Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Washington Pharmacy Advisory Committee Meeting

February 20, 2019

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Agenda Topics

- Overview of Disease State
- Indications
- Dosage & Formulations
- Guideline Updates

Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Oncology, Oral- Hematological

Overview of Disease State – Oncology, Oral- Hematological

- **Acute Myeloid Leukemia (AML)**
- Most common form of acute leukemia among adults estimated 5,930 cases diagnosed and 1,500 deaths in the US in 2019
- In patients who obtain a CR, 3 year survival is 45%, remission rates are inversely proportional to age
- Cytogenetics plays a large role in determining prognosis and treatment options
- Acute Promyelocytic Leukemia (APL) is a subtype of AML with distinct features and treatment
- **Chronic Myeloid Leukemia (CML)**
- Comprises 15% of all adult leukemias although does occur in all age groups, including pediatrics with an estimated 8,990 diagnosed cases and 1,140 deaths
- 3 phases of disease-chronic, accelerated and blast
- Gene mutation called the Philadelphia chromosome has been identified which involves a translocation t(9;22), also known as BCR-ABL translocation
- The discovery of tyrosine kinases that inhibit BCR-ABL has revolutionized the treatment of CML making long-term remission a reality
- **Multiple Myeloma**
- Accounts for > 15% of all hematologic malignancies with 32,110 projected diagnoses and 12,960 deaths projected in 2019
- Usually responds to initial chemotherapy but responses are often transient and patients often receive re-treatment with multiple different agents

Overview of Disease State – Oncology, Oral- Hematological

- **Multiple Myeloma, continued**
- Malignant neoplasm of plasma cells resulting in accumulation of plasma cells in the bone marrow
- Constellation of symptoms associated with multiple myeloma; often an indicator of more severe disease is known as “CRAB”- hypercalcemia, renal insufficiency, anemia and lytic bone lesions
- **Non-Hodgkin’s Lymphomas (NHL)**
- *Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL)*
  - Most prevalent adult leukemia with a median age at diagnosis of 72 years
  - Treatment is individualized as some patients may have indolent disease while others require treatment; a small percentage of patients undergo Richter’s transformation to a more aggressive non-Hodgkin’s lymphoma
  - Cytogenetic abnormalities are of prognostic significance and can help to drive treatment options
- *Mantle Cell Lymphoma (MCL)*
  - Possesses characteristics of both indolent and aggressive NHLs. Median OS is 3 years but no evidence of a survival plateau, similar to indolent leukemias
  - Chromosomal translocation t(11;14) is usually present

Oncology, Oral- Hematological – Indications

Drugs	Indications
Acute Myeloid Leukemia	
enasidenib (Idhifa)	▪ Relapsed or refractory acute myeloid leukemia (AML) with an isocitrate dehydrogenase-2 (IDH2) mutation as determined with an FDA-approved test
glasdegib (Daurismo)	• Newly diagnosed acute myeloid leukemia (AML), in combination with low-dose cytarabine in patients ≥ 75 years old or who have comorbidities that preclude the use of intensive induction chemotherapy
gilteritinib (Xospata)	• Adult patients with relapsed or refractory acute myeloid leukemia (AML) with a FMS-like tyrosine kinase 3 (FLT3) mutation as detected by an FDA-approved test
ivosidenib (Tibsovo)	▪ Adult patients with relapsed or refractory acute myeloid leukemia (AML) with a susceptible isocitrate dehydrogenase-1 (IDH1) mutation as approved by an FDA-approved test
midostaurin (Rydapt)	▪ Newly diagnosed AML that is FLT3 mutation-positive as detected by an FDA-approved test, in combination with standard cytarabine and daunorubicin induction and cytarabine consolidation ▪ Aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated hematological neoplasm (SM-AHN), or mast cell leukemia
tretinoin	▪ For remission induction in patients with acute promyelocytic leukemia (APL), FAB classification M3 characterized by the presence of the t(15;17) translocation and/or presence of the PML/RARα gene who are refractory to, have relapsed from, or have a contraindication to anthracycline chemotherapy
Chronic Myeloid Leukemia	
bosutinib (Bosulif)	▪ Newly diagnosed chronic phase (CP) Ph+ CML ▪ Treatment of chronic, accelerated, or blast phase Ph+ chronic myeloid leukemia (CML) with resistance or intolerance to prior therapy
busulfan (Myleran)	▪ Palliative treatment of chronic myelogenous (myeloid, myelocytic, granulocytic) leukemia
dasatinib (Sprycel)	▪ Treatment of adults with chronic, accelerated, or myeloid or lymphoid blast phase Ph+ CML with resistance or intolerance to prior therapy including imatinib (Gleevec) ▪ Treatment of adults with Ph+ acute lymphoblastic leukemia (ALL) with resistance or intolerance to prior therapy ▪ Newly diagnosed adult patients with Ph+ CML in chronic phase ▪ Treatment of pediatric patients with Ph+ CML in chronic phase
hydroxyurea	▪ Resistant CML ▪ Locally advanced squamous cell carcinomas of the head and neck (excluding lip), in combination with concurrent chemoradiation

