I. POLICY

It is the policy of UPMC Health Plan to maintain a prior authorization process that promotes appropriate utilization of specific drugs with potential for misuse or limited indications. This process involves a review using Food and Drug Administration (FDA) criteria to make a determination of Medical Necessity, as defined in CRM.015-Medical Necessity, and approval by the Pharmacy & Therapeutics Committee of the criteria for prior authorization, as described in RX.003-Prior Authorization Process.

The Intravenous immune globulin (IVIG) drugs are subject to the prior authorization process.

II. DEFINITIONS

N/A

III. PURPOSE

The purpose of this policy is to define the Prior Authorization Process for IVIG.

IV. SCOPE

This policy applies to members of the Pharmacy Services Department.
V. PROCEDURE

IVIG is used to increase circulation levels of gamma globulin in certain immunoglobulin deficiency states and in treatment of a limited number of specified diseases.

Criteria

FDA Approved Indications

1. Primary Immunodeficiency
   - Approve for one of the following if prescribed by an immunologist or hematologist or in consultation with an immunologist or hematologist:
     i. Common Variable Immunodeficiency (hypogammaglobulinemia)
     ii. Congenital Agammaglobulinemia
     iii. Bruton’s or X-linked Agammaglobulinemia
     iv. Severe Combined Immunodeficiency (SCID)
     v. X-linked Hyper-IgM Syndrome
     vi. Wiskott-Aldrich Syndrome
   - Approve for 1 year initially

2. Idiopathic or Immune Thrombocytopenic Purpura (ITP)
   (Platelet counts expressed per mm$^3$)
   - Children with ITP
     i. Approve for one of the following:
        o If platelet count < 20,000 and significant mucous membrane bleeding or if platelet count < 10,000 and minor purpura
        o If splenectomy planned and platelet count < 30,000
        o If platelet count < 20,000 and inaccessibility or noncompliance is a concern
        o If surgery, dental extractions, or other procedures likely to cause blood loss are needed
   - Adults with ITP
     ii. Approve for one of the following:
        o Member has tried a corticosteroid and the platelet count < 30,000 and there is acute bleeding
        o To increase platelet counts before major surgical procedures (e.g. splenectomy)
        o If platelet count is < 20,000 and the patient is considered to be at risk for intracerebral bleeding
        o If there will be predictable bleeding such as from surgery, dental procedures, or pregnancy/labor, then approve IVIG if the platelet counts are as follows: Dentistry ≤ 10,000,
teeth extractions $\leq 30,000$, regional dental block $\leq 30,000$
minor surgery $\leq 50,000$, major surgery $\leq 80,000$

- To defer or avoid splenectomy

- Pregnant Women with ITP
  - Approve for one of the following:
    - Platelet count is $< 100,000$
    - Pregnant women with past history of splenectomy
    - Pregnant women who have previously delivered infants
      with autoimmune thrombocytopenia
  - Approve for 1 month initially

3. Kawasaki Disease
   - Approve for 1 dose in the acute phase
   - May approve second dose in patients who fail to respond to initial therapy
   - Patients should receive a single dose of IVIG together with aspirin within
     the first 10 days of illness, and if possible, within 7 days of illness
   - Children presenting after the 10th day of illness with persistent fever
     without other explanation or aneurysms and ongoing systemic inflammation

4. Chronic B-cell Lymphocytic Leukemia
   - Members with Hypogammaglobulinemia (IgG $< 640\text{mg/dl}$) and/or with
     previous history of serious bacterial infection (requiring antibiotics)
   - Approve for 1 year initially

5. HIV in pediatric patients ($< 13$ years old) with CD4 count $\geq 200\text{/mm}^3$
   - Approve for one of the following:
     - Infants and children with recurrent (2 or more) serious bacterial
       infections such as bacteremia, meningitis, or pneumonia during a
       1-year period despite administration of highly active antiretroviral
       therapy (HAART) and prophylactic TMP-SMZ or other
       antimicrobials
     - HIV-infected infants and children with hypogammaglobulinemia
       (IgG $< 400\text{mg/dl}$)
     - Failure to form antibodies to common antigens, e.g., measles,
       pneumococcal, and/or haemophilus influenzae Type B
     - Absence of detectable antibody to measles in children who have
       received two measles immunizations and who live in regions with
       a high prevalence of measles
     - Chronic parvovirus B19 infection
     - Adjunctive therapy for bronchiectasis not optimally responsive to
       antibiotics and pulmonary therapy
vii. Passive immunization for measles if IM IG is contraindicated. IM injection contraindicated with severe thrombocytopenia or any coagulation disorder

- Approve for 1 year initially.

