Intravenous Immune Globulin (IVIG) - Adult/Pediatric - Inpatient/Ambulatory/Emergency Department

Consensus Care Guideline

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Population/Problem:

Intravenous Immunoglobulin (IVIG) is isolated from pooled human plasma and was originally developed as prophylaxis against infections for individuals with primary immunodeficiency disorders.[1,2] IVIG is used to prevent and treat a growing number of indications. The expanded use of IVIG is supported by varying quality of evidence. Numerous published guidelines highlight the uses associated with this agent. UW Health monitors the use of IVIG because of its association with both adverse events and high cost. Consensus care guidelines tailored to UW Health serve to optimize use of this resource. The current revision is a regularly scheduled review of available evidence to keep this guideline timely.

Definitions:

1. ABW: Actual Body Weight
2. Acute Idiopathic Thrombocytopenic Purpura: Acute bleeding with platelet count < 20,000/mm^3
3. GVHD: Graft Versus Host Disease
4. IBW: Ideal Body Weight
5. Order Weight: the weight used to calculate the total IVIG dose

Recommendations:

Ordering and Dosing

1. All patients must have a current documented weight and height prior to ordering IVIG. (*UW Health GRADE Very low quality evidence; strong recommendation*)
2. **Adult doses** should be based on ideal body weight (IBW) unless dosing to a specific and measurable IgG level[3,4] (*UW Health GRADE Low quality evidence; strong recommendation*)
   2.1. If actual body weight (ABW) is less than IBW, dose according to ABW.
3. **Pediatric doses** should be based on ABW.[5,6] (*UW Health GRADE High quality evidence; strong recommendation*)
4. Doses should be titrated to patient response. Aim for the minimum dose required to maintain optimal clinical response defined by the disease-specific monitoring parameters presented in the Appendix.[5,6] (*UW Health GRADE High quality evidence; strong recommendation*)
5. Doses should not exceed a maximum of 2 g/kg or 140 grams per day. (*UW Health GRADE Very low quality evidence; strong recommendation*)
6. IVIG should be used according to the specified criteria for each indication listed in the Appendix. (*UW Health GRADE quality of evidence varies; strength of recommendation varies*)
7. IVIG may limit the effectiveness of live attenuated virus vaccines, including the measles, mumps, rubella (MMR) and varicella vaccines. These vaccines should be administered 2 weeks prior to IVIG administration or delayed until 8 months after replacement of IVIG or 11 months following Kawasaki Disease treatment. (*UW Health GRADE Moderate quality evidence; strong recommendation*)
   7.1. The following live vaccines are not affected by IVIG administration: influenza, oral typhoid, yellow fever, and rotavirus vaccines.

Documentation

8. Documentation should clearly state the medical necessity for initiation and continued use of IVIG. (*UW Health GRADE Very low quality evidence; strong recommendation*)
9. Documentation should include:
   9.1. History and physical
   9.2. Test results, including written interpretation
   9.3. Prior treatment therapies
   9.4. When used for an appropriate indication, there should be evidence of a significant deficiency in IgG blood levels prior to initiation of treatment and impaired ability to make specific antibodies
   9.5. History of severe and recurrent infections when appropriate
   9.6. Treatment goals/expected response from IVIG initiation and subsequent treatment.
      9.6.1. For immune deficiency disorders, the prescriber should provide an IgG target goal.
   9.7. Evidence that IVIG therapy is effective when writing orders for continued therapy.

Administration

Filters

10. Gammagard Liquid® product requires no filtration. Gammagard S/D® low IgA requires filtration with a 15 micron filter. (*UW Health GRADE Moderate quality evidence; strong recommendation*)

Premedications

11. Not all patients require premedication for successful administration, and it may be reasonable to consider foregoing it. However, premedication increases the tolerability of IVIG for many patients.[7] Effective options are presented in the table below. They should be administered 30 minutes prior to the initiation the IVIG infusion. (*UW Health GRADE Moderate quality evidence; strong recommendation*)

