

Immunosuppressive Potential of Medications NOT Including Oncological Agents

Some medications affect and/or act on the immune system. There may be several reasons to determine a patient's immune status including:

- COVID-19 vaccine doses (moderately to severely immunocompromised patients are to receive 3 doses for the primary series; at times, moderately to severely immunocompromised status is an eligibility criterion for booster doses)
- eligibility for early COVID-19 therapeutics (e.g., Paxlovid™, remdesivir)
- potential for harm from live vaccines; reduced immune response from inactive vaccines; possibility of timing doses around vaccinations

Based on these nuances, along with the fact that information regarding immunosuppressive potential is often conflicting and/or based on limited clinical evidence, and that agents have varying degrees of immunosuppression, consider the individual patient and use clinical judgement.

This document contains a table of agents that affect and/or act on the immune system. Note this list is not exhaustive and agents are continually being introduced to the market. The last column (Mod-Severe IS) indicates whether medications are expected to cause *moderate to severe immunosuppression* for the purposes of determining COVID-19 vaccine doses and eligibility for early COVID-19 therapeutics in Saskatchewan.

- Agents in which the last column indicates ' $\sqrt{}$ ' are generally **considered** moderately to severely immunosuppressive.
- Agents in which the last column indicates 'X' are generally **not considered** moderately to severely immunosuppressive.

Live vaccines generally should not be given to patients taking medications that cause moderate to severe immunosuppression. If live vaccines are being considered for patients who are taking a medication indicated with an ' $\sqrt{}$ ', consult the patient's specialist or primary care provider.

Generic Name	Trade Name	Indications [‡]	Class	Additional Considerations/Comments	Mod- Severe IS [†]
Abatacept	Orencia®	JIA, PsA, RA, JRA	Selective T Cell Co- Stimulation Modulator	For Covid-19 vaccine considerations see references 1-3 [¶]	v
Adalimumab	Humira®	JIA, RA, AS, CD, UC, PsA, PsO, Uveitis	mAb TNF-α Inhibitor	For Covid-19 vaccine considerations see references 1-3,6 [¶] Biosimilars [¥] : Abrilada®, Amgevita®, Hadlima®, Hulio®, Hyrimoz®, Idacio®, Simlandi™, Yuflyma™	v
Alemtuzumab	Lemtrada®	MS	mAb Anti-CD52	For Covid-19 vaccine considerations see references 4,7,8 [¶] Transient immunosuppression during periods of severe lymphopenia, likely 4-8 weeks after end of treatment course. ²⁶	√/X (see comments)
Alirocumab	Praluent®	Antilipemic Agent	mAb PCSK9 Inhibitor	The role of PCSK9 in the immune system not understood but if anything, may have antiviral effects. ²⁸ Nothing to suggest immunosuppressive.	x
Anakinra	Kineret®	RA	IL-1 RA IL-1 Inhibitor	For Covid-19 vaccine considerations see references 1-3 [¶]	v
Apremilast	Otezla®	PsA, PsO, Behcet's Disease	Phosphodiesterase-4 Enzyme Inhibitor	For Covid-19 vaccine considerations see reference 2 [¶]	v
Auranofin	Ridaura®	RA	DMARD	Generally, not considered immunosuppressive ²⁵	x
Azathioprine	lmuran [®] , generic	RA, Anti-rejection	Immunosuppressant DMARD	Low doses (≤ 3mg/kg/day) are generally not considered immunosuppressive ¹⁴ ; however, for the purposes of this document, all doses are considered immunosuppressive	
Baricitinib	Olumiant®	RA	JAK Inhibitor	For Covid-19 vaccine considerations see references 1-3 [¶]	V
Basiliximab	Simulect®	Anti-Rejection	mAb IL-2 Inhibitor	For Covid-19 vaccine considerations see reference 8 [¶]	v
Belimumab	Benlysta	SLE	mAb BLyS Inhibitor	For Covid-19 vaccine considerations see references 2,3 [¶]	v
Benralizumab	Fasenra®	Asthma	mAb IL-5 Inhibitor	Specifically affects eosinophils. There may be concern with helminthic infections, but little immunosuppression otherwise. ¹⁰	х
Brodalumab	Siliq™	PsO	mAb IL-17 Inhibitor	For Covid-19 vaccine considerations see references 2,3 [¶]	٧
Canakinumab	llaris®	JIA	mAb IL- 1 Inhibitor	For Covid-19 vaccine considerations see references 2,3 ¹	٧
Certolizumab	Cimzia®	AS, PsA, PsO, RA	mAb TNF-α Inhibitor	For Covid-19 vaccine considerations see references 2,3 ¹	v

