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Dr. Helene Veillette is a dermatologist, clinical associate professor and division head at the CHU de Québec-Université Laval. She practices, teaches and is involved in many professional activities within her department and beyond.

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Dr. Veillette has a keen interest in hidradenitis suppurativa, as well as medical education and difficult clinical cases. She enjoys the human side of treating dermatological diseases and values teamwork. Since the beginning of her practice, she has held key positions and has initiated and collaborated in several initiatives for the advancement of her discipline.

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IN BRIEF: LABORATORY AND CLINICAL MONITORING REQUIREMENTS FOR JAK INHIBITORS

Janus kinase (JAK) inhibitors, more commonly referred to as JAK inhibitors (JAKi), are a class of drugs that target and block the JAK- signal transducer and activator of transcription (STAT) pathway, allowing regulation of immune responses and cell proliferation[1]. The JAK-STAT pathway is found in many immune cells and is known to augment the signal from cytokine receptors at the cell's surface to induce the transcription of messenger RNA in the nucleus. The key protein-encoding genes in this pathway were identified using primers to amplify, from the DNA of lymphoid tissue, a conserved kinase domain that phosphorylates tyrosine residues on substrate proteins. This eventually led to the discovery of 4 related protein tyrosine kinases (PTKs): JAK1, JAK2, JAK3 and tyrosine kinase 2 (TYK2).[2]

In June 2014, the first JAKi was approved and made available in the Canadian market for the treatment of rheumatoid arthritis: tofacitinib (Xeljanz®, also now indicated for the treatment of psoriatic arthritis and ulcerative colitis). Since then, several additional JAKi have entered the Canadian therapeutic armamentarium[2] for different indications (**Table 1**).

Numerous studies are underway that could lead to new indications for these agents, as well as the addition of new JAKi to the market[3]. The experience gained to date with these drugs, both in pivotal studies and in post-marketing use, has allowed a better understanding of the importance of clinical and laboratory monitoring when using these agents[4].

The side effects associated with JAKi are highly dependent on their target, i.e. their selectivity to block one of the four PTKs that make up the JAK family. Upper respiratory infections, acne, herpes simplex/zoster, cytopenia, elevated lipids, and nausea are common adverse events seen with JAKi that inhibit the JAK1 pathway.[2] Nasopharyngitis, headache, and diarrhea, are more commonly observed side effects of JAKi that inhibit the TYK2 pathway.[2] Finally, inhibition of the JAK2 pathway, which is involved in hematopoiesis, may potentiate side effects such as anemia and neutropenia[5].

Tofacitinib (Xeljanz®)	Rheumatoid arthritis, psoriatic arthritis, ulcerative colitis
Upadacitinib (Rinvoq®)	Rheumatoid arthritis, psoriatic arthritis, Moderate-to-severe atopic dermatitis, Ankylosing spondylitis, ulcerative colitis
Abrocitinib (Cibinqo®)	Moderate-to-severe atopic dermatitis
Deucravacitinib (Sotyktu™)	Moderate-to-severe plaque psoriasis
Ruxolitinib (Jakavi®)	Myelofibrosis, Polycythemia vera, Graft versus host disease (GVHD)
Fedratinib (Inrebic®)	Myelofibrosis
Baricitinib (Olumiant®)	Rheumatoid arthritis

Table 1. *List of approved JAK inhibitors in Canada (as of January 2023); courtesy of Helene Veillette, MD*

This article focuses on clinical and laboratory monitoring requirements for the use of JAKi therapy in dermatological indications. The main recommendations are based upon the three JAKi currently approved for a dermatological indication in Canada, upadacitinib[6], abrocitinib[7], and deucravacitinib[8], however, no laboratory monitoring is required for deucravacitinib according to the product monograph.

While product monographs are one source of information for dermatologists who wish to prescribe a JAKi,[6,7,8] they do not reflect the real-world monitoring requirements typically seen outside a clinical trial setting. As a result, it is important to develop robust and structured guidance based on the practical experience of treating patients in a natural setting. Clinicians are reminded that patients may have different lab monitoring and disease management requirements depending on their baseline health status, presence of underlying comorbidities, age, and other related factors.

Screening and risk assessment at BASELINE
a. History and physical examination: history of infection, neoplasia, venous thrombosis or pulmonary embolism, concomitant medications, possible pregnancy, breastfeeding
b. Complete blood count (CBC)
• Absolute lymphocyte count (ALC)
• Absolute neutrophil count (ANC)
• Hemoglobin (Hb)
c. Liver enzymes (ALT)
d. Creatinine
e. Lipid panel
f. Serologies: hepatitis B and C, HIV (if at risk)
g. Screening test for tuberculosis (e.g. Quantiferon®)

Table 2. *Suggested screening and risk assessment at baseline for JAKi approved in Canada; courtesy of Helene Veillette, MD*

In summary, the relevant clinical and laboratory monitoring for the use of JAKi currently approved in dermatological disease is as follows (**Table 2** and **Table 3**):

To facilitate laboratory monitoring for JAKi, a laboratory monitoring algorithm (**Figure 1**) was developed by 3 Canadian dermatologists: Dr. Melinda Gooderham, Dr. Mark Kirchhof and the author (H.V.) based on the product monographs,[6,7] personal experience, and previously published expert consensus.[5]

JAKi are new therapeutic tools at our disposal. Their use is relatively simple, with a safety profile that is similar to that of many drugs currently used in dermatology practices across Canada. With this said, it is important that updated guidance and clinical experience is shared around important clinical and laboratory parameters to ensure that patients are screened and monitored appropriately.

