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Practical Guidelines for Managing Patients With Psoriasis on Biologics: An Update

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Abstract

The paradigm for treating inflammatory diseases has shifted dramatically in the past 10 to 20 years with the discovery of targeted therapeutics or "biologic" agents. Patients with rheumatoid arthritis, inflammatory bowel disease, psoriatic arthritis, and psoriasis, among others, are reaping the benefits of decades of bench to bedside research, allowing them to live more productive lives with less side effects than traditional systemic therapies. Despite these advances, many physicians unfamiliar with biologics are left to care for the basic needs of these patients and may be unaware of the multisystem comorbidities associated with psoriasis and the screening, monitoring, and other special considerations required of biologics patients. This can be overwhelming to primary care physicians and inadvertently expose patients to undue risks. The aim of this review is to provide a practical approach for all health care providers caring for patients with psoriasis being treated with biologics to facilitate communication with their treating dermatologist and ultimately provide patients with more comprehensive care.

Keywords
psoriasis, guidelines, biologics, review

Approximately 1.7% of Canadians have psoriasis. Psoriasis can be debilitating and has an effect on quality of life that is similar to cancer, arthritis, hypertension, heart disease, diabetes, and depression.[1] The management of patients with psoriasis is complicated by the numerous comorbidities that are associated with the condition.[2,3] Over the past decade, with the introduction of novel targeted biological agents ("biologics"), skin disease and quality of life have improved in these patients without the toxicity seen with traditional agents such as cyclosporine, acitretin, and methotrexate. There are approximately 20 000 patients on biologics, and that number is currently increasing by 17% per year.[4] There are currently 8 unique biologics (and 1 biosimilar: Inflectra) approved in Canada for moderate to severe plaque psoriasis (Table 1). With the introduction of new biologics and discontinuation of others, an update on biologics in psoriasis is overdue. Understanding the benefits, risks, and monitoring of patients on biologics is becoming increasingly important to dermatologists and primary care physicians.

Prebiologics

Selecting the Right Patient for a Biologic

Patients with moderate to severe plaque psoriasis in Canada are generally treated with phototherapy and/or methotrexate, acitretin, or cyclosporine prior to being considered for a biologic (unless there are contraindications or access to phototherapy is limited). Biologics are costly medications, and to qualify for reimbursement, certain criteria (which vary from province to province) need to be met, including severity of disease and failed prior therapies.

Exclusion criteria. It is important when considering starting patients on an anti–tumour necrosis factor (TNF) agent to ask about moderate to severe heart failure, multiple sclerosis, optic neuritis, or other demyelinating disease.[5-7] Brodalumab is contraindicated in patients with Crohn disease and should be avoided in patients with a history of depression.[8] For all other biologics, physicians should screen for active malignancy within the past 5 years (other than nonmelanoma skin cancer),[9] active tuberculosis (TB),[10] and hepatitis or other severe active infections (see Table 2).[11-13]

Vaccines prior to biologics. Vaccine counselling is an essential component of psoriasis management on biologics. Given that

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Table 1. Biologic Agents Approved by Health Canada for Moderate to Severe Plaque Psoriasis.

Biologic Agent (Brand)	Health Canada Approval for Psoriasis	Target	Drug Delivery Route	Dosing	Half-Life, d	Time to Be Removed From Body, d
Etanercept (Enbrel)	2006	TNF-α	SQ	50 mg twice weekly × 12 weeks, then 50 mg weekly	4	16-20
Infliximab (Remicade)	2006	TNF-α	IV	5 mg/kg infusion at weeks 0, 2, and 6 and q8 weeks	8-9.5	32-48
Inflectra (Biosimilar infliximab)	2014					
Adalimumab (Humira)	2008	TNF-α	SQ	80 mg first week, 40 mg second week, then 40 mg q2 weeks	10-20	40-100
Ustekinumab (Stelara)	2008	p40 subunit of IL-12/23	SQ	45 mg (<100 kg) or 90 mg (>100 kg) at weeks 0 and 4 and then q12 weeks	15-45	60-225
Secukinumab (Cosentyx)	2015	IL-17A	SQ	300 mg at weeks 0, 1, 2, 3, and 4, then monthly	27	108-135
Ixekizumab (Taltz)	2016	IL-17A	SQ	160 mg at week 0, then 80 mg at weeks 2, 4, 6, 8, 10, and 12, then q4 weeks	13	52-65
Guselkumab (Tremfya)	2017	p19 subunit of IL-23	SQ	100 mg at weeks 0 and 4, then q8 weeks	15-18	75-90
Brodalumab (Siliq)	2018	IL-17RA	SQ	210 mg at weeks 0, 1, and 2, then q2 weeks	11	44-55