Oncology, Oral- Hematological – Indications

Drugs	Indications
Chronic Myeloid Leukemia, continued	
imatinib (Gleevec)	▪ Newly diagnosed adult and pediatric patients with Ph+ CML in chronic phase ▪ Patients with Ph+ CML in blast crisis, accelerated phase, or chronic phase after failure of interferon-alpha therapy ▪ Adult patients with relapsed or refractory Ph+ ALL ▪ Pediatric patients with newly diagnosed Ph+ ALL in combination with chemotherapy ▪ Adult patients with myelodysplastic/myeloproliferative diseases associated with platelet-derived growth factor receptor (PDGFR) gene re-arrangements as determined with an FDA-approved test† ▪ Adult patients with aggressive systemic mastocytosis without the D816V c-Kit mutation as determined with an FDA-approved test or with c-Kit mutational status unknown† ▪ Adult patients with hypereosinophilic syndrome and/or chronic eosinophilic leukemia who have the FIP1L1-PDGFRα fusion kinase (mutational analysis or FISH demonstration of CHIC2 allele deletion) and for patients with hypereosinophilic syndrome and/or chronic eosinophilic leukemia who are FIP1L1-PDGFRα fusion kinase-negative or unknown ▪ Adult patients with unresectable, recurrent, and/or metastatic dermatofibrosarcoma protuberans (DFSP) ▪ Patients with Kit (CD117)-positive unresectable and/or metastatic malignant gastrointestinal stromal tumors (GIST) ▪ Adjuvant treatment of adult patients following resection of Kit (CD117)-positive gastrointestinal stromal tumors (GIST)
nilotinib (Tasigna)	▪ Accelerated phase and chronic phase Ph+ CML in adult patients resistant to or intolerant to prior therapy that included imatinib (Gleevec) ▪ Newly diagnosed adult and pediatric patients at least 1 year of age with Ph+ CML in chronic phase ▪ Treatment of chronic phase Ph+ CML with resistance or intolerance to prior tyrosine-kinase inhibitor (TKI) therapy in pediatric patients at least 1 year of age
ponatinib (Iclusig)	▪ Treatment of adult patients with T315I-positive chronic myeloid leukemia (CML) (chronic phase, accelerated phase, or blast phase) or T315I-positive Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ALL) ▪ Treatment of adult patients with chronic phase, accelerated phase, or blast phase chronic myeloid leukemia or Ph+ALL for whom no other tyrosine kinase inhibitor (TKI) is indicated

Oncology, Oral- Hematological – Indications

Drugs	Indications
Multiple Myeloma	
ixazomib (Ninlaro)	▪ In combination with lenalidomide and dexamethasone for the treatment of multiple myeloma in patients who have received at least 1 prior therapy
lenalidomide (Revlimid)	▪ In combination with dexamethasone for the treatment of multiple myeloma ▪ As maintenance therapy for multiple myeloma following autologous hematopoietic stem cell transplantation (auto-HSCT) ▪ Treatment of transfusion-dependent anemia due to low-or intermediate-1-risk myelodysplastic syndromes associated with a deletion of 5q cytogenetic abnormality with or without additional cytogenetic abnormalities ▪ Treatment of mantle cell lymphoma after relapse or disease progression after 2 prior therapies, 1 of which included bortezomib
melphalan (Alkeran)	▪ Palliative treatment of multiple myeloma ▪ Palliation of non-resectable epithelial carcinoma of the ovary
panobinostat (Farydak)	▪ Treatment of multiple myeloma in combination with bortezomib and dexamethasone in patients who have received at least 2 prior regimens, including bortezomib and an immunomodulatory agent
pomalidomide (Pomalyst)	▪ For use in combination with dexamethasone for patients with multiple myeloma who have received at least 2 prior therapies including lenalidomide and a proteasome inhibitor and have demonstrated disease progression on or within 60 days of completion of the last therapy
thalidomide (Thalomid)	▪ Treatment of newly diagnosed multiple myeloma in combination with dexamethasone ▪ Acute treatment of cutaneous manifestations of moderate to severe erythema nodosum leprosum (ENL) ▪ Prevention and suppression of cutaneous manifestations of ENL recurrence as maintenance therapy

Oncology, Oral- Hematological – Indications

Drugs	Indications
Non-Hodgkin's Lymphomas	
Chronic Lymphocytic Leukemia	
chlorambucil (Leukeran)	▪ Treatment of chronic lymphatic (lymphocytic) leukemia, malignant lymphomas, including lymphosarcoma, giant follicular lymphoma, and Hodgkin's disease; chlorambucil is not curative in any of these disorders but may produce clinically useful palliation
duvelisib (Copiktra)	▪ Adult patients with relapsed or refractory CLL or SLL after at least 2 prior therapies ▪ Adult patients with relapsed or refractory follicular lymphoma (FL) after at least 2 prior systemic therapies
ibrutinib (Imbruvica)	▪ Mantle cell lymphoma (MCL) in patients who have received at least 1 prior therapy ▪ Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma ▪ Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma with 17p deletion ▪ Waldenström's macroglobulinemia ▪ Marginal zone lymphoma (MZL) requiring systemic therapy and patient has had prior anti-CD20-based therapy ▪ Chronic graft versus host disease (cGVHD) after failure of one of more lines of systemic therapy
idelalisib (Zydelig)	▪ Relapsed chronic CLL in combination with rituximab in patients for whom rituximab alone would be considered appropriate therapy due to other co-morbidities ▪ Relapsed follicular B cell non-Hodgkin's lymphoma (FL) in patients who have received at least 2 prior systemic therapies ▪ Relapsed small lymphocytic lymphoma (SLL) in patients who have received at least 2 prior systemic therapies
venetoclax (Venclexta)	▪ Treatment of CLL or SLL in patients with or without 17p deletion, as detected by an FDA-approved test, who have received at least 1 prior therapy
Mantle Cell Lymphoma	
acalabrutinib (Calquence)	▪ Treatment of adults with mantle cell lymphoma (MCL) treated with at least 1 prior therapy

Oncology, Oral- Hematological – Indications

Drugs	Indications
Miscellaneous Hematologic Malignancies	
mercaptopurine (Purixan)	▪ Acute lymphoblastic leukemia (ALL) as a component of a combination maintenance therapy regimen
procarbazine (Matulane)	▪ For use in combination with other anticancer drugs for the treatment of stage 3 and stage 4 Hodgkin's disease ; used as part of the MOPP regimen (nitrogen mustard, vincristine, procarbazine, prednisone)
ruxolitinib (Jakafi)	▪ Intermediate or high-risk myelofibrosis (MF), including primary MF, post-polycythemia vera MF and post-essential thrombocythemia MF ▪ Treatment of polycythemia vera in patients who have had an inadequate response to or are intolerant of hydroxyurea
thioguanine (Tabloid)	▪ For remission induction and remission consolidation of acute nonlymphocytic leukemias
vorinostat (Zolinza)	▪ Treatment of cutaneous manifestations of cutaneous T cell lymphoma (CTCL) in patients who have progressive, persistent, or recurrent disease on or following 2 systemic therapies

