Prior Authorization DRUG Guidelines

ZORTRESS (everolimus)

Effective Date: 10/20/2014
Date Developed: 10/14/2014
Last Approval Date: 01/26/16, 01/24/17
(Archive Date: 1/1/18)

Description: Zortress is a macrolide derivative which inhibits T-lymphocyte activation. The exact mechanism of action is not known. Experimental evidence suggests that Zortress binds to an intracellular protein, FKBP-12. A complex of tacrolimus-FKBP-12, calcium, calmodulin, and calcineurin is then formed and the phosphatase activity of calcineurin inhibited. This effect may prevent the dephosphorylation and translocation of nuclear factor of activated T-cells (NF-AT), a nuclear component thought to initiate gene transcription for the formation of lymphokines (such as interleukin-2, gamma interferon). The net result is the inhibition of T-lymphocyte activation (i.e., immunosuppression).

Authorization Criteria: Prophylaxis of organ rejection in liver transplants in adult patients in combination with corticosteroids and reduced doses of tacrolimus; and prophylaxis of organ rejection in renal transplants in adult patients at low to moderate immunologic risk in combination with basiliximab induction and concurrent with corticosteroids and reduced doses of cyclosporine.

Unlabeled Uses: Treatment of relapsed or refractory Waldenström’s macroglobulinemia; treatment of progressive advanced carcinoid tumors.

Note: Per VCHCP policy, unlabeled uses are not covered unless specific information is submitted. See VCHCP Policy on Coverage of Prescription Medication for Off-Label Use.

Dosing: Kidney 0.75 mg orally twice daily in combination with reduced dose cyclosporine and prednisone, administered as soon as possible after transplantation

Liver 1 mg orally twice daily in combination with reduced-dose tacrolimus, at least 30 days after transplantation

How Supplied: Tablets 0.25, 0.5, 0.75 mg

Contraindications/Warnings: Increased mortality often associated with serious infections within the first three months post-cardiac transplantation, therefore use of Zortress in heart
transplantation is not recommended; monitor drug levels if used with CYP3A4 medications; avoid live vaccines;

**Major Adverse Reactions:** Kidney graft thrombosis; hepatic artery thrombosis; serious infections; lymphomas/skin cancers; angioedema; delayed wound healing; hyperlipidemia; concomitant use of Zortress with cyclosporine may increase the risk of thrombotic microangiopathy/thrombotic thrombocytopenic purpura/hemolytic uremic syndrome

**Major Drug Interactions:** ACE inhibitors (increased risk of angioedema); CYP3a inducers (e.g., rifampin, rifabutin) and inhibitors (e.g., ketoconazole, itraconazole, voriconazole, clarithromycin, telithromycin, ritonavir, boceprevir, telaprevir, grapefruit juice) affect everolimus blood levels.

**REFERENCES**

1. Afinitor and Afinitor Disperz (everolimus) [prescribing information]. East Hanover, NJ: Novartis Pharmaceutical Co; February 2014.

**NOTE:** For those so disposed or curious, the chemical name of everolimus is:
**Revision History:**
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