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Monitoring DURING treatment
At 4 and no later than 12 weeks: CBC (i.e. ANC, ALC, and Hb) and liver enzymes
At no later than 12 weeks: lipid monitoring is recommended; patients should be managed according to international clinical guidelines for hyperlipidemia
Laboratory monitoring thereafter is based on clinical judgment: once or twice a year is probably sufficient for most patients.
For women of childbearing age, validate at follow-up if pregnancy is planned or if breastfeeding
Only if musculoskeletal symptoms are present: creatine phosphokinase (CPK)

Table 3. *Suggested ongoing monitoring requirements for JAKi approved in Canada; courtesy of Helene Veillette, MD*

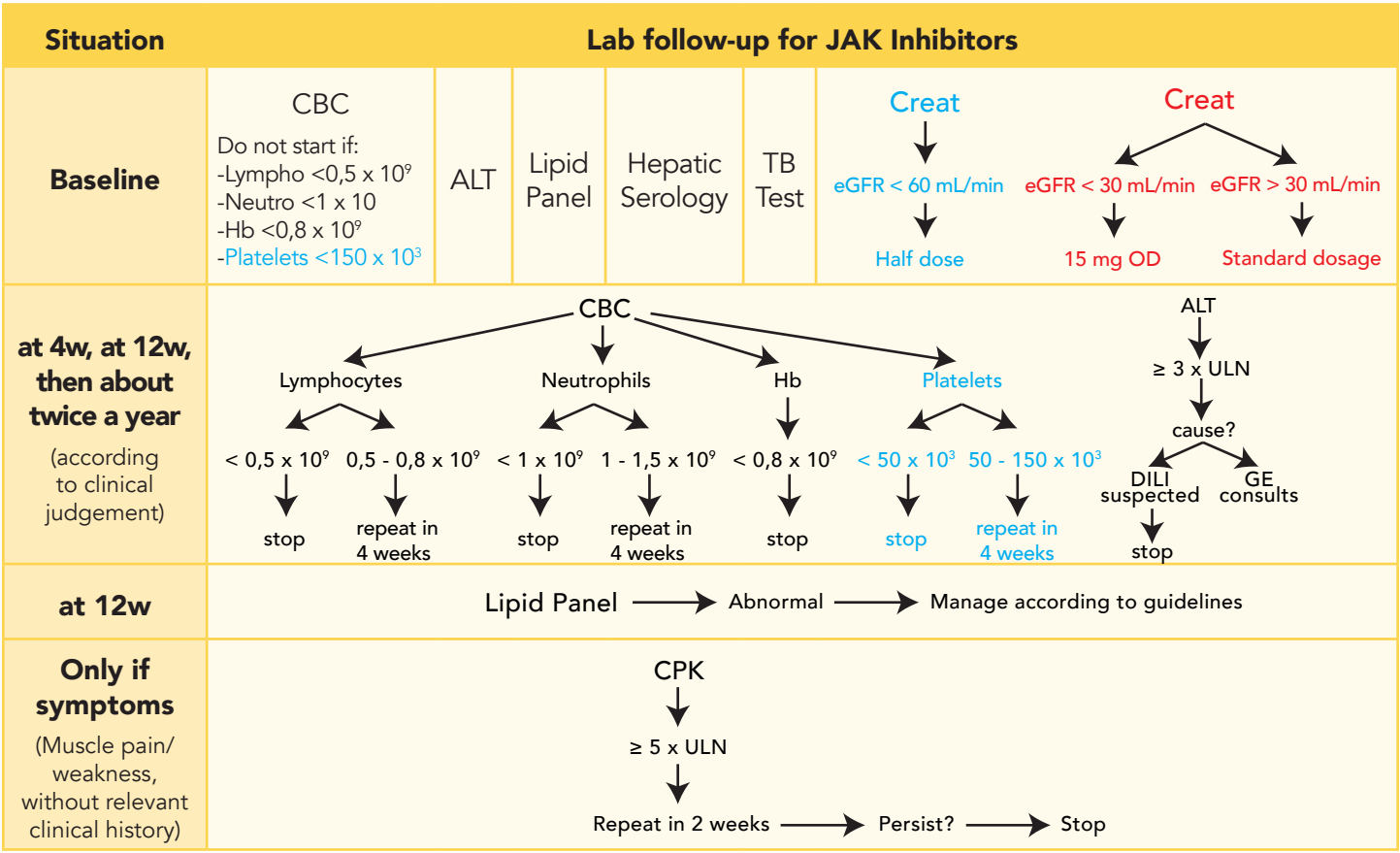

Figure 1. *Laboratory follow up algorithm for use of JAKi in Canada; courtesy of Helene Veillette, MD*

DILI: *drug-induced liver injury;* ***ULN:*** *upper limit of normal;* ***GE:*** *gastroenterology*

• Apply to all • Specific to Upadacitinib • Specific to Abrocitinib

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