Off-label Uses

1. Guillain-Barre Syndrome
   - Approve if IVIG initiated within 2 weeks and no longer than 4 weeks of onset of neuropathic symptoms in nonambulant adult patients
   - Approve for 1 month initially
   - Treatment after 4 weeks will be considered on a case by case basis since some patients may relapse

2. Dermatomyositis including juvenile and polymyositis
   - Member has unequivocal Dermatomyositis or Polymyositis AND
   - Approve in patients who have tried and failed or has contraindications to prednisone for 4 months AND adjuvant therapy
     i. Azathioprine, methotrexate, cyclosporine, or hydroxychloroquine
   - Approve for 6 months initially.

3. Systemic Lupus Erythematosus (SLE)
   - Member with severe active SLE AND
   - Member has tried and failed or has contraindications to first-line therapies
     i. NSAIDs
     ii. Steroids
     iii. Antimalarials (e.g., hydroxychloroquine)
   AND
   - Member has tried and failed or has contraindications to second-line therapies
     i. Immunosuppressants
        o Azathioprine, cyclophosphamide, methotrexate, cyclosporine, or mycophenolate
   - Approve for 1 year initially

4. Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)
   - Member has unequivocal CIDP AND
   - Member has impaired function by objective assessment AND
   - Trial and failure of or contraindications to steroid therapy for at least 2 months and/or plasma exchange
   - Approve for 1 year initially
5. **Multiple Sclerosis (MS)**
   - Approve for 1 year for relapsing, remitting MS after trial and failure for at least 3 months or contraindication to an interferon (e.g., Betaseron®, Avonex®, Rebi®) or glatiramer (Copaxone®)
   - Treatment of acute exacerbation of MS, primary-progressive MS, secondary-progressive MS, MS during pregnancy, and MS-related syndromes, such as muscle group weakness and optic neuritis, will NOT be covered due to lack of current scientific literature to support improvement in health outcomes.

6. **Autoimmune mucocutaneous blistering disease**
   - Member with pemphigus vulgaris, pemphigus foliaceus, bullous pemphigoid, mucous membrane pemphigoid (a.k.a., cichtral pemphigoid), and epidermolysis bullosa acquisita AND meets one of the following criteria
     i. Member has tried and failed or has contraindications to conventional therapies
        o Corticosteroids or immunosuppressive agents
     ii. In rapidly progressive, extensive, or debilitating cases
        o Give with conventional therapy
   - Approve for 4 months

7. **Myasthenia Gravis Syndrome**
   - Member has unequivocal Myasthenia Gravis Syndrome AND
   - Member has severely impaired function AND
   - Member has tried and failed for at least 3 months or has contraindications to other agents
     i. Cholinesterase inhibitors-pyridostigmine or neostigmine AND
     ii. Immunosuppresants or steroids
   - Approve for 1 month

8. **Parvovirus B19 Infection**
   - Member with Parvovirus B19 infection AND severe anemia associated with bone marrow suppression
   - Approve for 1 month

9. **Renal transplant rejection**
   - Indicated for desensitization of patients with a living donor who harbors or has harbored anti-HLA (human leukocyte antigen) antibody or isoagglutinins OR
   - Indicated in patients who have received a renal transplant from a living donor with post-transplant rejection
   - Approve for 1 month
10. Allogenic Bone Marrow Transplantation or Hematopoietic Stem Cell Transplantation (HSCT)

- **Severe** hypogammaglobulinemia (IgG < 400 mg/dL); does not have to be severe due to transplantation for multiple myeloma or malignant macroglobulinemia OR
- HSCT recipients with unrelated marrow grafts (allogeneic) with severe hypogammaglobulinemia within first 100 days after transplant
- Approve for 6 months

**Reauthorization Criteria:**
All prior authorization renewals will be reviewed to determine the Medical Necessity for continuation of therapy. Authorization may be extended based upon objective and subjective chart documentation from the provider that the member’s disease has significantly improved based upon the prescriber’s assessment while on therapy.

**Limitations:**

IVIG will NOT be covered for the following indications:

i. Epilepsy

ii. Rasmussen syndrome (345.70, 345.71)

iii. Amyotrophic Lateral Sclerosis (ALS) (335.20)

iv. Amyotrophic Lateral Dystrophy (ALD) (330.0)

v. Demyelinating polyneuropathy with IgM monoclonal gammopathy (273.1)

vi. Stiff-man syndrome (333.91)

vii. Paraneoplastic sensory neuropathy or polyneuropathy (355.9)

viii. Paraneoplastic cerebellar degeneration (334.9)

ix. Paraneoplastic encephalomyelitis (323.9)

x. Inclusion body myositis

xi. Diabetic Proximal Neuropathy (250.6x, 357.2)

xii. Undiagnosed neuropathy or weakness

xiii. Erythroblastosis (773.0, 773.1, 773.2)

xiv. Secondary thrombocytopenia (287.4)

xv. Malignancies with no causal link to coexisting neurological dysfunctions

xvi. Hemolytic anemia in members >18 years of age, without hepatomegaly or hepatosplenomegaly, or with splenomegaly alone

If a member does not meet the above approval criteria, the request will be sent for review by a UPMC Health Plan Medical Director.
VI. BIBLIOGRAPHY


