PEI Pharmacare
P.O. Box 2000
Charlottetown, PE
C1A 7N8
www.princeedwardisland.ca

Programmes provinciaux de medicaments
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PEI Pharmacare Bulletin

Issue (2024 - 17) **October 22, 2024**

NEW PRODUCT(S) ADDED TO THE PEI PHARMACARE FORMULARY (EFFECTIVE DATE: NOVEMBER 5, 2024)

Product (Generic name)	Product (Brand name)	Strength	Dosage Form	DIN	MFR
Ravulizumab	**Ultomiris**	**300 mg/30 mL** **300 mg/3 mL** **1,100 mg/11 mL**	**Vial** **Vial** **Vial**	**02491559** **02533448** **02533456**	**ALX**
Criteria	**Paroxysmal Nocturnal Hemoglobinuria** Initiation Criteria: For the treatment of patients with paroxysmal nocturnal hemoglobinuria (PNH) who meet the following criteria: • The diagnosis of PNH has been made based on the following confirmatory results: ○ Flow cytometry/FLAER exam with granulocytes or monocyte clone ≥ 10%; AND ○ LDH > 1.5 ULN; AND ○ At least one of the following: ▪ A thrombotic or embolic event which required the institution of therapeutic anticoagulant therapy, ▪ Minimum transfusion requirement of 4 units of red blood cells in the previous 12 months, ▪ Chronic or recurrent anemia where causes other than hemolysis have been excluded and demonstrated by more than one measure of less than or equal to 70g/L or by more than one measure of less than or equal to 100g/L with concurrent symptoms of anemia, ▪ Pulmonary insufficiency: Debilitating shortness of breath and/or chest pain resulting in limitation of normal activity (New York Heart Association Class III) and/or established diagnosis of pulmonary arterial hypertension, where causes other than PNH have been excluded, ▪ Renal insufficiency: History of renal insufficiency, demonstrated by an eGFR less than or equal to 60 mL/min/1.73m^2, where				

causes other than PNH have been excluded,
- Smooth muscle spasm: Recurrent episodes of severe pain requiring hospitalization and/or narcotic analgesia, where causes other than PNH have been excluded.

Renewal Criteria:

- Renewals will be considered for patients who;
  - Demonstrate clinical improvement while on therapy or
  - Where therapy has been shown to stabilize the patient's condition
- Requests for renewal should be accompanied by confirmation of granulocyte clone size (by flow cytometry).

Exclusion Criteria:

Exclusion criteria for both initiation and renewal requests:

- Small granulocyte or monocyte clone size - the treatment of patients with a granulocyte and monocyte clone size below 10% will not be eligible for treatment; OR
- Aplastic anemia with two or more of the following: neutrophil count below 0.5 x 10^9/L, platelet count below 20 x 10^9/L, reticulocytes below 25 x 10^9/L, or severe bone marrow hypocellularity; OR
- Patients afflicted with PNH and another life-threatening or severe disease where the long term prognosis is unlikely to be influenced by therapy (for example acute myeloid leukemia or high-risk myelodysplastic syndrome);

OR

- The presence of another medical condition that might reasonably be expected to compromise a response to therapy.

Exclusion criteria for renewal requests:

- The patient or treating physician fails to comply adequately with treatment or measures, including monitoring requirements, taken to evaluate the effectiveness of the therapy; OR
- If therapy fails to relieve the symptoms of disease that originally resulted in the patient being approved for subsidized treatment.

Clinical Notes:

- Patients with insufficient initial response or who have failed treatment with eculizumab at the Health Canada– recommended dosage are not eligible for reimbursement of ravulizumab.
- All patients must receive meningococcal vaccination with a tetravalent vaccine at least two weeks prior to receiving the first dose of ravulizumab.

Claim Notes:

- Approvals will be for a maximum of

Body Weight Range (kg)	Loading Dose (mg)	Maintenance Dose (mg)	Dosing Interval
≥ 5 to < 10	600	300	Every 4 weeks
≥ 10 to < 20	600	600	Every 4 weeks
≥ 20 to < 30	900	2,100	Every 8 weeks
≥ 30 to < 40	1,200	2,700	Every 8 weeks

≥ 40 to < 60	2,400	3,000	Every 8 weeks
≥ 60 to < 100	2,700	3,300	Every 8 weeks
≥ 100	3,000	3,600	Every 8 weeks

- Supplemental dosing following treatment with plasma exchange, plasmapheresis, or intravenous immunoglobulin is approved.
- Initial Approval: 6 months
- Renewal Approval: 1 year
- The patient must be under the care of a pediatric nephrologist, a nephrologist, a pediatric hematologist or a hematologist.

