MEDICATION COVERAGE POLICY

PHARMACY AND THERAPEUTICS ADVISORY COMMITTEE

Health Plan of San Joaquin | Mountain Valley Health Plan

POLICY	Transplant	**P&T DATE:**	12/10/2024
THERAPEUTIC CLASS	Immunosuppressive Agents	**REVIEW HISTORY** (MONTH/YEAR)	01/24, 12/22, 09/21, 9/20, 9/19, 9/18, 5/17, 5/16
LOB AFFECTED	Medi-Cal		

This policy has been developed through review of medical literature, consideration of medical necessity, generally accepted medical practice standards, and approved by the Health Plan Pharmacy and Therapeutic Advisory Committee.

Effective 1/1/2022, the Pharmacy Benefit is regulated by Medi-Cal Rx. Please visit https://medi-calrx.dhcs.ca.gov/home/ for portal access, formulary details, pharmacy network information, and updates to the pharmacy benefit.
All medical claims require that an NDC is also submitted with the claim. If a physician administered medication has a specific assigned CPT code, that code must be billed with the correlating NDC. If there is not a specific CPT code available for a physician administered medication, the use of unclassified CPT codes is appropriate when billed with the correlating NDC.

OVERVIEW

Organ transplant is a complex, high risk, and costly procedure. To minimize organ rejection, transplant patients usually take immunosuppressive therapy lifelong. However, these immunosuppressive agents carry their own risks, many related to increased risk of infections, metabolic syndrome, etc. The goal of immunosuppression therapy for organ transplant prevention is to minimize the side effects of immunosuppressants without compromising their efficacy. The below criteria, limits, and requirements for certain agents are in place to ensure appropriate use of those agents.
The purpose of this coverage policy is to review the available agents (Table 1) and to distinguish where the medications may be billed to. For agents listed for coverage under the medical benefit, this coverage is specific to outpatient coverage only (excludes emergency room and inpatient coverage).

Table 1. Available Transplant Rejection Prophylaxis, Treatment and Immunosuppressive Agents:
(Current as of 12/2024)

CPT code	Generic Name (Brand Name)	Available Strengths	Pharmacy Benefit	Outpatient Medical Benefit (Restrictions)
Calcineurin inhibitors				
J7507 J7525 for IV	**Tacrolimus (Prograf)**	IR Capsules: 0.5 mg, 1 mg, 5 mg IV solution: 5 mg/ml	Yes	Yes, for IV only
J7508	**Tacrolimus (Astagraf XL Envarsus XR)**	ER Capsule: 0.5 mg, 1 mg, 5 mg ER Tablet: 0.75 mg, 1 mg, 4 mg	Yes	No
--	**Cyclosporine, modified (Gengraf, Neoral)**	IR Capsules: 25 mg 50 mg 100 mg Oral Solution: 100mg/ml	Yes	No
J7516 J7515 J7502	**Cyclosporine (Sandimmune)**	Oral Solution: 100mg/ml IR Capsules: 25 mg, 50 mg, 100 mg IV: 50 mg/ml	Yes	Yes, for IV only
Anti-proliferative agents				
J7500 J7501 for IV	**Azathioprine (Imuran, Azasan)**	Tablets: 50 mg, 75 mg, 100 mg IV solution: 100 mg	Yes	Yes, for IV only

J7517	**Mycophenolate Mofetil (CellCept) Mycophenolate Acid (Myfortic DR)**	IR Tablets: 250 mg 500 mg DR Tablets: 180 mg 360 mg Oral Suspension: 200 mg/ml	Yes	No
mTOR (Mechanistic Target of Rapamycin) inhibitors				
J7527	**Everolimus (Zortress)**	Tablets: 0.25 mg, 0.5 mg, 0.75 mg, 1 mg	Yes	No
J7520	**Sirolimus (Rapamune)**	IR Tablets: 0.5 mg, 1 mg, 2 mg Oral Solution 1 mg/ml	Yes	No
Injectable Agents				
J0480	**Basiliximab (Simulect)**	IV Solution: 10 mg, 20 mg	Yes	Yes (PA)
J0485	**Belatacept (Nulojix)**	IV Solution: 250 mg	Yes	Yes (PA)
J0202	**Alemtuzumab (Lemtrada)**	IV Solution: 25 mg	Yes	Yes (PA)
J7511	**Antithymocyte Globulin Rabbit (Thymoglobulin)**	IV Solution: 25 mg	Yes	Yes (PA)
J7504	**Antithymocyte Globulin Equine (Atgam)**	IV Solution: 50 mg/mL	Yes	Yes (PA)
J3262	**Tocilizumab (Actemra)**	IV solution: 80 mg/4mL 300 mg/10 mL 400 mg /20 mL	Yes	Yes (PA)
Immune Globulin				
J1459	**Privigen**	5 gm/50 mL, 10 g/100 mL 20 g/200 mL 40 g/400 mL	Yes	Yes (PA)
J1551	**Cutaquig**	1GM/6ML 1.65 g/10 mL 2GM/12ML 3.3 g/20 mL 4GM/24ML 8GM/48ML	Yes	Yes (PA)
J1554	**Asceniv**	5 gm/50 mL	Yes	Yes (PA)
J1555	**Cuvitru**	1 g/5 mL 2 g/10 mL 4 g/20 mL 8 g/40mL 10 gm/50 mL	Yes	Yes (PA)
J1556	**Bivigam**	5 gm/50 mL 10 g/100 mL	Yes	Yes (PA)
J1557	**Gammaplex**	5 g/100 mL 5 gm/50 mL 10 g/100 mL 10 g/200 mL 20 g/200 mL 20 g/400 mL	Yes	Yes (PA)
J1558	**Xembify**	1 g/5 mL 2 g/10 mL 4 g/20 mL 10 gm/50 mL	Yes	Yes (PA)
J1559	**Hizentra**	1 g/5 mL	Yes	Yes (PA)