Abbreviations: IL, interleukin; IV, intravenous; q, every; SQ, subcutaneous; TNF-α, tumour necrosis factor–α.

administration of live vaccines is contraindicated while on therapy, patients should be vaccinated *prior to the start of biologic therapy*. Live vaccines include measles-mumps-rubella (MMR), varicella, herpes zoster (Zostavax), intranasal influenza, oral typhoid, yellow fever, oral polio virus, vaccinia/smallpox, oral cholera, bacille Calmette-Guerin (BCG), and rotavirus. Administering live vaccines 2 to 4 weeks prior to biologic therapy is considered adequate to prevent viral dissemination.[14-16] Live attenuated or inactivated vaccines can be given while on biologics but should also be administered if possible prior to biologic therapy as the immune response may be reduced. Hepatitis A and B vaccines are recommended in patients without confirmed immunity to viral hepatitis. It is recommended to administer annual inactivated influenza and pneumococcal vaccines while on biologic therapy. Meningococcal vaccines should be considered for high-risk patients (military personnel and college students).[16] In a multivariate cohort study of over 90 000 patients with psoriasis, single-agent biologic therapy was not associated with increased risk of herpes zoster (HZ).[17] However, when combined with methotrexate, their risk increased.[17] A recent metanalysis demonstrated an overall increased risk of HZ in patients with mixed inflammatory conditions but not those on treatment with anti-TNF biologic therapy.[18] Another review of the literature suggests infliximab increases the risk of HZ, while in patients treated with adalimumab, etanercept, and ustekinumab, HZ risk remains controversial in patients with psoriasis.[19] Nonetheless, HZ vaccination should be considered in all biologics patients older than 50 years, especially given that there is a non–live recombinant HZ vaccine that is now available (Shingrix). For a complete list of vaccinations recommended for adults older than 19 years, please refer to the Advisory Committee on Immunization Practices 2013 recommended immunization schedule.[20]

Required testing prior to biologics

i) Tuberculosis testing:
   a) Chest x-ray AND either
   b) Mantoux tuberculin skin test (TST)[21] or QuantiFERON Gold* (if immunocompromised or if previous BCG vaccination)[11]

*Interferon gamma release assay.

Tuberculosis

Although there have been few cases of TB in patients with psoriasis, data from randomized controlled trials in patients with rheumatoid arthritis in the 1990s revealed an increased incidence of TB in patients on anti-TNF therapy.[22] This led to screening recommendations that have been used in clinical trials with the newer biologic agents (anti-interleukin [IL]–17 and IL-12/23); therefore, it is unknown whether they possess the same risk of TB reactivation. Consequently, all biologics (according to their product monograph) are contraindicated in patients with active TB,[9] and appropriate screening should be done to rule out latent TB infection prior to initiation of the drug. The Centers for Disease Control and Prevention (CDC) recommend a TST for the diagnosis of latent TB infection (LTBI) in patients treated with anti-TNFs.[23] TST results can be interpreted as positive if >10 mm or >15 mm if they have no risk factors and

Table 2. Considerations Before Starting a Biologic Agent.

