جدول ۱– موارد اندیکاسیون مطلق کاربرد IVIG

	Condition	Indication for IVIG use
Primary and Secondary immunodeficiency	**Primary immunodeficiencies (associated with significant antibody defects)** such as common variable immunodeficiency, severe combined immunodeficiencies, transient hypogamm-aglobulinaemia of infancy, Wiskott Aldrich syndrome and X-linked agammaglobulinaemia	A specific PID diagnosis must be established by a clinical immunologist.
	Secondary antibody deficiency (any cause)	Underlying cause of hypogammaglobulinaemia cannot be reversed or reversal is contraindicated; OR Hypogammaglobulinaemia associated with NHL, CLL, MM, HSCT or other relevant B-cell malignancy confirmed by haematologist; AND - Recurrent or severe bacterial infection despite continuous oral antibiotic therapy for 3months. - IgG <5 g/L (excluding paraprotein) - Documented failure of serum antibody response to unconjugated pneumococcal or other polysaccharide vaccine challenge.
Nephrology	**Secondary hypogammaglobulinaemia**	Replacement therapy for life-threatening infection due to hypogammaglobulinaemia related to other diseases or medical therapy (Solid organ transplantation)
	ANCA-positive systemic necrotizing vasculitis	Control of vasculitic activity in rare cases of ANCA-positive systemic necrotising vasculitis failing to respond to corticosteroids and cytotoxic immunosuppression. IVIg has a limited role as one of several therapeutic options in relapsing disease.
	Kidney transplantation	**Pre-transplantation:** Patients in whom an antibody or antibodies prevent transplantation (donor specific anti‑human leukocyte antigen (HLA) antibody/ies or anti-blood group antibody).
	Kidney transplantation	**Post-transplantation:** To treat steroid-resistant acute rejection which may be cellular or antibody mediated. For prevention and/or treatment of rejection where other therapies are contraindicated or pose a threat to the graft or patient. When rejection is steroid resistant, IVIg is a safer therapy than anti-T cell antibody therapy with equal efficacy.
Hematology	**Acquired von willebrand disease**	Life or limb-threatening haemorrhage AND failure to respond to other treatments.
	HDN (hemolytic disease of the newborn)	Pediatric hematologists
	Idiopathic thrombocytopenic purpura- children	Pediatric hematologists

	Condition	Indication for IVIG use
	Idiopathic thrombocytopenic purpura- adults	Prior to surgery, IVIg is appropriate if unresponsive to steroids [platelet count will depend on surgery type: minor, >50 x109/L; major, >80 x109/L; critical (CNS/spinal), >100 x109/L] (grade C, level 4 evidence). **Acute (newly diagnosed) ITP** IVIg is appropriate in symptomatic ITP when steroids are contraindicated or a more rapid response is desirable, e.g. potentially life- threatening haemorrhage and/or bleeding into a critical area (grade B, level 2b evidence). IVIg is appropriate in symptomatic ITP that is unresponsive to steroids and when other treatments, e.g. splenectomy or immunosuppression, are considered inappropriate, aiming to keep patients symptom free. In such patients, the goal is to achieve platelet counts >30 x109/L (grade B, level 2c evidence). **Persistent ITP** For symptomatic cases unresponsive to all other treatments, IVIg is appropriate only for emergency management, e.g. potentially life-threatening haemorrhage and/or bleeding into a critical area (grade B, level 2b evidence). There is no evidence to guide a sequence of treatments for patients who have recurrent or persistent thrombocytopaenia associated with bleeding after an initial treatment course with corticosteroids or IVIg. Use 1 g/kg (0.8–1 for children) as a single infusion, to be repeated at later date if platelet count has not responded. **Chronic ITP:** Lifelong treatment with IVIg should be considered as exceptional and alternative approaches (splenectomy) and treatments(such as rituximab, thrombopoietin receptor agonists)should be considered.
	Pregnancy-associated idiopathic thrombocytopenic purpura	a.Platelets <30x109/L , b. Impending delivery; IVIg is appropriate for patients unresponsive to steroids or for whom there are contraindications to steroids or significant side effects (grade B, level 2b evidence).
Neurology	**Guillain-Barré syndrome**	First-line treatment for GBS and its variants with significant disability and progression.
	Chronic inflammatory demyelinating polyradiculoneuropathy	IVIg is recommended for CIDP in cases of significant impairment inhibiting normal daily activities (grade A, level Ia evidence); the choice of corticosteroids, plasma exchange or IVIg should be individualised.
	Multifocal motor neuropathy	as a first-line treatment
	Paraproteinaemic demyelinating neuropathy	IVIg is recommended for CIDP-like neuropathy (grade A recommendation, level Ia evidence); the choice of corticosteroids, plasma exchange or IVIg should be individualised.
	Myasthenia gravis	Intravenous immunoglobulin is an effective treatment for acute exacerbations of MG and for short-term treatment of severe MG.
	Stiff person syndrome (Moersch–Woltmann syndrome)	Patients with SPS incompletely responding to diazepam and/or baclofen and with significant disability requiring a cane or a walker due to truncal stiffness and frequent falls.
	Acute disseminated encephalomyelitis	

	Condition	Indication for IVIG use
	IgM paraproteinaemic neuropathy	Patients with IgM paraproteinaemic neuropathy with functional impairment in whom other therapies have failed or are contraindicated or undesirable.
	Inflammatory myopathies; Dermatomyositis (DM), Polymyositis (PM)	IVIg is appropriate in patients with resistant or aggressive disease (grade B recommendation, level IIb evidence).
Dermatology	**Cicatricial pemphigoid**	CP resistant to glucocorticoid and immunosuppressive therapy.
	Toxic epidermal necrolysis/Stevens–Johnson syndrome	To limit progression of TEN or SJS/TEN when administered in early stages.
Others	**HIV–associated idiopathic thrombocytopenic purpura**	Severe ITP associated with HIV infection.
	Kawasaki disease	Clinical diagnosis of Kawasaki disease by a pediatrician or immunologist.

