CADTH | pCODR PAN-CANADIAN ONCOLOGY DRUG REVIEW

PROVINCIAL FUNDING SUMMARY

Ruxolitinib (Jakavi) for Polycythemia Vera (pCODR 10065)

pERC Recommendation: Recommends

For further details, please see pERC Final Recommendation

Notification to Implement Issued by pCODR: March 18, 2016

This information is current as of November 1, 2019.

Note: Funding criteria as listed on the decision date. Please refer to the provincial drug programs for the most recent funding criteria and program eligibility.

PROVINCE	FUNDING STATUS	FUNDING DATE	FUNDING CRITERIA
BC	Funded	Apr 1, 2018	Polycythemia vera resistant or intolerant to hydroxyurea defined as below: • Resistance: after 3 months of hydroxyurea at the maximally tolerated dose. For patients showing one of the following: • need for phlebotomy to maintain HCT below 45%, or • platelet > 400 × 10^9 /L and WBC > 10 × 10^9 /L, or • failure to reduce splenomegaly extending greater than 10 cm below the costal margin by > 50%, as measured by palpation Intolerance: one of the following after any dose of hydroxyurea: • ANC < 1.0 × 10^9 /L or platelet < 100 × 10^9 /L or hemoglobin < 100 g/L at the lowest hydroxyurea dose required to achieve a response, defined as: • HCT < 45% without phlebotomy, and/or all of the followings: platelet < 400 × 10^9 /L, WBC < 10 × 10^9 /L and non-palpable spleen • Grade 3 to 4 non-hematologic toxicities (e.g., leg ulcers, mucocutaneous manifestations, GI symptoms, pneumonitis, or fever at any dose of hydroxyurea) • More than 1 week of grade 2 toxicities, permanent discontinuation of hydroxyurea, interruption of hydroxyurea until toxicity resolved, or hospitalization due to hydroxyurea toxicity. A BC Cancer "Compassionate Access Program" (CAP) request with appropriate clinical information (bone marrow report, cytogenetic report [if done], recent complete blood count and recent clinic progress note) for each patient must be approved prior to treatment. Initial CAP

PROVINCE	FUNDING STATUS	FUNDING DATE	FUNDING CRITERIA
			approval for 24 weeks. To continue treatment, apply to CAP for re-approval. Subsequent re-approvals through CAP will be required every 12 months.
AB	Funded	May 8, 2018	For the treatment of patients with polycythemia vera who have disease resistant to hydroxyurea or who are intolerant of hydroxyurea according to the modified European Leukemia NET criteria used in the RESPONSE trial and have good performance status. Treatment should continue until unacceptable toxicity or disease progression.
SK	Funded	Feb 23, 2018	For the treatment of patients with polycythemia vera who have disease resistant to Hydroxyurea or who are intolerant to Hydroxyurea according to the modified European LeukemiaNet Criteria used in the RESPONSE trial and have a good performance status Definition of Resistance to Hydroxyurea: After three (3) months of at least 2 g/day of Hydroxyurea, or at the maximally tolerated Hydroxyurea dose if that dose is less than 2 g/day, the patient shows any one or more of the following: o Need for phlebotomy to keep the hematocrit less than 45% o Uncontrolled myeloproliferation (platelet count >400 x 10^9/L and WBC >10 x 10^9/L o Failure to reduce massive splenomegaly greater than 50% as measured by palpation Definition of Intolerance to Hydroxyurea: During treatment with Hydroxyurea, at the lowest dose required to achieve a response*, the patient shows any one or more of the following: o ANC <1 x 10^9/L, or Platelets <100 x 10^9/L or Hemoglobin <100 g/L o Presence of leg ulcers o Non-hematologic toxicities related to hydroxyurea therapy (e.g., mucocutaneous manifestations, gastrointestinal symptoms, pneumonitis or fever) that are grade 3 to 4, or grade 2 for more than 1 week (CTCAE version 3.0) o Permanent discontinuation of Hydroxyurea, significant interruptions of therapy, or hospitalization due to Hydroxyurea toxicity *Response is defined as a hematocrit less than 45% without phlebotomy, and/or all of the following: platelets <400 x 10^9/L, WBC <10 x 10^9/L, and non-palpable spleen.
MB	Funded	Oct 19, 2017	For the treatment of patients with polycythemia vera who have disease resistant to hyroxyurea (HU) or who are intolerant of HU according ot the modified European LeukemiaNet Criteria used in the RESPONSE trial and have a good performance status.