Exclusion criteria:

1) **Absolute contraindications:**
   - □ Known hypersensitivity reaction
   - □ Infections
     - ○ Severe active infections (ie, sepsis, opportunistic infections)
     - ○ Active or latent tuberculosis (may be started after 2 months TB treatment if under supervision of multidisciplinary team)
   - □ Crohn disease (brodalumab only)
   - □ Moderate to severe heart failure (NYHA class III/IV)—anti-TNFs only
2) **Relative contraindications:**
   - □ History of depression (brodalumab only)
   - □ Demyelinating disease (ie, multiple sclerosis, optic neuritis)—anti-TNFs only
   - □ Malignancy (excluding BCC and SCC), especially lymphoma, melanoma, and breast cancer
   - □ Pregnancy
   - □ Planned surgery
   - □ Hepatitis B or C
   - □ HIV

Vaccines: (administering vaccines 2 to 4 weeks prior to starting biologics is considered adequate)

1) **Prior to starting (live attenuated vaccines):** measles-mumps-rubella, varicella, intranasal influenza, oral typhoid, yellow fever, oral polio virus, vaccinia/smallpox, BCG, rotavirus
2) **Prior to starting/may also be done while on biologics (inactivated vaccines):**
   - ○ Hepatitis A and B (if not immune)
   - ○ Varicella (if not immune)
   - ○ Herpes zoster virus (if aged >50 years)
   - ○ Meningococcal vaccine (military, college students)
   - ○ HPV vaccine

Monitoring:

- □ CXR + (PPD/TST or QFG[a]) for tuberculosis
- □ Serology: hepatitis A antibody; hepatitis B surface antigen (HepBsAg), hepatitis B surface antibody (anti-HBs), hepatitis B core total antibody (anti-HBc); hepatitis C antibody, HIV
- □ Liver function tests (infliximab only)

Comorbidities to check for:

- □ Psoriatic arthritis (morning joint stiffness > 30 minutes, swollen joints, nail changes)
- □ Metabolic syndrome (factors that increase risk of developing diabetes and cardiovascular disease: obesity, elevated blood pressure, fasting glucose, serum triglycerides, and low HDL)
- □ IBD (bloody diarrhea, diarrhea with weight loss, recurrent abdominal pain, anemia, perianal fistula)
- □ Uveitis (redness, eye pain, blurred vision, floaters)
- □ Depression (anhedonia, feeling down/depressed/hopeless)

Counsel patients at high risk for developing opportunistic infections:

- □ Health care professionals
- □ Water/soil workers (ie, farmer, gardener, construction, renovations)
- □ Pets: avoid cleaning fish tanks/litter boxes (or wear gloves)
- □ Avoid undercooked meat, eggs, poultry
- □ Caution if traveling to developing world (refer to travel clinic)

Abbreviations: BCC, basal cell carcinoma; BCG, bacille Calmette-Guerin; CXR, chest x-ray; HDL, high-density lipoprotein; HIV, human immunodeficiency virus; HPV, human papillomavirus; IBD, inflammatory bowel disease; NYHA, New York Heart Association; PPD, purified protein derivative; QFG, QuantiFERON Gold; SCC, squamous cell carcinoma; TB, tuberculosis; TNF, tumour necrosis factor; TST, tuberculin skin test.
[a]Interferon-gamma release assay.

are not immunosuppressed.[24] A history of latent TB is indicated by induration of 5 mm, even with a history of BCG vaccination, and is a contraindication to biologic use until appropriate chemoprophylaxis treatment and a negative chest x-ray to rule out active TB is established.[5,6] Patients diagnosed with latent tuberculosis who have received at least 2 months of chemoprophylaxis treatment can receive a TNF inhibitor with close supervision of a multidisciplinary team.[25] As all TB treatment in Canada must be given by regional TB clinics, refer to regional TB clinics for specific protocols on treating these patients and the Canadian tuberculosis standards.[26] For patients who have had previous BCG vaccination, interferon gamma release assays (ie, QuantiFERON Gold) are preferred to screening for LTBI as false-positive TST results are often seen in these patients.[27] Treatment with etanercept has a lower TB reactivation risk than other monoclonal antibody inhibitors (infliximab and adalimumab).[28-31]

ii) Serology:

- Hepatitis A, B, and C (if no confirmed immunity)[32,33]; human immunodeficiency virus (HIV)[34-36]