Oncology, Oral- Hematological – Dosing and Availability

Drug	Diagnosis						Administration	Dosage Forms
	CML	Ph+ ALL	CLL/SLL	NHL	MM	Other		
acalabrutinib (Calquence)	---	---	---	---	---	MCL: 100 mg every 12 hours	Swallow capsules whole with water; do not open, break, or chew capsules	100 mg capsules
bosutinib (Bosulif)	Newly diagnosed CP Ph+ CML: 400 mg once daily Resistant or intolerant CP, AP, BP Ph+ CML: 500 mg once daily May be increased to 600 mg daily if CHR is not reached by week 8 or a CCyR by week 12	---	---	---	---	---	Swallow tablets whole; do not crush or cut; take with food	100 mg, 400 mg, 500 mg tablets
busulfan (Myleran)	Remission induction: 60 mcg/kg or 1.8 mg/m2: usual dose between 4 mg and 8 mg orally daily	---	---	---	---	---	---	2 mg tablets
chlorambucil (Leukeran)	---	---	0.1 to 0.2 mg/kg once daily for 3 to 6 weeks	---	---	HD: 0.1 to 0.2 mg/kg once daily for 3 to 6 weeks	Take entire daily dose at 1 time	2 mg tablets

Oncology, Oral- Hematological – Dosing and Availability

Drug	Diagnosis						Administration	Dosage Forms
	CML	Ph+ ALL	CLL/SLL	NHL	MM	Other		
dasatinib (Sprycel)	CP CML: 100 mg to 140 mg daily AP CML: 140 mg to 180 mg daily BP CML: 140 mg daily Pediatric patients with CP Ph+ CML: weight based, starting dose not to exceed 100 mg, may increase up to 120 mg daily	Ph+ ALL: 140 mg to 180 mg daily	---	---	---	---	Swallow tablets whole; do not crush or cut; take with or without food either in the morning or in the evening	20 mg, 50 mg, 70 mg, 80 mg, 100 mg, 140 mg tablets
enasidenib (Idhifa)	---	---	---	---	---	AML: 100 mg once daily	Swallow tablets whole; do not crush or split; take with or without food at the same time each day	50 mg, 100 mg tablets
hydroxyurea (Hydrea)	Individualize dose based on patient risk factors, response to treatment and current clinical practice standards; base all dosing on body weight, either actual or ideal weight, whichever is less (see prescribing information for details)	---	---	---	---	Solid tumors: Individualize dose based on patient risk factors, response to treatment and current clinical practice standards; base all dosing on body weight, either actual or ideal weight, whichever is less (see prescribing information for details)	Prophylactic administration of folic acid is recommended; hydroxyurea capsules should not be opened	500 mg capsules
ibrutinib (Imbruvica)	---	---	420 mg once daily	MCL: 560 mg once daily MZL: 560 mg once daily	---	WM: 420 mg once daily cGVHD: 420 mg once daily	Swallow capsules whole with water; do not open, break or chew capsules	70 mg, 140 mg capsules 140 mg, 280 mg, 420 mg, 560 mg tablets
idelalisib (Zydelig)	---	---	150 mg twice daily	FL: 150 mg twice daily	---	---	Take with or without food; tablets should be swallowed whole	100 mg, 150 mg tablets

Oncology, Oral- Hematological – Dosing and Availability

Drug	Diagnosis						Administration	Dosage Forms
	CML	Ph+ ALL	CLL/SLL	NHL	MM	Other		
imatinib (Gleevec)	CP CML: 400 mg to 600 mg daily AP CML: 600 mg to 800 mg daily BP CML: 600 mg to 800 mg daily Pediatric patients with Ph+ CML CP: 340 mg/m2/day (not to exceed 600 mg/day)	Ph+ ALL in adults: 600 mg daily Ph+ ALL in children: 340 mg/m2/day (not to exceed 600 mg/day)	---	---	---	MDS/MPD: 400 mg daily ASM: 100 mg to 400 mg daily HES/CEL: 100 mg to 400 mg daily DFSP: 800 mg daily GIST: 400 to 800 mg daily	Take with a meal and a large glass of water; Doses of 400 mg or 600 mg should be administered once daily, whereas a dose of 800 mg should be administered as 400 mg twice daily; in children, imatinib (Gleevec) can be given as a once-daily dose in CML and Ph+ ALL, alternatively in children with CML, the daily dose may be split into 2 doses; For patients unable to swallow the film-coated tablets, the tablets may be dispersed in a glass of water or apple juice; administer suspension immediately after disintegration of tablet(s)	100 mg, 400 mg tablets
ivosidenib (Tibsovo)	---	---	---	---	---	IDH1 mutated AML: 500 mg once daily; treat for a minimum of 6 months to allow time for clinical response	May be taken with or without food but should not be administered with a high-fat meal; do not crush or split tablets	250 mg tablets
ixazomib (Ninlaro)	---	---	---	---	4 mg once weekly on days 1, 8, and 15 of a 28-day treatment cycle	---	Take at least 1 hour before or at least 2 hours after food; capsule should be swallowed whole with water; do not crush, chew or open capsule; ixazomib is used as part of a regimen that also includes lenalidomide and dexamethasone; consider antiviral prophylaxis to decrease the risk of herpes zoster reactivation	2.3 mg, 3 mg, 4 mg capsules