Generic Name	Trade Name	Indications [‡]	Class	Additional Considerations/Comments	Mod- Severe IS⁺
Cladribine	Mavenclad®	MS	Selective immunosuppressant	For Covid-19 vaccine considerations see reference 4,7,8 [¶] Transient immunosuppression during periods of severe lymphopenia, likely 2-3 months after end of treatment course. ²⁶	√/X (see comments)
Corticosteroids* (Systemic)				Generally speaking, doses <20mg/day of prednisone (or equivalent) or corticosteroids administered topically, inhaled, or intraarticular are not considered immunosuppressive. ^{3,14}	√ (depending on dose/ROA)
Cyclophosphamide	Procytox	Anti-Rejection, MS		For Covid-19 vaccine considerations see references 2,8 [¶]	v
Cyclosporine	Sandimmune [®] Neoral [®]	Anti-Rejection, RA, PsO	Calcineurin Inhibitor	For Covid-19 vaccine considerations see references 1-3,8 [¶]	v
Denosumab	Prolia®	Osteoporosis	mAb RANKL Inhibitor	The degree of immunosuppression – if any- from denosumab has not been well-established. It appears to be low, however, there is potential for increased infections. ¹¹ For Covid-19 vaccine considerations see references 5,11 [¶]	x
Dimethyl Fumarate	Tecfidera™, generic	MS	Fumaric Acid Derivative	For Covid-19 vaccine considerations see reference 4,7,8 [¶] May be immunosuppressive in some contexts ²⁷ , such as when lymphocyte count < 0.5 x 10 ⁹ /L	X (see comments)
Dupilumab	Dupixent®	Atopic Dermatitis, Asthma	mAb IL-4/IL-13 Inhibitor	IL-4 & IL-13 affect levels of IgE. There may be concern with helminthic infections, but little immunosuppression otherwise. ¹⁰ However, it is suggested to avoid live vaccines (such as MMR and varicella) when using dupilumab. ¹⁰	х
Eculizumab	Soliris®	↓ Hemolysis PNH, aHUS, gMG, NMOSD	mAb Complement C5 Inhibitor	For Covid-19 vaccine considerations see reference 9 ¹	v
Eptinezumab	Vyepti®	Migraine Prophylaxis	CGRP Binding Antibody	While CGRP receptors are found on some immune system cells, there is no evidence of immunosuppression. ²⁹	x
Erenumab	Aimovig®	Migraine Prophylaxis	CGRP Binding Antibody	While CGRP receptors are found on some immune system cells, there is no evidence of immunosuppression. ²⁹	x
Etanercept	Enbrel®	RA, JIA, PsA, PsO, AS	TNF-α Inhibitor	For Covid-19 vaccine considerations see references 2,3 [¶] Biosimilars [¥] : Brenzys [®] , Erelzi [®]	v
Everolimus	Afinitor [®] , generic		mTOR Kinase Inhibitor	Anti-rejection (off-label use) ¹⁹ For Covid-19 vaccine considerations see reference 8 [¶]	v

Generic Name	Trade Name	Indications [‡]	Class	Additional Considerations/Comments	Mod- Severe IS [†]
Evolocumab	Repatha®	Antilipemic Agent	mAb PCSK9 Inhibitor	The role of PCSK9 in the immune system is not understood but if anything, may have antiviral effects. ²⁸ Nothing to suggest immunosuppressive.	х
Fingolimod	Gilenya [®] , generic	MS	Spingosine 1-Phosphate Receptor Modulator	For Covid-19 vaccine considerations see references 4,7,8 [¶]	v
Fremanezumab	Ajovy®	Migraine Prophylaxis	CGRP Binding Antibody	While CGRP receptors are found on some immune system cells, there is no evidence of immunosuppression. ²⁹	х
Galcancezumab	Emgality [®]	Migraine Prophylaxis	CGRP Binding Antibody	While CGRP receptors are found on some immune system cells, there is no evidence of immunosuppression. ²⁹	х
Glatiramer	Copaxone [®] , Glatect™∆	MS		For Covid-19 vaccine considerations see references 4,7,8 [¶]	х
Golimumab	Simponi®	AS, PsA, RA, UC	mAB TNF-α Inhibitor	For Covid-19 vaccine considerations see references 1-3 [¶]	٧
Guselkumab	Tremfya®	PsO	mAb IL-23 Inhibitor	For Covid-19 vaccine considerations see references 1-3 [¶]	٧
Hydroxychloroquine	Plaquenil [®] , generic	RA, SLE	DMARD	Generally, not considered immunosuppressive. ²⁵	x
Infliximab	Remicade®	AS, CD, PsO, RA, UC	mAb TNF-α Inhibitor	For Covid-19 vaccine considerations see references 2,3,6 [¶] Biosimilars [¥] : Avsola™, Inflectra®, Remsima™ SC, Renflexa™	٧
Interferon Beta-1A Beta-1B Peginterferon Beta- 1A	Avonex®, Rebif® Betaseron® Plegridy™	MS		For Covid-19 vaccine considerations see references 4,7,8 [¶]	х
Intravenous Immunoglobulin (IVIG)		Autoimmune Diseases	Immune Globulin	For Covid-19 vaccine considerations see references 2,3 ¹	х
Ixekizumab	Taltz®	PsA, PsO	mAb IL-17 Inhibitor	For Covid-19 vaccine considerations see references 2,3. [¶]	v
Leflunomide	Arava [®] , generic	RA	DMARD	For Covid-19 vaccine considerations see references 2,3. ¹	٧
6–Mercaptopurine	Purinethol®, generic	Off-label use: CD, UC	Immunosuppressant DMARD	Low doses (≤1.5 mg/kg/day) generally not considered immunosuppressive ¹⁴ however, for the purposes of this document, all doses are considered immunosuppressive	√ (regardless of dose)