Atypical Hemolytic Uremic Syndrome

Initiation Criteria:

- For the treatment of adult and pediatric patients 1 month of age and older with atypical hemolytic uremic syndrome (aHUS) who meet all of the following criteria:
  - Confirmed diagnosis of aHUS at initial presentation, defined by presence of thrombotic microangiopathy (TMA), who meet all the following criteria:
    - A disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13 (ADAMTS13) activity ≥ 10% on blood samples taken before plasma exchange or plasma infusion (PE/PI); AND
    - Shiga toxin–producing Escherichia coli (STEC) test negative in patients with a history of bloody diarrhea in the preceding 2 weeks; and
    - TMA must be unexplained (not a secondary TMA).
  - Evidence of ongoing active TMA and progressing, defined by laboratory test abnormalities despite plasmapheresis, if appropriate. Patients must demonstrate:
    - Unexplained (not a secondary TMA) thrombocytopenia (platelet count < 150×10^9/L); and hemolysis as indicated by the documentation of 2 of the following: schistocytes on the blood film; low or absent haptoglobin; or lactate dehydrogenase (LDH) above normal. OR
    - Tissue biopsy confirms TMA in patients who do not have evidence of platelet consumption and hemolysis.
  - Evidence of at least 1 of the following documented clinical features of active organ damage or impairment:
    - Kidney impairment, as demonstrated by one of the following:
      - A decline in estimated glomerular filtration rate (eGFR) of > 20% in a patient with preexisting renal impairment; AND/OR
      - Serum creatinine (SCr) > upper limit of normal (ULN) for age or GFR < 60mL/min and renal function deteriorating despite prior PE/PI in patients who have no history of preexisting renal impairment (i.e., who have no baseline eGFR measurement); OR
      - SCr > the age-appropriate ULN in pediatric patients (as determined by or in consultation with a pediatric nephrologist) OR
    - The onset of neurological impairment related to TMA.

	▪ Other TMA-related manifestations, such as cardiac ischemia, bowel ischemia, pancreatitis, and retinal vein occlusion. • For transplant patients with a documented history of aHUS (i.e., history of TMA [not a secondary TMA only] with ADAMTS 13 > 10%) who meet the following criteria: o Develop TMA immediately (within hours to 1 month) following a kidney transplant; OR o Previously lost a native or transplanted kidney due to the development of TMA; OR o Have a history of proven aHUS and require prophylaxis with ravulizumab at the time of a kidney transplant • Patients should not have a history of ravulizumab treatment failure (i.e., treated with ravulizumab with a previous aHUS recurrence). Treatment failure is defined as: o Dialysis-dependent at 6 months, and failed to demonstrate resolution or stabilization of neurological or extrarenal complications if these were originally present; OR o On dialysis for ≥ 4 of the previous 6 months while receiving ravulizumab and failed to demonstrate resolution or stabilization of neurological or extrarenal complications if these were originally present; OR o Worsening of kidney function with a reduction in eGFR or increase in SCr ≥ 25% from baseline. Renewal Criteria: • Treatment with ravulizumab can be renewed as long as the patient exhibits a response to treatment or as per physician discretion (e.g., long-term funding based on factors like limited organ reserve or high-risk genetic mutation such as Factor H deficiency). o Response to treatment is defined as, but not limited to, hematological normalization (e.g., platelet count, LDH), stabilization of end-organ damage (such as acute kidney injury and brain ischemia), transplant graft survival in susceptible individuals, and dialysis avoidance in patients who are pre- end-stage kidney disease (ESKD). • Assessment of treatment response should be conducted at 6-months, at 12-months, then annually thereafter. o At the 6-month assessment, treatment response and no treatment failure (defined in Initiation Criteria) is required. o At the 12-month and annual assessments, treatment response, no treatment failure, and the patient has limited organ reserve or high-risk genetic mutation are required. ▪ Limited organ reserve is defined as significant cardiomyopathy, neurological, gastrointestinal, or pulmonary impairment related to TMA; or Grade 4 or 5 chronic kidney disease (eGFR < 30mL/min) is required. • A patient previously diagnosed with aHUS and who responded to treatment with ravulizumab and has not failed ravulizumab is eligible to restart ravulizumab if the patient redevelops a TMA related to aHUS and meets the following clinical conditions: o Significant hemolysis as evidenced by presence of schistocytes on the blood film, or low or absent haptoglobin, or LDH above normal; AND

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EITHER

Platelet consumption as measured by either ≥ 25% decline from patient baseline or thrombocytopenia (platelet count < 150,000 × 10^9/L); OR
TMA-related organ impairment (e.g., unexplained rise in serum creatinine with onset of urine dipstick positive for hemoglobin) including on recent biopsy.

Claim Notes:

Approvals will be for a maximum of:

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