Table 1. Frequently Used Premedications

Therapeutic Class	Population	
	Adults	**Pediatrics**
Analgesic	Acetaminophen 650 mg orally once	Acetaminophen 10 – 15 mg/kg orally once; maximum = 650 mg
Antihistamine	• Diphenhydramine 25 – 50 mg orally or intravenous once • Loratadine 10 mg orally once • Cetirizine 10 mg oral once • Fexofenadine 180 mg oral once	• Diphenhydramine 0.5 – 1 mg/kg oral or IV once; maximum = 50 mg • Loratadine oral once o 2-5 yrs: 5 mg o ≥ 6 yrs: 5 – 10 mg • Cetirizine oral once o 6 month – 2 yrs: 2.5 mg o 2 – 5 yrs: 2.5 – 5 mg o ≥ 6 yrs: 5 – 10 mg • Fexofenadine oral once o 2 – 11 yrs.: 60 mg o ≥ 12 yrs: 180 mg
Corticosteroid	• Dexamethasone 4 mg oral or IV once • Methylprednisolone 20 – 60 mg IV once	• Dexamethasone 0.5 mg/kg oral or IV once; maximum 4 mg • Methylprednisolone 0.5 – 1 mg/kg IV once (max 40 mg)

Adverse Reactions

12. The fluid status of the patient should be evaluated prior to administration. Overdose may lead to fluid overload and hyperviscosity.[8] (*UW Health GRADE Moderate quality evidence; strong recommendation*)
    - 12.1. Patients at risk of complications of fluid overload and hyperviscosity include elderly patients and those with cardiac or renal impairment.
    - 12.2. Strategies to lower risk of fluid overload are to use a low sodium product. The IVIG products available on UW Health formulary are low sodium products; Gammagard Liquid® (undetectable sodium) and Gammagard S/D® low IgA (0.85% sodium).
    - 12.3. Strategies to lower risk of hyperviscosity:
        - 12.3.1. Do not exceed the recommended dose
        - 12.3.2. Large doses may need to be infused over several days
        - 12.3.3. Ensure adequate hydration
        - 12.3.4. Infuse at the slowest practical rate
        - 12.3.5. Use a low osmolar product (e.g., Gammagard® Liquid)
        - 12.3.6. Encourage patients to limit immobility in the days immediately following the infusion.
13. Common adverse reactions (with frequency) include:
    - 13.1. Headache: 30.6%
    - 13.2. Nausea and/or vomiting: 22%
    - 13.3. Chills: 19.4%
    - 13.4. Hypotension: 14%
    - 13.5. Lightheadedness: ≤ 13%
    - 13.6. Fever: 11.1%
    - 13.7. Fatigue: 11.1%
    - 13.8. Backache: 8.3%
    - 13.9. Urticaria: 8%
    - 13.10. Leg cramps: 6%
    - 13.11. Flushing: 5.6%
14. Rare (<1%) but serious adverse reactions include: hemolysis transfusion-related acute lung injury, arterial thrombosis, deep vein thrombosis, pulmonary embolism, myocardial infarction, thromboembolism, aseptic meningitis syndrome, and acute renal failure.
    - 14.1. Certain patient populations may be predisposed to renal dysfunction when receiving IVIG products that contain sucrose. No UW Health formulary IVIG products contain sucrose.

14.1.1. Patients over 65 years old
14.1.2. Patients with diabetes mellitus
14.1.3. Patients with renal impairment prior to treatment with IVIG

15. Infusion related reactions that occur with IVIG are typically due to an infusion rate that is too fast for patient tolerability. Infusion reactions are more common in patients receiving their first IVIG infusions or when changing to a different IVIG product. If there is an infusion reaction, stop or slow the rate of infusion and treat as presented in Table 2 below.[7,9] (*UW Health GRADE Moderate quality evidence; strong recommendation*)
    15.1. Restart the infusion at a slower rate once the reaction subsides.[3,4] Decrease the infusion rate by one half the rate at which the reaction occurred. (*UW Health GRADE High quality evidence; strong recommendation*)
    15.2. The rate can be titrated to a faster rate again as the patient tolerates.[3,4] (*UW Health GRADE High quality evidence; strong recommendation*)
    15.3. If the patient has a history of infusion reactions, the prescriber should indicate in the order Admin Instructions the maximum infusion rate desired (gram/hr). (*UW Health GRADE Very low quality evidence; strong recommendation*)
    15.4. Consider switching to a different IVIG product in patients unable to tolerate a particular product[9] (*UW Health GRADE Low quality evidence; weak/conditional recommendation*)
    15.5. Consider checking for anti-IgA antibodies in patients with infusion reactions and consider product change to low IgA product (Gammagard S/D)[10,11] (*UW Health GRADE Low quality evidence; weak/conditional recommendation*)