Oncology, Oral- Hematological – Dosing and Availability

Drug	Diagnosis						Administration	Dosage Forms
	CML	Ph+ ALL	CLL/SLL	NHL	MM	Other		
lenalidomide (Revlimid)	---	---	---	---	MM: 25 mg once daily on days 1-21 of repeated 28-day cycles MM Maintenance Therapy following Auto-HSCT: 10 mg once daily continuously (Days 1-28 of repeated 28 day cycles); after 3 cycles of maintenance therapy, the dose can be increased to 15 mg once daily if tolerated	MCL: 25 mg/day on days 1-21 of repeated 28-day cycles MDS: 10 mg daily	MM: Administer with dexamethasone per recommended dosing schedule; concomitant dexamethasone is not administered with lenalidomide for maintenance therapy following Auto-HSCT	2.5 mg, 5 mg, 10 mg, 15 mg, 20 mg, 25 mg capsules
melphalan (Alkeran)	---	---	---	---	6 mg (3 tablets) daily	Ovarian CA: 0.2 mg/kg daily x 5 days	---	2 mg tablet
mercaptopurine (generic tablet, Purixan)	---	---	---	---	---	Maintenance dose in ALL: 1.5 to 2.5 mg/kg/day (50 to 75 mg/m2/day) as a single dose; doses are adjusted based on patient response and toxicity	Procedures for proper handling and disposal of anticancer drugs should be considered; shake suspension vigorously for at least 30 seconds before administration	50 mg tablets (generic only), 20 mg/mL oral suspension (Purixan; brand only) dispensed with 2 oral dispensing syringes (1 each 1 mL and 5 mL oral syringes)
midostaurin (Rydapt)	---	---	---	---	---	FLT3 mutation positive AML: 50 mg orally twice daily on Days 8 to 21 of each cycle of induction with cytarabine and daunorubicin and on Days 8 to 21 of each cycle of consolidation with high-dose cytarabine ASM, SM-AHN, MCL-100 mg twice daily with food continued until disease progression or unacceptable toxicity	Doses should be taken twice daily with food at approximately 12 hour intervals; do not open or crush midostaurin capsules	25 mg capsules

Oncology, Oral- Hematological – Dosing and Availability

Drug	Diagnosis						Administration	Dosage Forms
	CML	Ph+ ALL	CLL/SLL	NHL	MM	Other		
nilotinib (Tasigna)	Newly diagnosed CP-CML: 300 mg twice daily Resistant or Intolerant: CML-CP: 400 mg twice daily Pediatric patients with CP Ph+ CML: 230 mg/m2 twice daily; (round to nearest 50 mg and do not exceed single dose of 400 mg) CML-AP: 400 mg twice daily	---	---	---	---	---	Take on an empty stomach; no food for at least 2 hours before or at least 1 hour after dose; swallow capsules whole with water For patients unable to swallow capsules, the contents of each capsule may be dispersed in 1 teaspoon of applesauce and the mixture should be taken immediately	50 mg, 150 mg, 200 mg capsules
panobinostat (Farydak)	---	---	---	---	20 mg every other day for 3 doses per week in weeks 1 and 2 of each 21-day cycle for up to 8 cycles; the total duration of treatment may be extended to 16 weeks in appropriate patients	---	Take with or without food; capsules should be swallowed whole with a cup of water; do not open, crush, or chew capsules; panobinostat is administered in combination with bortezomib and dexamethasone	10 mg, 15 mg, 20 mg capsules
pomalidomide (Pomalyst)	---	---	---	---	4 mg once daily on days 1-21 of repeated 28-day cycles	---	Do not break, chew or open capsules; may be taken with or without food (at least 2 hours before or 2 hours after a meal); give in combination with dexamethasone	1 mg, 2 mg, 3 mg, 4 mg capsules

Oncology, Oral- Hematological – Dosing and Availability

Drug	Diagnosis						Administration	Dosage Forms
	CML	Ph+ ALL	CLL/SLL	NHL	MM	Other		
ponatinib (Iclusig)	Start dosing with 45 mg once daily; consider reducing the dose for CP-CML and AP-CML patients who have achieved a major cytogenetic response; consider discontinuing if response has not occurred by 3 months	Ph+ ALL: Start dosing with 45 mg once daily	---	---	---	---	May be taken with or without food; tablets should be swallowed whole, do not crush or dissolve tablets	15 mg, 45 mg tablets
procarbazine (Matulane)	---	---	---	---	---	HD: as part of a combination chemotherapy regimen (MOPP): 100 mg/m2 daily for 14 days; all dosages are based on actual weight or lean body mass if patient is obese	---	50 mg capsules
ruxolitinib (Jakafi)	---	---	---	---	---	Myelofibrosis: Initial dosing varies from 5 mg twice daily to 20 mg twice daily based on initial platelet count Polycythemia Vera: 10 mg twice daily	There are extemporaneous compounding instructions for administration through a nasogastric tube	5 mg, 10 mg, 15 mg, 20 mg, 25 mg tablets
thalidomide (Thalomid)	---	---	---	---	200 mg once daily	ENL: 100 mg to 300 mg once daily; up to 400 mg/day for severe cutaneous ENL	MM: take in combination with dexamethasone in 28-day treatment cycles Take with water, preferably at bedtime and at least 1 hour after the evening meal	50 mg, 100 mg, 150 mg, 200 mg capsules

