Pharmacy Policy Bulletin

Title: Everolimus (Zortress®)

Policy #: Rx.01.31

Application of pharmacy policy is determined by benefits and contracts. Benefits may vary based on product line, group, or contract. Some medications may be subject to precertification, age, gender or quantity restrictions. Individual member benefits must be verified.

This pharmacy policy document describes the status of pharmaceutical information and/or technology at the time the document was developed. Since that time, new information relating to drug efficacy, interactions, contraindications, dosage, administration routes, safety, or FDA approval may have changed. This Pharmacy Policy will be regularly and updated as scientific and medical literature becomes available. This information may include new FDA-approved indications, withdrawals, or other FDA alerts. This type of information is relevant not only when considering whether this policy should be updated, but also when applying it to current requests for coverage.

Members are advised to use participating pharmacies in order to receive the highest level of benefits.

Intent:

Everolimus (Zortress®) is indicated for the prophylaxis of organ rejection in adult patients at low-moderate immunologic risk receiving a kidney transplant.

The use of Everolimus (Zortress®) requires prior authorization (i.e. clinical pharmacy and/or Medical Director review).

Description:

Everolimus (Zortress®) inhibits antigenic and interleukin (IL-2 and IL-15) stimulated activation and proliferation of T and B lymphocytes. In cells, everolimus binds to a cytoplasmic protein, the FK506 binding protein-12 (FKBP-12), to form an immunosuppressive complex (everolimus:FKBP-12) that binds to and inhibits the mammalian target of rapamycin (mTOR), a key regulatory kinase. In the presence of everolimus phosphorylation of p70 S6 ribosomal protein kinase (p70S6K), a substrate of mTOR, is inhibited. Consequently, phosphorylation of the ribosomal S6 protein and subsequent protein synthesis and cell proliferation are inhibited. The everolimus:FKBP-12 complex has no effect on calcineurin activity.

Policy:

Everolimus (Zortress®) is approved when **all** of the following inclusion criteria are met:

- Documentation of at least 18 years of age
- Documenation of a diagnosis for the prevention of organ rejection of kidney transplants in adult patients at low to moderate immunologic risk
- Documentation that Zortress is given in combination with reduced doses of the calcineurin inhibitor (CNI) cyclosporine and corticosteroids

Guidelines:

Refer to the specific manufacturer's prescribing information for administration and dosage details and any applicable Black Box warnings.

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable benefit contract, the applicable drug(s) identified in this policy is (are) covered under the pharmacy benefits of the Company's products when the medical necessity criteria listed in this pharmacy policy are met. Any services that are experimental/investigational or cosmetic are benefit contract exclusions for all products of the Company.

References:

Everolimus (Zortress). In: Facts and Comparisons [online through Facts and Comparisons Online]. Indy, IN: Walter Kluwer Health Inc. Accessed December 06, 2010.

Everolimus (Zortress). In: Drugdex [online through Micromedex Healthcare Series]. Greenwood Village, CO: Thomson Micromedex. Accessed December 06, 2010.

Zortress (Everolimus) [package insert]. East Hanover, NJ: Novartis Pharmaceutical Co; March 2010.

Applicable Drugs:

Inclusion of a drug in this table does not imply coverage. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

Brand Name	Generic Name
Zortress	Everolimus

Cross References:

Policy Version Number:	1.00
P&T Approval Date:	November 10, 2011
Policy Effective Date:	February 01, 2012
Next Required Review Date:	November 10, 2012