Original Effective Date: 10/01/2016
Current Effective Date: 12/28/2022
Last P&T Approval/Version: 10/26/2022
Next Review Due By: 10/2023
Policy Number: C9720-A

Zortress (everolimus)

PRODUCTS AFFECTED

Zortress (everolimus), everolimus

COVERAGE POLICY

Coverage for services, procedures, medical devices, and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.
This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Prophylaxis of organ rejection

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by-case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review.

A. PROPHYLAXIS OF KIDNEY TRANSPLANT REJECTION:
1. Documentation member has had a kidney transplant
   AND
2. Documentation Member is NOT at high immunological risk: [One or more human leukocyte antigen (HLA) mismatches; Younger recipient, and older donor age; African American ethnicity (in the United States); Panel reactive antibody (PRA) greater than 0 percent; Presence of a donor-specific

antibody (DSA); Blood group incompatibility; Delayed onset of graft function; Cold ischemia time greater than 24 hours]
AND
3. Documentation of trial and failure (toxicity or signs of rejection) of an anti-rejection regimen containing TWO of the following: cyclosporine, tacrolimus, azathioprine, mycophenolate, corticosteroids
AND
4. Prescriber attests Zortress will be used in combination with basiliximab (Simulect), cyclosporine, and corticosteroids

B. PROPHYLAXIS OF LIVER TRANSPLANT REJECTION:
1. Documentation member has had a liver transplant
AND
2. Documentation that member is at least 30 days post-transplant
AND
3. Documentation of trial and failure (toxicity or signs of rejection) of an anti-rejection regimen containing TWO of the following: cyclosporine, tacrolimus, azathioprine, mycophenolate, corticosteroids
AND
4. Prescriber attests Zortress will be used in combination with tacrolimus and corticosteroids

CONTINUATION OF THERAPY:
A. PROPHYLAXIS OF ORGAN REJECTION:
1. Documentation member is responsive to therapy demonstrated by no signs or symptoms of acute/chronic organ rejection

DURATION OF APPROVAL:
Initial authorization: 6 months, Continuation of therapy: 12 months

PRESCRIBER REQUIREMENTS:
Prescribed by or in consultation with a transplant specialist. [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:
18 years of age or older

QUANTITY:
No requirements

PLACE OF ADMINISTRATION:
The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Oral

DRUG CLASS:
Macrolide Immunosuppressants

FDA-APPROVED USES:
Indicated for the prophylaxis of organ rejection in adult patients: *Kidney Transplant:* at low-moderate immunologic risk. Use in combination with basiliximab, cyclosporine (reduced doses) and

corticosteroids. *Liver Transplant:* Administer no earlier than 30 days post-transplant. Use in combination with tacrolimus (reduced doses) and corticosteroids.

Limitations of Use:
The safety and efficacy of Zortress has not been established in the following populations:

- Kidney transplant patients at high immunologic risk
- Recipients of transplanted organs other than kidney and liver
- Pediatric patients (less than 18 years).

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
None

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Zortress (everolimus) are considered experimental/investigational and therefore, will follow Molina's Off-Label policy. Contraindications to Zortress (everolimus) include: hypersensitivity to everolimus, sirolimus, or to components of the dug product, concurrent use of live vaccines.

OTHER SPECIAL CONSIDERATIONS:
Blackbox warning for malignancies and serious infections, kidney graft thrombosis; nephrotoxicity; and mortality in heart transplantation

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
N/A	

AVAILABLE DOSAGE FORMS:
Zortress TABS 0.25MG, 0.5MG, 0.75MG, 1MG
Everolimus TABS 0.25MG, 0.5MG, 0.75MG, 1MG

REFERENCES

1. Zortress [package insert]. Novartis. East Hanover, NJ. January 2021.
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3. Bortman GV, Ceruti B, Ahualli L, et al. South American Transplantation Registry of

PatientsReceiving Everolimus in Their Immunosuppressive Regimens. Trans Proceedings. 2010;42:324- 27.
4. Sanchez-Brotons JA, Sobrino-Marquez JM, Lage-Galle E, et al. Preliminary Experience with Conversion from Calcineurin Inhibitors to Everolimus in Cardiac Transplantation Maintenance Therapy. Trans Proceedings. 2008;40:3046-48.
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6. Lehmkuhl HB, Arizon J, Vigano M, et al. Everolimus with Reduced Dose Cyclosporine Versus MMF with Standard Cyclosporine in De Novo Heart Transplant Recipients. Transplantation. 2009;88:115- 122.
7. Gullestad L, Iversen M, Mortensen SA, et al. Everolimus with Reduced Calcineurin Inhibitor in Thoracic Transplant Recipients with Renal Dysfunction: A Mulricenter, Randomized Trial. Transplantation. 2010;89:864-872.
8. Simone PD, Metselaar HJ, Fischer L, et al. Conversion from a Calcineurin Inhibitor to Everolimus Therapy in Maintenance Liver Transplant Recipients: A Prospective, Randomized, Multicenter Trial. Liver Trans. 2009;15:1262-69.
9. Castroagudin JF, Molina E, Romero R, et al. Improvement of Renal Function After the Switch from a Calcineurin Inhibitor to Everolimus in Liver Transplant Recipients with Chronic Renal Dysfunction. Liver Trans. 2009;15:1792-97.
10. Bilbao I, Sapisochin G, Dopazo C, et al. Indications and Management of Everolimus after Liver Transplantation. Trans Proceedings. 2009;41:2172-76

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Products Affected Required Medical Information Contraindications/Exclusions/Discontinuation Available Dosage Forms	Q4 2022
Q2 2022 Established tracking in new format	Historical changes on file