Oncology, Oral- Hematological – Dosing and Availability

Drug	Diagnosis						Administration	Dosage Forms
	CML	Ph+ ALL	CLL/SLL	NHL	MM	Other		
thioguanine (Tabloid)	---	---	---	---	---	Acute nonlymphocytic leukemias: Doses varies according to the stage and regimen being utilized; dose should be drive by chosen protocol	---	40 mg tablets
tretinoin	---	---	---	---	---	APL: 45 mg/m2/day divided into 2 doses	---	10 mg capsule
venetoclax (Venclexta)	---	---	Ramp-Up phase dosing: 20 mg/day week 1; 50 mg/day week 2; 100 mg/day week 3; 200 mg/day week 4 and then 400 mg/day week 5 and beyond	---	---	---	Take with a meal and water; tablets should be swallowed whole and not chewed, crushed or broken prior to swallowing	10 mg, 50 mg, 100 mg tablets
vorinostat (Zolinza)	---	---	---	---	---	CTCL: 400 mg once daily	Take with food; capsules should not be opened or crushed	100 mg capsule

Oncology, Oral- Hematological – Guidelines

- NCCN AML Guidelines

Oncology, Oral- Hematological – Guidelines

- NCCN CML Guidelines

Oncology, Oral- Hematological – Guidelines

- NCCN Multiple Myeloma Guidelines

Oncology, Oral- Hematological – Guidelines

- NCCN Guideline for Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma

Washington State Health Care Authority

Antineoplastics and Adjunctive Therapy, Oral Agents, Hematologic Cancers

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February 20, 2019

Antineoplastics and Adjunctive Therapy, Oral Agents, Abbreviations

Abbreviation	Term
ALL	Acute Lymphoblastic Leukemia
AML	Acute Myeloid Leukemia
cGVHD	Chronic Graft Versus Host Disease
CLL	Chronic Lymphocytic Leukemia
CML	Chronic Myeloid Leukemia
FDA	Food and Drug Administration
IDH	Isocitrate Dehydrogenase
MCL	Mantel Cell Lymphoma
MOPP	Nitrogen mustard, vincristine, procarbazine, prednisone
MZL	Marginal Zone Lymphoma
Ph+	Philadelphia chromosome positive

Antineoplastics and Adjunctive Therapy, Oral Agents, Hematologic Cancers

Drug name (Brand Nane)	Mechanism of Action	FDA Approval
acalabrutinib (Calquence®)	Burton Tyrosine Kinase Inhibitor	2017
bosutinib (Bosulif®)	BCR-ABL Tyrosine Kinase Inhibitor	2012
busulfan (Myleran®)	Alkyl Sulfonate	1954
chlorambucil (Leukeran®)	Nitrogen Mustards	1957
cyclophosphamide*	Nitrogen Mustard	1959
dasatinib (Sprycel®)	BCR-ABL Tyrosine Kinase Inhibitor	2006
duvelisib (Copiktra®)	Phosphatidylinositol 3-Kinase Inhibitor	2018
enasidenib (Idhifa®)	IDH2 Inhibitors	2017
hydroxyurea (Hydrea®)*	Substituted Ureas	1998
ibrutinib (Imbruvica®)	Bruton Tyrosine Kinase Inhibitor	2013

*Generic available

Antineoplastics and Adjunctive Therapy, Oral Agents, Hematologic Cancers

Drug name (Brand Nane)	Mechanism of Action	FDA Approval
idelalisib (Zydelig®)	Phosphatidylinositol 3-Kinase Inhibitor	2014
imatinib (Gleevec®)*	BCR-ABL Tyrosine Kinase Inhibitor	2001
ivosidenib (Tibsovo®)	IDH1 Inhibitor	2018
ixazomib (Ninlaro®)	Proteasome Inhibitor	2015
lenalidomide (Revlimid®)	Systemic Immunomodulator	2005
lomustine (Gleostine®)	Alkylating Agents (Nitrosoureas)	1976
melphalan (Alkeran®)*	Nitrogen Mustards	1964
mercaptopurine (Purixan®)*	Purine Analog	1953
midostaurin (Rydapt®)	FLT3 Tyrosine Kinase Inhibitor	2017
nilotinib (Tasigna®)	BCR-ABL Tyrosine Kinase Inhibitor	2007

*Generic available

Antineoplastics and Adjunctive Therapy, Oral Agents, Hematologic Cancers

Drug name (Brand Nane)	Mechanism of Action	FDA Approval
panobinostat (Farydak®)	Histone Deacetylase Inhibitor	2015
pomalidomide (Pomalyst®)	Systemic Immunomodulator	2013
ponatinib (Iclusig®)	BCR-ABL Tyrosine Kinase Inhibitor	2012
procarbazine (Matulane®)	Alkylating Agent	1969
ruxolitinib (Jakafi®)	Janus-Associated Kinase Inhibitor	2011
thalidomide (Thalomid®)	Systemic Immunomodulator	1998
thioguanine (Tabloid®)	Purine Analog	1966
tretinoin*	Retinoid	1995
venetoclax (Venclexta®)	B-Cell Lymphoma-2 Inhibitor	2016
vorinostat (Zolinza®)	Histone Deacetylase Inhibitor	2006

*Generic available

Antineoplastics and Adjunctive Therapy, Oral Agents, Hematologic Cancers

Initial request:

- Diagnosis that is listed in FDA-approved label **OR** in compendia recognized by Medicaid (defined in Section 1927 of the Social Security Act); **AND**
- If an FDA-approved companion diagnostic test for the requested agent exists, documentation that the test was performed to confirm the diagnosis; **AND**
- If a test with adequate ability to confirm a disease mutation exists, documentation that the test was performed to confirm the diagnosis; **AND**
- If not indicated as a first line agent, documentation of all previous therapies; **AND**
- Must be used in combination with other chemotherapeutic or adjuvant agents according to the FDA approved prescribing information; **AND**

Antineoplastics and Adjunctive Therapy, Oral Agents, Hematologic Cancers

Initial request (continued):

- Prescribed by, or in consultation with, a specialist in oncology or hematology; **AND**
- The patient does not have any contraindications to the requested oral oncology medication; **AND**
- The prescribed quantity and dosing regimen falls within the manufacturer's published dosing guidelines and is appropriate for the patient's age; **AND**
- Documentation from the provider on what measure they'll use to determine whether the patient has had a positive clinical response