Table 2. Treatment of Adverse Reactions

Therapeutic Class	Population	
	Adults	**Pediatrics**
Antihistamine	• Diphenhydramine 25 – 50 mg intravenous once	• Diphenhydramine 0.5 – 1 mg/kg IV; maximum = 50 mg once
Corticosteroid	• Dexamethasone 4 mg IV once	• Dexamethasone 0.5 mg/kg IV once; maximum 4 mg • Hydrocortisone sodium succinate 1 mg/kg IV once; maximum 100 mg

Monitoring

16. All patients should be continually monitored for adverse effects related to the administration of IVIG and the infusion rate. (*UW Health GRADE High quality evidence; strong recommendation*)
    16.1. Monitor for signs and symptoms of thrombosis, blood hyperviscosity, hemolysis, hemolytic anemia, and acute lung injury. (*UW Health GRADE High quality evidence; strong recommendation*)
17. The following vital signs can be monitored to assess the safety of the infusion: blood pressure, heart rate, respiratory rate, oxygen saturation, and temperature. They can be measured before, during, and/or after the infusion OR if the patient experiences new or worsening symptoms of an infusion reaction. (*UW Health GRADE High quality evidence; strong recommendation*)
18. Periodic monitoring of renal function is recommended in patients that are judged to be at risk of acute renal failure. (*UW Health GRADE High quality evidence; strong recommendation*)

Infusion Rates

19. Patient tolerability is always the first consideration for infusion rate. (*UW Health GRADE High quality evidence; strong recommendation*)
20. IVIG infusion rate calculations should use the patient's order weight (the same weight used to calculate the total IVIG dose) (*UW Health GRADE Very low quality evidence; conditional recommendation*)
    20.1. For most adult patients, this will be IBW. If ABW is less than IBW, use ABW
    20.2. For most pediatric patients, this will be ABW
    20.3. If a patient has previously tolerated IVIG rates based on a different weight type, the use of a weight other than the order weight may be specified in the Admin Instructions of the IVIG order

21. Generally, infusion rates should be slower for the first two infusions or when IVIG products are changed. The infusion rate for the first two administrations is presented for adults and pediatric patients below in Table 3. If patients tolerate the initial infusions, an incrementally faster rate can be used for subsequent infusions.[7] For all infusions, a gradual titration approach to the maximal infusion rate is recommended. (*UW Health GRADE High quality evidence; strong recommendation*)
22. Consider a slower infusion rate (e.g., maximum rate 2 mL/kg/hour) in patients with underlying renal disease or who are at risk for developing thrombotic events, including individuals with a history of thrombosis and those with cardiovascular risk factors. To decrease these risks, the patient should be optimally hydrated. A product with a lower osmolality should be considered.[3,4] (*UW Health GRADE High quality evidence; strong recommendation*)
23. An infusion time longer than the maximum calculated infusion duration (8-12 hours) may be considered for **inpatients** to decrease the risk of adverse reactions. A prolonged infusion time in excess of the maximum calculated infusion duration may be considered when:
    23.1. A dedicated line will be available for the full duration of the infusion and the administration of other medications will not be delayed
    23.2. The patient's discharge time is not anticipated within 24 hours and will not be postponed to complete infusion. *(UW Health GRADE Very low quality evidence; conditional recommendation)*
24. Patients being treated for Kawasaki Disease or Multisystem Inflammatory Syndrome in Children (MIS-C) receive a high dose of IVIG at a slower rate due to high oncotic/volume load. The minimum infusion time for these patients should not be less than 10 hours.[127] *(UW Health GRADE Moderate quality evidence; strong recommendation)*

Table 3. IVIG Infusion Rates for 10% Product (1 mL = 100 mg)
Use order weight for rate calculations unless otherwise specified in Admin Instructions

