

Pharmacy Benefit Determination Policy

Policy Subject: Afinitor Policy Number: SHS PBD8 Category: Antineoplastic Policy Type: <input type="checkbox"/> Medical <input checked="" type="checkbox"/> Pharmacy Department: Pharmacy	Dates: Effective Date: June 30, 2016 Revision Date: Approval Date: April 25, 2018 Next Review Date: April 2019
Product (check all that apply): <input checked="" type="checkbox"/> Group HMO/POS <input checked="" type="checkbox"/> Individual HMO/POS <input checked="" type="checkbox"/> PPO <input checked="" type="checkbox"/> ASO	Clinical Approval By: Medical Directors Peter Graham, MD Pharmacy and Therapeutics Committee Peter Graham, MD

Policy Statement:

Physicians Health Plan, PHP Insurance & Service Company, and Sparrow PHP will cover Afinitor through the Pharmacy Benefit based on approval by the Clinical Pharmacist or Medical Director using the following determination guidelines

Drugs and Applicable Coding:

NA

Clinical Determination Guidelines:

Document the following with chart notes

A. Breast Cancer

1. Diagnosis & severity:
 - a. Postmenopausal
 - b. Advanced HR+ disease
 - c. HER2-negative
2. Other therapies: Failed or had significant adverse effects
 - a. Femora (letrozole po) OR
 - b. Arimidex (anastrozole po)
3. Dosage regimen (everolimus po)
 - a. 10mg 1x/day
 - b. Combination w Aromasin (exemestane po)
4. Approval
 - a. Initial: 6 mons
 - b. Re-approval: 6 mons until disease progression or unacceptable toxicity

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- B. Neuroendocrine Tumors
1. Diagnosis & severity:
 - a. Progressive, unresectable, locally advanced or metastatic disease
 - Pancreatic neuroendocrine tumors (PNET)
 - Well-differentiated, nonfunctional GI or lung neuro-endocrine tumors
 2. Other therapies: None
 3. Dosage regimen (everolimus po): 10mg 1x/day
 4. Approval
 - a. Initial: 6 mons.
 - b. Re-approval: 6 mons. until disease progression or unacceptable toxicity
- C. Renal Angiomyolipoma (AML)
1. Diagnosis & severity:
 - a. Tuberous sclerosis complex (TSC) AND
 - b. AML
 2. Other therapies: Failed or contraindicated
 - a. Surgery: AML's > 4cm; symptoms refractory to conservative measures; high suspicion of malignancy
 - b. Radiofrequency ablation & cryo-ablation: AML's <4cm
 3. Dosage regimen (everolimus po): 10mg 1x/day
 4. Approval
 - a. Initial: 6 mons.
 - b. Re-approval: 6 mons. until disease progression or unacceptable toxicity
- D. Renal Cell Carcinoma (RCC), advanced
1. Diagnosis & severity:
 - a. Advanced RCC w predominant clear cell histology
 - b. Relapsed or medically unresectable RCC w non-clear cell histology
 2. Other: Failure or significant adverse effects (1 below)
 - a. Listed in FDA approved indication: Sutent (sunitinib po) or Nexavar (sorafenib po) OR
 - b. Not listed in indication: Votrient (pazopanib po) or Inlyta (axitinib)
 3. Dosage regimen (everolimus po): 10mg 1x/day
 4. Approval
 - a. Initial: 6 mons
 - b. Re-approval: 6mons until disease progression or unacceptable toxicity
- E. Sub-ependymal Giant Cell Astrocytoma (SEGA)
1. Diagnosis & severity:
 - a. Tuberous sclerosis complex (TSC) AND
 - b. SGCT needs intervention & not curably resectable or symptomatic/growing after surgery
 2. Other therapies: Surgery if advisable
 3. Dosage regimen:
 - a. Initial (everolimus po): 4.5mg/m² (round to the nearest 2mg tab for po susp. or 2.5mg tab)
 - b. Adjustment: Trough < 5mg/mL - ↑ 2-2.5mg/day; >5mg/mL - ↓ 2-2.5mg/day (@ lowest dose give qod)
 4. Approval
 - a. Initial: 6 mons.
 - b. Re-approval: 6 mons. until disease progression or unacceptable toxicity

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Appendix I: Patient Safety and Monitoring

Drug	Adverse Reactions	Monitoring	REMS
Afinitor everolimus	<ul style="list-style-type: none"> • CV: edema (13-39%), HTN (4-13%) • CNS: Malaise (\leq45%), fatigue (14-44%), HA (19-29%), migraine (\leq30%), behavioral problems (21%), insomnia (6-14%), dizziness (7-12%) • Derm: Skin rash (21-59%), cellulitis (29%), acne (10-22%), nail dx (5-22%), pruritus 13-20%), xeroderma (13%) • Endo/metab: \uparrowcholesterol (81-85%), \downarrow Na bicarb (56%), \uparrow tri-glycerides (27-52%), \uparrowPO3 (9-49%), \downarrowCa (37%), \downarrow albumin (13-33%), \uparrow glucose (14-25%), amenorrhea (15-17%) • GI: Stomatitis (62-78%), diarrhea (14-50%), abdominal pain (9-36%), \downarrow appetite (6-30%), N/V (15-29%), weight loss (9-28%), anorexia (25%), dysgeusia 5-22%), mucositis (19%), constipation (10-14%), xerostomia (8-11%) • GU: UTI (5-16%), irregular menses (10-11%) • Hem/Onc: \uparrow PPT, anemia (41-61%), \downarrow LYMP (45-54%), \downarrowplts (45-54%), neutropenia (46%), leukopenia (37%) • Hep: \uparrow alk phos. (32-74%), \uparrow AST (23-69%), \uparrowALT (48-51%) • MSK: Weakness (13-33%), arthralgia (13-20%), back/limb pain (8-15%) • Resp: Resp tract inf. (31%), cough (20-30%), rhinitis (25%), nasopharyngitis (6-25%), URI (5-11%), dyspnea (20-24%), epistaxis (5-22%), pneumonitis (1-19%), oral pain (11%) • Misc: Fever (15-31%), Infection (37-50%) • Preg category: C 	<ul style="list-style-type: none"> • Labs (prior & during): CBC w diff.; LFT, Cr, Urinary protein & BUN; serum glucose & lipid profile. • HEM/Onc: monitor for S & Sx of malignancy • Infection: monitor for S & Sx • Resp: Monitor S & Sx of non-infectious pneumonitis 	None Needed

References and Resources:

1. Lexicomp Online®, Lexi-Drugs®, Hudson, Ohio: Lexi-Comp, Inc.; Afinitor, accessed March 2018
2. Metastatic well-differentiated pancreatic neuroendocrine tumors: Systemic therapy options to control tumor growth and symptoms of hormone hypersecretion. UpToDate [internet] Accessed April 2016. Available from: <http://www.uptodate.com /contents/metastatic-well-differentiated-pancreatic-neuroendocrine>
3. Tuberous Sclerosis complex: Management. UpToDate [internet] Accessed April 2016. Available from: <http://www.uptodate.com /contents/tuberous-sclerosis-complex-management>
4. Renal manifestations of tuberous sclerosis complex. UpToDate [internet] Accessed April 2016. Available from: <http://www.uptodate.com /contents/renal-manifestations-of-tuberous-sclerosis-complex>.
5. Long-term everolimus treatment in individuals with tuberous sclerosis complex: a review of current literature. 2015. Pediatric Neurology: 53;23-30.

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Approved By:	
	4/25/18
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	4/25/18
Human Resources – Kurt Batteen	Date