Immunosuppressive Drugs **Policy Number: M-0025**
Revision: 1 **Last Update: 3/19/2013**

Payment will not be made for any use of these drugs outside of the criteria without prior authorization. The member may not be billed unless the member explicitly agrees in writing to be responsible for the charges in accordance with the contract/provider manual. Prior authorization will only be given if the provider demonstrates the intended use meets Medicare coverage guidelines.

Indications and Limitations:

A Medicare covered transplant means that the beneficiary must have received the transplant from a Medicare approved facility and was entitled to Medicare Part A at the time of the transplant. (If the patient had an organ transplant NOT covered by Medicare coverage of transplant drugs would be by Part D). For kidney transplants ONLY: after 36 months if the beneficiary is no longer eligible to receive coverage under Part B, the beneficiary may be eligible for coverage under the Part D benefit if enrolled in a Medicare Prescription Drug Plan.

For immunosuppressive drugs covered under this policy, the dosage, frequency and route of administration must conform to generally accepted medical practice and must be medically necessary to prevent or treat the rejection of an organ transplant. For the items addressed in this local coverage determination, the criteria for "reasonable and necessary", based on Social Security Act §1862(a)(1)(A) provisions, are defined by the following indications and limitations of coverage and/or medical necessity.

Coverage of parenteral azathioprine (J7501) or methylprednisolone (J2920, J2930) is limited to those situations in which the medication cannot be tolerated or absorbed if taken orally and is self-administered by the beneficiary. Claims for parenteral azathioprine or methylprednisolone that do not meet this criterion will be denied as not medically necessary.

Parenteral cyclosporine (J7516), antithymocyte globulin (J7504, J7511), muromonab-CD3 (J7505), tacrolimus (J7525) and daclizumab (J7513) are not proven to be safe when

administered in the home setting and therefore they will be denied as not medically necessary when provided in that setting.

Drugs may be covered only if dispensed and billed to Medicare by the entity that actually dispenses the drug to the Medicare beneficiary, and that entity must be permitted under all applicable federal, state, and local laws and regulations to dispense drugs. Only entities licensed in the state where they are physically located may bill the DME MAC for immunosuppressive drugs. Physicians may bill the DME MAC for drugs if all of the following conditions are met: the physician is 1) enrolled as a Durable Medical Equipment, Prosthetics, Orthotics, and Suppliers (DMEPOS) supplier with the National Supplier Clearinghouse, and 2) dispensing the drug(s) to the Medicare beneficiary, and 3) authorized by the State to dispense drugs as part of the physician's license. Claims submitted by entities not licensed to dispense drugs will be denied for lack of medical necessity.

The quantity of immunosuppressive drugs dispensed is limited to a 30-day supply. Quantities of immunosuppressive drugs dispensed in excess of a 30-day supply will be denied as not medically necessary. If a drug is denied as not medically necessary, the related supply fee (Q0510, Q0511 and Q0512) will be denied as not medically necessary.

Coding Information:

HCPCS Code(s)

J0485	INJECTION, BELATACEPT, 1 MG
J2920	INJECTION, METHYLPREDNISOLONE SODIUM SUCCINATE, UP TO 40 MG
J2930	INJECTION, METHYLPREDNISOLONE SODIUM SUCCINATE, UP TO 125 MG
J7500	AZATHIOPRINE, ORAL, 50 MG
J7501	AZATHIOPRINE, PARENTERAL, 100 MG
J7502	CYCLOSPORINE, ORAL, 100 MG
J7504	LYMPHOCYTE IMMUNE GLOBULIN, ANTITHYMOCYTE GLOBULIN, EQUINE, PARENTERAL, 250 MG
J7505	MUROMONAB-CD3, PARENTERAL, 5 MG
J7506	PREDNISONE, ORAL, PER 5MG
J7507	TACROLIMUS, ORAL, PER 1 MG
J7509	METHYLPREDNISOLONE ORAL, PER 4 MG