Antineoplastics and Adjunctive Therapy, Oral Agents, Hematologic Cancers

Reauthorization criteria:

- Documentation from the provider that the patient has had a positive clinical response and is able to tolerate therapy

Antineoplastics and Adjunctive Therapy, Oral Agents, Hematologic Cancers

acalabrutinib (Calquence)

- Treatment of adults with mantle cell lymphoma (MCL) treated with at least 1 prior therapy

bosutinib (Bosulif)

- Newly diagnosed chronic phase (CP) Ph+ CML
- Treatment of chronic, accelerated, or blast phase Ph+ chronic myeloid leukemia (CML) with resistance or intolerance to prior therapy

busulfan (Myleran)

- Palliative treatment of chronic myelogenous (myeloid, myelocytic, granulocytic) leukemia

chlorambucil (Leukeran)

- Treatment of chronic lymphatic (lymphocytic) leukemia, malignant lymphomas, including lymphosarcoma, giant follicular lymphoma, and Hodgkin's disease; chlorambucil is not curative in any of these disorders but may produce clinically useful palliation

Antineoplastics and Adjunctive Therapy, Oral Agents, Hematologic Cancers

cyclophosphamide

- Lymphomas: Hodgkin's disease, lymphocytic lymphoma, mixed-cell type lymphoma, histiocytic lymphoma, Burkitt's lymphoma
- Other malignant diseases: multiple myeloma, leukemias, mycosis fungoides, neuroblastoma, adenocarcinoma of ovary, retinoblastoma, breast carcinoma
- Nephrotic syndrome: biopsy proven minimal change nephrotic syndrome in pediatric patients who failed to adequately respond to or are unable to tolerate adrenocorticosteroid therapy

dasatinib (Sprycel)

- Treatment of adults with chronic, accelerated, or myeloid or lymphoid blast phase Ph+ CML with resistance or intolerance to prior therapy including imatinib (Gleevec)
- Treatment of adults with Ph+ acute lymphoblastic leukemia (ALL) with resistance or intolerance to prior therapy
- Newly diagnosed adult patients with Ph+ CML in chronic phase
- Treatment of pediatric patients with Ph+ CML in chronic phase

Antineoplastics and Adjunctive Therapy, Oral Agents, Hematologic Cancers

duvelisib (Copiktra)

- treatment of adult patients with relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) after at least 2 prior therapies and relapsed or refractory follicular lymphoma (FL) who have received at least 2 prior systemic therapies

enasidenib (Idhifa)

- Relapsed or refractory acute myeloid leukemia (AML) with an isocitrate dehydrogenase-2 (IDH2) mutation as determined with an FDA-approved test

hydroxyurea (Hydrea)

- Resistant CML
- Locally advanced squamous cell carcinomas of the head and neck (excluding lip), in combination with concurrent chemo-radiation

Antineoplastics and Adjunctive Therapy, Oral Agents, Hematologic Cancers

ibrutinib (Imbruvica)

- Mantle cell lymphoma (MCL) in patients who have received at least 1 prior therapy
- Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma
- Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma with 17p deletion
- Waldenström's macroglobulinemia
- Marginal zone lymphoma (MZL) requiring systemic therapy and patient has had prior anti-CD20-based therapy
- Chronic graft versus host disease (cGVHD) after failure of one of more lines of systemic therapy

idelalisib (Zydelig)

- Relapsed chronic CLL in combination with rituximab in patients for whom rituximab alone would be considered appropriate therapy due to other co-morbidities
- Relapsed follicular B cell non-Hodgkin's lymphoma (FL) in patients who have received at least 2 prior systemic therapies
- Relapsed small lymphocytic lymphoma (SLL) in patients who have received at least 2 prior systemic therapies

Antineoplastics and Adjunctive Therapy, Oral Agents, Hematologic Cancers

imatinib (Gleevec)

- Newly diagnosed adult and pediatric patients with Ph+ CML in chronic phase
- Patients with Ph+ CML in blast crisis, accelerated phase, or chronic phase after failure of interferon-alpha therapy
- Adult patients with relapsed or refractory Ph+ ALL
- Pediatric patients with newly diagnosed Ph+ ALL in combination with chemotherapy
- Adult patients with myelodysplastic/myeloproliferative diseases associated with platelet-derived growth factor receptor (PDGFR) gene re-arrangements as determined with an FDA-approved test†
- Adult patients with aggressive systemic mastocytosis without the D816V c-Kit mutation as determined with an FDA-approved test or with c-Kit mutational status unknown
- Adult patients with hypereosinophilic syndrome and/or chronic eosinophilic leukemia who have the FIP1L1-PDGFRα fusion kinase (mutational analysis or FISH demonstration of CHIC2 allele deletion) and for patients with hypereosinophilic syndrome and/or chronic eosinophilic leukemia who are FIP1L1-PDGFRα fusion kinase-negative or unknown
- Adult patients with unresectable, recurrent, and/or metastatic dermatofibrosarcoma protuberans (DFSP)
- Patients with Kit (CD117)-positive unresectable and/or metastatic malignant gastrointestinal stromal tumors (GIST)
- Adjuvant treatment of adult patients following resection of Kit (CD117)-positive gastrointestinal stromal tumors (GIST)

Antineoplastics and Adjunctive Therapy, Oral Agents, Hematologic Cancers

ivosidenib (Tibsovo)

- Adult patients with relapsed or refractory acute myeloid leukemia (AML) with a susceptible isocitrate dehydrogenase-1 (IDH1) mutation as approved by an FDA-approved test

ixazomib (Ninlaro)

- In combination with lenalidomide and dexamethasone for the treatment of multiple myeloma in patients who have received at least 1 prior therapy

lenalidomide (Revlimid)

