Table 5e. Characteristics of Immunomodulators

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- The information in this table is derived from data on the use of these drugs for FDA-approved indications or from clinical trials that evaluated their use in patients with COVID-19.
- For dose modifications for patients with organ failure or those who require extracorporeal devices, please refer to product labels or EUAs, when available.
- There are currently not enough data to determine whether certain medications can be safely coadministered with therapies for the treatment of COVID-19. When using concomitant medications with similar toxicity profiles, consider performing additional safety monitoring.
- The potential additive, antagonistic, or synergistic effects and the safety of using certain combination therapies for the treatment of COVID-19 are unknown. Clinicians are encouraged to report AEs to the FDA *MedWatch* program.
- For drug-drug interaction information, please refer to product labels and visit the Liverpool COVID-19 Drug Interactions website.
- For the Panel's recommendations on using the drugs listed in this table, please refer to the drug-specific sections of the Guidelines; Therapeutic Management of Nonhospitalized Adults With COVID-19; Therapeutic Management of Hospitalized Adults With COVID-19; Therapeutic Management of Hospitalized Children With COVID-19; and Pregnancy, Lactation, and COVID-19 Therapeutics.

Drug Name	Dosing Regimens	Adverse Events	Monitoring Parameters	Drug-Drug Interaction Potential	Comments
Corticosteroid (Systemic) *Recommended by the Panel for the treatment of COVID-19 in certain hospitalized patients.*					
Dexamethasone	**Dose for Adults With COVID-19** • DEX 6 mg IV or PO once daily for up to 10 days or until hospital discharge, whichever comes first[1]	• Hyperglycemia • Secondary infections • Reactivation of latent infections (e.g., HBV, HSV, strongyloidiasis, TB) • Psychiatric disturbances • Avascular necrosis • Adrenal insufficiency • Increased BP • Peripheral edema • Myopathy (particularly if used with NMBAs)	• Blood glucose • BP • Signs and symptoms of new infection	• Moderate CYP3A4 inducer • CYP3A4 substrate	• If DEX is not available, an alternative corticosteroid (e.g., prednisone, methylprednisolone, hydrocortisone) can be used. • For these drugs, the total daily dose equivalencies to DEX 6 mg (IV or PO) are: • Prednisone 40 mg • Methylprednisolone 32 mg • Hydrocortisone 160 mg

Drug Name	Dosing Regimens	Adverse Events	Monitoring Parameters	Drug-Drug Interaction Potential	Comments
Janus Kinase Inhibitors *Recommended by the Panel for the treatment of COVID-19 in certain hospitalized patients.*					
Baricitinib	**FDA-Approved Doses for COVID-19 in Adults Aged ≥18 Years, per eGFR[2]** *≥60 mL/min/1.73 m²* • BAR 4 mg PO once daily for 14 days or until hospital discharge, whichever comes first *30 to <60 mL/min/1.73 m²* • BAR 2 mg PO once daily for 14 days or until hospital discharge, whichever comes first *15 to <30 mL/min/1.73 m²* • BAR 1 mg PO once daily for 14 days or until hospital discharge, whichever comes first *<15 mL/min/1.73 m²* • **Not recommended** **FDA EUA Dose for COVID-19 in Children Aged 9–17 Years[3]** • Same as adults **FDA EUA Doses for COVID-19 in Children Aged 2 to <9 Years, per eGFR[3]** *≥60 mL/min/1.73 m²* • BAR 2 mg PO once daily for 14 days or until hospital discharge, whichever comes first *30 to <60 mL/min/1.73 m²* • BAR 1 mg PO once daily for 14 days or until hospital discharge, whichever comes first *<30 mL/min/1.73 m²* • **Not recommended**	• Lymphoma and other malignancies • Thrombotic events (e.g., PE, DVT, arterial thrombosis) • GI perforation • Treatment-related changes in lymphocytes, neutrophils, Hgb, liver enzymes • HSV reactivation • Herpes zoster • Secondary infections • Serious cardiac-related events (e.g., MI, stroke)	• CBC with differential • Renal function • Liver enzymes • Signs and symptoms of new infections	• Dose modification recommended when coadministering BAR with a strong OAT3 inhibitor.	• See the FDA label[2] and EUA[3] for dosing guidance in patients with: • ALC <200 cells/μL • ANC <500 cells/μL • If increases in ALT or AST are observed and DILI is suspected, interrupt BAR treatment until the diagnosis of DILI is excluded. • BAR tablets can be taken PO or crushed, dispersed in water, and given via gastrostomy tube.[2] **Availability** • BAR is approved by the FDA for the treatment of COVID-19 in adults aged ≥18 years.[2] • BAR is available through an FDA EUA for children aged 2–17 years who require supplemental oxygen, NIV, MV, or ECMO.[3]

