DRUG DETERMINATION POLICY

Title: DDP-16 Immune Globulins

Effective Date: 05/05/2022

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. General Use Considerations.

A. Ideal Body Weight (IBW): immune globulin dosage calculated using IBW (See Appendix II).

B. Switching routes of administration: subcutaneous initial weekly dose (grams) = [1.37x intravenous dose (grams)] divided by [intravenous dose interval (weeks)].

C. Site of care: intravenous immune globulins are subject to the site-of-care policy.

D. Appropriate medication use [must meet all listed below]:

1. Diagnosis: meets standard diagnostic criteria that designates signs, symptoms and test results to support specific diagnosis.

2. Food and Drug Administration (FDA) approval status [must meet one listed below]:

a. FDA approved: product, indication, and/or dosage regimen.

b. Non-FDA approved: compendium support (Lexicomp™) for use of a drug for a non-FDA approved indication or dosage regimen.

3. Place in therapy: sequence of therapy supported by national or international accepted guidelines and/or studies (e.g., oncologic, infectious conditions).

a. Oncology: National Comprehensive Cancer Network (NCCN) category of evidence and consensus 2A (based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate).

II. Immune Deficiency.

A. Diagnosis.[must meet all listed below]:

1. Primary Immune Deficiency [must meet one listed below]:

a. Agammaglobulinemia due to the absence of B cells; OR

b. Hypogammaglobulinemia with impaired specific antibody production (e.g. common variable immunodeficiency).

2. Secondary Immune Deficiency: B-cell CLL

B. Severity based on Immune Globulin (IgG) level [must meet one listed below]:

1. Below 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 .

1. Primary or secondary immune deficiency:

a. Intravenous (IV): 0.4 grams per kg every three to four weeks.

b. Subcutaneous (SQ): 100mg per kg every week.

2. Dose titration: maintain trough IgG blood levels 10g/L or less, and/or to reduce incidence of infection (see Appendix I).

D. Approval:

1. Initial: six months.

2. Re-approval criteria:

a. IgG trough level: must be drawn after at least three consecutive months of treatment

b. IgG blood level range [must meet one listed below]:

- Approve: below 10g/L blood level

- Approve: IgG at or above 10g/L blood level with dose decrease by 5 to 10g (only decrease dose if no significant/frequent infections).

- Denial: IgG above 10g/L blood level without immune globulin dose decrease and or significant incidence of infections (see Appendix I).

c. Duration: six to twelve months.

III. Neuropathies.

A. Chronic Inflammatory Demyelinating Polyneuropathy CIDP [must meet all listed below]:

1. Diagnosis and severity.
    a. Systemic proximal and distal weakness [must meet both listed below]:
        - Progressive or relapsing course for over two months.
        - Absent/diminished deep tendon reflexes.
    b. Electro-diagnostic testing indicates demyelination in two nerves [must meet one listed below]:
        - Partial motor conduction block.
        - Increased distal CMAP duration.
        - Abnormal temporal dispersion.
        - Decreased conduction velocity.
        - Increased distal motor latency.
        - Absent of or increased F-wave latency.
2. Other therapies: contraindicated, inadequate response after four months or significant adverse effects to one category listed below:
    a. Severe fulminant CIDP: pulse steroids.
    b. Insidious CIDP [must meet one of the following]: pulse steroids, methotrexate, cyclosporine, mycophenolate, azathioprine.
3. Dosage regimen: immune globulin:
    a. Intravenous (IV): 2g per kg over two to five days, then 1g per kg over one to two days every three weeks.
    b. Subcutaneous (SQ): 200 to 400mg per kg per week over one to two sessions.
4. Approval.
    a. Initial: six months.
    b. Re-approval: six months to one year.

B. Multifocal Motor Neuropathy (MMN) [must meet all listed below]:
1. Diagnosis and severity [must meet all listed 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 intravenous.
    a. 2g per kg over five days, then 0.4gms per Kg monthly, titrate dose down depending on improvement of symptoms.
3. Approval.
    a. Initial: one course.
    b. Re-approval: four months.

III. Miscellaneous.

A. Idiopathic thrombocytopenia (ITP) [must meet all listed below]:
1. Diagnosis and severity [must meet one listed below]:

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

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

2. Dosage regimen: immune globulin intravenous.

a. Acute ITP:

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

b. Chronic ITP (adults and pediatrics): 0.4g per kg as needed to maintain platelet count at or above 30,000 per mm^3.

3. Approval: chronic ITP:

a. Initial: six months.

b. Re-approval: six months.

B. Kawasaki disease

1. Dosage regimen for immune globulin intravenous: 2g per kg times one dose within ten days of onset of illness and before an aneurysm occurs.

4.0 Coding:

COVERED CODES				
Code	**Brand**	**Generic**	**Billing unit**	**Prior Approval**
J1459	Privigen	Immune globulin	500mg	Y
J1556	Bivigam	Immune globulin	500mg	Y
J1557	Gammaplex	Immune globulin	500mg	Y
J1561	Gamunex, C/Gammarked	Immune globulin	500mg	Y
J1566	Carimmune NF	Immune globulin	500mg	Y
J1568	Octagam	Immune globulin	500mg	Y
J1569	Gammagard	Immune globulin	500mg	Y
J1572	Flebogamma, DIF	Immune globulin	500mg	Y
NA	Cutaquig	Immune globulin, SQ		Y
J1555	Cuvitru	Immune globulin, SQ	500mg	Y
J1559	IGSC (Hizentra)	Immune globulin	100mg	Y
J1575	Hyqvia	Immune globulin, SQ	100mg	Y
J1599	Panzyga	Immune globulin		Y
J1558	Xembify	Immune globulin, SQ		Y
J1554	Asceniv	Immune globulin		Y

5.0 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 2022.
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.
8. Maintenance immunosuppression in Myasthenia Gravis; Journal of Neurological Sciences 2016;369:294-302.

6.0 Appendices:

See pages 6-7.

7.0 Revision History:

Original Effective Date: 06/16/2005

Next Review Date: 03/24/2023

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
9/20	Off cycle review, added general dosing consideration section, formatting, replaced abbreviations, no significant content change
2/21	
02/23/2022	Annual review; added compendium support to appropriate use section

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 Immune Globulin Intravenous or Subcutaneous

Age	Body Weight (BW)	Dose Rounding
Pediatrics (<17 years old)	Actual BW	<20gs: exact dose ≥20gs: rounded down to nearest vial >1g per kg given over several days: may divide in unequal doses
Adults (≥17years old)	IBW	<20gs: rounded down to nearest vial ≥20gs: round down to nearest vial >1g per 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, Intravenous Subcutan-eous	• Central Nervous System: fatigue (6-24%), headache (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 reaction (4-15%), pain (7-14%), pyrexia (11-35%) • Pregnancy Category: C	• Renal Function: assess BUN/Cr prior to and during treatment • Hemolysis: watch for signs and symptoms, confirm with lab test. • Thrombosis: check blood viscosity in those at risk, watch for signs and symptoms • Aseptic meningitis: watch for signs and symptoms, conduct neuro exam if needed • Respiratory: watch for signs and symptoms of transfusion-related acute lung injury	• Nothing required