	Initial IVIG Rate Titration (1st or 2nd Dose)	Subsequent IVIG Infusions
Adults	• 0.5 mL/kg/hour x 15 minutes; then • 1 mL/kg/hour x 15 minutes; then • 1.5 mL/kg/hour x 15 minutes; then • 2 mL/kg/hour for remaining volume	• 0.5 mL/kg/hour x 15 minutes; then • 1 mL/kg/hour x 15 minutes; then • 1.5 mL/kg/hour x 15 minutes; then • 2 mL/kg/hour* x 15 minutes; then • 3 mL/kg/hour x 15 minutes; then • 4 mL/kg/hour x 15 minutes; then • 5 mL/kg/hour for remaining volume
	Initial IVIG Rate Titration (1st or 2nd Dose)	**Subsequent IVIG Infusions**
Pediatrics (except Kawasaki Disease or MIS-C)	• 0.5 mL/kg/hour x 30 minutes; then • 1 mL/kg/hour x 30 minutes; then • 2 mL/kg/hour* x 30 minutes; then • 3 mL/kg/hour x 30 minutes; then • 4 mL/kg/hour for remaining volume	• 0.5 mL/kg/hour x 30 minutes; then • 1 mL/kg/hour x 30 minutes; then • 2 mL/kg/hour* x 30 minutes; then • 3 mL/kg/hour x 30 minutes; then • 4 mL/kg/hour x 30 minutes; then • 5 mL/kg/hour for remaining volume
	IVIG Rate Titration	
Kawasaki Disease or MIS-C	• 0.5 mL/kg/hour x 30 minutes; then • 0.8 mL/kg/hour x 30 minutes; then • 1 mL/kg/hour x 30 minutes; then • 1.5 mL/kg/hour x 30 minutes; then • Infuse remaining volume at 2.3 mL/kg/hour over 8 hours	

*2 mL/kg/hour is the suggested maximum rate for inpatients, age > 65 years, history of thrombosis, presence of cardiovascular risk factors, renal insufficiency, or diabetes

The following tools are available in Health Link to help communicate and calculate IVIG infusion rates:

Tool Description	Tool Name	How to Use/Purpose
SmartPhrase	.RXRIVIGINFUSIONRATE	Verifying pharmacist adds SmartPhrase to Admin Instructions field of IVIG orders to communicate weight and maximum infusion rate for nurse to use in IVIG rate calculator

IVIG Rate Calculator	Adult IVIG Calculator	How to Find the IVIG Calculator in Health Link Nurse inputs order weight (kg), total IVIG dose (grams), and maximum infusion rate (if applicable). The calculator will recommend how to program the IV pump.
	Pediatric IVIG Calculator	
	Pediatric – Kawasaki or MIS-C	

Immune Globulin Administered by Subcutaneous Route

25. Administration by the subcutaneous route may be considered in patients who are treated for immunodeficiencies, including clinically significant hypogammaglobulinemia secondary to protein losses or chylous effusions. Subcutaneous administration is less likely to result in adverse effects and may achieve more sustained IgG levels. Traditional immune globulin products labeled for subcutaneous administration and available on the UW Health formulary include Gammagard Liquid®. HyQvia®, indicated for hyaluronidase facilitated subcutaneous administration in patients aged 12 years and older, is also available on the UW Health formulary on a restricted basis. The goal is to ultimately transition patients to self-administration (or administration by caregiver) in the home. However HyQvia® is approved for outpatient administration during the initial dose ramp-up in patients naïve to immune globulin or those transitioning from intravenous administration. *(UW Health GRADE High quality evidence; strong recommendation)*
26. Subcutaneous immune globulins are often more concentrated (e.g., 20%) than product used for IVIG. Independent insurance screening is necessary for subcutaneous immune globulin products and administration. Previous insurance coverage of intravenous administration may not extend to subcutaneous administration, even when using the same product.

Disclaimer
Consensus care models assist clinicians by providing a framework for the evaluation and treatment of patients. This guideline outlines the preferred approach for most patients. It is not intended to replace a clinician's judgment or to establish a protocol for all patients. It is understood that some patients will not fit the clinical condition contemplated by a guideline and that a guideline will rarely establish the only appropriate approach to a problem.

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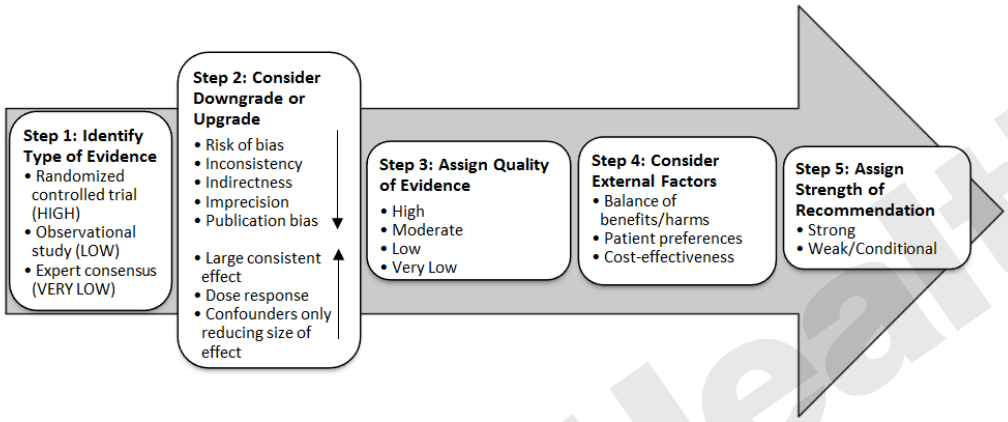
Methodology

Methods Used to Collect/Select the Evidence:
Electronic database searches (e.g., PUBMED) were conducted by the guideline author(s) and workgroup members to collect evidence for review. Expert opinion and clinical experience were also considered during discussions of the evidence.