Generic Name	Trade Name	Indications [‡]	Class	Additional Considerations/Comments	Mod- Severe IS⁺
Mepolizumab	Nucala	Asthma	mAb IL-5 Inhibitor	Specifically affects eosinophils. There may be concern with helminthic infections, but little immunosuppression otherwise ¹⁰	x
Methotrexate	generics	PsA, PsO, RA	DMARD	Low doses (≤ 0.4 mg/kg/week) generally not considered immunosuppressive ¹⁴ ; however, for the purposes of this document, all doses are considered immunosuppressive	√ (regardless of dose)
Mitoxantrone	generic	MS	Topoisomerase II Inhibitor	For Covid-19 vaccine considerations see references 4,7,8. [¶]	v
Mycophenolate	Cellcept [®] , Myfortic [®] , generic	Anti-Rejection	Antiproliferative	For Covid-19 vaccine considerations see references 2,8. [¶]	V
Natalizumab	Tysabri®	MS	mAb	For Covid-19 vaccine considerations see references 4,7,8. [¶]	х
Ocrelizumab	Ocrevus [®]	MS	mAb Anti-CD20	For Covid-19 vaccine considerations see references 2,4,7,8. [¶]	v
Ofatumumab	Kesimpta™	MS	mAb Anti-CD20	For Covid-19 vaccine considerations see references 4,7,8. [¶]	v
Omalizumab	Xolair®	Asthma, Chronic Urticaria	mAb Anti-IgE	Specifically binds IgE. There may be concern with helminthic infections, but little immunosuppression otherwise ¹⁰	x
Ozanimod	Zeposia®	MS	S1P Receptor Modulator	For Covid-19 vaccine considerations see references 4,7,8. [¶]	
Ponesimod	Ponvory™	MS	S1P Receptor Modulator	For Covid-19 vaccine considerations see references 4,7,8. [¶]	v
Prednisone/ prednisolone	generics/ Pediapred®			Generally speaking, doses <20mg/day of prednisone (or equivalent) are not considered immunosuppressive. ^{3,14}	
Reslizumab	Cinqair™	Asthma	mAb IL-5 Inhibitor	Specifically affects eosinophils. There is concern with helminthic infections but little immunosuppression otherwise. ¹⁰	x
Risankizumab	Skyrizi®	PsO	mAb IL-23 Inhibitor	For Covid-19 vaccine considerations see reference 2. ¹	
Rituximab	Rituxan®	RA, GPA, MPA, MS	mAb Anti-CD20	For Covid-19 vaccine considerations see references 2-4,8. [¶] Biosimilars [¥] : Riabni™, Riximyo ^{®,} , Ruxience™, Truxima™	
Romosozumab	Evenity™	Osteoporosis	mAb Sclerostin Inhibitor	The degree of immunosuppression – if any- from romosozumab has not been well-established; there does not appear to be increased risk of infection. ¹¹ For Covid-19 vaccine considerations see references 5,11. [¶]	x

