Consensus Guidelines for COVID-19 Drug Therapies

Updated: March 9, 2023

organization last update	**NIH (adults)** March 8, 2023	**NIH (peds)** March 8, 2023	**IDSA** February 8, 2023	**WHO** January 13, 2023
general guideline principles and/or definitions	give COVID pts inactivated influenza vaccine; give COVID-19 vaccines ASAP per ACIP/CDC; consider monoclonal antibodies for PrEP or PEP, 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; consult multidisciplinary team when using immunomodulating therapy for MIS-C *also see NIH (adults)*	consider local SARS-CoV-2 variant susceptibility when assessing monoclonal antibody tx options low co-infxn rates; super-infxns may be 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

abbreviations: PrEP = pre-exposure prophylaxis; PEP = post-exposure prophylaxis

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**
nirmatrelvir/ritonavir	for outpts w/ mild-mod dz at high risk for dz progression	for outpts ≥12 yo and ≥40 kg w/ mild-mod dz at high risk for dz progression	suggest use for outpts w/ mild-mod dz at high risk for dz progression	for adult pts w/ non-severe dz at highest risk for hospitalization[1] suggest *against* use in pts w/ non-severe dz at low risk for hospitalization
molnupiravir	for outpts w/ mild-mod dz at high risk for dz progression ONLY if other outpt options not available or appropriate	rec *against* use	suggest use for outpts ≥18 yo w/ mild-mod dz at high risk for dz progression, if no other tx options	suggest use for pts ≥18 yo w/ non-severe dz who are not pregnant or breastfeeding, and at highest risk for hospitalization[1]
remdesivir (RDV)	outpts: for pts w/ mild-mod dz at high risk for dz progression[2] inpts: for pts requiring O_2 but *not* rec if mech vent or ECMO;[2] IE for pts not requiring O_2; rec *against* routine use after discharge	outpts: for pts ≥12 yo and ≥40 kg w/ mild-mod dz at high risk for dz progression[2] inpts not requiring O_2: consider use for pts ≥12 yo at highest risk for dz progression inpts requiring conventional O_2: use RDV; use in combo w/ DEX if increasing O_2 needs inpts requiring high flow O2 or noninvasive vent: use in combo w/ DEX	outpts: suggest use in pts w/ mild-mod dz at high risk for dz progression[2] inpts w/ mild-mod dz: suggest use in pts at high risk for dz progression[2] inpts w/ severe dz (SpO_2 ≤94%): suggest use but not if mech vent or ECMO[2]	suggest use for pts ≥12 yo and ≥40 kg w/ non-severe dz at highest risk for hospitalization[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
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
ribavirin (RBV)	--	--	IE (in vitro data only)	--
lopinavir/ ritonavir (LPV/r)	rec *against* use	rec *against* use	rec *against* use	rec *against* use
other HIV protease inhibitors (e.g. darunavir (DRV))	rec *against* use	rec *against* use	DRV: IE (no activity at normal doses, no viral clearance per mfr)	--
famotidine	--	--	suggest *against* COVID tx use in outpts w/ mild-mod dz and inpts w/ severe dz	--
ivermectin	rec *against* use	rec *against* use	rec *against* use	*not* rec outside clinical trial

nitazoxanide	*not* rec outside clinical trial	*not* rec outside clinical trial	--	--
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 – pts w/ highest risk if >10% chance of hospitalization; in absence of risk prediction tools, greatest risk factors incl. unvaccinated status, older age, immunodeficiencies, or chronic comorbidities
2 – RDV duration recs: NIH: 3 days for outpts; 5 days for inpts; IDSA: 3 days for outpts or inpts w/ mild-mod dz; 5 days for inpts requiring O_2

