin allergy when possible and update medical record if patient able to tolerate beta-lactams
• Refer to the Sanford Guide or MMC ASP website:
  http://www.einstein.yu.edu/departments/medicine/divisions/infectious-diseases/antimicrobial-stewardship/

SCENARIO #1: Initial Patient Presentation (DAY 0-1)

Workup (while in recommended PPE):

• Obtain the following:
  o SARS-CoV-2 testing
  o Blood cultures x 2 sets
  o Chest imaging
  o Respiratory culture (if possible)
  o Urinary pneumococcal and legionella antigens
  o Procalcitonin at baseline
  o EKG to monitor QTc (especially if considering empiric azithromycin or levofloxacin)

Treatment:

• Explore experimental COVID treatments while risk stratifying for concurrent bacterial infection

<table>
<thead>
<tr>
<th>Risk Stratification</th>
<th>Antibiotic Management</th>
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</thead>
<tbody>
<tr>
<td>• Lower O₂ supplementation requirements (e.g. nasal cannula, non-rebreather, etc.)</td>
<td>• HOLD empiric antibiotics and continue workup</td>
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<tr>
<td>• Not critically ill</td>
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<tr>
<td>• Not in respiratory failure</td>
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<tr>
<td>• Illness most likely from viral pneumonia</td>
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<tr>
<td>• Higher O₂ supplementation requirements (e.g. high flow O₂, NIPPV, or intubation due to respiratory failure)</td>
<td>• Consider starting empiric antibiotics based on etiology:</td>
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<tr>
<td></td>
<td>o Community acquired pneumonia (CAP) coverage if from home</td>
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<td></td>
<td>o Hospital acquired pneumonia (HAP) coverage if from LTC facility</td>
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</tbody>
</table>

CAP coverage:
• Ceftriaxone 1g IV daily + Azithromycin 500mg PO OR Doxycycline 100mg PO twice daily (if QTc > 500ms)
• **Severe allergy to penicillin:** Monotherapy with levofloxacin PO 250mg to 750mg; 750mg dose recommended if CrCl >50 ml/min; elderly and patient with diminished renal function require lower dose (250-500mg)

### HAP coverage, risk factors for MRSA or Pseudomonas

• Normal renal function: Piperacillin/tazobactam 4.5g IV every 6 hours OR Cefepime 2g IV every 8 hours + Vancomycin 15-20mg/kg IV
  - **Contact ID/stewardship to assist with renal dose adjustment to above regimen or for alternative anti-Pseudomonal and anti-MRSA agents**
  - Consider MRSA nasal swab to help de-escalate vancomycin IV if negative
• **Severe allergy to penicillin:** Levofoxacin 750mg PO/IV daily if CrCl >50ml/min (or equivalent dose adjusted for renal function) + vancomycin 15-20mg/kg IV
• Consider 1 dose of gentamicin 5mg/kg IV ideal body weight if CrCl>30 ml/min for added Pseudomonal coverage, please adjust dose according to renal function

### DAY 2-3 FOLLOW-UP:

• Is patient clinically improved or unchanged?
  - If improving and on antibiotics, **define a duration**
  - If unchanged or not improving, **consult ID for assistance**
• Any positive microbiology results to guide treatment?
  - If yes, refer to pathogen-directed treatment guidance on page 4
  - Stop atypical coverage if Legionella antigen is negative and low suspicion for other atypicals (other Legionella serogroups, Mycoplasma, etc.)
  - If micro results negative, consider stopping antibiotics or consult ID for assistance
  - If high suspicion of bacterial PNA - continue antibiotics for a total of 5 days
  - Consider nasal MRSA swab to help de-escalate vancomycin IV
• Unclear what is going on?
  - Consult ID to help determine ongoing antimicrobial treatment

### SCENARIO #2: Floor or ICU patient, ongoing or new fevers, respiratory decline, hypotension or shock, rise in WBC count not due to steroids

**Work up:**
• Obtain the following:
  o Repeat blood cultures x 2 sets
  o Chest imaging
  o Respiratory culture if possible
  o Follow-up PCT level
  o Check stool *C.difficile* if patient having diarrhea, has been on antibiotics or steroids, not on laxatives or stool softeners
• Change any old central lines and urinary catheters

Treatment:

• Normal renal function: Piperacillin/tazobactam 4.5g IV every 6 hours OR Cefepime 2g IV every 8 hours + Vancomycin 15-20mg/kg IV
  o **Contact ID/stewardship to assist with renal dose adjustment to above regimen or for alternative anti-Pseudomonal and anti-MRSA agents**
• Consider nasal MRSA swab to help de-escalate IV vancomycin
• **Severe allergy to penicillin**: levofoxacin 750mg PO/IV daily if CrCl >50ml/min (or equivalent dose adjusted for renal function) + vancomycin 15-20mg/kg IV
• Consider 1 dose of gentamicin 5mg/kg IV ideal body weight if CrCl>30 ml/min for added Pseudomonal coverage), please adjust dose according to renal function
• Consider adding micafungin 100mg IV if patient in septic shock, has received steroids, and has central lines

***Consult ID for assistance, especially if patient has already been on antibiotics and is getting worse***

48-HOURS LATER:

• Is patient clinically improved or unchanged?
  o If improving, **define a duration**, i.e. 5-7 days
  o If unchanged or not improving, **consult ID for assistance**
• Any positive microbiology results to guide treatment?
  o If yes, refer to pathogen-directed treatment guidance below.
  o Is PCT ≥ 0.5mg/dL suggestive of bacterial infection?
• Unclear what is going on?
  o Consult ID to help determine ongoing antimicrobial treatment and duration

**Pathogen-directed treatment, susceptibilities known**

• De-escalate antibiotics as indicated and define a duration
• If multi-drug resistant organism (MDRO), consult ID/ASP to escalate antibiotics as indicated and define duration