

COVID-19: ANTIBIOTIC MANAGEMENT IN AMBULATORY PATIENTS



A Rapid Guidance Summary from the Penn Medicine Center for Evidence-based Practice
Last updated April 21, 2020 1:00 pm. Sources rechecked April 19 unless otherwise noted.

Key questions answered in this summary

- What are indications for antibiotic use in COVID-19 patients being cared for in the ambulatory setting?
- What are best practices related to antibiotic management in an ambulatory COVID-19 patient?
- Which antibiotics are preferred for use with an ambulatory COVID-19 patient?

Summary of major recommendations

- Antibiotic therapy may be indicated in COVID-19 patients with mild pneumonia when a bacterial etiology has not been ruled out.
- Antibiotic therapy in the ambulatory setting should be initiated as soon as a bacterial co-infection with COVID-19 is suspected.
- There is limited and controversial evidence related to the use of azithromycin + hydroxychloroquine combination therapy to treat COVID-19.
- Antibiotic use is dependent on the clinical diagnosis. However, doxycycline and amoxicillin may be viable options for first-line therapy in a patient with no co-morbidities.

Public health agency guidance on antibiotic indications in COVID+ patients or patients under investigation (PUI)

Source	Recommendations
WHO April 11	Indications: Adults with pneumonia but no signs of severe pneumonia and no need for supplemental oxygen may be isolated in a community facility or home care and given an appropriate antibiotic. Pneumonia may be managed in an outpatient setting depending on its severity, which may be determined by the combination of clinical judgement and CURB-65 score. Antibiotics are not indicated in patients with mild illness , defined as upper respiratory viral infection presenting with fever, fatigue, cough (with or without sputum production), anorexia, malaise, muscle pain, sore throat, dyspnea, nasal congestion, or headache.
NICE April 3	Oral antibiotics may be considered in patients with pneumonia or presumed pneumonia in the case where objective diagnosis is not possible who can or wish to be treated in the community if: the likely cause is bacterial , or if it is unclear whether the cause is bacterial or viral and symptoms are more concerning , or they are at high risk for complications (ex. older, have a pre-existing comorbidity such as immunosuppression or heart or lung disease, or have a history of severe illness following lung infection).
CDC April 3	The CDC offers no guidance specific to the use of antibiotics in COVID+ patients in the outpatient setting.

Professional society guidance on antibiotic indications in COVID+ patients or patients under investigation (PUI)

Source	Recommendations
IDSA April 13	The IDSA offers no guidance specific to the use of antibiotics in COVID+ patients in the outpatient setting.
ASP April 2	For patients in an ambulatory setting, antibacterial therapy (including azithromycin) is not routinely recommended for patients with COVID-19 outside of approved clinical trials or where other indications would justify its use.

Medical center guidance on antibiotic indications in COVID+ patients or patients under investigation (PUI)

Source	Recommendations
MGH April 18	Routine empiric antibiotics are not recommended. Thus far, MGH has detected low rates of bacterial superinfection in COVID-19 patients [ambulatory vs. inpatient setting not specified].

Public health agency guidance on antibiotic selection and best practices

Source	Recommendations
NICE April 3	When starting antibiotic treatment, the first-choice oral antibiotic is: doxycycline 200 mg on the first day, then 100 mg once a day for 5 days in total (not in pregnancy). Alternative: amoxicillin 500 mg 3 times a day for 5 days [specific to ambulatory setting].
WHO March 13	Empiric antibiotic treatment should be based on the clinical diagnosis (community acquired pneumonia, health care-associated pneumonia [if infection was acquired in health care setting] or sepsis), local epidemiology and susceptibility data, and national treatment guidelines.

Medical center guidance on antibiotic selection and best practices

Source	Recommendations
MGH April 11	If started, usual course is 5 days. For non-pregnant patients, doxycycline is preferred over azithromycin [ambulatory vs. inpatient setting not specified].

