Consensus Guidelines for COVID-19 Drug Therapies

Updated: July 19, 2021

organization last update	**NIH (adults)** July 8, 2021	**NIH (peds)** July 8, 2021	**IDSA** June 25, 2021	**WHO** July 6, 2021	**SCCM** January 29, 2021	**PIDS** January 3, 2021
general guideline principles and/or definitions	give COVID pts inactivated influenza vaccine; refer to ACIP/CDC for SARS-CoV-2 vaccine recs; antiviral prophylaxis not rec outside clinical trial; tx pregnant pts based on shared decision-making	infection generally milder in children than adults; most w/ mild-mod dz can be managed w/ supportive care alone; limited data in children, recs based on adults if inadequate data	low co-infxn rates but limited data; super-infxns more common w/ immune modulators; prolonged empiric antimicrobials incr. resistance risk	antiviral prophylaxis or tx *not* rec outside clinical trial; start empiric antimicrobial tx ASAP in severe dz for likely pathogens, incl. seasonal influenza	severe dz = pneumonia signs, and respiratory rate <30, severe respiratory distress, or O_2 sat <90% on room air; critical dz = ARDS, sepsis, septic shock, or requiring ventilation	supportive care only rec for peds outpts or mild-mod dz but consider antiviral tx case-by-case in peds pts w/ confirmed COVID and underlying condition[1]

1 – possible severe dz risk factors: medical complexity (multiple chronic health conditions, medical technology dependence, functional limitations), >12 yo, severe immunosuppression, severe underlying cardiac or pulmonary dz, obesity

antiviral agents

	NIH (adults)	**NIH (peds)**	**IDSA**	**WHO**	**SCCM**	**PIDS**
remdesivir (RDV)	for inpts requiring O_2 but *not* rec if mech vent or ECMO[1]; IE for pts not requiring O_2; rec *against* routine use after discharge	for inpts ≥16 yo w/ incr. O_2 needs, or ≥12 yo w/ incr. O_2 and severe dz risk; rec *against* routine use after discharge (may consider use for all ages w/ peds ID consult)	for inpts w/ severe dz (requires O_2 or w/ SpO_2 ≤94%)[1,2]; rec *against* routine use in inpts not requiring O_2	*not* rec in inpts regardless of dz severity	suggest use in adults w/ severe dz not requiring mech vent; suggest *against* use in adults w/ critical dz requiring mech vent	*not* rec outside clinical trial in outpts or mild-mod dz; suggest use in peds pts w/ confirmed COVID and severe or critical dz, but *not* routinely for MIS-C[1]
hydroxychloroquine (HCQ) *FDA EUA revoked June 15, 2020*	rec *against* use	rec *against* use	*not* rec in inpts w/ or w/o AZ	rec *against* use	rec *against* use in adults w/ severe or critical dz	rec *against* use outside clinical trial w/ or w/o AZ
chloroquine (CQ) *FDA EUA revoked June 15, 2020*	rec *against* use	rec *against* use	*not* rec in inpts w/ or w/o AZ	rec *against* use	--	--
azithromycin (AZ)	rec *against* use	rec *against* use	combo w/ HCQ or CQ *not* rec in inpts	*not* rec outside clinical trial	--	rec *against* combo w/ HCQ outside clinical trial
ribavirin (RBV)	--	--	IE (in vitro data only)	--	--	rec *against* combo w/ LPV/r outside clinical trial
lopinavir/ ritonavir (LPV/r)	*not* rec outside clinical trial	*not* rec outside clinical trial	*not* rec in inpts	rec *against* use	--	rec *against* use outside clinical trial w/ or w/o RBV
other HIV protease inhibitors (e.g. darunavir (DRV))	*not* rec outside clinical trial	*not* rec outside clinical trial	DRV: IE (no activity at normal doses, no viral clearance per mfr)	--	--	--
famotidine	--	--	suggest *against* COVID tx use outside clinical trial	--	--	--
ivermectin[4]	IE	IE	suggest *against* COVID tx use outside clinical trial	*not* rec outside clinical trial	--	--
nitazoxanide	rec *against* use	rec *against* use	--	--	--	--
neuraminidase inhibitors (e.g. oseltamivir)	--	--	IE (unclear mechanism since no target on virus)	--	--	--

abbreviations: -- = not discussed in guidelines; IE = insufficient evidence; EUA = emergency use authorization; inpts = inpatients/hospitalized pts; outpt = outpatients; MIS-C = multisystem inflammatory syndrome in children

1 – NIH and IDSA: 5 days if NOT requiring mech vent or ECMO (consider extending for up to 10 days if inadequate improvement); IDSA only: 10 days if requiring mech vent or ECMO; PIDS: 5 days for severe dz, 5-10 days for critical dz

2 – if limited RDV supply, prioritize use for pts requiring supplemental O_2 but not mech vent or ECMO

