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SASKATCHEWAN FORMULARY BULLETIN
Update to the 62nd Edition of the Saskatchewan Formulary

Temporary Non-Interchangeable Full Formulary Benefit Due to Shortages:

- **vigabatrin, sachet, 500mg (US-Labelled Vigabatrin) effective December 22, 2025**

Additional Biosimilar Formulation of an Existing Exception Drug Status (EDS) Benefit with Same Criteria:

- **denosumab, prefilled syringe, 60mg/mL (Stoboclo)**

Additional Formulation of an Existing Exception Drug Status (EDS) Benefit According to the Following Criteria:

- **rivaroxaban, granules for suspension, 51.7mg, 103.4mg (Xarelto Granules)**
  For the treatment and prevention of venous thromboembolism (VTE) in pediatric patients.

Additional Criteria for an Existing Exception Drug Status (EDS) Benefit:

- **burosumab, solution for injection, 10mg/mL, 20mg/mL, 30mg/mL (mg) (Crysvita)**
  B) Initiation Post-Epiphyseal Closure
  For the treatment of X-linked hypophosphatemia (XLH) when initiated in patients who have ALL of the following:
  - Age of 18 years or older, or younger than 18 years with epiphyseal closure, who have not previously received treatment with burosumab; AND
  - A diagnosis of XLH supported by:
    - Classic clinical features of adult XLH (such as, but not limited to, short stature or bowed legs); AND
    - A confirmed phosphate-regulating endopeptidase homolog, X-linked (PHEX) gene variant in the patient. If a PHEX gene variant is not confirmed, diagnosis may be confirmed using serum intact fibroblast growth factor 23 (FGF23) level[1]; AND
  - Estimated glomerular filtration rate (eGFR) of 60 mL/min or greater; or eGFR ranging from 45 mL/min to less than 60 mL/min with confirmation that the renal insufficiency is not due to nephrocalcinosis; AND
  - Presence of skeletal pain that the treating physician attributes to XLH and/or osteomalacia; AND
  - Insufficient response or refractory to conventional therapy with active vitamin D and oral phosphate supplementation, as shown by:
    - Presence of either radiographic evidence of osteomalacia, nonhealing complete fractures, or nonhealing incomplete fractures after 1 year of conventional therapy, OR
    - The development of hyperparathyroidism or nephrocalcinosis on conventional therapy.

[1] Examples of serum intact FGF23 level confirming XLH may include a level > 30 pg/mL by Kainos Assay or equivalent level through an alternative validated assay, as determined by the diagnosing specialist.

Burosumab should be prescribed by a physician working in a comprehensive team of health care providers who are experienced in the diagnosis and management of XLH.
Initial approval duration = 13 months

Renewal Criteria:

- Coverage of burosumab may be renewed if NONE of the following develop or progress while on treatment:
  - Hyperparathyroidism
  - Nephrocalcinosis
  - Evidence of fracture or pseudofracture based on radiographic assessment
  - Fasting hypophosphatemia.

Renewal approval duration = 12 months

- **ravulizumab, intravenous solution, 10mg/mL (30mL vial), 100mg/mL (3mL vial), 100mg/mL (11mL vial) (mg) (Ultomiris)**
  INDICATION: Generalized Myasthenia Gravis (gMG):
  Initiation Criteria:
  For the treatment of adult patients with generalized myasthenia gravis (gMG) who:
  - Have a positive serologic test for anti-acetylcholine receptor (anti-AChR) antibodies; AND,
  - Have a Myasthenia Gravis Activities of Daily Living (MG-ADL) score[1] at baseline of ≥6; AND,
  - Have Myasthenia Gravis Foundation of America (MGFA) class II to IV disease; AND,
  - Have symptoms persisting despite an adequate trial of conventional therapy[2] for gMG; AND,
  - Will not have ravulizumab initiated during a gMG exacerbation or crisis, or within 12 months of a thymectomy; AND,
  - Will not be using ravulizumab concomitantly with rituximab, a neonatal Fc receptor antagonist, or another complement inhibitor; AND,
  - Are under the care of a neurologist with expertise in the diagnosis and management of gMG.

