DRUG DETERMINATION POLICY

Title: DDP-16 Immune Globulins

Effective Date: 06/03/2020

Physicians Health Plan
PHP Insurance Company
PHP Service Company

Important Information - Please Read Before Using This Policy

The following policy applies to health benefit plans administered by PHP and may not be covered by all PHP plans. Please refer to the member's benefit document for specific coverage information. If there is a difference between this general information and the member's benefit document, the member's benefit document will be used to determine coverage. For example, a member's benefit document may contain a specific exclusion related to a topic addressed in a coverage policy.

Benefit determinations for individual requests require consideration of:

1. The terms of the applicable benefit document in effect on the date of service.
2. Any applicable laws and regulations.
3. Any relevant collateral source materials including coverage policies.
4. The specific facts of the particular situation.

Contact PHP Customer Service to discuss plan benefits more specifically.

1.0 Policy:

This policy describes the determination process for coverage of specific drugs that require prior approval.

This policy does not guarantee or approve Benefits. Coverage depends on the specific Benefit plan. Pharmacy Benefit Determination Policies are not recommendations for treatment and should not be used as treatment guidelines.

2.0 Background or Purpose:

Immune globulins are specialty drugs indicated for a number of diagnoses and are associated with significant toxicity. These criteria were developed and implemented to ensure appropriate use for the intended diagnoses and mitigation of toxicity, if possible.

3.0 Clinical Determination Guidelines:

Document the following with chart notes:

I. Immune Deficiency.
   A. Diagnosis.
      1. Primary Immune Deficiency (one below):
         a. Agammaglobulinemia due to the absence of B cells; OR
         b. Hypogammaglobulinemia with impaired specific antibody production (e.g. CVID).
      2. Secondary Immune Deficiency: B-cell CLL
   B. Severity based on IgG level (one below):
      1. Less than 6g/L IgG blood level; OR
      2. Over 6g/L blood level and continued hard to treat infections (one in Appendix I).
   C. Dosage regimen: Immune globulin IV/SC (see Appendix II).
      1. Primary or secondary immune deficiency:
         a. IV: 0.4g/kg every three to four weeks.

b. SC: 100mg/kg every week.

2. Dose titration: maintain trough IgG blood levels over 5 to 10g/L or to reduce incidence of infection.

D. Approval:

1. Initial: six months.

2. Re-approval:

a. IgG trough level drawn (at least three consecutive months of treatment).

b. Target blood level range:

i. Approve: below 10g/L blood level or at or above 10g/L blood level (with dose decrease by 5 to 10g).

ii. Deny: above 10g/L blood level without dose decrease.

c. Duration: six to 12 months.

II. Neuropathies.

A. Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

1. Diagnosis and severity.

a. Systemic proximal and distal weakness (both below):

i. Progressive or relapsing course for over two months.

ii. Absent/diminished deep tendon reflexes.

b. Electro-diagnostic testing indicates demyelination in two nerves (one below):

i. Partial motor conduction block.

ii. Increased distal CMAP duration.

iii. Abnormal temporal dispersion.

iv. Decreased conduction velocity.

v. Increased distal motor latency.

vi. Absent of or increased F-wave latency.

2. Other therapies:

a. Severe fulminant CIDP: pulse steroids.

b. Insidious CIDP (one of the following): pulse steroids, methotrexate, cyclosporine, mycophenolate, azathioprine.

3. Dosage regimen (immune globulin IV/SC).

a. IV: 2g/kg over two to five days, then 1g/kg over one to two days every three weeks.

b. SC: 200 to 400mg/kg per week over one to two sessions.

4. Approval.

a. Initial: six months.

b. Re-approval:

i. Six months to one year depending on improvement of symptoms.

ii. Continuing high dose immune globulin: add steroid.

B. Multifocal Motor Neuropathy (MMN).

1. Diagnosis and severity (all below):

a. Slow/stepwise, progressive, focal asymmetric limb weakness in motor nerve distribution of greater than two nerves for over one month.

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 five days every two to six weeks, titrate dose down depending on improvement of symptoms.