Methods Used to Formulate the Recommendations:
The workgroup members agreed to adopt recommendations developed by external organizations and/or arrived at a consensus through discussion of the literature and expert experience. All recommendations endorsed or developed by the guideline workgroup were reviewed and approved by other stakeholders or committees (as appropriate).

Methods Used to Assess the Quality of the Evidence/Strength of the Recommendations:
Internally developed recommendations, or those adopted from external sources without an assigned evidence grade, were evaluated by the guideline workgroup using an algorithm adapted from the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology.

GRADE Methodology adapted by UW Health



GRADE Ranking of Evidence

High	We are confident that the effect in the study reflects the actual effect.
Moderate	We are quite confident that the effect in the study is close to the true effect, but it is also possible it is substantially different.
Low	The true effect may differ significantly from the estimate.
Very Low	The true effect is likely to be substantially different from the estimated effect.

GRADE Ratings for Recommendations for or Against Practice

Strong (S)	Generally, should be performed (i.e., the net benefit of the treatment is clear, patient values and circumstances are unlikely to affect the decision.)
Conditional (C)	May be reasonable to perform (i.e., may be conditional upon patient values and preferences, the resources available, or the setting in which the intervention will be implemented.)

Collateral Tools & Resources

The following collateral tools and resources support staff execution and performance of the evidence-based model recommendations in everyday clinical practice.

Metrics
- Adverse event reporting

Guidelines
- Kawasaki Disease: Diagnosis and Management- Pediatric- Inpatient
- MIS-C – Pediatric/Neonatal – Inpatient/Emergency Department

Order Sets & Smart Sets
- Inpatient Immune Globulin Infusion Adult Supplement Order Set [#1317]
- Inpatient Immune Globulin Infusion Pediatric Supplemental Order Set [#4161]
- Inpatient -Kawasaki Disease- Pediatric Supplemental Order Set [#8152]
- UWRX Infusion Center Order Set [#930]
- Inpatient – Multisystem Inflammatory Syndrome (MIS-C) – Pediatric – Admission Order Set [#9498]

Patient Resources
- Health Facts For You [#6868] – Intravenous Immune Globulin (IVIG)

Policies
- Medication Use in Outpatient Care Areas [UW Health Policy #15.2]
- Alaris System [UW Health Nursing Patient Care Policy # 1.24]
- Medication Delivery Via Tube System [UW Health Policy # 4.1]

Appendix. Indications for IVIG

Immunology					
Indication	**Criteria for Use**	**Dose and Duration**	**Monitoring Parameters**	**Evidence Ranking**	**UW Health Recommendation Rating**
Primary Immunodeficiency • Congenital agammaglobulinemia[12-15] • Common variable immunodeficiency[16,17] • Wiskott-Aldrich syndrome[18] • X-linked agammaglobulinemia[19,20] • Severe combined immunodeficiency	IgG value 2 standard deviations below normal for age	400-600 mg/kg every 4 weeks	Goal of therapy is to prevent infections (i.e. bronchiectasis). Ideal trough IgG values: within age and gender appropriate normal range.	Low	Strong
Kawasaki syndrome[21,22]	Progressive form of the disease, ongoing inflammation, and/or elevated acute inflammatory markers and fever	2 gram/kg once, beginning within 7 days of onset of fever	Inflammatory markers. • Defervescence • CRP • ESR	High	Strong
		Re-treatment with 2 gram/kg in a single dose may be given when ongoing inflammation is documented		High	Strong
Idiopathic Thrombocytopenic Purpura (ITP)[23-26]	Management of acute bleeding due to severe thrombocytopenia and/or platelet count less than 20,000/mm^3 in adults, or less than 30,000/mm^3 in children.	Acute: 1 gram/kg daily for 1-2 days	Maintain platelet count ≥ than 20,000/mm3 in adults, or ≥ greater than 30,000/mm3 in children: • Acute: Monitor platelet count daily • Chronic: Monitor platelet count every 4 weeks Documented bleeding episodes	Moderate	Strong
		Chronic: 1 gram/kg intermittently as to maintain platelet count			
Secondary Immunodeficiency due to CLL[27,28]	IgG of less than 400 mg/dL	400 mg/kg every 4 weeks	Maintain a serum trough level IgG values ≥400 mg/dL	Moderate	Strong
Systemic Juvenile Idiopathic Arthritis (JIA)[29,30]	Resistant to other forms of therapy	1 to 2 gram/kg bimonthly for the first 2 months, then monthly for up to 6 months.	Efficacy appears to be short lived, Substantial clinical improvement must be shown and document after 4-6 courses	Moderate	Weak/Conditional