J7510	PREDNISOLONE ORAL, PER 5 MG
J7511	LYMPHOCYTE IMMUNE GLOBULIN, ANTITHYMOCYTE GLOBULIN, RABBIT, PARENTERAL, 25MG
J7513	DACLIZUMAB, PARENTERAL, 25 MG
J7515	CYCLOSPORINE, ORAL, 25 MG
J7516	CYCLOSPORIN, PARENTERAL, 250 MG
J7517	MYCOPHENOLATE MOFETIL, ORAL, 250 MG
J7518	MYCOPHENOLIC ACID, ORAL, 180 MG
J7520	SIROLIMUS, ORAL, 1 MG
J7525	TACROLIMUS, PARENTERAL, 5 MG
J7527	EVEROLIMUS, ORAL, 0.25 MG
J7599	IMMUNOSUPPRESSIVE DRUG, NOT OTHERWISE CLASSIFIED
J8530	CYCLOPHOSPHAMIDE; ORAL, 25 MG
J8610	METHOTREXATE; ORAL, 2.5 MG
Q0510	PHARMACY SUPPLY FEE FOR INITIAL IMMUNOSUPPRESSIVE DRUG(S), FIRST MONTH FOLLOWING TRANSPLANT
Q0511	PHARMACY SUPPLY FEE FOR ORAL ANTI-CANCER, ORAL ANTI-EMETIC OR IMMUNOSUPPRESSIVE DRUG(S); FOR THE FIRST PRESCRIPTION IN A 30-DAY PERIOD
Q0512	PHARMACY SUPPLY FEE FOR ORAL ANTI-CANCER, ORAL ANTI-EMETIC OR IMMUNOSUPPRESSIVE DRUG(S); FOR A SUBSEQUENT PRESCRIPTION IN A 30-DAY PERIOD

Refill Requirements:

For DMEPOS items and supplies provided on a recurring basis, billing must be based on prospective, not retrospective use. For DMEPOS products that are supplied as refills to the original order, suppliers must contact the beneficiary prior to dispensing the refill and not automatically ship on a pre-determined basis, even if authorized by the beneficiary. This shall be done to ensure that the refilled item remains reasonable and necessary, existing supplies are approaching exhaustion, and to confirm any changes or modifications to the order. Contact with the beneficiary or designee regarding refills must take place no sooner than 14 calendar days prior to the delivery/shipping date. For delivery of refills, the supplier must deliver the DMEPOS product no sooner than 10 calendar days prior to the end of usage for the current product. This is regardless of which delivery method is utilized. (CMS Program Integrity Manual, Internet-Only Manual, CMS Pub. 100-8, Chapter 5, Section 5.2.6).

For all DMEPOS items that are provided on a recurring basis, suppliers are required to have contact with the beneficiary or caregiver/designee prior to dispensing a new supply of items. Suppliers must not deliver refills without a refill request from a beneficiary. Items delivered without a valid, documented refill request will be denied as not reasonable and necessary.

Suppliers must not dispense a quantity of supplies exceeding a beneficiary's expected utilization. Suppliers must stay attuned to changed or atypical utilization patterns on the part of their clients. Suppliers must verify with the ordering physicians that any changed or atypical utilization is warranted. Regardless of utilization, a supplier must not dispense more than a 1-month quantity at a time.

Black Box Warning:

Azasan Oral (Tablet)
Chronic immunosuppression with azathioprine, a purine antimetabolite, increases risk of malignancy in humans. Reports of malignancy include post-transplant lymphoma and hepatosplenic T-cell lymphoma (HSTCL) in patients with inflammatory bowel disease. Physicians using this drug should be very familiar with this risk as well as with the mutagenic potential to both men and women and with possible hematologic toxicities. Physicians should inform patients of the risk of malignancy with azathioprine.

Cellcept Oral (Capsule; Tablet; Powder for Suspension)
Increased susceptibility to infection and the possible development of lymphoma may result from immunosuppression. Only physicians experienced in immunosuppressive therapy and management of organ transplant recipients should prescribe, and they should have complete information requisite for the follow-up of the patient. Female contraception must be used due to increased risk of congenital malformations and pregnancy loss.