PROVINCE	FUNDING STATUS	FUNDING DATE	FUNDING CRITERIA
ON	Funded	Nov 20, 2017	Initial: For the treatment of patients with polycythemia vera who meet the following criteria: -Demonstrated resistance or demonstrated intolerance to hydroxyurea (HU); AND -Have a good performance status (ECOG ≤ 3) Resistance to Hydroxyurea as defined by: Use of HU for at least 3 months of treatment at a dose of at least 2 grams per day (or at maximally tolerated doses if unable to take 2 grams per day) meeting one of the following: -Patient continues to require phlebotomy to keep hematocrit (HCT) at less than 45%; OR -Patient demonstrates uncontrolled myeloproliferation (i.e. platelet count > 400 x 10^9/L and white blood cell count > 10 x 10^9/L); OR -Symptomatic splenomegaly Intolerance to Hydroxyurea as defined: After any dose of hydroxyurea, patient demonstrates one of the following: -Absolute neutrophil count < 1 x 10^9/L or platelet < 100 x 10^9/L or hemoglobin < 100 g/L at the lowest dose of HU required to achieve a response; OR -Presence of leg ulcers or other unacceptable HU-related grade 3 or 4 non-hematological toxicities (eg. Mucocutanous manifestations, gastrointestinal symptoms, pneumonitis, fever); OR -If patient demonstrates non-hematological grade 2 toxicities for at least one week: ORr -If toxicity requires permanent discontinuation of HU, interruption of HU until resolution of toxicity, or requiring hospitalization as a result of HU toxicity. Renewal: Patient continues to respond to treatment and has not experienced disease progression. Response defined by any one or more of the following; -Hematocrit <45% without phlebotomy; AND/OR -Platelet count ≤ 400 x 10^9/L; AND/OR -White blood cell count ≤ 10 x 10^9/L; AND/OR -non-palpable spleen.

PROVINCE	FUNDING STATUS	FUNDING DATE	FUNDING CRITERIA
NS	Funded	Sep 3, 2019	For the treatment of patients with polycythemia vera who have demonstrated resistance or intolerance to hydroxyurea (HU), and have a good performance status. Treatment should continue until unacceptable toxicity or disease progression. Resistance is considered if, after at least 3 months of HU therapy at the maximum tolerated dose, patients experience at least one of the following: • Need for phlebotomy to keep the hematocrit less than 45%. • Uncontrolled myeloproliferation (platelet count > 400 x 10^9/L and WBC > 10 x 10^9/L). • Failure to reduce massive splenomegaly > 50% as measured by palpation. Intolerance to HU is considered if patients experience at least one of the following: • Absolute neutrophil count < 1.0 x 10^9/L, platelet count < 100 x 10^9/L or hemoglobin<100g/L at the lowest dose of HU required to achieve a response.A response to HU is defined as HCT < 45% without phlebotomy and, and/orall of the following: platelet count ≤ 400x 10^9/L, white blood cell count ≤ 10 x 10^9/L, andnon-palpable spleen. • Presence of leg ulcers or other unacceptable HU-related non-hematologicaltoxicities (defined as grade 3 or 4, or more than 1 week of grade 2) such asmucocutaneous manifestations, gastrointestinal symptoms, pneumonitis or fever • Toxicity requiring permanent discontinuation of HU, or interruption of HU until toxicityresolved, or hospitalization due to HU toxicity.

