University of Michigan Health Plan

DRUG DETERMINATION POLICY

Title: DDP-16 Immune Globulins

Effective Date: 2/26/25

Important Information - Please Read Before Using This Policy

The following policy applies to health benefit plans administered by UM Health Plan and may not be covered by all UM Health Plan. 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 UM Health Plan 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 treatment recommendations and should not be used as treatment guidelines.

2.0 Background or Purpose:

Immune globulins are specialty drugs indicated for several 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 Considerations.

A. Use Ideal Body Weight (IBW): immune globulin dosage is calculated using IBW (See Appendix II), unless Actual Body Weight is less than Ideal Body Weight

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

C. 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 the 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 relevant clinical 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).

D. Required site-of-care as determined by the Health Plan (DDP-08 Site of Care for Administration of Parenteral Specialty Drugs).

E. Pharmaceutical sample use: The Plan does not recognize samples as a medication trial or for continuation of therapy.

F. Adherence to requested medication required for re-approval [must meet one listed below]:

1. Medications processed under the medical benefit: consistent utilization (at least 80% of days covered) based on medical claims history or chart notes.

2. Medications processed under the pharmacy benefit: consistent (at least 80% of days covered) fill history electronically or verbally from the pharmacy.

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 the 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]:

i. Approve: below 10g/L blood level

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

iii. Deny: 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]:

i. Progressive or relapsing course for over two months.

ii. Absent/diminished deep tendon reflexes.

b. Electro-diagnostic testing indicates demyelination in two nerves [must meet one listed 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 trial of one drug in the pertinent category below is required unless contraindicated. Trials must result in an inadequate response after four consecutive months of use per medication or severe adverse effects. Severe fulminant CIDP: pulse steroids.

a. Insidious CIDP: 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 the 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 0.4g per Kg monthly, titrate dose down depending on improvement of symptoms.

3. Approval.
   a. Initial: one course.
   b. Re-approval: four months.

IV. 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:
      i. Adult: 1g per kg times one (may repeat in 24 to 48 hours);
      ii. 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 for one dose within ten days of onset of illness and before an aneurysm occurs.

4.0 Coding:

COVERED CODES – MEDICAL BENEFIT				
Code	**Brand**	**Generic**	**Billing Units (1 unit)**	**Prior Approval**
J1459	Privigen	Immune globulin	500 mg	Y
J1554	Asceniv	Immune globulin	500 mg	Y
J1555	Cuvitru	Immune globulin, SQ	100 mg	Y
J1556	Bivigam	Immune globulin	500 mg	Y
J1557	Gammaplex	Immune globulin	500 mg	Y
J1559	Hizentra	Immune globulin, SQ	100 mg	Y
J1561	Gamunex-C/Gammaked	Immune globulin	500 mg	Y
J1566	Carimune NF/Gamastan	Immune globulin	500 mg	Y
J1568	Octagam	Immune globulin	500 mg	Y
J1569	Gammagard	Immune globulin	500 mg	Y
J1572	Flebogamma, DIF	Immune globulin	500 mg	Y
J1575	Hyqvia	Immune globulin, SQ	100 mg	Y
J1576	Panzyga	Immune globulin	100 mg	Y

COVERED PRODUCTS – PHARMACY BENEFIT		
Brand	**Generic**	**Prior Approval**
Cutaquig	Immune globulin, SQ	Y

EXCLUDED ~~NON-COVERED~~ CODES				
Code	**Brand**	**Generic**	**Billing unit**	**Benefit Plan Reference/Reason**
J1551	Cutaquig	Immune globulin, SQ	100 mg	Covered on the pharmacy benefit with prior approval
J1558	Xembify	Immune globulin, SQ	100 mg	Not a Preferred Agent

5.0 References, Citations & Resources:

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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 December 2024.
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.

9. The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. Blood 2011;117(16):4190-4207.
10. Evidence-based guideline: Intravenous immunoglobulin in the treatment of neuromuscular disorders [RETIRED] Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology 2012:78(13).
11. Joint Task Force on Practice Parameters, representing the American Academy of Allergy, Asthma & Immunology; the American College of Allergy, Asthma & Immunology; and the Joint Council of Allergy, Asthma & Immunology. Practice parameter for the diagnosis and management of primary immunodeficiency. J Allergy Clin Immunol. 2015;136(5):1186-1205.e1-78. doi:10.1016/j.jaci.2015.04.049[PubMed 26371839]
12. 2021 American College of Rheumatology/Vasculitis Foundation guideline for the management of Kawasaki disease. Arthritis Care Res (Hoboken). 2022;74(4):538-548. doi:10.1002/acr.24838[PubMed 35257507]
13. American Society of Hematology 2019 guidelines for immune thrombocytopenia. Blood Adv. 2019;3(23):3829-3866. doi:10.1182/bloodadvances.2019000966[PubMed 31794604]
14. International consensus guidance for management of myasthenia gravis: Executive summary. Neurology. 2016;87(4):419-425. doi: 10.1212/WNL.0000000000002790.[PubMed 27358333]

6.0 Appendices:

See page 7.

7.0 Revision History:

Original Effective Date: 06/16/2005

Next Review Date: 03/01/2026

Revision Date	Reason for Revision
4/19	Transfer to the 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	Annual review
2/22	
1/23	Annual review, updated coding, IBW or ABW whichever is less to match Sparrow IVIG updated policy, reference update, added non-covered code table
12/23	Annual review, added references, revised general considerations and other therapies section, removed patient safety and monitoring section, updated coding section
12/24	Annual review; clarify place in therapy, update reference.

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