3 – provided that shared decision-making used, data collected, pt warrants investigational tx, and no drug shortage
4 – ivermectin: avail. data currently doesn't support clinical effectiveness and safety per manufacturer

immunomodulators

	NIH (adults)	NIH (peds)	IDSA	WHO	SCCM	PIDS
systemic corticosteroids (e.g. dexamethasone (DEX))	COVID tx: use DEX for pts requiring O_2, incl. mech vent pts[1,2]; rec *against* DEX use in pts not requiring O_2; rec *against* routine use after discharge underlying condition: continue tx, give PRN supplement doses refractory shock: low-dose tx rec over no tx	COVID tx: use DEX for inpts requiring high flow O2, noninvasive vent, mech vent, or ECMO[1,2]; rec *against* routine use after discharge underlying condition: continue tx, give PRN supplement doses refractory shock: low-dose tx rec over no tx	COVID tx: rec DEX for critically ill pts; suggest DEX in inpts w/ severe dz requiring O_2 or w/ SpO_2 $\leq$94%;[1,2] rec *against* steroids in inpts not requiring O_2	COVID tx: for pts w/ severe or critical dz; rec *against* use in non-severe dz[1-3] ARDS: may use per SOC viral pneumonia: routine use *not* rec other indications: may use per SOC	rec short course systemic steroids (DEX preferred) in adults w/ severe or critical dz[1,2]	--
tocilizumab (IL-6 inhibitor)	use in combo w/ DEX in 1) pts in ICU <24h on high flow O_2 or mech vent or 2) non-ICU pts on high flow O_2 or noninvasive vent w/ significant inflammation (CRP $\geq$75)[4] IE for all other inpts w/ hypoxemia	COVID tx: IE (if used, give in combo w/ DEX) MIS-C: IE	suggest use in severe or critical dz if inflammatory markers elevated (CRP $\geq$75)	use in combo w/ steroids for pts w/ severe or critical dz	--	--
sarilumab (IL-6 inhibitor)	IE for pts in ICU <24h on high flow O_2, mech vent, or noninvasive vent	COVID tx: *not* rec outside clinical trial MIS-C: *not* rec outside clinical trial	IE	use in combo w/ steroids for pts w/ severe or critical dz	--	--
siltuximab (IL-6 inhibitor)	*not* rec outside clinical trial	*not* rec outside clinical trial	--	--	--	--
IL-1 inhibitors	IE	COVID tx: IE MIS-C: may consider use in refractory cases in consultation w/ multidisciplinary team	--	--	--	--
baricitinib (JAK inhibitor)	inpts requiring O_2 but not on high-flow O_2 or noninvasive vent: IE inpts requiring high-flow O_2 or noninvasive vent: rec baricitinib + steroids +/- RDV if progression or significant inflammation; if can't use steroids, rec baricitinib + RDV; rec	IE	for inpts w/ severe dz (SpO_2 $\leq$94% and not intubated) who can't use steroids, consider combo w/ RDV rather than RDV alone use combo w/ RDV plus steroids in clinical trial *only* in inpts	--	--	--

	against routine use after discharge inpts on mech vent: IE					
other JAK inhibitors (e.g. ruxolitinib)	*not* rec outside clinical trial	*not* rec outside clinical trial	--	--	--	--
BTK inhibitors	*not* rec outside clinical trial	*not* rec outside clinical trial	--	--	--	--
interferons (IFN)	all IFNs: *not* rec outside clinical trial in severe or critical dz IFN-β: IE for early mild-mod dz	all IFNs: *not* rec outside clinical trial in severe or critical dz IFN-β: IE for early mild-mod dz	--	IFN-β-1a *not* rec outside clinical trial	--	--
colchicine	inpts: rec *against* use outside clinical trial outpts: IE	inpts: rec *against* use outside clinical trial outpts: IE	--	--	--	--
fluvoxamine	IE	IE	--	--	--	--

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1 – NIH/IDSA/SCCM recommended adult dose: dexamethasone 6 mg/day for up to 10 days; WHO recommended adult dose: dexamethasone 6 mg/day or hydrocortisone 50 mg IV q8h x7-10 days; NIH recommended peds dose: 0.15 mg/kg/dose (max 6 mg) once daily for up to 10 days

2 – equivalent daily glucocorticoid dose may be substituted if dexamethasone unavailable: dexamethasone 6 mg/day = methylprednisolone 32 mg/day OR prednisone 40 mg/day OR hydrocortisone 150-160 mg/day

3 – pregnant pts: benefit may outweigh risk if mild COVID and at risk for preterm birth (24-34 wks gest)