immunomodulators

	NIH (adults)	NIH (peds)	IDSA	WHO
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	COVID tx: use DEX for inpts requiring high flow O_2, noninvasive vent, mech vent, or ECMO[1,2]; rec *against* DEX use in pts not requiring O_2 or requiring conventional O_2, but may consider if increasing O_2 needs; rec *against* routine use after discharge MIS-C: use low-moderate dose methylprednisolone (or equivalent) in combo w/ IVIG; consider higher doses if no improvement w/in 24h underlying condition: continue tx, give PRN supplement doses	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
inhaled corticosteroids (e.g. budesonide)	IE	IE	suggest *against* use for mild-mod dz outside clinical trial	--
tocilizumab (IL-6 inhibitor)	inpts requiring conventional O_2: use if rapidly increasing O_2 needs, systemic inflammation, and already receiving DEX[4,5] inpts requiring high-flow O_2, noninvasive vent, mech vent, or ECMO: use in combo w/ DEX[4,5]	consider use in pts >2 yo requiring high-flow O2, noninvasive vent, mech vent, or ECMO if no oxygenation improvement w/in 24h of DEX	suggest use in severe or critical dz if inflammatory markers elevated (CRP ≥ 75)[5]	use in combo w/ steroids for pts w/ severe or critical dz
sarilumab (IL-6 inhibitor)	use as alternative to tocilizumab[5]	*not* rec in inpts outside clinical trial	IE[5]	use in combo w/ steroids for pts w/ severe or critical dz
siltuximab (IL-6 inhibitor)	*not* rec outside clinical trial	IE	--	--
baricitinib (JAK inhibitor)	inpts conventional O_2: use if rapidly increasing O_2 needs, systemic inflammation, and already receiving DEX[6]; rec *against* routine use after discharge inpts requiring high-flow O_2, noninvasive vent, mech vent, or ECMO: use in combo w/ DEX[6]; rec *against* routine use after discharge	consider use in pts >2 yo requiring high-flow O2, noninvasive vent, mech vent, or ECMO if no oxygenation improvement w/in 24h of DEX	suggest use w/ steroids in inpts w/ severe dz ($SpO_2 \leq 94\%$) for inpts w/ severe dz ($SpO_2 \leq 94\%$ and not intubated) who can't use steroids, suggest combo w/ RDV	rec baricitinib + steroids in severe or critical dz
tofacitinib (JAK inhibitor)	use as alternative to baricitinib[6]	use as alternative to baricitinib[6]	for inpts w/ severe dz ($SpO_2 \leq 94\%$ and no mech vent)	suggest *against* use[7]
ruxolitinib (JAK inhibitor)	*not* rec outside clinical trial	*not* rec outside clinical trial	--	suggest *against* use[7]
other JAK inhibitors	*not* rec outside clinical trial	*not* rec outside clinical trial	--	--
BTK inhibitors	*not* rec outside clinical trial	*not* rec outside clinical trial	--	--
anakinra (IL-1 inhibitor)	IE	MIS-C: consider use at high doses if no improvement w/in 24h	--	--

canakinumab (IL-1 inhibitor)	*not* rec outside clinical trial	IE	--	--
infliximab (TNF-alpha inhibitor)	--	MIS-C: consider use if no improvement w/in 24h	--	--
interferons (IFN)	all IFNs: *not* rec outside clinical trial in outpts w/ mild-mod dz IFN-α or λ: *not* rec outside clinical trial in inpts IFN-β: rec *against* use in inpts	IE	--	IFN-β-1a *not* rec outside clinical trial
colchicine	inpts: rec *against* use outpts: *not* rec outside clinical trial	IE	rec *against* use	rec *against* use for non-severe dz
fluvoxamine	IE	IE	inpts: IE outpts: rec *against* use outside clinical trial	rec *against* use for non-severe dz outside clinical trial

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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; avoid use if significant immunosuppression, GI perforation risk, uncontrolled non-SARS-CoV-2 infection, ALT >5x ULN, ANC <500, or Plt <50,000

5 – may use sarilumab IV as an alternative when tocilizumab IV is not available or not feasible to use

6 – may use tofacitinib as an alternative when baricitinib is not available or not feasible to use

