CUH
Ospidéal Ollscoile Chorcaí
Cork University Hospital

Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive

JAK inhibitors
GP information sheet

JAK inhibitors

They are potent selective inhibitor of the JAK family. It works by reducing the activity of an enzyme in the body called 'Janus kinase', which is involved in inflammation. Inhibition of JAK 1, JAK 2 and JAK 3 by different JAK inhibitors attenuates signalling of proinflammatory interleukins and interferon which modulates immune and inflammatory response. By reducing the activity of this enzyme, JAK inhibitors helps to reduce pain, stiffness, swelling in the joints, and helps to slow the damage to the bone and cartilage in the joints.

Screening pre commencement

- FBC/ Renal profile/ Liver profile
- Screen for latent or active TB infection i.e. Quantiferon.
  -Treat latent TB with standard anti tuberculosis medication.
- Screen for viral Hepatitis
- Up to date on vaccinations in agreement with current immunisation guidelines.
- Vaccination with live vaccines should occur at least 4 weeks prior to initiation.

Precautions and contraindications

- Contraindicated if active TB/ serious infection/ opportunistic infection
- Contraindicated if
  - Lymphocyte count <0.75 cellsx10^9/l
  - Neutrophil count <1.0 cellsx10^9/l
  - Haemoglobin <8 g/dl
- Hepatic impairment
  - Not recommended in Severe hepatic impairment (Child Pugh C)
  - Dose reduction in moderate hepatic impairment
- Renal impairment
  - Dose reduction in Severe renal impairment (CrCl<30ml/min)
  - Not recommended in patients with CrCl<15ml/min
- Contraindicated in pregnancy and breastfeeding
  - Women of childbearing age should use effective contraception during treatment and for at least 4 weeks after the last dose.

- If a new infection develops
  - Interrupt JAK inhibitors treatment and investigation as appropriate for an immunocompromised patient
  - If patients presents with new onset abdominal signs and symptoms- promptly investigate for Gastrointestinal perforation (risk factors: history of diverticulitis, steroid or NSAID use)

Lab Monitoring

- FBC and LFTs should be monitored monthly for the first 3 months and every 3 months thereafter. **Blood cholesterol must be monitored after the first 3 months of treatment**

Neutrophil Count(ANC)	
≥1 cells	Dose should be maintained.
0.5- 1 cells	For persistent (2 sequential values in this range on routine testing) decreases in this range, dosing should be interrupted until ANC≥ 1cell. When ANC≥1, resume.
≤0.5 cells	Dosing should be discontinued and repeat testing within 7 days.

Lymphocyte count (ALC)	
≥0.75 cells	Dose should be maintained.
0.5- 0.75 cells	For persistent (2 sequential values in this range on routine testing) Decrease in this range, dosing should be interrupted until ALC ≥0.75. When ALC is ≥0.75, resume JAKi.
<0.5cells	If lab value confirmed by repeat testing within 7 days, Dosing should be discontinued.

Haemoglobin (Hb)	
If Hb value reduces by ≤ 2g/dL and Total Hb remains ≥8g/dL	Dose should be maintained.

Liver Function	
>2 but < 3 fold rise in AST/ALT from upper limit of reference range	Repeat LFTs in 4 weeks
>3 fold rise in AST/ALT from upper limit of reference range	Hold JAKi. Repeat LFTs within 2-4 weeks

Renal Function	
Creatinine clearance (CrCl) <30	Hold JAKi. Contact Rheumatology department for advice.

Possible Side Effects

Infections -Increased risk of infections such as upper respiratory tract infections. If an infection develops, JAK inhibitor therapy should be temporarily interrupted. Treatment should not be resumed until the infection resolves.

Tuberculosis – JAK inhibitors should not be given to patients with active TB. Anti-TB therapy should be considered prior to initiation of JAK inhibitors in patients with previously untreated latent TB.

Viral reactivation- Viral reactivation, including cases of herpes virus reactivation (e.g., herpes zoster, herpes simplex), were reported in clinical studies. JAK inhibitor treatment should be temporarily interrupted until the episode resolves. Patients may be considered to have herpes vaccination prior to start of therapy.

Venous Thromboembolism - Events of deep venous thrombosis (DVT) and pulmonary embolism (PE) have been reported in patients receiving JAK inhibitors. If clinical features of DVT/PE occur, treatment should be temporarily interrupted and patients should be evaluated promptly.

Contact Details

Davida Hehir, Clinical Nurse Specialist in Rheumatology: (021) 4922645
Arun Augustine, Clinical Nurse Specialist in Rheumatology: (021) 4234517

Please consult up to date relevant literature (data sheets) or BNF when prescribing JAK inhibitors. Please contact the Rheumatology team if you have any other queries regarding the prescribed medication.