Hepatitis B

It is generally accepted that biologics should not be initiated in patients with active hepatitis B as rare cases of reactivation have been reported, albeit most of these patients would likely be on other immunosuppressive medications.[5-7] Moreover, high-risk patients should have screening hepatitis B surface antigen (anti-HBsAg), antibody to hepatitis B surface antigen (anti-HBs), and antibody to hepatitis B core antigen (anti-HBc) serology performed.[37] Because of the potentially serious complications associated with hepatitis B virus (HBV) reactivation, it is important to measure viral load in patients with a history of HBV infection prior to initiation of biologic therapy.[38] Comanagement with a hepatologist should be considered in the case of chronic carriers of hepatitis B virus or those with positive serology along with monitoring for symptoms such as appetite loss, fatigue, nausea, widespread pruritus, hepatic tenderness, jaundice, dark urine, and pale stool.[39]

Hepatitis C

The association with biologic therapy and hepatitis C is less clear. Screening with anti–hepatitis C virus (HCV) antibodies is recommended and treatment with antiviral therapy for active infection prior to initiation with biologics. There is some suggestion that treatment with anti-TNFs may be beneficial in these patients, but comanagement with a hepatologist in these patients is recommended.[40,41]

HIV

The treatment of HIV+ patients with psoriasis with biologic therapy is somewhat controversial. If patients have stable disease (ie, low viral load, acceptable CD4 counts, and no evidence of active opportunistic infection), it is reasonable to consider biologic therapy in consultation with their infectious disease specialist.[40,42]

iii) Blood tests:

- Complete blood count (CBC)

Since the withdrawal of efalizumab (2009) and alefacept (2011) from the market, none of the currently approved biologics are associated with cytopenias. Therefore, routine CBC testing is no longer indicated.

- Liver function tests (infliximab only)

There is no evidence in support of routine baseline laboratory investigations prior to biologic therapy, with the exception of infliximab. Rarely, infliximab has been associated with hepatitis; therefore, baseline liver function tests in these patients are recommended and should be repeated while on therapy at periodic intervals (ie, 3-6 months), except for those at high risk of liver injury, in which case collaboration with hepatology and more frequent monitoring is advised.[7,43,44] Antinuclear antibody (ANA) screening is controversial based on case reports of drug-induced lupus.[45-52] ANA positivity is known to be high in patients with psoriasis and psoriatic arthritis being treated with biologics despite a low number of patients developing drug-induced lupus.[53] In addition, when it develops, it is usually milder and spontaneously resolves upon discontinuation of the drug.[54]

*Comorbidities to screen for (*primary care recommendations).* Systemic inflammation is the driving force behind psoriasis and many other inflammatory disorders, which explains the multiple comorbidities seen in these patients. Screening for psoriasis comorbidities, especially amongst patients with moderate to severe psoriasis, is critical.

i) Psoriatic arthritis

Psoriatic arthritis is a progressive inflammatory arthritis present in up to 30% of patients with psoriasis, with a greater risk in more extensive psoriasis. Where possible, a single biologic should be used in the management of both psoriasis and psoriatic arthritis. Most of the currently available psoriasis biologic agents have been approved to treat psoriatic arthritis with 2 exceptions: guselkumab, in which early studies are promising and phase III studies are under way in psoriatic arthritis, and brodalumab, which is not approved to treat psoriatic arthritis.

*Physicians should specifically ask about joint pain and stiffness lasting longer than an hour after waking and, if necessary, refer to a rheumatologist.

ii) Cardiovascular disease

Patients with psoriasis carry an elevated risk of metabolic syndrome, which includes abdominal obesity, high blood pressure, high fasting blood glucose, high serum triglycerides, and low high-density lipoprotein (HDL) levels.[2,55-59] Metabolic syndrome increases the risk of developing type 2 diabetes and cardiovascular disease. Compared to the general population, obesity rates in psoriasis can be 1.3- to 1.8-fold higher, and they can be more pronounced in more severe forms. Prospective cohort studies have found patients with severe psoriasis have an increased risk of myocardial infarction compared with the general population[2] and 50% increased risk of cardiovascular (CV)–related mortality.[57,59]

*Primary care physicians should specifically monitor cardiovascular risk factors among patients with psoriasis. This includes routine blood pressure measurements, lipid profile, and screening for diabetes. Counselling about smoking cessation, weight loss strategies for obese patients, diet, and exercise should be provided.

iii) Inflammatory bowel disease (IBD)