Drug Name	Dosing Regimens	Adverse Events	Monitoring Parameters	Drug-Drug Interaction Potential	Comments
Janus Kinase Inhibitors, continued					
Tofacitinib	**Dose for COVID-19 in Clinical Trials** • Tofacitinib 10 mg PO twice daily for up to 14 days or until hospital discharge, whichever comes first[4]	• Thrombotic events (e.g., PE, DVT, arterial thrombosis) • Anemia • Secondary infections • GI perforation • Diarrhea • Headache • Herpes zoster • Lipid elevations • Liver enzyme elevations • Lymphoma and other malignancies • Serious cardiac-related events (e.g., MI, stroke)	• CBC with differential • Liver enzymes • Signs and symptoms of new infections	• Requires dose modification when administered with strong CYP3A4 inhibitors or when used with a moderate CYP3A4 inhibitor that is coadministered with a strong CYP2C19 inhibitor • Coadministration with strong CYP3A4 inducers **is not recommended**.	• Avoid use in patients with ALC <500 cells/μL, ANC <1,000 cells/μL, or Hgb <9 g/dL. • May require dose modification in patients with moderate to severe renal impairment or moderate hepatic impairment
Interleukin-6 Inhibitors (Anti-Interleukin-6 Receptor Monoclonal Antibodies) *Recommended by the Panel for the treatment of COVID-19 in certain hospitalized patients.*					
Sarilumab	**Dose for COVID-19 in Clinical Trials** • 1 dose of sarilumab 400 mg by IV infusion over 1 hour[5,6]	• Neutropenia • Thrombocytopenia • GI perforation • HSRs • Liver enzyme elevations • HBV reactivation • Infusion-related reactions	• HSRs • Infusion-related reactions • CBC with differential • Liver enzymes	• Elevated IL-6 may downregulate CYP enzymes; thus, use of sarilumab may lead to increased metabolism of coadministered drugs that are CYP substrates. • The effects of sarilumab on CYP enzymes may persist for weeks after the drug is stopped.	• Sarilumab **is not recommended** in patients with ALT or AST >1.5 times the upper limit of the reference range, ANC <2,000 cells/μL, or PLT <150,000 cells/μL.[7] **Availability** • The IV formulation of sarilumab is not approved by the FDA, but in clinical trials, a single SUBQ dose (using the prefilled syringes, **not** the prefilled pen) of sarilumab 400 mg was reconstituted in 100 cc 0.9% NaCl and given as an IV infusion over 1 hour.[6,8]

Drug Name	Dosing Regimens	Adverse Events	Monitoring Parameters	Drug-Drug Interaction Potential	Comments
Interleukin-6 Inhibitors (Anti-Interleukin-6 Receptor Monoclonal Antibodies), continued					
					• IV infusion of sarilumab should occur within 4 hours of its preparation; it can be stored at room temperature until administered.
Tocilizumab	**FDA-Approved Dose for COVID-19 in Hospitalized Adults** • 1 dose of tocilizumab 8 mg/kg actual body weight (up to 800 mg) by IV infusion over 1 hour **FDA EUA Doses for COVID-19 in Hospitalized Children** *Body Weight ≥30 kg* • Tocilizumab 8 mg/kg by IV infusion over 1 hour *Body Weight <30 kg* • Tocilizumab 12 mg/kg by IV infusion over 1 hour **For All Doses** • If clinical signs or symptoms worsen or do not improve following the first IV infusion, 1 additional dose may be administered at least 8 hours after the first dose.	• HSRs • Infusion-related reactions • GI perforation • Hepatotoxicity • Treatment-related changes on laboratory tests for neutrophils, platelets, lipids, and liver enzymes • HBV reactivation • Secondary infections • Cases of disseminated strongyloidiasis have been reported in patients with COVID-19 during treatment with tocilizumab and corticosteroids.	• HSRs • Infusion-related reactions • CBC with differential • Liver enzymes	• Inhibition of IL-6 may lead to increased metabolism of coadministered drugs that are CYP450 substrates. • The effects of tocilizumab on CYP enzymes may persist for weeks after the drug is stopped.	• Tocilizumab **is not recommended** in patients with ALT or AST >10 times the upper limit of the reference range, ANC <1,000 cells/μL, or PLT <50,000 cells/μL.[9] • SUBQ formulation of tocilizumab **is not intended** for IV administration. **Availability** • IV tocilizumab is approved by the FDA for the treatment of COVID-19 in hospitalized adults aged 18 years.[10] • Tocilizumab is available through an FDA EUA for the treatment of COVID-19 in certain hospitalized children aged 2–17 years.[9]