  Initial Coverage Duration: 6 months

  Initial Renewal Criteria:
  Renewal of ravulizumab coverage will be considered in individuals who:
  - Have a documented improvement (decrease) in MG-ADL score[1] of 2 or more points; AND,
  - Will not be using ravulizumab concomitantly with rituximab, a neonatal Fc receptor antagonist, or another complement inhibitor; AND,
  - Remain under the care of a neurologist with expertise in the diagnosis and management of gMG.

  Subsequent Renewal Criteria:
  Ongoing coverage of ravulizumab will be considered in individuals who:
  - Have maintained the improvement in MG-ADL score[1] demonstrated at the initial renewal; AND,

- Will not be using ravulizumab concomitantly with rituximab, a neonatal Fc receptor antagonist, or another complement inhibitor; AND,
- Remain under the care of a neurologist with expertise in the diagnosis and management of gMG.

Renewal Duration: 12 months

[1]The MG-ADL score must be measured and provided by the physician at baseline and with each renewal request.
[2]Conventional therapy should include an adequate trial of, or intolerance to, rituximab. If rituximab is not appropriate, an adequate trial of another preventative treatment (including, but not limited to, other monoclonal antibodies, acetylcholinesterase inhibitors (AChEIs), azathioprine, mycophenolate, etc.) should have been tried.

INDICATION*:* Neuromyelitis Optica Spectrum Disorder (NMOSD):
For the treatment of neuromyelitis optica spectrum disorder (NMOSD) in adult patients who meet ALL of the following:

- The patient is anti–aquaporin 4 (AQP4) seropositive; and
- The patient has had at least one NMOSD attack or relapse in the previous 12 months; and
- The patient has experienced an inadequate response or intolerance following a trial of rituximab, or has a contraindication to rituximab; and
- The patient has an Expanded Disability Status Scale (EDSS) score of 7 points or less; and
- Ravulizumab is being prescribed by a neurologist with expertise in treating NMOSD; and
- Ravulizumab will not be used in combination with rituximab, satralizumab, eculizumab, or inebilizumab.

Initial approval duration: 12 months

Note: Ravulizumab should not be initiated during a NMOSD relapse episode.

Renewal
To be eligible for ongoing coverage of ravulizumab, the patient must:

- Maintain an EDSS score of 8 points or less (measured annually); and
- Remain under the care of a neurologist with expertise in treating NMOSD; and
- Not be using ravulizumab in combination with rituximab, satralizumab, eculizumab, or inebilizumab.

Renewal duration: 12 months

Exception Drug Status (EDS) Benefit According to the Following Criteria:

- **eculizumab, intravenous solution, 10mg/mL (30mL vial) (mL) (Soliris)**
  INDICATION: Atypical Hemolytic Uremic Syndrome (aHUS):
  Initiation Criteria
  For the treatment of atypical hemolytic uremic syndrome (aHUS), when prescribed by or in consultation with a nephrologist or hematologist, in patients meeting ALL of the following:

  1. Confirmed diagnosis of aHUS at initial presentation, defined by presence of thrombotic microangiopathy (TMA) as follows:

- ADAMTS-13* 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 (i.e., not attributed to any secondary cause).

AND

2. Evidence of ongoing active TMA that is progressing (despite use of plasmapheresis, if appropriate), as demonstrated by the following:

- Unexplained thrombocytopenia (platelet count < 150 × 10^9/L and not a secondary TMA); 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
- TMA confirmed by tissue biopsy, in patients who do not have evidence of platelet consumption and hemolysis.