Immunology

Indication	Criteria for Use	Dose and Duration	Monitoring Parameters	Evidence Ranking	UW Health Recommendation Rating
Normogammaglobulinemia with impaired specific antibody production (Qualitative antibody deficiency) [31]	Recurrent infections requiring antibiotic treatment and well-documented severe polysaccharide non-responsiveness	400 mg/kg every 4 weeks; Consider discontinuation or drug holiday (5 months) preferably in temperate climate) to assess efficacy	Decrease number of infections	Very Low	Weak/Conditional

Neurology and Neuromuscular

Indication	Criteria for Use	Dose and Duration	Monitoring	Evidence Ranking	UW Health Recommendation Rating
Autoimmune Encephalopathy[32]	Used in combination with corticosteroids or plasmapheresis.	400 mg/kg for 5 days	Improvement in functional status (neurologic, psychiatric)	Very low	Weak/Conditional
Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) [33-40]	Used as monotherapy Can be used in combination with corticosteroids or immunosuppressants or as an alternative to plasmapheresis	Induction: 2 gram/kg administered as divided doses over 2 to 5 consecutive days Maintenance: 1 gram/kg given over 1 to 2 days every 3 weeks for 2 to 3 months before determining response to therapy. Further tapering of dose or frequency and duration of treatment depend on clinical response	IVIG should be used for 2 to 3 months before determining whether the patient has responded. If there is no benefit after 2 to 3 months, IVIG therapy should be discontinued Aim for minimum dose to maintain optimal functional status. (i.e. physical function; mobility/ambulation, fatigue)	High	Strong
Guillain-Barre Syndrome (GBS)[37,41-44]	Used as first line agent for rapidly progressive form of disease. May be used as an alternative to plasmapheresis	400 mg/kg daily for 5 days or 1 gram/kg for 2 days	Improvement in functional status (i.e. physical function, mobility, respiratory status)	High	Strong
Moderate-Severe Myasthenia Gravis (MG) [45-49]	Used when other treatments have been ineffective. Unresponsive/Intolerant to steroids	Induction: 400 mg/kg daily for 5 days or 1gram/kg for 2 days	Measurable response must be documented within 6 months. (i.e. physical function;	High	Strong

Neurology and Neuromuscular					
Indication	**Criteria for Use**	**Dose and Duration**	**Monitoring**	**Evidence Ranking**	**UW Health Recommendation Rating**
	Myasthenic Crisis: First line therapy As an alternative treatment to plasma exchange or thymectomy	Maintenance: 400mg/kg every 4 weeks	mobility/ambulation, fatigue) If there is no benefit after 6 courses, IVIG therapy should be discontinued.		
Multifocal Motor Neuropathy (MMN) [50]	Multifocal motor neuropathy with persistent conduction block as diagnosed by a neurologist	Induction: 2 gram/kg in 2 to 5 divided doses. Maintenance: 400 mg/kg to 1 gram/kg every 2-6 weeks after induction dosing regimen The amount per dose should be titrated to the individual's response. Aim for minimum dose to maintain optimal functional status.	Improvement in functional status	Moderate	Weak/ Conditional
Stiff Person Syndrome (SPS) [51,52]	Significant functional impairment in patients who have a verified diagnosis of stiff person syndrome made by a neurologist Used when standard treatment with diazepam is no longer effective	Induction: 2 gram/kg in 2 to 5 divided doses	Improvement in functional status Duration of benefit ranges from 6 weeks to one year.	Moderate	Strong
		Maintenance: 1 gram/kg x 2 days monthly x 3 months		Moderate	Strong