		2 g/10 mL 4 g/20 mL 10 gm/50 mL		
J1561	**Gamunex-hyphenc/ Gammaked**	1 g/10 mL 2.5 g/25 mL 5 gm/50 mL 10 g/100 mL 20 g/200 mL 40 g/400 mL	Yes	Yes (PA)
J1562	**Vivaglobin**	0.48 g/3 mL 1.6 gm/10 mL 3.2 g/20 mL	Yes	Yes (PA)
J1566	**Carimune**	3, 6, 12 grams	Yes	Yes (PA)
J1568	**Octagam**	1 g/20 mL 2 g/20 mL 2.5 gm/50 mL 5 g/100 mL 5 gm/50 mL 10 g/100 mL 10 g/200 mL 20 g/200 mL 30 g/300 mL	Yes	Yes (PA)
J1569	**Gammagard**	5 g, 10 g vial	Yes	Yes (PA)
J1572	**Flebogamma / Flebogamma Dif**	5 g/100 mL 10 g/200 mL 20 g/400 mL	Yes	Yes (PA)
J1575	**Hyqvia**	2.5 g/25 mL 5 gm/50 mL 10 g/100 mL 20 g/200 mL 30 g/300 mL	Yes	Yes (PA)
J1576	**Panzyga**	1 g/10 mL 2.5 g/25 mL 5 gm/50 mL 10 g/100 mL 20 g/200 mL 30 g/300 mL	Yes	Yes (PA)
J1599	**Alyglo**	5 gm/50 mL 10 g/100 mL 20 g/200 mL	Yes	Yes (PA)

PA = Prior Authorization

EVALUATION CRITERIA FOR APPROVAL/EXCEPTION CONSIDERATION

Below are the coverage criteria and required information for agents with medical benefit restrictions. This coverage criteria has been reviewed and approved by the Health Plan Pharmacy & Therapeutics (P&T) Advisory Committee. For agents that do not have established prior authorization criteria, Health Plan will make the determination based on Medical Necessity criteria as described in Health Plan Medical Review Guidelines (UM06).

Intravenous Immunosuppressant
Basiliximab (Simulect)

- ❒ **Coverage Criteria:** Approval is determined by medical necessity criteria.
- ❒ **Limits:** NONE
- ❒ **Required Information for Approval:** Please submit clinic notes with documentation of acute organ rejection in patients receiving kidney or liver transplant.

Intravenous Immunosuppressant
Antithymocyte Globulin (Thymoglobulin, Atgam)

- ❒ **Coverage Criteria:** Approval is determined by medical necessity criteria.
- ❒ **Limits:** NONE
- ❒ **Required Information for Approval:** Please submit clinic notes with documentation of acute organ rejection in patients receiving kidney transplant.

Intravenous Immunosuppressant
Belatacept (Nulojix)

- ❒ **Coverage Criteria:** Approval is determined by medical necessity criteria.
- ❒ **Limits:** NONE
- ❒ **Required Information for Approval:** Please submit clinic notes with documentation of organ transplant in patients who are EBV seropositive.

Intravenous Immunosuppressant
Alemtuzumab (Lemtrada)

- ❒ **Coverage Criteria:** Approval is determined by medical necessity criteria.
- ❒ **Limits:** NONE
- ❒ **Required Information for Approval:** Approval is determined by medical necessity criteria. Please submit clinic notes with documentation of acute organ rejection in patients receiving kidney transplant where Basiliximab or Antithymocyte Globulin is inappropriate.
- ❒ **Notes:** Can cause significant lymphopenia that can lasts from 6 months to several years. Occasionally used off-label for kidney transplants.