Drug Name	Dosing Regimens	Adverse Events	Monitoring Parameters	Drug-Drug Interaction Potential	Comments
Cytotoxic T-Lymphocyte–Associated Antigen 4 Agonist *Recommended by the Panel for the treatment of COVID-19 in certain hospitalized patients.*					
Abatacept	**Dose for COVID-19 in Clinical Trials** • 1 dose of abatacept 10 mg/kg actual body weight (up to 1,000 mg) by IV infusion over 30 minutes[11]	• HSRs, including anaphylaxis • Infusion-related reactions • HBV reactivation • Secondary infections • Patients with COPD may develop more frequent respiratory AEs. • Headache • Upper respiratory infection, nasopharyngitis • Nausea • Anemia • HTN • Decrease in CD4 count • Hypermagnesemia • Acute kidney injury[12]	• HSRs • Infusion-related reactions • CBC with differential • Electrolytes • Renal function	• Drug-drug interactions are unlikely between abatacept and medications that are CYP substrates, inhibitors, or inducers.	• The IV formulation of abatacept includes maltose, which may give falsely elevated blood glucose readings with certain blood glucose monitors (e.g., GDH-PQQ–based monitoring systems) on the day of infusion. • In the ACTIV-1 trial, 1 case of anaphylaxis and 2 infusion-related reactions were reported among abatacept recipients.[11] **Availability** • The IV formulation of abatacept is commercially available.
Tumor Necrosis Factor–Alpha Inhibitor *Recommended by the Panel for the treatment of COVID-19 in certain hospitalized patients.*					
Infliximab	**Dose for COVID-19 in Clinical Trials** • 1 dose of infliximab 5 mg/kg actual body weight by IV infusion over 2 hours[11]	• HSRs, including anaphylaxis • Infusion-related reactions • The following AEs are associated with chronic use of infliximab: • Hepatotoxicity • Cytopenia (e.g., leukopenia, neutropenia, thrombocytopenia, pancytopenia	• HSRs • Infusion-related reactions • CBC with differential • PLT • Liver enzymes • If infliximab is administered to patients with heart failure, they should be closely monitored.	• Inhibition of cytokine activity may lead to increased metabolism of coadministered drugs that are CYP450 substrates.	**Availability** • Infliximab is available as an originator biologic or a biosimilar.

Drug Name	Dosing Regimens	Adverse Events	Monitoring Parameters	Drug-Drug Interaction Potential	Comments
Tumor Necrosis Factor–Alpha Inhibitor, continued					
		• HBV reactivation • Secondary infections (e.g., invasive fungal infections, reactivation of latent TB) • Heart failure • CVA, MI, hypotension, hypertension, arrhythmias • Transient vision loss • Demyelinating disease • Lupus-like syndrome • Headache • Abdominal pain[13]			
Anti-C5a Monoclonal Antibody *Received an FDA EUA for the treatment of COVID-19 when it is administered within 48 hours of MV or ECMO. There is insufficient evidence for the Panel to recommend either for or against its use.*					
Vilobelimab	**FDA EUA Dose for COVID-19 in Hospitalized Adults Receiving MV or ECMO** • Vilobelimab 800 mg by IV infusion after dilution, up to 6 doses; start treatment within 48 hours of intubation (Day 1) followed by administration on Days 2, 4, 8, 15, and 22 if patient is still hospitalized (even if discharged from ICU)	• Secondary infections • Infusion-related reactions • Delirium • PE • HTN • Pneumothorax • DVT • Liver enzyme elevations • Hypoxemia • Thrombocytopenia • Pneumomediastinum • Supraventricular tachycardia • Constipation • Rash	• Signs and symptoms of new infections • Infusion-related reactions • CBC with differential • Liver enzymes	• None expected	**Availability** • Vilobelimab is not approved by the FDA, but it is commercially available for use in hospitalized adults with COVID-19, as authorized by the EUA.[14]