- In combination with dexamethasone for the treatment of multiple myeloma
- As maintenance therapy for multiple myeloma following autologous hematopoietic stem cell transplantation (auto-HSCT)
- Treatment of transfusion-dependent anemia due to low-or intermediate-1-risk myelodysplastic syndromes associated with a deletion of 5q cytogenetic abnormality with or without additional cytogenetic abnormalities
- Treatment of mantle cell lymphoma after relapse or disease progression after 2 prior therapies, 1 of which included bortezomib

Antineoplastics and Adjunctive Therapy, Oral Agents, Hematologic Cancers

lomustine (Gleostine)

- Brain tumors, primary and metastatic, following appropriate surgical and/or radiotherapeutic procedures
- Hodgkin's hymphoma in combination with other chemotherapies, following disease progression with initial chemotherapy

melphalan (Alkeran)

- Palliative treatment of multiple myeloma
- Palliation of non-resectable epithelial carcinoma of the ovary

mercaptopurine (Purixan)

- Acute lymphoblastic leukemia (ALL) as a component of a combination maintenance therapy regimen

midostaurin (Rydapt)

- Newly diagnosed AML that is FLT3 mutation-positive as detected by an FDA-approved test, in combination with standard cytarabine and daunorubicin induction and cytarabine consolidation
- Aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated hematological neoplasm (SM-AHN), or mast cell leukemia

Antineoplastics and Adjunctive Therapy, Oral Agents, Hematologic Cancers

nilotinib (Tasigna)

- Accelerated phase and chronic phase Ph+ CML in adult patients resistant to or intolerant to prior therapy that included imatinib (Gleevec)
- Newly diagnosed adult and pediatric patients at least 1 year of age with Ph+ CML in chronic phase
- Treatment of chronic phase Ph+ CML with resistance or intolerance to prior tyrosine-kinase inhibitor (TKI) therapy in pediatric patients at least 1 year of age

panobinostat (Farydak)

- Treatment of multiple myeloma in combination with bortezomib and dexamethasone in patients who have received at least 2 prior regimens, including bortezomib and an immunomodulatory agent

Antineoplastics and Adjunctive Therapy, Oral Agents, Hematologic Cancers

pomalidomide (Pomalyst)

- For use in combination with dexamethasone for patients with multiple myeloma who have received at least 2 prior therapies including lenalidomide and a proteasome inhibitor and have demonstrated disease progression on or within 60 days of completion of the last therapy

ponatinib (Iclusig)

- Treatment of adult patients with T315I-positive chronic myeloid leukemia (CML) (chronic phase, accelerated phase, or blast phase) or T315I-positive Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ALL)
- Treatment of adult patients with chronic phase, accelerated phase, or blast phase chronic myeloid leukemia or Ph+ALL for whom no other tyrosine kinase inhibitor (TKI) is indicated

Antineoplastics and Adjunctive Therapy, Oral Agents, Hematologic Cancers

procarbazine (Matulane)

- For use in combination with other anticancer drugs for the treatment of stage 3 and stage 4 Hodgkin's disease ; used as part of the MOPP regimen (nitrogen mustard, vincristine, procarbazine, prednisone)

ruxolitinib (Jakafi)

- Intermediate or high-risk myelofibrosis (MF), including primary MF, post-polycythemia vera MF and post-essential thrombocythemia MF
- Treatment of polycythemia vera in patients who have had an inadequate response to or are intolerant of hydroxyurea

Antineoplastics and Adjunctive Therapy, Oral Agents, Hematologic Cancers

thalidomide (Thalomid)

- Treatment of newly diagnosed multiple myeloma in combination with dexamethasone
- Acute treatment of cutaneous manifestations of moderate to severe erythema nodosum leprosum (ENL)
- Prevention and suppression of cutaneous manifestations of ENL recurrence as maintenance therapy

thioguanine (Tabloid)

- For remission induction and remission consolidation of acute nonlymphocytic leukemias

Antineoplastics and Adjunctive Therapy, Oral Agents, Hematologic Cancers

tretinoin

- For remission induction in patients with acute promyelocytic leukemia (APL), FAB classification M3 characterized by the presence of the t(15;17) translocation and/or presence of the PML/RARα gene who are refractory to, have relapsed from, or have a contraindication to anthracycline chemotherapy

venetoclax (Venclexta)

- Treatment of CLL or SLL in patients with or without 17p deletion, as detected by an FDA-approved test, who have received at least 1 prior therapy

vorinostat (Zolinza)

- Treatment of cutaneous manifestations of cutaneous T cell lymphoma (CTCL) in patients who have progressive, persistent, or recurrent disease on or following 2 systemic therapies

Antineoplastics and Adjunctive Therapy, Oral Agents, Hematologic Cancers

Motion:

- "I move that the Apple Health Medicaid Program implement the clinical criteria listed on slides 27-29 as recommended. The hematologic oncology drugs listed on Magellan slides 6-10 are considered safe and efficacious for their respective FDA indications. All drugs are preferred for their FDA labeled indications."
  - Motion: Storhaug
  - 2nd: Schwilke

Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Oncology, Oral- Prostate

Overview of Disease State – Oncology, Oral- Prostate

- Prostate cancer is the most commonly diagnosed cancer in U.S. men
  - Prostate cancer is the 2nd leading cause of death among men in US and accounts for 10% of all cancer deaths in U.S. men
- Disproportionately affects black men with ~ 60% higher incidence and 110% higher mortality
- Prostate cancer is rare in men < 40 years but the risk increases with each subsequent decade of life
- In 2019, there are expected to be 174,650 cases of prostate cancer diagnosed and 31,620 deaths due to prostate cancer in the U.S.
- Prostate cancer often has an indolent course; active surveillance is an option in some cases; localized prostate cancer can be cured by surgery or radiation therapy
- The use of prostate-specific antigen (PSA) testing as a screening tool for prostate cancer is controversial due to the risk of overdiagnosis and subsequent risk of unnecessary treatment
  - In 2018 the USPSTF revised their recommendations regarding routine PSA screening and now say the decision should be individualized for men ages 55 to 69 years of age
- Androgens (specifically testosterone) are known growth signals for the prostate and the majority of prostate cancers are hormonally dependent, therefore androgen deprivation therapy (ADT) is a cornerstone of treatment
- Prognosis and thus treatment decisions are dependent on several factors including tumor size, histologic grade (Gleason score), PSA level, disease stage and patient life expectancy

