Pharmacy Benefit Determination Policy

Policy Subject: IGIV/SC	**Dates:**
Policy Number: SHS PBD12	**Effective Date:** June 16, 2005
Category: Oncology & Anti-Infectives	**Revision Date** March 29, 2018
Policy Type: ☒ **Medical** ☒ **Pharmacy**	**Approval Date:** April 25, 2018
Department: Pharmacy	**Next Review Date:** April 2019
Product (check all that apply):	**Clinical Approval By:**
☒ Group HMO/POS	**Medical Directors**
☒ Individual HMO/POS	Peter Graham, MD
☒ PPO	**Pharmacy and Therapeutics Committee**
☒ ASO	Peter Graham, MD

Policy Statement:

Physicians Health Plan, PHP Insurance & Service Company, and Sparrow PHP will cover IGIV/SC through the Medical/Pharmacy Benefit based on approval by the Clinical Pharmacist or Medical Director using the following determination guidelines

Drugs and Applicable Coding:

J-code: Privigen - J1459, Bivigam - J1556, Gammaplex - J1557, Gamunex & C/Gammarked - J1561, IVIG lyophilized NOS - J1566, Octagam - J1568, Gammagard - J1569, Febogamma & Dif - J1572, IVIG non-lyophilized NOS - J1599 (1U/500mg); Cuvitru - J1555, IGSC (Hizentra) - J1559 (1U/100mg)

Clinical Determination Guidelines:

Document the following with chart notes

I. Immune Deficiency
- A. Diagnosis
  1. Primary Immune Deficiency (1 below)
     a. Agammaglobulinemia due to the absence of B cells OR
     b. Hypogammaglobulinemia w impaired specific antibody production (eg. CVID)
  2. Secondary Immune Deficiency: B-cell CLL; Multiple Myeloma (MM)
- B. Severity based on IgG level (1 below)
  1. 5 - 6 g/L or IgG level OR
  2. > 6 g/L & continued hard to treat infections (1 in Appendix I.)
- C. Dosage regimen: Immune globulin IV/SC (See Appendix II)
  1. Primary or secondary immune deficiency:
     a. IV: 0.4 g/Kg q 3 - 4 wks.
     b. SC: 100mg/Kg q wk.
  2. Dose titration: Maintain trough IgG levels > 5-10 g/L or to reduce incidence of infection
- D. Approval:
  1. Initial: 6 mons
  2. Re-approval: IgG trough level drawn (≥ 3 consecutive mons of tx); 6-12 mons.

II. Neuropathies
- A. Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)
  1. Diagnosis & severity
     - a. Systemic proximal & distal weakness (both below)
       - Progressive or relapsing course for > 2 mons
       - Absent/diminished deep tendon reflexes
     - b. Electro-diagnostic testing indicates demyelination in 2 nerves (1 of the following): Partial motor conduction block, ↑distal CMAP duration, abnormal temporal dispersion, ↓conduction velocity, ↑distal motor latency, absent of or ↑F-wave latency
  2. Other therapies:
     - a. Severe fulminant CIDP: Pulse steroids
     - b. Insidious CIDP (1 following): Pulse steroids, MTX, cyclosporin, mycophenolate, azathioprine
  3. Dosage regimen (immune globulin IV/SC)
     - a. IV: 2g/Kg over 2-5 days, then 1g/Kg over 1-2 days q 3 wks
     - b. SC: 200-400mg/Kg/wk. over 1-2 sessions
  4. Approval
     - a. Initial: 6 mons (1/3 of patients don't respond)
     - b. Re-approval:
       - 6 mons - 1 yr. depending on improvement of symptoms
       - Continuing high dose IVIG: Add steroid
- B. Multifocal Motor Neuropathy (MMN)
  1. Diagnosis & severity
     - a. Slow/stepwise, progressive, focal asymmetric limb weakness in motor nerve distribution of $\underline{\geq}$ 2 nerves for > 1 mon.
     - b. No objective sensory abnormalities except for minor vibration sense in lower limb
     - c. Electro-diagnostic testing indicates focal demyelination and conduction block
  2. Dosage regimen (immune globulin IV)
     - a. IV: 2g/Kg over 5 days every 2-6 weeks, titrate dose down depending on improvement of sx.
  3. Approval
     - a. Initial: 1 course
     - b. Re-approval: 3 months

