swissmedic

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Inrebic® (active substance: fedratinib as dihydrochloride monohydrate)

Temporary authorisation in Switzerland: 1 July 2021

Medicinal product (hard capsule) as second-line treatment for certain forms of myelofibrosis

About the medicinal product

Inrebic contains the active substance fedratinib as dihydrochloride monohydrate and has been authorised in Switzerland in the form of a hard capsule at the dosage strength of 100 mg.

Inrebic is a prescription-only medicine used for treating the forms of intermediate-risk and high-risk myelofibrosis listed below in patients who do not (or no longer) respond to, or are unable to tolerate, drugs containing the active substance ruxolitinib:

- Primary myelofibrosis
- Secondary myelofibrosis that has occurred as a consequence of polycythaemia vera (PV) or essential thrombocytopenia (ET)

Myelofibrosis is a rare disease that affects the bone marrow and leads to a change in the bone marrow tissue and the formation of fibres. Healthy blood cells can no longer be formed in sufficient numbers and blood cell formation is outsourced to other organs, resulting in an enlarged spleen, for example.

Since this is a rare disease, the medicine has been authorised as an orphan drug. "Orphan drug" is a designation given to important medicinal products for rare diseases.

Inrebic was authorised under Article 13 of the Therapeutic Products Act (TPA). This means that the medicinal product is already authorised in another country with comparable medicinal product control. In this case, Swissmedic takes into consideration the results of checks carried out by the foreign regulatory agency, provided certain requirements are fulfilled. These involve checks on the quality, efficacy and safety of the medicinal product, and the extent to which the results can be accepted for Switzerland.

The consideration of the results of foreign authorisation procedures is intended to help ensure that medicines that are already authorised abroad can be made available to patients in Switzerland as quickly as possible.

In deciding whether to authorise Inrebic in Switzerland, Swissmedic has accepted parts of the assessment and approval decision of the U.S. Food and Drug Administration (FDA).

Mode of action

Inrebic contains the active substance fedratinib, which belongs to the group of Janus kinase[1] inhibitors (JAK) and specifically inhibits the Janus kinase "JAK-2".

Use

Inrebic is a prescription-only medicine available as a hard capsule containing a 100 mg dose of active substance. Treatment is administered at the recommended dosage of 400 mg taken once a day by mouth.

Efficacy

The efficacy of Inrebic as second-line treatment was evaluated on the basis of study ARD12181 (JAKARTA2). The study participants were 97 patients with myelofibrosis who were previously treated with the active substance ruxolitinib and who did not respond to, or were unable to tolerate, this treatment.

The primary efficacy endpoint was the proportion of patients achieving a ≥35% reduction in spleen volume, compared to the spleen volume at the start of treatment, by the end of the 6th treatment cycle. After the 6 treatment cycles, a reduction in spleen volume of ≥35% was observed in 22.7% of the patients (22 patients out of 97 study participants).

Precautions, undesirable effects & risks

Inrebic must not be used in those who are hypersensitive to the active substance or any of the excipients.

Like all medicines, Inrebic can produce side effects, although not necessarily in everyone.

Serious effects and fatal cases of encephalopathy (brain damage) have occurred during the use of Inrebic. Therefore, before treatment with Inrebic is started, the thiamine levels (vitamin B1) should be checked and then monitored at regular intervals, and additional thiamine should be taken if the levels are too low.

The most common undesirable effects (affecting more than one in 10 patients) are urinary tract infections, anaemia (low red blood cell count), thrombocytopenia (low platelet count), bleeding, neutropenia (low white blood cell count), blood lipase level increased, blood amylase level increased, headache, dizziness, diarrhoea, nausea, vomiting, constipation, blood liver enzyme levels increased, muscle spasms, blood level of muscle breakdown products increased and fatigue/loss of strength.

All precautions, risks and other possible undesirable effects are listed in the Information for patients (package leaflet) and the Information for healthcare professionals.

[1] Janus kinase: This specific tyrosine kinase is an enzyme responsible for signal transmission within cells.

Why the medicinal product has been authorised

The prognosis for myelofibrosis patients who do not (or no longer) respond to, or are unable to tolerate, medicines containing the active substance ruxolitinib is currently poor, since no other relevant treatments are available.

A reduction in spleen volume was observed in the clinical trial described above.

Due to the premature discontinuation of the pivotal clinical trials, only limited data are available on efficacy and safety, and particularly on long-term results. Moreover, the treatment with Inrebic is associated with significant risks, including the possibility of triggering serious episodes of encephalopathy.

Considering all the available data, the advantages of Inrebic for the treatment of certain forms of myelofibrosis outweigh the risks. The medicinal product Inrebic was authorised temporarily in Switzerland (in accordance with Art. 9a TPA) since not all clinical trials were available or had been concluded at the time of authorisation. The temporary authorisation is contingent on the timely submission of the data requested by Swissmedic. Once these authorisation conditions have been met, the temporary authorisation can be converted into an ordinary authorisation in the event of a positive benefit-risk assessment of the results.

Further information on the medicinal product

Information for healthcare professionals: Information for healthcare professionals Inrebic®

Information for patients (package leaflet): Information for patients Inrebic®

Healthcare professionals (doctors, pharmacists and others) can answer any further questions.

The date of revision of this text corresponds to that of the SwissPAR. New information concerning the authorised medicinal product in question will not be incorporated into the Public Summary SwissPAR.

Swissmedic monitors medicinal products authorised in Switzerland. Swissmedic initiates the necessary action in the event of newly discovered adverse drug reactions or other safety-relevant signals. New findings that could impair the quality, efficacy or safety of this medicinal product are recorded and published by Swissmedic. If necessary, the medicinal product information is adapted.