Generic Name	Trade Name	Indications [‡]	Class	Additional Considerations/Comments	Mod- Severe IS⁺
Sarilumab	Kevzara®	RA	mAb IL-6 Inhibitor	For Covid-19 vaccine considerations see references 2,3. [¶]	
Secukinumab	Cosentyx®	AS, PsO, PsA	mAb IL-17 Inhibitor	For Covid-19 vaccine considerations see references 2,3. [¶]	V
Siltuximab	Sylvant®	Multicentric Castleman's Disease	mAb IL-6 Inhibitor		v
Siponimod	Mayzent®	MS	S1P Receptor Modulator	For Covid-19 vaccine considerations see references 4,7,8. ¹	V
Sirolimus	Rapamune [®]	Anti-Rejection	mTOR Kinase Inhibitor	For Covid-19 vaccine considerations see reference 8. [¶]	v
Sulfasalazine	Salazopyrin®	CD, RA, UC	DMARD	Generally, not considered immunosuppressive. ²⁵	Х
Tacrolimus	Advagraf [®] , Prograf [®] , Envarsus PA [®] , generic	RA, Anti-Rejection	Calcineurin Inhibitor	For Covid-19 vaccine considerations see references 3,7,8. [¶]	V
Teriflunomide	Aubagio®	MS	Pyrimidine Synthesis Inhibitor	For Covid-19 vaccine considerations see references 4,7,8. [¶]	
Tildrakizumab	llumya™	PsO	mAb IL-23 Inhibitor	For Covid-19 vaccine considerations see reference 2. ¹	
Tocilizumab	Actemra®	JIA, RA	mAb IL-6 Inhibitor	For Covid-19 vaccine considerations see references 2,3,6. [¶]	
Tofacitinib	Xeljanz®	PsA, RA, UC	JAK Inhibitor	For Covid-19 vaccine considerations see references 2,3. [¶] V	
Upadacitinib	Rinvoq®	RA	JAK Inhibitor	For Covid-19 vaccine considerations see references 2,3. [¶]	
Ustekinumab	Stelara®	CD, PsA, PsO	mAb IL-12/IL-23 Inhibitor	For Covid-19 vaccine considerations see references 2,3,6. [¶]	
Vedolizumab	Entyvio®	CD, UC	mAb Selective Adhesion- Molecule Inhibitor	For COVID-19 vaccine considerations see reference 6. [¶] This agent is gut-specific and deemed not to causesystemic immunosuppression. ³⁰ However, caution isadvised until lack of systemic immunosuppression is firmlyestablished.	
 Please note: Some ho abiraterone anastrozole apalutamide 	rmonal medications indic bicalutamide buserelin cyproterone	ated for cancer are • darolut • degare • enzalut	amide • lix •	flutamide • letrozole • ralox	amide kifene oxifen

aHUS=atypical hemolytic uremic syndrome; AS=ankylosing spondylitis; CD=Crohn's disease; CGRP = calcitonin gene-related peptide; DMARD = disease modifying antirheumatic drug; gMG=generalized myasthenia gravis; GPA = granulomatosis with polyangiitis; Ig = immune globulin; IL = interleukin; JAK = janus kinase; JIA=juvenile idiopathic arthritis; JRA = juvenile rheumatoid arthritis; mAb = monoclonal antibody; MMR = measles, mumps, rubella; MPA = microscopic polyangiitis; MS=multiple sclerosis; mTOR = mammalian target of rapamycin; NMOSD=neuromyelitis optica spectrum disorder; PCSK9 = proprotein convertase subtilisin kexin type 9; PNH=paroxysmal nocturnal hemoglobinuria; PsA=psoriatic arthritis; PsO=plaque psoriasis; RA=rheumatoid arthritis; RANKL = receptor activator of nuclear factor kappa-B ligand; S1P = sphingosine-1-phosphate; SLE=systemic lupus erythematosus; SPA = granulomatosis with polyangitis; TNF α= tumor necrosis factor-alpha; UC=ulcerative colitis

+Mod-Sev IS = moderately to severely immunosuppressive for the purposes of determining COVID-19 vaccine doses and early COVID-19 therapeutics in Saskatchewan V Agent is generally considered to cause moderate to severe immunosuppression

x While the agent may affect the immune system, it is generally not considered to cause moderate to severe immunosuppression

[‡] Some drugs are used for several autoimmune diseases, often off-label. Some uncommon indications not included.

¶ Note that the information in these references is subject to change – please see the most current version.

*Corticosteroids: in the context of immunosuppression, only concerned with systemic corticosteroids (oral, parenteral), not topical, inhaled, or local injections. Physiologic dose is ~5 mg prednisone PO daily. See Corticosteroids and equivalent doses below.

[¥]Biosimilar. Not all biosimilars have the same indications as the reference product; check product monographs.

^A Subsequent entry non-biologic complex drug

Corticosteroid	Approximate Equivalent Dose	Route of Administration
Prednisone/Prednisolone	5 mg	PO
Betamethasone	0.6 mg to 0.75 mg	IM
Cortisone	25 mg	PO
Dexamethasone	0.75 mg	PO
Hydrocortisone	20 mg	PO
Methylprednisolone	4 mg	PO
Triamcinolone	4 mg	IM

Approximate Equivalent Doses of Systemic Corticosteroids (based on mineralocorticoid activity)

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