Zortress(R): Increased susceptibility to infection and the possible development of lymphoma and other malignancies may result from immunosuppression. Only physicians experienced in immunosuppressive therapy and management of transplant patients should prescribe everolimus. Reduced doses of cyclosporine should be used in combination with everolimus in order to reduce renal dysfunction and monitoring of cyclosporine and everolimus whole blood trough concentrations is recommended. The use of everolimus has resulted an increase risk of graft loss within the first 30 days posttransplantation. Use in heart transplantation is not recommended.

Neoral Oral (Capsule, Liquid Filled; Solution)

Cyclosporine, a systemic immunosuppressant, may increase the susceptibility to infection and development of neoplasia. Hypertension and nephrotoxicity can occur at recommended dosages, and the risk increases with increasing dose and duration of cyclosporine therapy. Monitor blood levels and renal function to avoid toxicity. Neoral(R) and Sandimmune(R) are not bioequivalent and cannot be used interchangeably without physician supervision. Psoriasis patients previously treated with PUVA and to a lesser extent, methotrexate or other immunosuppressive agents, UVB, coal tar, or radiation therapy, are at an increased risk of developing skin malignancies when taking cyclosporine

Prograf Intravenous (Solution)

Increased susceptibility to infection and the possible development of lymphoma and other malignancies may result from immunosuppression. Only physicians experienced in immunosuppressive therapy and management of organ transplant patients should prescribe, and they should have complete information requisite for the follow-up of the patient [6].

Prograf Oral (Capsule)

Increased susceptibility to infection and the possible development of lymphoma and other malignancies may result from immunosuppression. Only physicians experienced in immunosuppressive therapy and management of organ transplant patients should prescribe, and they should have complete information requisite for the follow-up of the patient [6].

Prograf Topical (Ointment)

Long-term safety of topical calcineurin inhibitors has not been established and rare cases of malignancy (eg, skin and lymphoma) have been reported in patients treated with topical calcineurin inhibitors, including tacrolimus ointment. Avoid continuous long-term use in any age group, and apply to limited areas of involvement with atopic dermatitis. Not indicated for use in children less than 2 years of age. Only 0.03% tacrolimus ointment is indicated for use in children 2-15 years of age.

Rapamune Oral (Tablet; Solution)

Increased susceptibility to infection and the possible development of lymphoma and other malignancies may result from immunosuppression. Only physicians experienced in immunosuppressive therapy and management of renal transplant patients should prescribe sirolimus, and they should have complete information requisite for the follow-up of the patient. The use of sirolimus in combination with cyclosporine or tacrolimus was associated with excess mortality, graft loss, and hepatic artery thrombosis in studies in de novo liver transplant patients. Cases of bronchial anastomotic dehiscence, most fatal, have been reported in de novo lung transplant patients when sirolimus has been used as part of an immunosuppressive regimen. The safety and efficacy of sirolimus as immunosuppressive therapy have not been established in liver or lung transplant patients, and therefore, such use is not recommended.

Sandimmune Intravenous (Solution)

Cyclosporine should be administered with adrenal corticosteroids but not with other immunosuppressive agents. Increased susceptibility to infection and the possible development of lymphoma may result from immunosuppression. SANDIMMUNE(R) and NEORAL(R) are not bioequivalent and cannot be used interchangeably without physician supervision. Monitor cyclosporine blood levels to avoid toxicity due to high levels and possible organ rejection due to low levels as a result of the erratic absorption of cyclosporine during chronic administration of SANDIMMUNE ®

Sandimmune Oral (Capsule; Capsule, Liquid Filled; Solution)

Cyclosporine should be administered with adrenal corticosteroids but not with other immunosuppressive agents. Increased susceptibility to infection and the possible development of lymphoma may result from immunosuppression. SANDIMMUNE(R) and NEORAL(R) are not bioequivalent and cannot be used interchangeably without physician supervision. Monitor cyclosporine blood levels to avoid toxicity due to high levels and possible organ rejection due to low levels as a result of the erratic absorption of cyclosporine during chronic administration of SANDIMMUNE®

Definitions:

HCPCS Code—Healthcare Common Procedure Coding System - A system of letter and number codes assigned to procedures, medications, supplies and equipment used for pricing and billing.