PROVINCE	FUNDING STATUS	FUNDING DATE	FUNDING CRITERIA
NB	Funded	May 8, 2018	For the treatment of patients with polycythemia vera who have demonstrated resistance or intolerance to hydroxyurea (HU). Renewal Criteria: Written confirmation that the patient has responded to treatment and there is no evidence of disease progression. Clinical Notes: 1. Patients must have a good performance status. 2. Treatment should be discontinued upon disease progression or unacceptable toxicity. 3. Resistance is considered if, after at least 3 months of HU therapy at the maximum tolerated dose, patients experience at least one of the following: - Need for phlebotomy to maintain hematocrit (HCT) < 45% - Uncontrolled myeloproliferation (i.e., platelet count > 400 x 10^9/L and white blood cell count > 10 x 10^9/L) - Failure to reduce massive splenomegaly by greater than 50%, as measured by palpation 4. Intolerance to HU is considered if patients experience at least one of the following: - Absolute neutrophil count < 1.0 x 10^9/L, platelet count < 100 x 10^9/L or hemoglobin < 100 g/L at the lowest dose of HU required to achieve a response. A response to HU is defined as HCT < 45% without phlebotomy, and/or all of the following: platelet count < 400 x 10^9/L, white blood cell count < 10 x 10^9/L, and non-palpable spleen. - Presence of leg ulcers or other unacceptable HU-related non-hematological toxicities (defined as grade 3 or 4 or, more than one week of grade 2) such as mucocutaneous manifestations, gastrointestinal symptoms, pneumonitis, or fever - Toxicity requiring permanent discontinuation of HU, interruption of HU until toxicity resolved, or hospitalization due to HU toxicity.

PROVINCE	FUNDING STATUS	FUNDING DATE	FUNDING CRITERIA
NL	Funded	Aug 1, 2019	For the treatment of patients with polycythemia vera who have disease resistant to hydroxyurea (HU) or who are intolerant of HU according to the modified European LeukemiaNet Criteria* used in the RESPONSE trial and have a good performance status. Renewal Criteria: • Written confirmation that the patient has responded to treatment and there is no evidence of disease progression *Modified European LeukemiaNet Criteria HU Resistance (defined after 12 weeks into a course of HU therapy at a dose of at least 2 grams/day or at the subjects maximally tolerated dose if that dose is less than 2 grams/day): • need for phlebotomy to keep hematocrit < 45%, or • platelet count > 400 x 10^9/L and white blood cell count > 10 x 10^9/L, or • failure to reduce splenomegaly extending greater than 10 cm below the costal margin by more than 50%, as measured by palpation; HU Intolerance: • Absolute neutrophil count < 1.0 x 10^9/L OR platelet count < 100 x 10^9/L OR hemoglobin <100 g/L (i.e. 10 g/dL) at the lowest dose of HU required to achieve a response (with response modified from Barosi et al 2009B: hematocrit < 45% without phlebotomy AND/OR all of the following three items: platelet count ≤ 400 x 10^9/L, white blood cell count ≤ 10 x 10^9/L, and non-palpable spleen), or o Presence of leg ulcers or other unacceptable HU-related non-hematological toxicities (such as mucocutaneous manifestations, gastrointestinal symptoms, pneumonitis or fever at any dose of HU), defined as: • CTCAE version 3.0 Grade 3-4, OR • more than 1 week of CTCAE version 3.0 Grade 2 OR • permanent discontinuation of HU, OR • interruption of HU until toxicity resolved, OR • hospitalization due to HU toxicity.
PEI	Under provincial consideration		

Under provincial consideration means that the province is reviewing pCODR's recommendation. This may include the province working with the drug manufacturer to reach an agreement for a drug product that both parties can accept, in particular in cases where the pCODR Expert Review Committee has recommended that the drug be funded only on the condition of cost-effectiveness being improved to an acceptable level. This may occur before or after the pan-Canadian Pharmaceutical Alliance negotiations. Please contact the specific provincial drug program and/or cancer agency in your province for information about the status of a given drug product.