Hematology					
Indication	**Criteria for Use**	**Dose and Duration**	**Monitoring**	**Evidence Ranking**	**UW Health Recommendation Rating**
Bone Marrow Transplantation (prevention of Graft Versus Host Disease (GVHD) and infection) Adult and Pediatric[53-57]	Low Ig levels pre-transplant defined as IgG of less than 500 mg/dL.	Pre-transplant: 250 mg/kg to a maximum of 20 grams on days -7 and -2 before transplant.	IgG values ≥500 mg/dL. IgG levels be monitored every 2 weeks in patients receiving IVIG due to the shorter half-life	Moderate	Strong
		Post-transplant: Weekly through day 100.		Moderate	Strong
Autoimmune Hemolytic Anemia[58]	Following failure of immunosuppression with corticosteroids and cytotoxic agents prior to consideration for splenectomy	500 mg/kg/day for 5 days	Hemoglobin level ; Clinical status	Low	Weak/Conditional
Persisting hypogammaglobulinemia secondary to rituximab therapy[59,60]	Documentation of recurrent and/or severe infections, significant hypogammaglobulinemia, and impaired specific antibody production	200 – 400 mg/kg monthly until IVIG level exceed 550 mg/d; then as needed to maintain IVIG nadir between 550-600 mg/dL	Resolution of severe infection and IVIG level	Very Low	Weak/Conditional
Severe thrombocytopenia (Hematology consult required)[61]	Severe thrombocytopenia and at least ONE of the following • Severe or life-threatening bleeding • Urgent need for invasive diagnostic procedure or surgery • Severe thrombocytopenia duration of at least 7 days expected after high dose chemotherapy (HLA-matched or cross matched platelets should be tried first)	1 gram/kg/day as continuous IV infusion for 2 days PLUS apheresis platelets given at rate of 1 unit per 4 hours, as continuous infusion, started concurrently with IVIG and continued x 72 hours	Platelet levels	Low	Weak/Conditional

Transplantation					
Indication	**Criteria for Use**	**Dose and Duration**	**Monitoring**	**Evidence Ranking**	**UW Health Recommendation Rating**
Antibody Mediated Rejection[62-76]	Evidence of acute or chronic active rejection; presence of rejection established by biopsy and laboratory test to assess the presence and strength of antibodies to donor.	See UW Health Kidney Rejection Treatment Protocols for definitions of rejection type by Banff criteria and timing. Also see concurrent therapy. • Early rejection: 100 mg/kg for 4-6 doses after plasma exchange then 500 mg/kg/week x 4 weeks • Late rejection and persistent rejection: 500 mg/kg/week x 4 weeks	Reduction in donor-specific antibodies and graft function by biopsy	Moderate	Weak/Conditional
BK virus (polyoma) associated nephropathy[77]	Failure of decreased immunosuppression to clear viremia	500 mg / kg (maximum of 70 grams) every week for four doses;	Viral clearance and graft function	Very Low	Weak/Conditional
Cytomegalovirus associated disease[78-80]	Failure of decreased immunosuppression in combination with anti-viral therapy to clear viremia	500 mg/kg once; may repeat once weekly for three doses with severe disease; total dose should not exceed 2 gram/kg	Viral clearance and graft function	Low	Weak/Conditional
Transplant Desensitization[81-87]	Dependent on type of transplant (living or deceased) and amount of preformed antibodies detected in solid antigen bead testing done prior to transplant	See Solid Organ Transplant Departmental Protocol for live (D2) and deceased (D5c) donors • 100 mg/kg after each plasma exchange o D2- X2-3 doses before and after transplant o D5c- one dose before transplant and X2-3 doses after transplant	Post reperfusion biopsy	Low	Weak/Conditional
Waitlist Desensitization[88-90]	Candidates on the kidney transplant waitlist approved for waitlist desensitization by the desensitization committee.	Solid Organ Transplant Departmental Protocol should be followed and referred to as a resource OR 2 gram/kg administered monthly for 6 months with monitoring of donor specific antibodies	After 6 months, the clinical response is assessed by the desensitization committee to determine whether the patient should receive second cycle of 6 monthly doses of IVIG.	Low	Weak/ conditional