Psoriasis is well known to be associated with IBD such as Crohn disease and ulcerative colitis, with several studies showing a 1.5- to 3-fold increased risk of IBD. Currently, infliximab and adalimumab are approved for treatment of both Crohn disease and ulcerative colitis, whereas ustekinumab is approved for Crohn disease. With the IL-17s (ixekizumab and secukinemab), patients with IBD should be followed closely as new cases/exacerbations of IBD were observed during clinical trials.[60,61] Brodalumab is contraindicated in patients with Crohn disease.[8]

*Primary care physicians or dermatologists should consider referral to a gastroenterologist in patients who exhibit inflammatory bowel disease signs and symptoms.

iv) Depression

Patients with psoriasis are more likely to have depressive symptoms, with up to 10% of patients having clinical depression. In general, biologic medications are not known to exacerbate depressive symptoms, with the exception of brodalumab. Although a causal association between treatment with brodalumab and increased risk of suicidal ideation and behaviour has not been established, there were patients with suicidal ideation and behaviour, including completed suicides, in clinical trials. Therefore, prior to prescribing brodalumab, it is recommended to screen for and treat patients with a history of depression and/or suicidal ideation or behaviour.[8] In contrast, recent real-world data obtained from the Psoriasis Longitudinal Assessment and Registry (PSOLAR) population suggested that patients treated with biologics (excluding brodalumab) compared with conventional therapy (methotrexate/cyclosporine) had a reduced risk of depressive symptoms (hazard ratio [HR], 0.76; 95% confidence interval [CI], 0.59-0.98).[62] It is not known whether this effect is direct or indirect.

*Patients who exhibit signs of significant anxiety or depression should be treated appropriately by the primary care physician and, if necessary, referred to a mental health professional.

Opportunistic infections: suggested screening/counselling for high-risk activities/occupations/food or animal exposures. The risk of endemic mycoses (histoplasmosis, coccidioidomycosis, and blastomycosis) and TB varies according to geography.[62] Thus, the overall risk of opportunistic infections should be considered before initiating therapy. Notable infections associated with infliximab and etanercept use were histoplasmosis, candidiasis, listeriosis, non-TB mycobacterial infections, and aspergillosis.[18] Counselling patients with psoriasis on biologics about how to mitigate risks of opportunistic infections is prudent (Table 3).

Table 3. High-Risk Behaviours Predisposing Biologics Patients to Opportunistic Infections.

Occupation
Work with ocean water/fresh fish/aquarium water (*Mycobacterium marinum*)
Farmers, gardeners, construction/excavators, landscapers, or those who work with soil (dimorphic fungi—histoplasmosis, coccidioidomycosis, blastomycosis)
Health care professionals (tuberculosis, hepatitis B and C, human immunodeficiency virus)
Sewage repair, pipe installation, air conditioners, or those with exposure to contaminated water (atypical mycobacteria, *Legionella pneumophila*)
Interests:
Spelunking (soil contaminated with bird or bat feces: histoplasmosis) **avoid
Renovations (buildings with mold spores) **wear protective respiratory mask
Farming (chicken coops: histoplasmosis, cryptococcus) **wear mask
Gardening (rose thorns: sporotrichosis) **wear gloves
Animal contacts/pets:
Fish tank cleaning (*Mycobacterium marinum*) **wear gloves
Litter box cleaning—cat feces (toxoplasmosis) **avoid cleaning litter box[63]
Contact with reptiles or amphibians (salmonella)[64,65]
Food preferences:
Avoid unpasteurized dairy (ie, soft cheeses) or processed meats (ie, hot dogs, meat pates, deli meats) (listeria)[66-68]
Avoid undercooked meat, raw eggs, poultry (salmonella[69,70] listeria)
Travel:
Caution if travelling to developing world
Refer to travel clinic for vaccinations
Consider drinking bottled water, no ice cubes, don't brush teeth with tap water, no street vendor food, no salads, only fruit you can peel (salmonella, listeria, atypical mycobacteria)

Considerations During Treatment With Biologics

Monitoring

Please see Table 4 for a complete list of monitoring suggested for patients with psoriasis being treated with biologics. Product monographs recommend baseline TB testing but do not mandate further TB testing. Most physicians who prescribe biologics do not perform annual TB screening, except in high-risk patients (health care workers or those who travel to endemic areas).[71,72] Interval monitoring of liver function tests in patients being treated with infliximab is recommended. A complete skin check for skin cancer, including cutaneous T-cell lymphoma, is recommended, although the overall cancer risk with biologic therapy is equivocal.[73-75] In patients with psoriasis, some studies have found an increased risk of lymphoma,[76] while others have not.[77] Interestingly, most randomized trials in patients with psoriasis treated with

Table 4. Recommended Monitoring for Patients With Psoriasis on Biologics.

