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**EPAR summary for the public**

# Jakavi

ruxolitinib

This is a summary of the European public assessment report (EPAR) for Jakavi. It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the medicine to reach its opinion in favour of granting a marketing authorisation and its recommendations on the conditions of use for Jakavi.

## What is Jakavi?

Jakavi is a medicine that contains the active substance ruxolitinib. It is available as tablets (5, 10, 15 and 20 mg).

## What is Jakavi used for?

Jakavi is used to treat the following conditions:

- myelofibrosis in adults who have splenomegaly (enlarged spleen) or symptoms related to the disease such as fever, night sweats, bone pain and weight loss. Myelofibrosis is a disease in which the bone marrow becomes very dense and rigid and produces abnormal, immature blood cells. Jakavi can be used in three types of the disease: primary myelofibrosis (also known as chronic idiopathic myelofibrosis, where the cause is unknown), post-polycythaemia vera myelofibrosis (where the disease is linked to an overproduction of red blood cells) and post-essential thrombocythaemia myelofibrosis (where the disease is linked to an overproduction of platelets, components that help the blood to clot).
- polycythaemia vera in adults who are resistant or intolerant to treatment with the medicine hydroxyurea. Polycythaemia vera is a disease that mainly causes too many red blood cells to be produced, which can cause reduced blood flow to the organs due to 'thickening' of the blood and occasionally the formation of blood clots.

The medicine can only be obtained with a prescription.

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## How is Jakavi used?

Treatment with Jakavi should only be started by a doctor who is experienced in treating patients with cancer medicines. The patient's complete blood cell count must be taken before starting treatment and monitored during treatment.

In myelofibrosis, the recommended starting dose is up to 20 mg twice a day depending on the platelet count. In polycythaemia vera, the recommended starting dose is 10 mg twice a day.

If the treatment is not considered effective enough, the dose can be increased by 5 mg up to 25 mg twice a day.

A lower dose should be used in certain cases, including in patients reduced liver function or severely reduced kidney function, and in patients taking certain other medicines. Treatment should be stopped if the patient's blood levels of platelets or neutrophils (a type of white blood cell) fall below certain thresholds, or if no improvement in spleen size or symptoms is seen after six months. In polycythaemia vera treatment should also be stopped when haemoglobin levels are very low.

## How does Jakavi work?

The active substance in Jakavi, ruxolitinib, works by blocking a group of enzymes known as Janus kinases (JAKs), which are involved in the production and growth of blood cells. In myelofibrosis and polycythaemia vera, there is too much JAK activity, leading to the abnormal production of blood cells. These blood cells migrate to organs including the spleen, causing them to become enlarged. By blocking JAKs, Jakavi reduces the abnormal production of blood cells, thereby reducing the symptoms of the diseases.

## How has Jakavi been studied?

In myelofibrosis, Jakavi was investigated in two main studies involving 528 patients. The first study compared Jakavi with placebo (a dummy treatment). The second study compared Jakavi with the best available treatment, which included different types of medicines such as anti-cancer agents, hormones and immunosuppressants. The main measure of effectiveness was the proportion of patients whose spleen had reduced in size by at least 35%, measured after six months in the first study and after one year in the second study.

In polycythaemia vera, Jakavi was studied in one main study which involved 222 patients who were resistant or intolerant to treatment with hydroxyurea. This study, which compared Jakavi with best available treatment, looked at the percentage of patients who showed improvement in their condition, measured as requiring none or no more than one phlebotomy (a procedure to remove excess blood from the body) and whose spleen reduced by at least 35% in size, after 8 months of treatment.

## What benefit has Jakavi shown during the studies?

In myelofibrosis, Jakavi was more effective than placebo and the best available treatment at reducing the size of the spleen. In the first study, the target reduction in spleen size was achieved in 42% of patients treated with Jakavi (65 out of 155) compared with less than 1% of patients given placebo (1 out of 153). In the second study, the target reduction in spleen size was achieved in 29% of patients treated with Jakavi (41 out of 144) compared with 0% of patients receiving the best available treatment (0 out of 72).

In polycythaemia vera, 21% (23 out of 110) of patients given Jakavi showed an improvement after 8 months of treatment, compared with 1% (1 out of 112) of patients given the best available treatment.

## What is the risk associated with Jakavi?

In myelofibrosis, the most common side effects with Jakavi (seen in more than 1 patient in 10) are thrombocytopenia (low blood platelet counts), anaemia (low red blood cell counts), neutropenia (low levels of neutrophils), urinary tract infections (infection of the structures that carry urine), bleeding, bruising, weight gain, hypercholesterolaemia (high blood cholesterol levels), dizziness, headache and raised liver enzyme levels.

In polycythaemia vera, the most common side effects with Jakavi (seen in more than 1 patient in 10) are thrombocytopenia (low blood platelet counts), anaemia (low red blood cell counts), bleeding, bruising, hypercholesterolaemia (high blood cholesterol levels), hypertriglyceridemia (high blood fat levels), dizziness, raised liver enzyme levels and high blood pressure.

Jakavi must not be used in women who are pregnant or breastfeeding. For the full list of all side effects and restrictions with Jakavi, see the package leaflet.

## Why has Jakavi been approved?

The CHMP decided that Jakavi's benefits are greater than its risks and recommended that it be given marketing authorisation. In myelofibrosis the CHMP considered that the reduction in spleen size and symptoms seen in patients taking Jakavi is clinically important. The Committee noted that the quality of life of patients treated with Jakavi was improved but that the medicine's effects had still to be evaluated in terms of extending the life of patients or delaying the progress of the disease or the onset of leukaemia. With regard to safety, the Committee considered that the risk of infections is acceptable but should be monitored further, while other known risks, such as bleeding or a reduction in blood cell counts, can be appropriately managed.

In polycythaemia vera the CHMP considered that Jakavi is of benefit to patients who do not respond or are intolerant to treatment with hydroxyurea, while the safety profile is acceptable. However, the long-term effects of the medicine will need to be further investigated.

## What measures are being taken to ensure the safe and effective use of Jakavi?

A risk management plan has been developed to ensure that Jakavi is used as safely as possible. Based on this plan, safety information has been included in the summary of product characteristics and the package leaflet for Jakavi, including the appropriate precautions to be followed by healthcare professionals and patients.

In addition, the company that makes Jakavi is extending the main studies on myelofibrosis and will provide annual data on the effects of Jakavi in terms of how long patients live and how long they live without their disease getting worse or developing leukaemia. In polycythaemia vera, the company will extend the main study to provide long-term data on the safety and effectiveness of Jakavi.

## Other information about Jakavi

The European Commission granted a marketing authorisation valid throughout the European Union for Jakavi on 23 August 2012.

The full EPAR for Jakavi can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European public assessment reports. For more information about treatment with Jakavi, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

This summary was last updated in 03-2015.