3. Approval.

a. Initial: one course.

b. Re-approval: three months.

III. Miscellaneous.

A. Idiopathic thrombocytopenia (ITP)

1. Diagnosis and severity.

a. Adults: platelets below 30,000 and severe bleeding or below 50,000 and surgery pending.

b. Pediatrics: platelets below 20,000 and significant bleeding or below 10,000 with no or minimal bleeding.

2. Dosage regimen (immune globulin IV).

a. Acute ITP: Adult - 1g/kg times one (may repeat in 24 to 48 hours); Pediatrics: 0.8-1g/kg times one.

b. Chronic ITP (adults and pediatrics): 0.4 g/kg every three to four weeks.

3. Approval (chronic):

a. Initial: six months.

b. Re-approval: six to twelve months depending on the platelet count.

B. Kawasaki disease

1. Dosage regimen (immune globulin IV): 2g/kg times one dose within ten days of onset of illness and before an aneurysm occurs.

C. Other: non-FDA approved use of immune globulins requires literature support, prior approval from a clinical pharmacist and may be subject to SHS Collaborative P and T Committee review.

IV. Coverage of immune globulins is subject to the site-of-care policy.

4.0 Coding:

COVERED CODES				
Code	**Brand**	**Generic**	**Billing unit**	**Prior Approval**
J1459	Privigen	Immune globulin	500mg	Y
J1556	Bivigam	Immune globulin	500mg	Y
J1567	Gammaplex	Immune globulin	500mg	Y
J1561	Gamunex, C/Gammarked	Immune globulin	500mg	Y
J1566	Carimmune NF	Immune globulin	500mg	Y

COVERED CODES				
Code	**Brand**	**Generic**	**Billing unit**	**Prior Approval**
J1568	Octagam	Immune globulin	500mg	Y
J1569	Gammagard	Immune globulin	500mg	Y
J1572	Febogamma, DIF	Immune globulin	500mg	Y
NA	Cutaquig	Immune globulin, SC		Y
J1565	Cuvitru	Immune globulin, SC	500mg	Y
J1559	IGSC (Hizentra)	Immune globulin	100mg	Y
NA	GammaSTAN	Immune globulin, IM		Y
J1575	Hyqvia	Immune globulin, SC	100mg	Y
NA	Panzyga	Immune globulin		Y
NA	Xembify	Immune globulin, SC		Y
J1566	NA	IVIG lyophilized NOS	500mg	Y
J1599	NA	IVIG non-lyophilized NOS	500mg	Y
NA	Asceniv	Immune globulin		Y

5.0 Unique Configuration/Prior Approval/Coverage Details:

None.

6.0 References, Citations & 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. Lexicomp Online® Lexi-Drugs® Lexi-Comp, Inc. IGIV/SC; Accessed March 2020.
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.

7.0 Appendices:

See pages 5-6.

8.0 Revision History:

Original Effective Date: 06/16/2005

Next Review Date: 03/25/2021

Revision Date	Reason for Revision
4/19	Transfer to new format
3/20	Annual review; revised indication, replaced abbreviations, added new drugs Carimune NF; Cutaquig; GamaSTAN; GamaSTAN S/D; Hyqvia; Panzyga; Xembify, Asceniv

Appendix I: Hard to Treat Infections

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	• Central nervous system: fatigue (6-24%), HA (15-45%) • Dermatologic: infusion site reactions (75%) • Gastrointestinal: diarrhea (6-20%), nausea (7-22%) • Hematological: ecchymosis (40%) • Musculoskeletal: back pain (4-17%) • Respiratory: sinusitis (8-44%) • Miscellaneous: chills (6-19%), injection site Rx (4-15%), pain (7-14%), pyrexia (11-35%) • Pregnancy Category: C	• Renal function: assess BUN/Cr prior to and during treatment • Hemolysis: watch signs and symptoms (S & S), confirm with lab test. • Thrombosis: check blood viscosity in those at risk, watch S & S • Aseptic meningitis: watch for S & S, conduct neuro exam if needed • Respiratory: watch for S & S of transfusion-related acute lung injury	• Nothing required