Intervention	Frequency	Notes
Liver function tests	Every 3-6 months	In infliximab patients only, consider more frequent dosing if risk factors for hepatitis or elevated LFTs at baseline
TB—TST/PPD or QFG	Yearly	High-risk patients: health care workers or travel to an endemic area
Complete skin survey for skin cancer, including cutaneous T-cell lymphoma	Yearly	
Screen for chronic opportunistic infection	At each visit	Persistent fever, cough, flu-like symptoms, chronic open wounds, skin lesions, infections lasting longer than usual
Ask about travel plans	At each visit	Refer to travel clinic if traveling to developing world
Ask about upcoming surgery or pregnancy	At each visit	Consider stopping during pregnancy or 4-5 half-lives before surgery
Update vaccines	Yearly Age >50 years	Inactivated influenza (not flu-mist) and pneumococcal vaccines Consider herpes zoster vaccine

Abbreviations: LFT, liver function tests; PPD, purified protein derivative; QFG, QuantiFERON Gold; TB, tuberculosis; TST, tuberculin skin test.

Table 5. When to Consider Stopping a Biologic.

Elective surgery
Hold biologic agent for 4 to 5 half-lives if major surgical procedures (conservative approach) in consultation with dermatologist
Vaccinations
Inactivated vaccines may be given
Live vaccines: hold biologic for 4 to 5 half-lives prior to vaccine administration in consultation with dermatologist (drug efficacy might be lost)
Infections
Most common: cellulitis, pneumonia
Hold biologic agent if serious infection requiring hospitalization or intravenous antibiotics, severe fever and chills, or oral antibiotics for moderate infections

biologics reported no cases of lymphoma, or the incidence of lymphoma was on par or only slightly higher than that of the general population.[14,15,17-23,78]

For nonmelanoma skin cancers (NMSCs), a review of 9 high-quality publications found 8 of 9 trials demonstrated an increased risk of NMSC while on biologic therapy, especially those with risk factors of previous skin cancer or actinic damage, concurrent or history of immunosuppressive therapies, or therapies known to increase skin cancer risk[73] (ie, cyclosporine[79] and phototherapy, especially psoralen and ultraviolet A [PUVA][80]). A recent meta-analysis and European guidelines confirmed that the highest risk in terms of cancer in patients with psoriasis is for skin cancer, and there is no increased risk of lymphoma or melanoma.[81,82]

When to Consider Stopping a Biologic

Surgery. There is limited evidence as to whether biologic therapy should be stopped or continued in patients with psoriasis who are undergoing surgical procedures.[9] Current guidelines based primarily on rheumatologic data recommend a planned break for 4 half-lives (see Table 1) of biologic therapy in those undergoing major surgical procedures (Table 5). This is despite the fact that the use or preoperative discontinuation of TNF-α antagonists does not appear to influence the rates of surgical complications, including incidence of infections.[71,83-87] Not surprisingly, there was a significant risk of disease flare when biologics were held perioperatively.[9,88] A practical approach would be to stop a biologic only for mouth/gastrointestinal surgery and to continue for "clean surgeries."