Intravenous *Immunoglobulins*
Alyglo; Asceniv; Bivigam; Carimune NF; Cutaquig; Cuvitru; Flebogamma DIF; GamaSTAN; Gammagard; Gammagard S/D Less IgA; Gammaked; Gammaplex; Gamunex-C; Hizentra; Hyqvia; Octagam; Panzyga; Privigen; Xembify

- ❒ **Coverage Criteria:** Reserved for patients with one or more of the following:
  - **Prevention of acute humoral rejection** for high-risk solid organ transplant patients, including those who are highly sensitized, have positive cross match, or have a live donor with ABO incompatibility.
  - **Treatment of acute humoral rejection** for patients with documentation of antibody-mediated rejection (AMR) post-transplant.
  - **Hypogammaglobulinemia** to prevent post-transplant infections for patients with documented low IgG levels (e.g. <400 mg/dL).
  - **Refractory BK viremia** in kidney transplant patients who have persistent viral titers despite reduced immunosuppression.
  - Other off-label indications supported by society guidelines
- ❒ **Limits:** NONE
- ❒ **Required Information for Approval:** Approval is determined by medical necessity criteria. Relevant information for approval may include high panel-reactive antibody (PRA) levels, presence of donor-specific antibodies (DSAs) pre-transplant, documented ABO incompatibility, histological evidence of AMR (e.g. via biopsy), presence of donor-specific antibodies during AMR, clinical signs of graft dysfunction, IgG levels, history of recurrent infections, BK virus titer.
- ❒ **Notes: N/A**

CLINICAL JUSTIFICATION

The goal of immunosuppression therapy for organ transplant prevention is to minimize the side effects of immunosuppressants without compromising their efficacy. Depending on the transplant type, a prophylaxis

regimen can consist of monotherapy or a combination of agents. Immunosuppressive agents can be classified into 2 main categories: induction or maintenance.

Organ transplants with the highest risk for transplant rejection (e.g. heart, kidney, liver) may require induction therapy (i.e. Basiliximab, Thymoglobulin) to prevent acute organ rejection since the risk for organ rejection is highest within the first 6 months post-transplantation. Induction agents can also be used to delay the initial add-on of nephrotoxic calcineurin inhibitors (Cyclosporine, Tacrolimus).

Maintenance therapies are typically oral agents (cyclosporine, tacrolimus, sirolimus, mycophenolate, etc) and need to be taken lifelong. The dosing of these agents are titrated based on the serum concentration in the body—with target serum levels higher initially post-transplantation. It is generally not recommended to switch in between agents once a patient is stable on a particular agent. The current trend is to use a combination of 3 maintenance therapies—usually a calcineurin-inhibitor (cyclosporine or tacrolimus), an antimetabolite agent (mycophenolate mofetil or azathioprine), and a glucocorticoid over the first year post-transplantation. Sirolimus and everolimus are Mammalian Target of Rapamycin (mTOR) inhibitors which are structurally similar to Tacrolimus but considered to be a safer alternative for patients with renal insufficiency, although the use of everolimus within 3 months post-cardiac transplantation is not recommended due to a higher incidence of mortality from infections. Corticosteroids are used to lower the immune response. They are highly effective for the prevention and treatment of acute rejection, but their long-term use is associated with a number of adverse effects (i.e. worsening metabolic syndrome, fluid retention, osteoporosis, opportunistic infections, etc). Therefore, it is common to use corticosteroids in relatively high doses initially, then tapered to low doses or discontinued after 6 to 12 months post-transplantation. Patients with a history of one or more organ rejection may need to optimize drug therapies (switch from azathioprine to mycophenolate mofetil or switch from antimetabolite agents to an mTOR inhibitor).

The KDIGO guidelines suggest treating antibody-mediated acute rejection with one or more of the following alternatives, with or without corticosteroids): plasma exchange, intravenous immunoglobulin, anti-CD20 antibody, or lymphocyte-depleting antibody.

Recommendations for the off-label use of immune globulin (IVIG) are based on various society guidelines and literature demonstrating positive outcomes, including desensitization of high-sensitivity patients prior to transplant, treatment of antibody mediated rejection, and the prevent and treatment of infections.[19,20]

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⌖ REVIEW & EDIT HISTORY

Document Changes	Reference	Date	P&T Chairman
Creation of Policy	HPSJ Coverage Policy – Immunology – Transplant 2016-05.docx	5/2016	Johnathan Yeh, PharmD
Update to Policy	HPSJ Coverage Policy – Immunology – Transplant 2017-05.docx	5/2017	Johnathan Yeh, PharmD
Update to Policy	HPSJ Coverage Policy – Immunology – Transplant 2018-09.docx	9/2018	Johnathan Yeh, PharmD
Update to Policy	HPSJ Coverage Policy – Immunology – Transplant 2019-09.docx	9/2019	Matthew Garrett, PharmD
Update to Policy	HPSJ Coverage Policy – Immunology – Transplant 2020-09.docx	9/2020	Matthew Garrett, PharmD
Update to Policy	Transplant	9/2021	Matthew Garrett, PharmD
Review of Policy	Transplant	12/2022	Matthew Garrett, PharmD
Review of Policy	Transplant	1/2024	Matthew Garrett, PharmD
Update to Policy	Transplant	12/2024	Matthew Garrett, PharmD

Note: All changes are approved by the Health Plan P&T Committee before incorporation into the utilization policy