Professional society guidance regarding use of azithromycin to treat COVID-19

IDSA April 13	Because of the potential for toxicity, the panel recommends that the HCQ+AZ combination only be used in the context of a clinical trial. Additional randomized controlled trials and prospective outcome registries are needed to inform research for treatment with HCQ alone or in combination with azithromycin for patients with COVID-19 This recommendation does not address the use of azithromycin for secondary bacterial pneumonia in patients with COVID-19.
AAFP April 8	The AAFP cautions against the use of off-label medications, including azithromycin, for the treatment of COVID-19. There have been limited studies performed with varying degrees of success, the data do not support improved patient-oriented outcomes with these medications [ambulatory vs. inpatient setting not specified].

Evidence review: The use of azithromycin to treat COVID-19

ASHP April 17	Current data insufficient to establish pros and cons of adjunctive use of azithromycin in management of COVID-19. Additional data needed before any conclusions can be made regarding possible benefits of using a combined regimen of hydroxychloroquine and azithromycin in pts with COVID-19.
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	Contraindication: Because both azithromycin and hydroxychloroquine are associated with QT prolongation, caution is advised if considering use of both drugs in pts at risk for QT prolongation or receiving other drugs associated with arrhythmias and in those with chronic medical conditions (e.g., renal failure, hepatic disease) diagnostic testing and monitoring recommended to minimize risk of drug-induced cardiac effects
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Medical center guidance regarding the use of azithromycin to treat COVID-19

Nebraska April 17	Studies of azithromycin combination therapy with hydroxychloroquine does not convincingly suggest added benefit, given multiple study limitations and concern for antibiotic overuse.
USC April 14	A small non-randomized study -- which subsequent to publication received an expression of concern from the sponsoring society -- has suggested a benefit of combining hydroxychloroquine with azithromycin for treating COVID-19. Larger studies are needed to further evaluate the safety of combining these meds, as the combination of the two can potentiate cardiac complications [ambulatory vs. inpatient setting not specified].
Mt. Sinai April 11	For the patient not requiring hospitalization : In conjunction with hydroxychloroquine, may add azithromycin 500 mg PO x 1 dose then 24 hours later start 250 mg PO q 24 hours x 4 doses for a total of 5 days of therapy OR 500 mg PO q 24 hours x 3 doses for a total of 3 days of therapy. If patient able to tolerate oral hydroxychloroquine, then patient should receive oral azithromycin. Intravenous azithromycin use is discouraged. Contraindications: Combination Azithromycin and Hydroxychloroquine are contraindicated in persons with known WPW and prolonged QT.
Yale March 23	Outpatient prescribing of hydroxychloroquine, HIV-1 protease inhibitors, and azithromycin should be reserved only for patients who have medical conditions where their use has been established and there are no other alternatives.

Key sources searched

Public health agency guidance: World Health Organization (WHO), Center for Disease Control and Prevention (CDC), National Health Service (NHS) (UK), National Institute for Health and Care Excellence (NICE) (UK), European Center for Disease Prevention and Control (ECDC), Public Health Agency of Canada

Professional society guidance: American Academy of Family Practice (AAFP), American Board of Family Medicine (ABFM), American Board of Internal Medicine (ABIM), American College of Chest Physicians (ACCP), American Society of Health-System Pharmacists (ASHP), Antimicrobial Stewardship Program (ASP)

Medical center guidance: MGH, UCSF, University of Washington, Cleveland Clinic, Sinai, OHSU, Weill-Cornell, NYU Langone, Hopkins, Mayo, Nebraska, USC, UPHS, Yale, Stanford, University of Michigan

About this report

A Rapid Guidance Summary is a focused synopsis of recommendations from selected guideline issuers and health care systems, intended to provide guidance to Penn Medicine providers and administrators during times when latest guidance is urgently needed. It is not based on a complete systematic review of the evidence. Please see the CEP web site for further details on the methods for developing these reports.

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