Vaccines. There is a lack of evidence to show vaccinating biologics patients causes harm. The basic norms followed in clinical practice with patients with psoriasis are derived from transplant guidelines.[72] In general, however, avoidance of live vaccines (in patients and household contacts) while on biologics is prudent.[89] If a live vaccine is needed while on biologics, holding the agent for 4 to 5 half-lives prior to vaccine administration is appropriate.[14-16] Consultation with the treating dermatologist is imperative, however, as stopping a biologic agent may result in lack of response of the biologic.[90,91]

Infection risk on biologics. Although infection risk for immune-mediated inflammatory diseases like psoriasis is generally thought to be higher than normal due in part to baseline disease activity or the disease pathophysiology itself,[92] the risk of infections, especially TB, reflects key safety concerns regarding the use of anti-TNF biologics. Safety data from psoriasis clinical trials with biologics indicate that opportunistic infections are relatively rare. The most commonly reported types of serious infections in a multicenter, longitudinal, disease-based registry at dermatology centers (PSOLAR) were pneumonia and cellulitis with adalimumab and infliximab. No increased risk was observed with ustekinumab or etanercept.[93]

In general, biologic therapy should be withheld if a patient develops a serious infection requiring hospitalization or intravenous antibiotics, has severe fever and chills, or requires oral antibiotics for moderate infections.[5-8,60,61,94,95]

Special Considerations for Biologics

Travel while on biologics. Patients who plan to travel overseas, especially to the developing world, should be assessed at a travel clinic for the appropriate vaccinations and counselling regarding endemic infections and protective practices. As stated prior, live vaccines should be given before initiating biologics, or the biologic should be held for 4 to 5 half-lives. Travellers to the developing world may be recommended to receive yellow fever, oral typhoid, or oral cholera vaccine, in addition to updating their MMR vaccines, so this is important to note. Hepatitis A and B vaccine (Twinrix) should be considered if travelling to a resort. Hepatitis B vaccine is recommended if travel to China is anticipated and can be given without interruption of the biologic treatment.

Injection site reactions. Injection site reactions can occur up to 12 days post-treatment and, although rare, can be debilitating and force patients who may be responding to a biologic to stop. Most common signs are redness, rash, swelling, itching, and bruising at the site of injections. This may be complicated by hyper- or hypotension, headaches, rash, urticarial, and flu-like symptoms. Some proposed remedies have included avoiding the site (at least 3 cm from previous site) and applying a damp towel or ice pack to the site for 10 to 15 minutes after the injection. Patients treated with intravenous (IV) infusion require monitoring during the infusion and 1 hour after.

Pregnancy. While the use of biologics during pregnancy is considered category B (no known toxicity in humans), there exists a growing body of literature to suggest their safety. A recent meta-analysis of 13 studies found that while complications were increased over the general population, there was no increased risk of pregnancy or neonatal complications in anti-TNF-treated patients over those with the same disease state not receiving anti-TNFs.[96] This has been confirmed by other meta-analyses in both the rheumatologic and gastrointestinal literature.[97-99]

In general, this offers women who are afraid of disease flare some data to make an informed decision about stopping their biologic, but without prospective data, the use of biologics in pregnancy is not recommended.[5-8,60,61,94,95] If used in pregnancy, live vaccines should not be administered to infants for 4 to 5 half-lives after the mother's last dose of biologic.

Children and the elderly. Only 1 biologic agent has been recently approved in Canada for plaque psoriasis in children. Ustekinumab is indicated for the treatment of moderate to severe plaque psoriasis in patients aged 12 to 17 years.[95]

Etanercept has not yet been approved for psoriasis in children in Canada, although in November 2016, it was approved in the United Staes for moderate to severe plaque psoriasis in patients aged 4 to 17 years. It is indicated in Canada for treatment of juvenile idiopathic arthritis in patients aged 4 to 17 years.[6]

Etanercept has been studied in patients 65 years or older and was found to be equivalent in efficacy and safety to younger age groups.[6]

Summary

Biologic therapies for psoriasis offer patients improved quality of life over traditional systemic therapy in terms of improved efficacy and less toxicity and monitoring. The primary care physician should be aware of the major risks in patients being treated with biologics for psoriasis: infection and nonmelanoma skin cancer malignancy. Incidence of both of these event categories is low, however, particularly if appropriate screening and counselling is done.

In terms of long-term data, the oldest anti-TNF (etanercept) has been approved in North America for 19 years, which is reassuring in and of itself, but does not preclude ongoing vigilance in monitoring these patients. Finally, it is critical that specialists in family medicine, dermatology, gastroenterology, psychiatry, and rheumatology work together to identify and reduce the impact of known comorbidities in patients with psoriasis.

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Dedication

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