Dermatology					
Indication	**Criteria for Use**	**Dose and Duration**	**Monitoring**	**Evidence Ranking**	**UW Health Recommendation Rating**
Pemphigus Vulgaris/Pemphigus Foliaceus with IVIG as monotherapy[91-95]	Treatment refractory patients; failure of systemic corticosteroids and immunosuppressants; paraneoplastic disease	1-2 gram/kg ; total dose divided equally and given daily for 3-5 days every 4 weeks; decrease frequency after disease controlled (every 6, 8, 10, 12, 14, 16 weeks) When given 16 weeks x 2 consider discontinuation for disease remission	Reduction or discontinuation of steroid; disease remission	Moderate	Weak/Conditional
Pemphigus Vulgaris Rituximab + IVIG[96,97]	Treatment refractory (inadequate response to conventional immune suppressive therapy + IVIG) patients when given in combination with rituximab	2 gram/kg every 3 weeks for 2 doses starting in week 3 of rituximab therapy; then once monthly for 4 doses	Discontinuation of steroid; disease remission	Low	Weak/conditional
Bullous pemphigoid and Mucous-membrane (cicatricial) pemphigoid[91,93-95]	Treatment refractory patients; failure of systemic corticosteroids and immunosuppressants; paraneoplastic disease	1-2 gram/kg ; total dose divided equally and given daily for 3-5 days every 4 weeks; decrease frequency after disease controlled (every 6, 8, 10, 12, 14, 16 weeks) When given 16 weeks x 2 consider discontinuation for disease remission	Reduction or discontinuation of steroid; disease remission	Low	Weak/Conditional
Stevens-Johnson Syndrome; toxic epidermal necrolysis[98-102]	First line for treatment of severe disease in conjunction with withdrawal of offending medication and supportive care	1-2 gram/kg daily for up to 3 consecutive days or until symptoms resolve; pt should be evaluated daily before each dose	Symptom resolution	Low	Weak/ Conditional
Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)[103-105]	Life-threatening reaction refractory to corticosteroids	1 gram/kg daily for up to 3 consecutive days or until symptoms resolve; pt should be evaluated daily before each dose	Symptom resolution	Low	Weak/ Conditional

Infectious Disease					
Indication	**Criteria for Use**	**Dose and Duration**	**Monitoring**	**Evidence Ranking**	**UW Health Recommendation Rating**
HIV-associated thrombocytopenia[106]	When platelets are less than 50,000	1 gram/kg/day for two consecutive days per week for 4 weeks	Platelet count; Signs and symptoms of IVIG adverse effects	Moderate	Weak/Conditional
Necrotizing Fasciitis[107-112]	Critically ill patients with staph or strep necrotizing soft tissue infection	Between 200 mg/kg/day and 2 gram/kg/day for 1 to 5 days	Improvement of soft tissue infection	High	Weak/Conditional
Multisystem Inflammatory Syndrome in Children (MIS-C)[113,114]	MIS-C with features of Kawasaki Disease (KD), or moderate to severe disease without KD features (i.e., shock or myocardial dysfunction)	2 gram/kg (IBW) once; max dose = 100 grams For patients with concern for significant cardiac dysfunction: 1 gram/kg once daily x 2 days; max dose = 50 grams	Cardiac function and fluid status Inflammatory markers. • Defervescence • CRP • ESR Additional labs: • CBC (w/ Diff) • CMP	Very Low	Weak/Conditional

Connective Tissue Disease					
Indication	**Criteria for Use**	**Dose and Duration**	**Monitoring**	**Evidence Ranking**	**UW Health Recommendation Rating**
Lupus erythematosus (cutaneous or systemic)[115-119]	Severe, refractory disease	1 gram/kg on 2 consecutive days then Systemic: 1 gram/kg once monthly until symptoms resolve Cutaneous: between 400 mg/kg and 2 gram/kg per month until symptoms resolve	Erythrocyte sedimentation rate, C-reactive protein, urine protein, serum creatinine, anti-double stranded RNA, and complement (C3 & C4)	Low	Weak/Conditional
Refractory Dermatomyositis[120-123]	Unresponsive/intolerant to steroids and immunosuppressants; Significant skin involvement; paraneoplastic disease	1 gram/kg x 2 consecutive days monthly for 3 to 6 months	Improved clinical status (increase muscle strength, improved cutaneous disease, decreased CK level); able to taper steroids	Moderate	Weak/Conditional
Refractory Polymyositis[120,123]	Second line therapy for patients not responding to immunosuppressive treatment; paraneoplastic disease	1 gram/kg x 2 consecutive days monthly for 3 to 6 months	Improved clinical status (increase muscle strength, improved cutaneous disease, decreased CK level); able to taper steroids	Low	Weak/Conditional

Inappropriate Uses
1. Alzheimer's disease[124] (*UW Health GRADE Moderate quality evidence; strong recommendation*) 2. Wegener's granulomatosis[125] (*UW Health GRADE Moderate quality evidence; strong recommendation*)

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