AND

3. Evidence of at least ONE of the following documented clinical features of active organ damage or impairment:

- Kidney impairment, as demonstrated by one of the following:

Patient Characteristics	Kidney Impairment Level
Adult, preexisting renal impairment	eGFR decline of > 20%
Adult, no history of preexisting renal impairment (including patients with no baseline eGFR measurement)	SCr > ULN for age, or eGFR < 60mL/min and renal function deteriorating despite prior PE/PI
Pediatric patients	SCr > the age-appropriate ULN (as determined by or in consultation with a pediatric nephrologist)

eGFR = estimated glomerular filtration rate
SCr = serum creatinine
ULN = upper limit of normal

and/or

- The onset of neurological impairment related to TMA; and/or
- Other TMA-related manifestations, such as cardiac ischemia, bowel ischemia, pancreatitis, and retinal vein occlusion.

Initial coverage duration: 6 months

*Notes: ADAMTS-13 = A disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13.

Initiation Criteria for Kidney Transplant Patients

Transplant patients with a documented history of aHUS (i.e., history of TMA [not a secondary TMA only] with ADAMTS-13 activity ≥ 10%) may be eligible for eculizumab coverage, when

prescribed by or in consultation with a nephrologist or hematologist, if ANY of the following occur:

- Development of TMA immediately (within hours to 1 month) following a kidney transplant; or
- Experiencing aHUS recurrence after previous loss of a native or transplanted kidney due to the development of TMA; or
- The patient will be receiving a kidney transplant and requires prophylaxis with eculizumab at the time of the transplant.

Initial coverage duration: 6 months

Exclusion Criteria (for initial and renewal requests)
Patients with a history of eculizumab treatment failure (i.e., treated with eculizumab for a previous aHUS occurrence/recurrence) will not be eligible for coverage.

Treatment failure is defined as ANY of the following occurring while receiving eculizumab:

- Dialysis dependence at 6 months of eculizumab treatment, and failure to demonstrate resolution or stabilization of neurological or extrarenal aHUS complications (if these were originally present); or
- On dialysis for ≥ 4 of the previous 6 months of eculizumab treatment, and failure to demonstrate resolution or stabilization of neurological or extrarenal aHUS complications (if these were originally present); or
- Worsening of kidney function with a reduction in eGFR or increase in SCr ≥ 25% from baseline at the start of eculizumab treatment.

Patients will not be eligible for eculizumab coverage if receiving concurrent treatment with another C5 inhibitor drug (e.g., ravulizumab, etc.).

Initial Renewal Criteria (at 6 months)
After the initial 6 months of eculizumab treatment, coverage may be renewed if ALL of the following are met:

- The patient has demonstrated response to treatment, defined as, but not limited to:
  - Hematological normalization (e.g., platelet count, LDH); and
  - Stabilization of aHUS-related end-organ damage (such as acute kidney injury and brain ischemia); and
  - Transplant graft survival in susceptible individuals; and
  - Dialysis avoidance, in patients who are pre-end stage kidney disease (ESKD); and
- The patient has not experienced treatment failure, as defined in the Exclusion Criteria above; and
- Eculizumab therapy continues to be managed by or in consultation with a nephrologist or hematologist.

Initial Renewal coverage duration: 6 months

Subsequent Renewal Criteria (at 12 months and thereafter)
For patients requiring ongoing eculizumab treatment, coverage may be renewed if ALL of the following are met:

- The patient continues to demonstrate response to treatment, as defined in the Initial Renewal Criteria above; and
- The patient has not experienced treatment failure, as defined in the Exclusion Criteria above; and
- The patient has limited organ reserve, or a high-risk genetic mutation (e.g., Factor H deficiency) associated with aHUS recurrence.
    - Limited organ reserve is defined as significant cardiomyopathy, neurological, gastrointestinal, or pulmonary impairment related to TMA; or Stage 4 or 5 chronic kidney disease (eGFR < 30mL/min).

AND

- Eculizumab therapy continues to be managed by or in consultation with a nephrologist or hematologist.

