RUXOLITINIB

Ruxolitinib is a medication used to treat myeloproliferative neoplasms (MPNs). In Australia its trade name is Jakavi® and it is licensed for the treatment of patients with primary myelofibrosis (MF), polycythemia vera (PV) patients who are resistant to or intolerant of hydroxycarbamide (hydroxyurea), or patients with myelofibrosis occurring as a complication of polycythaemia vera (post-PV myelofibrosis) or essential thrombocythaemia (post-ET myelofibrosis). It is under investigation in clinical trials for patients with ET. It is an oral medication which is available in 5 mg, 10 mg, 15 mg and 20 mg tablets.

HOW DOES IT WORK?

Blood cells originate from stem cells. Stem cells are master cells which divide and mature into the different types of blood cells: red blood cells, white blood cells and platelets. The marrow in our bones acts as a factory for the division and maturation of these stem cells into blood cells. Once the blood cells have matured, they leave the bone marrow and enter our blood stream. In MPNs the processes involved in controlling blood cell production are disordered and for most patients this is thought to be due to over-activation of the JAK-STAT pathway via driver mutations in JAK2, CALR or MPL.

Ruxolitinib works by interfering with the function of the JAK2 enzyme and its relation JAK1. This slows down blood cell production and the production of signalling chemicals involved in inflammation, known as cytokines.

Ruxolitinib's most important actions in patients with MPNs are to reduce spleen size, improve symptoms and to decrease blood cell production. Most patients with an enlarged spleen will notice a rapid improvement in the size of the spleen and its associated symptoms. Many of the symptoms patients experience with MF and PV (e.g. sweating, itching, fatigue and abdominal discomfort after meals) also improve with ruxolitinib therapy. Blood cell production is reduced on ruxolitinib and hence it can improve high blood counts but it may also exacerbate (make worse) pre-existing anaemia (low red cells) or thrombocytopenia (low platelets).

You will need frequent blood tests and monitoring whilst taking ruxolitinib to ensure that the dose you are taking is correct for you.

WHAT ARE THE SIDE EFFECTS?

Most people taking this drug tolerate it well and have few side effects. However, it is important that you inform your doctor if you are experiencing any side effects listed below or develop any new symptoms, even if mild.

Common side effects

Approximately 1- 20% of people taking ruxolitinib will experience some of these common side effects:

- Reduced red blood cells (anaemia). If your red blood cells drop too low you may notice that you are becoming breathless and tire easily.
- Reduced platelets (thrombocytopenia). If your platelet count drops too low you may experience nose bleeds, bleeding gums when you clean your teeth, a rash of tiny red spots or increased bruising.
- Reduced white blood cells (neutropenia). If your white blood cells drop too low you may have an increased risk of developing infections. You may experience a high temperature, fever, shivers or chills.

If you experience any of the symptoms above, you must contact your haematologist immediately. Sudden and unexpected changes in blood cell levels may occur, although this is uncommon, therefore it is important to attend appointments to have your blood counts checked and to discuss any symptoms with your haematologist.

Other common side effects

- Painful skin rash with blisters (possible symptoms of shingles (herpes zoster))
- High level of cholesterol
- Abnormal liver function test results
- Dizziness
- Headache
- Weight gain
- Frequently passing wind (flatulence)

If you experience any side effects, talk to your doctor. This includes any possible side effects not listed here.

The above list is not fully comprehensive and some other side effects can occur. Please consult the official product information if you are experiencing any side effects and it is important that patients inform their doctor if they do experience any side effects.

Ruxolitinib and infections

Ruxolitinib treatment has been shown to be associated with increased risk of infections varying from simple chest and urine infections to reactivation or occurrence of more serious infections such as shingles, hepatitis, TB and certain rare infections (including a disease called Progressive Multifocal Leucoencephalopathy). It is therefore important that other doctors involved in your care, as well as your haematologist are aware of your medical history.

Increased risk of non-melanoma skin cancer

All patients with myeloproliferative neoplasms have an increased risk of non-melanoma skin cancers. This risk is likely to be further increased by ruxolitinib therapy. It is sensible to avoid sun exposure, and to wear SPF >50 sunblock and protective clothing. While a causal relationship to ruxolitinib has not been definitively established, regular and vigilant skin examinations are essential for all patients on ruxolitinib.

TAKING RUXOLITINIB

How to take ruxolitinib

- It is usually taken twice a day, with or without food. It is recommended to be taken at the same time each day.
- Wash your hands thoroughly before and after taking the tablets
- Swallow ruxolitinib tablets whole with plenty of water.
- Do not chew, crush or break the tablets.
- If a dose is missed do not take an additional dose.
- It is important to not stop taking your tablets without consulting your haematologist.