Drug Name	Dosing Regimens	Adverse Events	Monitoring Parameters	Drug-Drug Interaction Potential	Comments
Interleukin-1 Inhibitors *Anakinra: Received an FDA EUA for the treatment of COVID-19 in certain hospitalized adults. There is insufficient evidence for the Panel to recommend either for or against its use.* *Canakinumab: The Panel recommends against the use of canakinumab for the treatment of COVID-19, except in a clinical trial.*					
Anakinra	**FDA EUA Dose for COVID-19 in Hospitalized Adults Aged ≥18 Years** • Anakinra 100 mg SUBQ once daily for 10 days **Dose for Patients With CrCl <30 mL/min** • Anakinra 100 mg SUBQ every other day for 5 total doses over 10 days[15]	• Neutropenia, particularly when used concomitantly with other agents that can cause neutropenia • HSRs, including anaphylaxis and angioedema • Secondary infections • Injection site reactions • Liver enzyme elevations • Hyperkalemia • Hypernatremia • Rash	• CBC with differential; assess neutrophils before starting treatment and during therapy. • BMP • Liver enzymes • Renal function	• Use with TNF-blocking agents **is not recommended** due to potential increased risk of infection.	• Contraindicated in patients with known hypersensitivity to proteins derived from *Escherichia coli*, anakinra, or any component of the product[15]
Canakinumab	**Dose for COVID-19 in Clinical Trials** • Canakinumab 450–750 mg (based on body weight) by IV infusion over 2 hours[16,17] **FDA-Approved Dose for Systemic JIA** • Canakinumab 4 mg/kg (up to 300 mg) SUBQ every 4 weeks[18]	• HSRs • Neutropenia • Nasopharyngitis • Diarrhea • Respiratory tract infections • Bronchitis • Gastroenteritis • Pharyngitis • Musculoskeletal pain • Vertigo • Abdominal pain • Injection site reactions • Liver enzyme elevations	• HSRs • CBC with differential • Liver enzymes	• Binding of canakinumab to IL-1 may increase formation of CYP enzymes and alter metabolism of drugs that are CYP substrates. • Use with TNF-blocking agents **is not recommended** due to potential increased risk of infection.	**Availability** • The IV formulation of canakinumab is not approved by the FDA for use in the United States.[18]

Drug Name	Dosing Regimens	Adverse Events	Monitoring Parameters	Drug-Drug Interaction Potential	Comments
Corticosteroids (Inhaled) *There is insufficient evidence for the Panel to recommend either for or against the use of inhaled corticosteroids for the treatment of COVID-19.*					
Budesonide (Inhaled)	**Dose for COVID-19 in Clinical Trials** • Budesonide 800 µg oral inhalation twice daily until symptom resolution or for up to 14 days[19,20]	• Secondary infections • Oral thrush • Systemic AEs are not common, but they may occur when budesonide is coadministered with a strong CYP3A4 inhibitor.	• Signs of AEs involving the oral mucosa or throat, including thrush • Signs of systemic corticosteroid effects (e.g., adrenal suppression)	• CYP3A4 substrate • **Do not use** with strong CYP3A4 inhibitors.	• No comments
Ciclesonide (Inhaled)	**Dose for COVID-19 in Clinical Trials** • Ciclesonide 160 µg as 2 MDI inhalations twice daily for 30 days[21]	• Secondary infections • Oral thrush • Systemic AEs (less common)	• Signs of AEs involving the oral mucosa or throat, including thrush • Signs of systemic corticosteroid effects (e.g., adrenal suppression)	• CYP3A4 substrate • Strong CYP3A4 inhibitors are expected to have less effect on ciclesonide exposure than on budesonide or fluticasone exposure.	• No comments
Fluticasone (Inhaled)	**Dose for COVID-19 in Clinical Trials** • Fluticasone 200 µg as 1 MDI inhalation once daily for 14 days[22]	• Secondary infections • Oral thrush • Systemic AEs are not common, but they may occur when fluticasone is coadministered with a strong CYP3A4 inhibitor.	• Signs of AEs involving the oral mucosa or throat, including thrush • Signs of systemic corticosteroid effects (e.g., adrenal suppression)	• CYP3A4 substrate • **Do not use** with strong CYP3A4 inhibitors.	• No comments

Key: AE = adverse event; ALC = absolute lymphocyte count; ALT = alanine transaminase; ANC = absolute neutrophil count; AST = aspartate aminotransferase; BAR = baricitinib; BMP = basic metabolic panel; BP = blood pressure; CBC = complete blood count; CD4 = CD4 T lymphocyte; COPD = chronic obstructive pulmonary disease; CrCl = creatinine clearance; CVA = cerebral vascular accident; CYP = cytochrome P450; DEX = dexamethasone; DILI = drug-induced liver injury; DVT = deep vein thrombosis; ECMO = extracorporeal membrane oxygenation; eGFR = estimated glomerular filtration rate; EUA = Emergency Use Authorization; FDA = Food and Drug Administration; GDH-PQQ = glucose dehydrogenase pyrroloquinoline quinone; GI = gastrointestinal; HBV = hepatitis B virus; Hgb = hemoglobin; HSR = hypersensitivity reaction; HSV = herpes simplex virus; HTN = hypertension; ICU = intensive care unit; IL = interleukin; IV = intravenous; JIA = juvenile idiopathic arthritis; MDI = metered dose inhaler; MI = myocardial infarction; MV = mechanical ventilation; NaCl = sodium chloride; NIV = noninvasive ventilation; NMBA = neuromuscular blocking agent; OAT = organic anion transporter; the Panel = the COVID-19 Treatment Guidelines Panel; PE = pulmonary embolism; PLT = platelet count; PO = oral; SUBQ = subcutaneous; TB = tuberculosis; TNF = tumor necrosis factor

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