Subsequent Renewal coverage duration: 12 months

Reinitiation Criteria

Patients previously diagnosed with aHUS who responded to treatment with eculizumab (without treatment failure, as defined in the Exclusion Criteria above) may be eligible for coverage to restart eculizumab, if a TMA related to aHUS redevelops and ALL of the following are present:

- Significant hemolysis, as evidenced by presence of schistocytes on the blood film, low or absent haptoglobin, or LDH above normal;

AND

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

AND

- Eculizumab therapy is being prescribed by or in consultation with a nephrologist or hematologist.

Reinitiation Coverage duration: 6 months, with renewal considered according to Initial Renewal Criteria and Subsequent Renewal Criteria above.

<u>INDICATION: Paroxysmal Nocturnal Hemoglobinuria (PNH):</u>

Initiation Criteria

For the treatment of Paroxysmal Nocturnal Hemoglobinuria (PNH) in patients diagnosed based on both of the following confirmatory results:

- Flow cytometry/FLAER exam with granulocyte or monocyte clone size ≥ 10%; and
- Lactate dehydrogenase (LDH) > 1.5 x upper limit of normal (ULN);

AND

the patient is exhibiting at least ONE of the following features attributed to PNH:

- A thrombotic or embolic event which required the initiation of therapeutic anticoagulant therapy; and/or
- Transfusion requirement of ≥ 4 units of red blood cells in the previous 12 months; and/or

- Chronic or recurrent anemia where causes other than hemolysis have been excluded, and demonstrated by more than one hemoglobin measure of ≤ 70g/L or more than one hemoglobin measure of ≤ 100 g/L with concurrent symptoms of anemia; and/or
- Pulmonary insufficiency, as defined by 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; and/or
- Renal insufficiency, demonstrated by an eGFR ≤ 60mL/min/1.73m^2, where causes other than PNH have been excluded; and/or
- Smooth muscle spasm, as defined by recurrent episodes of severe pain requiring hospitalization and/or narcotic analgesia, where causes other than PNH have been excluded;

AND

eculizumab is being prescribed by or in consultation with a hematologist or nephrologist with experience managing PNH.

Initial approval duration: 6 months

Renewal Criteria

After the initial approval period, a patient may receive approval for further coverage of eculizumab where:

- There has been relief in the PNH symptoms that had qualified the patient for their initial eculizumab approval; and
- There is demonstrated clinical improvement in the patient, or stabilization of the patient's condition, while receiving treatment with eculizumab; and
- The patient and treating physician have been adequately adherent to treatment and to measures, including monitoring requirements, taken to evaluate the effectiveness of the therapy; and
- Eculizumab is being prescribed by or in consultation with a hematologist or nephrologist with experience in managing PNH.

Requests for renewal must be accompanied by current confirmation of granulocyte and monocyte clone size (by flow cytometry), in accordance with the Exclusion Criteria below.

Renewal duration: 1 year

Exclusion Criteria (for initial and renewal requests)

Patients meeting any of the following criteria will not be eligible for eculizumab coverage:

- Prior treatment failure with a C5 inhibitor (e.g., eculizumab, ravulizumab, etc.);
- Receiving concurrent treatment with another C5 inhibitor drug (e.g. ravulizumab);
- Granulocyte and monocyte clone size both below 10%;
- Presence of 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;
- Presence of 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

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

The Following Products were NOT RECOMMENDED for Formulary listing:

- **avacopan, capsule, 10mg (Tavneos)** – for anti-neutrophil cytoplasmic autoantibody associated vasculitis and microscopic polyangiitis
- **avatrombopag, tablet, 20mg (Doptelet)** – for chronic immune thrombocytopenia
- **deucravacitinib, tablet, 6mg (Sotyktu)** – for plaque psoriasis
- **tralokinumab, pre-filled syringe, 150mg/1mL (Adtralza)** – for atopic dermatitis

The Following Products have been DELISTED from the Formulary at the request of the Manufacturer:

- **clotrimazole, vaginal suppository/1% topical cream, 500mg (Canesten Combi-Pak 1)**
- **clotrimazole, vaginal tablet, 200mg (Canesten Combi-Pak 3)**

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