جدول ۲– موارد اندیکاسیون نسبی کاربرد IVIG. در موارد ذیل تجویز IVIG منوط به ارائه توضیحات و مستندات معتبر می باشد.

Condition	Indication for IVIG use
Primary and Secondary immunodeficiency	
Thymoma with immunodeficiency	Profound B cell depletion and/or significant antibody deficiency.
HSCT in primary immunodeficiencies	PID patients undergoing HSCT.
Specific antibody deficiency	Approval by a clinical immunologist, AND Severe, persistent, opportunistic or recurrent bacterial infections despite continuous oral antibiotic therapy for 3 months, AND Documented failure of serum antibody response to unconjugated pneumococcal or other polysaccharide vaccine challenge.
Nephrology	
Haemolytic uraemic syndrome	
Henoch–Schonlein purpura	
Hematology	
Acquired red cell aplasia	IVIg is recommended for patients with red cell aplasia due to parvovirus B19
Autoimmune hemolytic anemia	1. Symptomatic or severe AIHA (Hb <60 g/L, except patients with co-morbidities) refractory to conventional therapy with corticosteroids; OR 2. As a temporising measure before splenectomy; OR 3. As initial and maintenance therapy in AIHA in patients unsuitable for splenectomy or immunosuppression.
Autoimmune neutropenia	IVIg may be considered among treatment options in rare circumstances when the standard treatment of G-CSF fails.
Evans syndrome	1. Refractory to conventional therapy with corticosteroids; OR 2. Where corticosteroids are contraindicated; OR 3. As a temporising measure before splenectomy.
F/NAIT (Foeto/neonatal alloimmune	Pediatric hematologis

Thrombocytopenia)	
PTP (post-transfusion purpura)	IVIg is recommended therapy in patients with post transfusion purpura with decreased platelets 2–14 days post-transfusion and bleeding (grade C, level III evidence).
Aplastic anemia	IVIG is not recommended for treatment of aplastic anemia
Neurology	
Opsoclonus-myoclonus ataxia	Long-term maintenance therapy of OMA in association with other tumour therapies.
Lambert–Eaton myasthenic syndrome	Short-term therapy for severely affected nonparaneoplastic LEMS patients.in whom other therapy (e.g. with 3,4-diaminopyridine) has failed.
Post-polio syndrome	IVIG has a minor to moderate positive effect on muscle strength and some aspects of quality of life in PPS.
Relapsing remitting multiple sclerosis	-IVIG could still be considered as a second or third-line therapy in RRMS if conventional immunomodulatory therapies are not tolerated because of side effects or concomitant diseases -And in particular in pregnancy where other therapies may not be used (good clinical practice point).
Amyotrophic lateral sclerosis	IVIg is sometimes used when the diagnosis of motor neuron disease has not yet been established and an alternative diagnosis of multifocal motor neuropathy has not been ruled out.
Diabetic amyotrophy (diabetic proximal neuropathy or diabetic lumbosacral radiculoplexus neuropathy)	IVIg may be considered in exceptional circumstances for intractable pain or progressive muscle weakness in patients in whom steroids are ineffective or cannot be tolerated.
Acute uremic polyneuropathy	
Paraneoplastic polyneuropathy	
Dermatology	
Bullous pemphigoid	BP resistant to topical and systemic glucocorticoids and immunosuppressive therapy.
Pyoderma gangrenosum	Patients with significant pyoderma gangrenosum, diagnosed by a dermatologist, unresponsive to corticosteroids and other immunosuppressive agents.
Infectious Diseases	
Staphylococcal or streptococcal toxic shock syndrome	For staphylococcal TSS when other therapies have failed.
Necrotising (PVL-associated) staphylococcal sepsis	For necrotising PVL-associated staphylococcal sepsis when all other treatments have failed.
Severe or recurrent Clostridium difficile colitis	Only recommended for severe or multiple recurrent *C. difficile* colitis when all other treatments have failed or are inappropriate.
Others	

Adrenoleukodystrophy	
Female infertility/Poor responders with ART	

جدول ۳– مواردیکه IVIG برای درمان اندیکاسیون ندارد و توصیه نمی شود.

Condition	Indication for IVIG use
Nephrology	
Catastrophic antiphospholipid syndrome	IVIg may be appropriate therapy for catastrophic antiphospholipid syndrome (with multiple organ failure). It is not indicated for the treatment of antiphospholipid syndrome in other cases.
Glomerulonephritis — IgA nephritis	
Nephrotic syndrome	IVIg is not supported in this setting; preferable alternative treatments are available.
Hematology	
Hemolytic transfusion reaction	IVIG may be considered among the options for treatment of serious, life-threatening, delayed hemolytic transfusion reactions in patients with SCD.
Virus-associated hemophagocytic syndrome	IVIG is not recommended for routine use in the treatment of VAHS. Based on consensus by the expert panel, IVIG may be considered among the options for treatment of severe life-threatening VAHS.
Others	
Autoimmune congenital heart block (neonatal lupus)	IVIg therapy may be indicated during pregnancy when there is a history of autoimmune congenital heart block in at least one previous pregnancy and maternal SS-A and/or SS-B antibodies are present.
Acute exacerbations of MS	IVIG does not seem to have any valuable effect as add-on therapy to methylprednisolone
Critical illness polyneuropathy	