ICD-9 Code—International Classification of Disease, 9th edition. A standardized classification of disease, injuries, and causes of death, by etiology and anatomic localization and codified into a 6-digit number, which allows clinicians, statisticians, politicians, health planners and others to speak a common language, both US and internationally.

References:

1. Local Coverage Determination (L11521) (Revision 3) available at http://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=11521&ContrId=140&ver=47&ContrVer=2&Date=01%2f01%2f2013&DocID=L11521&bc=iAAAAAgAAAAAAA%3d%3d& Accessed March 19, 2013.
2. Micromedex Website available at http://www.thomsonhc.com.ezproxy.samford.edu/micromedex2/librarian/ND_T/evidencexpert/ND_PR/evidencexpert/CS/F9267F/ND_AppProduct/evidencexpert/DUPLICATIONSHIELDSYNC/6E2661/ND_PG/evidencexpert/ND_B/evidencexpert/ND_P/evidencexpert/PFActionId/evidencexpert.DisplayDrugpointDocument?docId=928039&contentSetId=100&title=Mycophenolate+Sodium&servicesTitle=Mycophenolate+Sodium&topicId=dosingAndIndicationsSection&subtopicId=fdaSection. Accessed July 25, 2012.
3. Myfortic Package Insert available at http://www.pharma.us.novartis.com/product /pi/pdf/myfortic.pdf. Accessed July 25, 2012.
4. Azasan Package Insert available at http://www.salix.com/assets/pdf/prescribe_info/azasanpi.pdf. Accessed July 23, 2012.
5. Micromedex Website available at http://www.thomsonhc.com.ezproxy.samford.edu/micromedex2/librarian/ND_T/evidencexpert/ND_PR/evidencexpert/CS/4B0649/ND_AppProduct/evidencexpert/DUPLICATIONSHIELDSYNC/823D19/ND_PG/evidencexpert/ND_B/evidencexpert/ND_P/evidencexpert/PFActionId/evidencexpert.DoIntegratedSearch?SearchTerm=azasan. Accessed July 23, 2012.
6. CellCept Package Insert available at http://www.gene.com/gene/product s/information/cellcept /pdf/pi.pdf. Accessed July 23, 2012.
7. Micromedex Website. Available at: http://www.thomsonhc.com.ezproxy.samford.edu/micromedex2/librarian/ND_T/evidencexpert/ND_PR/evidencexpert/CS/10D07A/ND_AppProduct/evidencexpert/DUPLICATIONSHIELDSYNC/E6015A/ND_PG/evidencexpert/ND_B/evidencexpert/ND_P/evidencexpert/PFActionId/evidencexpert.GoToDashboard?docId=923344&contentSetId=100&title=Mycophenolate+Mofetil&servicesTitle=Mycophenolate+Mofetil&brandName=Cellcepthttp://www.thomsonhc.com.ezproxy.samford.edu/micromedex2/librarian/ND_T/evidencexpert/ND_PR/evidencexpert/CS/10D07A/ND_AppProduct/evidencexpert/DUPLICATIONSHIELDSYNC/E6015A/ND_PG/evidencexpert/ND_B/evidencexpert/ND_P/evidencexpert/PFActionId/evidencexpert.GoToDashboard?docId=923344&contentSetId=100&title=Mycophenolate+Mofetil&servicesTitle=Mycophenolate+Mofetil&brandName=Cellcept. Accessed July 25, 2012.
8. Micromedex Website available at http://www.thomsonhc.com.ezproxy.samford.edu/micromedex2/librarian/ND_T/evidencexpert/ND_PR/evidencexpert/CS/177670/ND_AppProduct/evidencexpert/DUPLICATIONSHIELDSYNC/98DA7D/ND_PG/evidencexpert/ND_B/evidencexpert/ND_P/evidencexpert/PFActionId/evidencexpert.Displa

yDrugpointDocument?docId=927997&contentSetId=100&title=Cyclosporine%2C+Modified&servicesTitle=Cyclosporine%2C+Modified&topicId=blackBoxWarningSection&subtopicId=null. Accessed July 25, 2012.