7 – may consider tofacitinib or ruxolitinib only if baricitinib, tocilizumab, or sarilumab not available

antibody-based therapies

	NIH (adults)	NIH (peds)	IDSA	WHO
bamlanivimab *FDA EUA for monotherapy revoked Apr 16, 2021*	rec *against* monotherapy (see recs for bamlanivimab and etesevimab)	rec *against* monotherapy (see recs for bamlanivimab and etesevimab)	--	--
bamlanivimab and etesevimab *FDA EUA not currently authorized as of Jan 24, 2022*	COVID tx for outpts: rec *against* use[1] COVID tx for inpts: rec *against* use[1] COVID PEP: rec *against* use[1]	COVID tx for outpts: rec *against* use[1] COVID tx for inpts: rec *against* use[1] COVID PEP: rec *against* use[1]	--	--
casirivimab and imdevimab *FDA EUA not currently authorized as of Jan 24, 2022*	COVID tx for outpts: rec *against* use[1] COVID tx for inpts: rec *against* use[1] COVID PEP: rec *against* use[1]	COVID tx for outpts: rec *against* use[1] COVID tx for inpts: rec *against* use[1] COVID PEP: rec *against* use[1]	--	rec *against* use
sotrovimab *FDA EUA not currently authorized as of Mar 25, 2022*	outpts: rec *against* use[1] inpts: rec *against* use[1]	outpts: rec *against* use[1] inpts: rec *against* use[1]	--	rec *against* use
tixagevimab and cilgavimab *FDA EUA not currently authorized as of Jan 26, 2023*	COVID PrEP: rec *against* use[1]	COVID PrEP: rec *against* use[1]	--	--
bebtelovimab *FDA EUA not currently authorized as of Nov 4, 2022*	outpts: rec *against* use[1]	IE	--	--
convalescent plasma (CP) *FDA EUA for low-titer CP revoked Feb 4, 2021*	outpts: IE inpts w/o impaired immunity: rec *against* inpts w/ impaired immunity: IE	rec *against* CP in inpts if mech vent; rec *against* CP in inpts outside clinical trial if not mech vent; may consider high-titer	outpts: suggest use of high-titer CP for outpts w/ mild-mod dz at high risk for dz progression, if no other tx options inpts: rec *against* use	non-severe dz: rec *against* use severe dz: *not* rec outside clinical trial

		CP use on case-by-case basis with peds ID consult		
immune globulin (IVIG)	*not* rec outside clinical trial	COVID tx: IE MIS-C: use in combo w/ low-moderate dose methylprednisolone; rec *against* IVIG monotherapy unless glucocorticoid contraindicated	IE	--
SARS-CoV-2-specific IGs	IE	IE	--	--

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1 – NIH: not expected to be effective due to high non-susceptible variant proportion; IDSA: may use if predominant regional variant susceptible

adjunct therapies

	NIH (adults)	NIH (peds)	IDSA	WHO
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; rec *against* antiplatelet tx to prevent dz progression or death inpts not requiring O_2: give VTE prophylaxis w/ prophylactic dose heparin (LMWH preferred) unless contraindicated inpts requiring conventional O_2: give VTE prophylaxis w/ therapeutic dose heparin (LMWH preferred) if D-dimer >ULN and no incr. bleeding risk, otherwise give prophylactic dose heparin unless contraindicated; rec *against* therapeutic-dose oral anticoagulants for VTE prophylaxis except in clinical trial; rec *against* antiplatelet tx to prevent dz progression or death inpts requiring high-flow O_2, noninvasive vent, mech vent, or ECMO: give VTE prophylaxis w/ prophylactic dose heparin unless contraindicated, rec *against* intermediate or therapeutic doses except in clinical trial; switch to prophylactic dose if therapeutic dose started before ICU transfer unless VTE; rec *against* antiplatelet tx to prevent dz progression or death in non-critically ill pts, IE for critically ill pts pregnant inpts: give VTE prophylaxis w/ prophylactic dose heparin unless	COVID-19 tx: VTE prophylaxis per SOC MIS-C: use low-dose aspirin if no bleeding risk; add therapeutic anticoagulation for pts w/ large CAAs or moderate-severe LV dysfunction, otherwise consider adding therapeutic vs prophylactic anticoagulation on an individual basis	--	use standard prophylaxis dose in inpts if no indication for intermediate or therapeutic doses[1]

	contraindicated, IE for therapeutic doses if no known VTE			
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	--	--	--
NSAIDs	continue underlying condition tx; no antipyretic strategy preference	--	no evidence link to COVID worsening per FDA, EMA, WHO	--
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