Dosage

Your doctor will determine the dose of ruxolitinib you are to take. Your doctor may recommend that you take your medication twice a day. Please be sure to follow the instructions precisely. Depending upon your response and the presence of side effects your doctor may alter the dose of ruxolitinib.

Keeping track

Some patients find it helpful to keep a record to remember when to take your tablets (e.g. medication reminder app on a smart phone) and record any side effects.

Non-compliance - It is important that you follow the directions precisely. Failure to do so may increase your risk of vascular and thrombotic disease related complications.

Storage and disposal of ruxolitinib

- Store in a dry place at room temperature and definitely less than 30ºC.
- As with all medications ruxolitinib can be harmful to others. Keep all medications in a secure location well out of reach of children and pets.
- Return any unused tablets to your local pharmacy or hospital. Do not dispose of them in the bin or flush them down the toilet.
- Do not use tablets after the expiry date stated on the packaging.

INTERACTIONS WITH OTHER MEDICATIONS OR VITAMINS, HERBAL SUPPLEMENTS OR REMEDIES

Whenever you take ruxolitinib (or in fact any medication), always provide the names of other medicines prescribed for you as well as any over-the-counter medications (e.g vitamins, herbal supplements or remedies) to the health care team who are treating you. It can be very helpful to carry a list of the names and dosages of all your medicines to show to your haematologist at appointments.
The MPN AA has a wallet card which provides for medications to be listed.

Other medications and supplements to avoid whilst taking ruxolitinib.

- **FOOD** Avoid grapefruit, grapefruit juice and supplements that contain grapefruit extract as well as Seville oranges (used in making marmalade) while taking ruxolitinib as these products may increase the amount of ruxolitinib in your blood.
- Ruxolitinib is metabolized through a pathway known as CYP3A4 and many drugs can increase or reduce its activity. A list of such medications (e.g. clarithromycin, fluconazole and others including the herbal product St Johns Wort) will be in the package insert or ask a pharmacist before taking any new medicine.

WHAT SHOULD I EXPECT?

How fast does it work?

Ruxolitinib may take several weeks to begin having an effect on your blood cells, but often its effects on spleen and symptoms occur in 2-4 weeks. Your blood cell counts may not stabilise for up to 16 weeks.

How will I feel?

You will hopefully notice a reduction in your MPN-related symptoms. It may help to keep track of these so you can monitor how you are feeling. Most people taking this drug tolerate it well with relatively few side effects.

Will I need follow up?

You will need more frequent blood tests during the first weeks of treatment to determine how your body is responding to the medication. Once your body has adjusted to the medication you will need checks less frequently, perhaps every 2 to 3 months. Your kidney and liver function may also be checked with blood tests.

Important tips for taking ruxolitinib

Ruxolitinib works fast to reduce spleen size and symptoms but these benefits are rapidly lost when the medication is stopped. This relapse of symptoms and increase in spleen size can occur rapidly and can make patients very ill. For this reason **it is important not to stop this medication suddenly, and generally your medical team will slowly reduce the dose before stopping this drug. Experience has shown that it is very important not to cease ruxolitinib if you contract COVID 19.**

It is advisable to have an annual cholesterol check with your GP.
If you are admitted to hospital for any reasons, emergency or routine, it is important that you keep taking ruxolitinib and ask the medical team to liaise with your haematologist.
Keep a regular check on your skin and if any changes are noticed, report these to your haematologist**.**

WHAT IF I HAVE OTHER MEDICAL CONDITIONS?

Ruxolitinib should be used under supervision if you have now or have had any of the following conditions:

- Allergies to any of the ingredients in the medicine (these will be listed on the information leaflet that came with your tablets)
- HIV infection or AIDS
- Previous infections such as TB (tuberculosis) or hepatitis B
- Kidney problems
- If you are planning pregnancy
- If you have radiation therapy planned
- Previous skin cancer or melanoma skin cancer.

If you think you may have or have had one of these conditions, please discuss this with your doctor.

FREQUENTLY ASKED QUESTIONS

Can I eat and drink normally?
Yes. We recommend that you eat a normal, healthy diet and drink plenty of water.

Can I drink alcohol?
While it is safe to drink alcohol in moderation whilst taking ruxolitinib, Australian NHMRC guidelines state that for healthy women and men drinking no more than two standard drinks on any day reduces your risk of harm from alcohol-related disease. Alcohol can cause dehydration, and it is important to avoid becoming dehydrated if you have an MPN. Please ask your doctor if you require more information regarding alcohol consumption.

