Reference number
2021-A

SPECIALTY GUIDELINE MANAGEMENT

AFINITOR (everolimus)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications[1]
1. Postmenopausal women with advanced hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (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 (pNETs) that are unresectable, locally advanced or metastatic
3. Adults with progressive, well-differentiated, non-functional neuroendocrine tumors of gastrointestinal or lung origin that are unresectable, locally advanced or metastatic
4. Adults with advanced renal cell carcinoma (RCC) after failure of treatment with sunitinib or sorafenib
5. Adults with renal angiomyolipoma and tuberous sclerosis complex (TSC), not requiring immediate surgery
6. Adults and pediatric patients with tuberous sclerosis complex (TSC) who have subependymal giant cell astrocytoma (SEGA) that requires therapeutic intervention but cannot be curatively resected
7. Adjunctive treatment of adult and pediatric patients aged 2 years and older with TSC-associated partial-onset seizures

B. Compendial Uses[2]
1. Relapsed or surgically unresectable stage IV renal cell carcinoma:
   a. Systemic therapy for non-clear cell histology
   b. Subsequent therapy for predominant clear cell histology
2. Soft tissue sarcoma subtypes:
   a. Perivascular epithelioid cell tumors (PEComa)
   b. Recurrent angiomyolipoma
   c. Lymphangioleiomyomatosis
   d. Gastrointestinal stromal tumors
3. Neuroendocrine tumor of the thymus
4. Thymomas and thymic carcinomas
5. Osteosarcoma
6. Classical Hodgkin lymphoma
7. Papillary, Hürthle cell, and follicular thyroid carcinoma
8. Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma
9. Endometrial carcinoma
10. Recurrent or stage IV hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer in combination with exemestane, fulvestrant, or tamoxifen in patients who have had prior endocrine therapy within 1 year.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Breast Cancer[1,2-5]
Authorization of 12 months may be granted for treatment of hormone receptor HR-positive, human epidermal growth factor receptor 2 (HER2)-negative recurrent or metastatic breast cancer when prescribed in combination with exemestane, fulvestrant, or tamoxifen and the patient has received endocrine therapy within 1 year.

B. Renal Cell Carcinoma[1,2,6]
Authorization of 12 months may be granted for treatment of relapsed, metastatic, or unresectable RCC when either of the following criteria are met:
1. Disease is of non-clear cell histology.
2. Disease is of predominantly clear cell histology and has progressed on prior therapy.

C. Neuroendocrine Tumors[1,2]
Authorization of 12 months may be granted for treatment of neuroendocrine tumors of pancreatic, gastrointestinal, lung, or thymic origin.

D. Renal Angiomyolipoma, Subependymal Giant Cell Astrocytoma, or Partial-Onset Seizures Associated With Tuberous Sclerosis Complex (TSC)[1,7]
Authorization of 12 months may be granted for treatment of renal angiomyolipoma, subependymal giant cell astrocytoma, or partial-onset seizures associated with TSC.

E. Soft Tissue Sarcoma[2,8]
Authorization of 12 months may be granted for treatment of any of the following subtypes of soft tissue sarcoma: perivascular epithelioid cell (PEComa), angiomyolipoma, lymphangioleiomyomatosis or gastrointestinal stromal tumors.

F. Thymomas and Thymic Carcinomas[2,9]
Authorization of 12 months may be granted for treatment of thymomas and thymic carcinomas.

G. Osteosarcoma[2]
Authorization of 12 months may be granted for treatment of osteosarcoma.

H. Classical Hodgkin Lymphoma[2,10,11]
Authorization of 12 months may be granted for treatment of classical Hodgkin lymphoma.

I. Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma[2,12]
Authorization of 12 months may be granted for treatment of Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma.

J. Thyroid Carcinoma[2,13]
Authorization of 12 months may be granted for treatment of thyroid carcinoma with any of the following histologies: papillary, Hurthle cell, follicular.

K. Endometrial Carcinoma[14]
Authorization of 12 months may be granted for treatment of endometrial carcinoma.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Afinitor [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; April 2018.
2. The NCCN Drugs & Biologics Compendium® © 2018 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed May 22, 2018.
3. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Breast Cancer. Version 1.2018. Accessed May 22, 2018. https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf.
4. Baselga J, Campone M, Piccart M, et al. Everolimus in postmenopausal hormone-receptor–positive advanced breast cancer. *N Engl J Med*. 2012;366(6):520-529.
5. Yardley DA, Noguchi S, Pritchard KI, et al. Everolimus plus exemestane in postmenopausal patients with HR(+) breast cancer: BOLERO-2 final progression-free survival analysis. *Adv Ther* 2013;30:870-884.
6. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Kidney Cancer. Version 4.2018. Accessed May 22, 2018. https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf.
7. Sampson JR. Therapeutic targeting of mTOR in tuberous sclerosis. *Biochem Soc Trans*. 2009;37:259-264.
8. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Soft Tissue Sarcoma. Version 2.2018. Accessed May 22, 2018. https://www.nccn.org/professionals/physician_gls/pdf/sarcoma.pdf.
9. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Thymomas and Thymic Carcinomas. Version 2.2018. Accessed May 22, 2018. https://www.nccn.org/professionals/physician_gls/pdf/thymic.pdf.
10. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Hodgkin Lymphoma. Version 3.2018. Accessed May 22, 2018. https://www.nccn.org/professionals/physician_gls/pdf/hodgkins.pdf.
11. Johnston PB, Inwards DJ, Colgan JP, et al. A Phase II trial of the oral mTOR inhibitor everolimus in relapsed Hodgkin lymphoma. *Am J Hematol* 2010;85:320-324.
12. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma. Version 1.2018. Accessed May 22, 2018. https://www.nccn.org/professionals/physician_gls/pdf/waldenstroms.pdf.
13. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Thyroid Carcinoma. Version 1.2018. Accessed May 22, 2018. https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf.
14. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Uterine Neoplasms. Version 1.2018. Accessed May 22, 2018. https://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf.

DOCUMENT HISTORY

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Reviewed:	CDPR: 04/2009, WLF 06/2009; KP 05/2010, 11/2010, 05/2011, 08/2011, 02/2012, 03/2012, 05/2012, 08/2012; DNC 07/2013, MCM 08/2014; ADA 08/2015, LCB 11/2015; DNC 03/2016, MM 05/2016, DNC 08/2016, ME 05/2017, SD 08/2017, ME 04/2018, EPA 05/2018
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