4 – IE for repeated dosing or use in peds pts; avoid use if significant immunosuppression, GI perforation risk, uncontrolled non-SARS-CoV-2 infection, ALT >5x ULN, ANC <500, or Plt <50,000

antibody-based therapies

	NIH (adults)	NIH (peds)	IDSA	WHO	SCCM	PIDS
bamlanivimab *FDA EUA for monotherapy revoked Apr 16, 2021*	rec *against* monotherapy (see recs for bamlanivimab and etesevimab)	--	rec *against* monotherapy	--	--	suggest *against* routine use in peds pts
bamlanivimab and etesevimab	rec *against* use	rec *against* use	suggest use in mild-mod dz if high risk for progession[2], incl. outpts or inpts w/ mild-mod dz admitted for non-COVID reason	--	--	--
casirivimab and imdevimab	outpts: for mild-mod dz in pts at high risk for progression[1,2] inpts: consider use in pts w/ mild-mod dz admitted for non-COVID reason if EUA criteria met[1,2], otherwise *not* rec outside clinical trial	IE (consider case-by-case use for outpts if EUA criteria met, especially if 1+ criteria or if ≥16 yo, w/ peds ID consult)	suggest use in mild-mod dz if high risk for progession[2], incl. outpts or inpts w/ mild-mod dz admitted for non-COVID reason	--	--	suggest *against* routine use in peds pts, incl. high-risk pts as designated by FDA[2]
sotrovimab	outpts: for mild-mod dz in pts at high risk for progression[1,2] inpts: consider use in pts w/ mild-mod dz admitted for non-COVID reason if EUA	IE (consider case-by-case use for outpts if EUA criteria met, especially if 1+ criteria or if ≥16 yo, w/ peds ID consult)	suggest use in mild-mod dz if high risk for progession,[2] incl. outpts or inpts w/ mild-mod dz admitted for non-COVID reason	--	--	--

	criteria met[1,2], otherwise *not* rec outside clinical trial					
convalescent plasma (CP) *FDA EUA for low-titer CP revoked Feb 4, 2021*	rec *against* low-titer CP outpts: IE for high-titer CP inpts w/o impaired immunity: rec *against* high-titer CP if mech vent; rec *against* high-titer CP outside clinical trial if not mech vent inpts w/ impaired immunity: IE for high-titer CP	rec *against* CP in inpts if mech vent; rec *against* CP in inpts outside clinical trial if not mech vent; may consider high-titer CP use on case-by-case basis with peds ID consult	outpts: use in clinical trial *only* in mild-mod dz[3] inpts: suggest *against* use	*not* rec outside clinical trial	suggest *against* use in adults w/ severe or critical dz in outside clinical trials	--
immune globulin (IVIG)	*not* rec outside clinical trial	COVID tx: IE MIS-C: may consider use in consultation w/ multidisciplinary team	IE	--	suggest *against* routine use in critical adult pts	--
SARS-CoV-2-specific IGs	IE	IE	--	--	--	--

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1 – consider use in peds pts and pregnant pts on case-by-case basis
2 – outpts w/ mild-mod COVID-19 at high risk for progression to severe dz or hospitalization as defined by the FDA Emergency Use Authorization (EUA) for bamlanivimab, bamlanivimab and etesevimab, casirivimab and imdevimab, and sotrovimab
3 – greatest likely benefit if admin. w/in <3 days of COVID dx or hospitalization; critically ill pts unlikely to benefit (IDSA/AABB Joint Statement)

adjunct therapies

	NIH (adults)	NIH (peds)	IDSA	WHO	SCCM	PIDS
antibacterials	*not* rec in outpts if not otherwise indicated	--	--	--	--	--
antithrombotics	underlying condition: continue tx outpts: prophylaxis *not* rec outside clinical trial if not otherwise indicated inpts: give VTE prophylaxis, IE for higher prophylactic doses or thrombolytics; VTE tx per SOC	--	--	use standard prophylaxis dose in inpts if no indication for intermediate or therapeutic doses[1]	give VTE prophylaxis in adults w/ severe or critical dz; suggest *against* routine therapeutic anticoagulation in adults w/ severe or critical dz outside clinical trials if no VTE evidence	--
ACEIs/ARBs	underlying conditions: continue tx COVID tx: *not* rec outside clinical trial	--	underlying conditions: continue tx per AHA/ACC/HFSA COVID tx: IE	--	--	--
inhaled pulmonary vasodilators (e.g. nitric oxide, prostacyclins)	nitric oxide: rec *against* routine use all agents: may give trial as rescue tx, taper off if not rapidly improved	--	--	--	nitric oxide: rec *against* routine use in mech vent adults w/ ARDS all agents: may give trial as rescue tx in mech vent adults w/ severe ARDS and	--

					hypoxemia, taper off if not rapidly improved	
NSAIDs	continue underlying condition tx; no antipyretic strategy preference	--	no evidence link to COVID worsening per FDA, EMA, WHO	--	suggest acetaminophen for fever control in critical adult pts	--
statins	underlying conditions: continue tx COVID tx: *not* rec outside clinical trial	--	--	--	--	--
vitamin C	IE	--	--	--	--	--
vitamin D	IE	--	--	--	--	--
zinc	COVID tx: IE COVID prevention: rec *against* exceeding RDA outside clinical trial[2]	--	--	--	--	--

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1 - intermediate dose = 2x standard thromboprophylaxis dose; therapeutic dose = acute VTE tx dose

2 – recommended dietary allowance (RDA): adult females = 8 mg/day; adult males = 11 mg/day; see NIH Zinc Fact Sheet for RDAs in other populations