9. Neoral Package Insert available at http://www.pharma.us.novartis.com/product/pi/pdf/neoral.pdf. Accessed July 25, 2012.
10. Micromedex Website available at http://www.thomsonhc.com.ezproxy.samford.edu/micromedex2/librarian/ND_T/evidencexpert/ND_PR/evidencexpert/CS/CF2C89/ND_AppProduct/evidencexpert/DUPLICATIONSHIELDSYNC/88F125/ND_PG/evidencexpert/ND_B/evidencexpert/ND_P/evidencexpert/PFActionId/evidencexpert.DisplayDrugpointDocument?docId=922304&contentSetId=100&title=Tacrolimus&servicesTitle=Tacrolimus&topicId=dosingAndIndicationsSection&subtopicId=fdaSection. Accessed July 25, 2012.
11. Prograf Package Insert available at http://www.astellas.us/docs/prograf.pdf. Accessed July 25, 2012.
12. Micromedex Website available at http://www.thomsonhc.com.ezproxy.samford.edu/micromedex2/librarian/ND_T/evidencexpert/ND_PR/evidencexpert/CS/D7A366/ND_AppProduct/evidencexpert/DUPLICATIONSHIELDSYNC/678350/ND_PG/evidencexpert/ND_B/evidencexpert/ND_P/evidencexpert/PFActionId/evidencexpert.DisplayDrugpointDocument?docId=925033&contentSetId=100&title=Sirolimus&servicesTitle=Sirolimus&topicId=dosingAndIndicationsSection&subtopicId=fdaSection. Accessed July 26, 2012.
13. Rapamune Package Insert available at https://www.rapamune.com/files/ Rapamune _US_PI_ July_2011.pdf. Accessed July 26, 2012.
14. Micromedex Website available at http://www.thomsonhc.com.ezproxy.samford.edu/micromedex2/librarian/ND_T/evidencexpert/ND_PR/evidencexpert/CS/1C0E18/ND_AppProduct/evidencexpert/DUPLICATIONSHIELDSYNC/C2738E/ND_PG/evidencexpert/ND_B/evidencexpert/ND_P/evidencexpert/PFActionId/evidencexpert.DisplayDrugpointDocument?docId=151625&contentSetId=100&title=Cyclosporine&servicesTitle=Cyclosporine&topicId=dosingAndIndicationsSection&subtopicId=nonfdaSection. Accessed July 26, 2012.
15. Sandimmune Package Insert available at http://www.pharma.us.novartis.com/ product/pi/pdf /sandimmune.pdf. Accessed July 26, 2012.
16. Micromedex Website available at http://www.thomsonhc.com.ezproxy.samford.edu/micromedex2/librarian/ND_T/evidencexpert/ND_PR/evidencexpert/CS/C52CC6/ND_AppProduct/evidencexpert/DUPLICATIONSHIELDSYNC/2174BD/ND_PG/evidencexpert/ND_B/evidencexpert/ND_P/evidencexpert/PFActionId/evidencexpert.DisplayDrugpointDocument?docId=929332&contentSetId=100&title=Everolimus&servicesTitle=Everolimus&topicId=dosingAndIndicationsSection&subtopicId=fdaSection. Accessed July 26, 2012.
17. Zortress Package Insert available at http://www.pharma.us.novartis.com/product/pi/pdf/zortress.pdf. Accessed July 26, 2012.

Document History:

Date Written: 8/7/12
Effective Date: 4/1/13
Revision 1: 3/19/2013
Internal Review: 3/24/2013
External Review: 3/26/2013

For the Archived Policy, please go to http://www.vivaprovider.com/Resources/CoveragePolicies.aspx and click on the Archived Policies Link.