III. Miscellaneous
- A. Idiopathic thrombocytopenia (ITP)
  1. Diagnosis & severity
     - a. Adults: Platelets (plts) <30,000 & severe bleeding or < 50,000 & surgery pending
     - b. Pediatrics: Plts < 20,000 & significant bleeding or < 10,000 w no or minimal bleeding
  2. Dosage regimen (immune globulin IV)
     - a. Acute ITP: Adult - 1g/Kg x 1 (may repeat in 24-48hrs.); Pediatrics: 0.8-1g/Kg x 1
     - b. Chronic ITP (Adults & Pediatrics): 0.4 g/kg q 3 - 4 weeks
  3. Approval (Chronic):
     - a. Initial: 6 mons
     - b. Re-approval: 6-12 mons depending on plts
- B. Kawasaki disease
  1. Dosage regimen (immune globulin IV): 2gm/Kg x 1 dose within 10 days of onset of illness & before aneurysms occur.
- C. Other: Non-FDA approved use of IGIV requires literature support, prior approval from a clinical pharmacist & may be subject to SHS Collaborative P & T Committee review.

Appendix I: Hard to treat infections[7]

Infection/Treatment	Frequency		Duration	
Age	**Child**	**Adult**	**Child**	**Adult**
Ear	≥4	≥2	1 year	1 year
Sinus	≥2 (serious)	≥2 (new w/o allergies)	1 year	1 year
Pneumonia	≥2	≥2	1 year	2 years
Abscess of skin or organ (deep)	Recurrent	Recurrent	NA	NA
Deep-seated (including septicemia)	≥2	NA	NA	NA
IV antibiotics to clear	≥2	≥2	NA	NA

Appendix II: Dose Determination for IGIV/SC

Age	Body Weight (BW)	Dose Rounding
Pediatrics (<17yo)	Actual BW	<20gs: exact dose ≥20gs: rounded ↓ to nearest vial >1g/Kg given over several days: may divide in unequal doses
Adults (≥ 17yo)	IBW	<20gs: rounded ↓to nearest vial ≥20gs: Round ↓to nearest vial >1g/Kg given over several days: may divide in unequal doses
Formulas	**Ideal BW**	
Male	[(height in inches – 60) x 2.3] + 50	
Female	[(height in inches – 60) x 2.3] + 45.5	

Appendix III: Patient Safety and Monitoring

Drug	Adverse Reactions	Monitoring	REMS
Immune globulin, IV/SC	• CNS: Fatigue (6-24%), HA (15-45%) • Derm (SC): Infusion site reactions (75%) • GI: Diarrhea (6-20%), Nausea (7-22%) • Hematological: Ecchymosis (40%) • MS: Back Pain (4-17%) • Resp: Sinusitis (8-44%) • Misc.: Chills (6-19%), Injection site Rx (4-15%), Pain (7-14%), pyrexia (11-35%) • Pregnancy category C	• Renal Function: Assess BUN/Cr prior to & during tx • Hemolysis: Watch signs & symptoms (S & S), confirm with lab test. • Thrombosis: Check blood viscosity in those at risk, watch S & S • Aseptic meningitis watch for S & Sx, conduct neuro exam if needed • Resp: Watch for S & Sx of transfusion-related acute lung injury	• Nothing required

References and Resources:

1. Sparrow Health System Department of Pharmacy Services. IVIG Medication Use policy 3/15/16
2. Multifocal Motor Neuropathy. UpToDate [internet] Accessed April 2016. Available from: http://www.uptodate.com /contents/multifocal-motor-neuropathy
3. IGIV/SC. Lexicomp Online® Lexi-Drugs® Lexi-Comp, Inc. Accessed March 2016.
4. Joint Task Force of the EFNS and PNS. J Peripher Nerv Syst. 2010;15(1):1-9.
5. Evaluating dose ratio of SC to IV immunoglobulin therapy among patients with primary immunodeficiency disease switching to 20% SC immunoglobulin therapy. AMJC Supplement. 2016:22(15 Sup);S473-s481
6. Update on the use of immunoglobulin in human disease: A review of the evidence J Allergy Clin Immunol 2017;139:S1-46.
7. 10 Warning signs of Primary Immunodeficiency. Jeffery Modell Foundation Medical Advisory board 2016.

Approved By:

4/26/18

Peter Graham, MD – PHP Executive Medical Director — Date

4/25/18

Human Resources – Kurt Batteen — Date