What if I want to have a child?
We strongly recommend that you use contraception whilst taking ruxolitinib, because this medication can be harmful to a developing foetus. When planning to conceive or to father a child, you should stop taking ruxolitinib AFTER discussion with your doctor.

It is imperative to discuss your plans together with your haematologist prior to becoming pregnant or fathering a child. Your doctor can recommend treatment options for you that will not cause harm to your developing baby and will increase your chance of a successful pregnancy. If you or your partner becomes pregnant while taking this drug please contact your doctor immediately for further advice.

Can I breastfeed while taking ruxolitinib?
Breastfeeding while taking ruxolitinib is not recommended.

Can I drive?
There is no evidence that taking ruxolitinib would stop you from driving.

Do I need to take any special precautions?
As noted previously, it is important not to stop taking ruxolitinib suddenly as this can cause a withdrawal type syndrome which consists of a return of symptoms and growth of your spleen which may be sudden and has occasionally made patients very unwell.

Can I have vaccinations such as the flu and COVID-19 vaccines while taking ruxolitinib?
Yes, you can have most vaccinations, including the flu and COVID-19 vaccines, whilst taking ruxolitinib. Some vaccinations are live vaccines (e.g. measles, mumps and varicella virus vaccines) and these should not be taken with ruxolitinib. It is important you tell the person giving you the vaccine that you are taking ruxolitinib and we would recommend consulting with your haematologist.

COVID-19 - Can I take antivirals while on ruxolitinib?
If you test positive for COVID-19, you may be eligible for antiviral treatments. **Some antivirals are not suitable for patients taking ruxolitinib but it is important that you do not stop taking your ruxolitinib**. The antiviral most suitable for you will depend on what other medications you are taking and your kidney function. Your doctor will advise which antivirals are suitable for you and treatment must be commenced within 5 days of symptom onset, or as soon as possible if you have no symptoms but test positive. Please contact your GP or haematologist to arrange antiviral therapy immediately if required.

Need to have a medical procedure – what to do?
You may occasionally be required to adjust or stop your ruxolitinib if you need an operation. It is important that you inform the doctor or dentist planning the procedure or operation that you are taking ruxolitinib and that they coordinate your treatment with your haematologist. We always recommend that you inform your haematologist if you have any procedures or operations planned. It is very important NOT TO STOP taking ruxolitinib without a discussion with your haematology team.

WHAT CAN I DO TO HELP MYSELF IF I HAVE AN MPN?

It's important to take good care of yourself. There are many things you can do to feel better.

- **Don't neglect your general health, particularly your cardiovascular health including stopping smoking and managing your cholesterol.** It is a good idea to have regular physical checkups, including skin checks, eye health examinations and the recommended screening tests for breast cancer, bowel cancer, cervical cancer and prostate cancer.
- **Be blood clot aware.** Having an MPN puts patients at higher risk of having a blood clot. It's good to know the signs and how to prevent blood clots. See STOP THE CLOT website at: https://www.stoptheclot.org/learn_more/signs-and-symptoms-of-blood-clots/
- **Have regular and vigilant skin cancer check ups for both melanoma and non melanoma skin cancers,** especially if you are also on treatment regimes such as hydroxycarbamide (hydroxyurea) or ruxolitinib
- **Good nutrition is important**. Eat a balanced diet including lots of fresh fruit and vegetables, lean protein and whole grains.
- **Drink plenty of water and prevent dehydration** by avoiding excessive alcohol and caffeinated drinks.
- **Maintain a normal weight and maintain your muscle mass** to help keep your cholesterol and blood sugar within normal limits.
- **Exercise is very beneficial** for people with MPNs and helps to fight fatigue. Before starting on any new programme, check with your GP or haematologist and start slowly and gently.
- **Stop smoking.** Ask your GP if you need help.
- **Consider wellness activities** such as yoga, aerobic activity, strength training, meditation, massages, support groups, improved nutrition etc – an international study of hundreds of MPN patients showed wellness activities had a pattern of decreased levels of symptom burden, fatigue, depression, and a higher quality of life for MPN patients. (Survey of Integrative Medicine in Myeloproliferative neoplasms – the SIMM study).

More information on living well with an MPN is available at www.mpnallianceaustralia.org.au

GENERAL ADVICE

This leaflet is intended to give you general information about taking ruxolitinib, or as a reference for people already taking this medication. It is important that in addition to this leaflet you read the product information available from your pharmacist about ruxolitinib and discuss any concerns with your general practitioner or haematologist.