BlueCross BlueShield
Federal Employee Program

AFINITOR and, AFINITOR DISPERZ, **TORPENZ** (**everolimus**)

Preferred products: generic everolimus, Torpenz

RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Everolimus (Afinitor, Afinitor Disperz, and Torpenz) is a macrolide immunosuppressant and a mechanistic target of rapamycin (mTOR) inhibitor which helps control cell division and reduce the growth of new blood vessels. The mTOR pathway is dysregulated in several human cancers and in tuberous sclerosis complex (TSC). Everolimus reduces protein creation and cell growth by binding to the FK binding protein-12 (FKBP-12), an intracellular protein, to form a complex that inhibits activation of mTOR (mechanistic target of rapamycin) serine-threonine kinase activity. Inhibition of mTOR by everolimus has been shown to reduce cell proliferation, angiogenesis, and glucose uptake in in vitro and/or in vivo studies (1-3).

Regulatory Status

FDA-approved indications:

Afinitor is a kinase inhibitor that is indicated for: (2)

1. Postmenopausal women with advanced hormone receptor-positive (HR-positive), HER2-negative breast cancer in combination with exemestane after failure of treatment with letrozole or anastrozole.
2. Adults with progressive neuroendocrine tumors of pancreatic origin (PNET) and adults with progressive, well-differentiated, non-functional neuroendocrine tumors (NET) of gastrointestinal (GI) or lung origin that are unresectable, locally advanced or metastatic.
3. Adults with advanced renal cell carcinoma (RCC) after failure of treatment with sunitinib or sorafenib.
4. Adults with renal angiomyolipoma and tuberous sclerosis complex (TSC), not requiring immediate surgery.

Afinitor Disperz is a kinase inhibitor indicated for: (2)

1. The treatment of adult and pediatric patients aged 2 years and older with TSC-associated partial-onset seizures.

Torpenz is a kinase inhibitor indicated for: (3)

1. Postmenopausal women with advanced hormone receptor-positive (HR-positive), HER2-negative breast cancer (advanced HR+ BC) in combination with exemestane after failure of treatment with letrozole or anastrozole.

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2. Adults with renal angiomyolipoma and tuberous sclerosis complex (TSC), not requiring immediate surgery.

Afinitor, Afinitor Disperz and Torpenz are kinase inhibitors indicated for the treatment of: (2-3)

1. Pediatric and adult patients with tuberous sclerosis complex (TSC) who have subependymal giant cell astrocytoma (SEGA) that requires therapeutic intervention but cannot be curatively resected.

Limitations of Use: (2-3)

Afinitor and Torpenz are not indicated for the treatment of patients with functional carcinoid tumors.

Off-Label Uses for Afinitor and Torpenz: (4-5)

Through randomized control trials and phase II studies, Afinitor has been found effective in the following disease states:

1. Lung neuroendocrine tumors
2. Waldenstrom's macroglobulinemia/lymphoplasmacytic lymphoma
3. Soft Tissue sarcoma:
    a. Perivascular epithelioid cell tumors (PEComa)
    b. Recurrent angiomyolipoma
    c. Lymphangioleiomyomatosis
4. Classical Hodgkin lymphoma
5. Advanced HR-positive, HER2-negative breast cancer
    a. Used in combination with exemestane that progressed within 12 months, has been previously treated with a nonsteroidal aromatase inhibitor, or previously treated with tamoxifen
    b. Used in combination with an endocrine agent (e.g., exemestane, faslodex, or tamoxifen)
6. Gastrointestinal (GI) neuroendocrine tumors – metastatic or unresectable progressive disease
7. Thymus neuroendocrine tumors: metastatic or unresectable progressive disease
8. Osteosarcoma
9. Thymomas/Thymic carcinomas
10. Thyroid carcinoma: Papillary, Hürthle cell, and follicular thyroid carcinoma

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11. Relapse or stage IV RCC:
    a. Systemic therapy for non-clear cell histology
    b. Subsequent therapy for predominant clear cell histology
12. Gastrointestinal stromal tumors (GIST): treatment in combination with either imatinib, sunitinib, or regorafenib for disease progression after single-agent therapy with imatinib, sunitinib, and regorafenib
13. Endometrial carcinoma: in combination with letrozole

Summary

Everolimus (Afinitor, Afinitor Disperz, and Torpenz) is a macrolide immunosuppressant and a mechanistic target of rapamycin (mTOR) inhibitor which helps control cell division and reduce the growth of new blood vessels. The mTOR pathway is dysregulated in several human cancers and in tuberous sclerosis complex (TSC). Inhibition of mTOR by everolimus has been shown to reduce cell proliferation, angiogenesis, and glucose uptake in in vitro and/or in vivo studies (1-3).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Afinitor, Afinitor Disperz, and Torpenz while maintaining optimal therapeutic outcomes.

References

1. Everolimus. Drug Facts and Comparisons. eFacts [online]. 2021. Available from Wolters Kluwer Health, Inc.
2. Afinitor/Afinitor Disperz [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; February 2022.
3. Torpenz [package insert]. Maple Grove, MN: Upsher-Smith Laboratories, LLC; March 2024.
4. NCCN Drugs & Biologics Compendium® Everolimus 2025. National Comprehensive Cancer Network, Inc. Accessed on January 15, 2025.
5. Royce M, Bachelot T, Villaneuva C, et al. Everolimus Plus Endocrine Therapy for Postmenopausal Women with Estrogen Receptor-Positive, Human Epidermal Growth Factor Receptor 2-negative Advanced breast Cancer. JAMA Oncol. 2018;4(7): 977-984.