Oncology, Oral- Prostate – Indications

Drugs	Generic	Indications
abiraterone acetate (Zytiga)	---	▪ In combination with prednisone for the treatment of patients with metastatic castration-resistant prostate cancer (mCRPC) or metastatic high-risk castration-sensitive prostate cancer (mCSPC)
abiraterone acetate (Yonsa)	---	▪ In combination with methylprednisolone for the treatment of patients with mCRPC
apalutamide (Erleada)	---	▪ Treatment of patients with non-metastatic, castration-resistant prostate cancer (NM-CRPC)
bicalutamide (Casodex)	---	▪ In combination therapy with a luteinizing hormone-releasing hormone (LHRH) analog for the treatment of stage D2 metastatic carcinoma of the prostate
enzalutamide (Xtandi)	---	▪ Treatment of patients with mCRPC
estramustine (emcyt)	---	▪ Palliative treatment of metastatic and/or progressive carcinoma of the prostate
flutamide	---	▪ In combination with LHRH agonists for the management of locally confined stage B2-C and stage D2 metastatic carcinoma of the prostate
nilutamide (Nilandron)	---	▪ In combination with surgical castration for the treatment of metastatic prostate cancer (stage D2)†

abiraterone acetate- androgen biosynthesis inhibitor; must be coadministered with corticosteroids
apalutamide, enzalutamide bind to and inhibit the androgen receptor and are considered 2nd generation antiandrogens
bicalutamide, flutamide, nilutamide- 1st generation anatiandrogens
estramustine- cytotoxic chemotherapy

Oncology, Oral- Prostate – Dosing and Availability

Drugs	Dose	Administration Notes	Available Strengths
abiraterone acetate (Zytiga)	▪ mCRPC: 1,000 mg (two 500 mg tablets or four 250 mg tablets) once daily along with prednisone 5 mg twice daily ▪ Metastatic high-risk CSPC: 1,000 mg (two 500 mg tablets or four 250 mg tablets) once daily along with prednisone 5 mg once daily	Take on an empty stomach 1 hour before or 2 hours after meals Swallow tablets whole; do not crush or chew tablets	250 mg tablet (film-coated and uncoated), 500 mg tablet (film-coated)
abiraterone acetate (Yonsa)	▪ mCRPC: 500 mg (four 125 mg tablets) once daily in combination with methylprednisolone 4 mg administered orally twice daily	May be taken with or without food; tablets should be swallowed whole with water; do not crush or chew tablets	125 mg tablet
apalutamide (Erleada)	▪ 240 mg (four 60 mg tablets) once daily	Take with or without food at the same time each day, and swallow the tablets whole	60 mg tablet
bicalutamide (Casodex)	▪ 50 mg once daily ▪ Treatment should be started at the same time as treatment with an LHRH agonist	Take with or without food at the same time each day (morning or evening)	50 mg tablet
enzalutamide (Xtandi)	160 mg (four 40 mg capsules) once daily	Take with or without food Swallow capsules whole; do not chew, dissolve or open the capsules	40 mg capsules
estramustine (Emcyt)	14 mg/kg/day divided into 3 to 4 oral daily doses; (doses often range from 10 mg/kg/day to 16 mg/kg/day)	Store in the refrigerator; Take 1 hour before or 2 hours after meals with water; Milk, milk products and calcium-rich foods or drugs must not be taken simultaneously	140 mg capsule
flutamide	250 mg (two 125 mg capsules) every 8 hours for a total daily dose of 750 mg	Stage D2 metastatic carcinoma: treatment should be started at the same time as treatment with an LHRH agonist Stage B2-C prostatic carcinoma: treatment should be started with goserelin acetate implant 8 weeks prior initiating radiation and continue during radiation therapy	125 mg capsule
nilutamide (Nilandron)	300 mg once a day for 30 days, followed thereafter by 150 mg once a day	Take with or without food	150 mg tablet

Oncology, Oral- Prostate – Guidelines

- **Localized Disease**
- Shared decision making is recommended based on an explanation of risks vs benefits
- Active surveillance for low risk disease is recommended
- Patients found to have lymph node metastasis via surgery as well as those with initial high or very high risk should receive ADT (Category 1) assuming the patient has a life expectancy of ≥ 5 years
- Patients who undergo surgery (radical prostatectomy) or radiation therapy and who subsequently experience a rising PSA should receive ADT
- Patients who experience disease progression while receiving ADT are designated as castration-recurrent (or resistant) prostate cancer (CRPC)
  - Disease progression as demonstrated clinically, radiographically or biochemically
- CRPC may occur in either the non-metastatic setting or the metastatic setting

Oncology, Oral- Prostate – Guidelines

- **Non-metastatic CRPC**
- If patients experience a PSA doubling time ≤ 10 months- enzalutamide or apalutamide (category 1)-based on improvement in metastasis-free survival- SPARTAN, PROSPER trials
- ICER report available for these therapies in this setting
- **Metastatic CRPC**
- May be either metastatic castration-sensitive prostate cancer (mCSPC) or metastatic CRPC (mCRPC)
- ADT therapy is the backbone of therapy for all metastatic prostate cancer
  - Antiandrogens may be utilized at the start of ADT therapy to minimize tumor flare
- mCSPC-docetaxel (STAMPEDE, CHAARTED trials) or abiraterone (LATITUDE, STAMPEDE trials) (both category 1) superior to ADT alone
  - Favors abiraterone selection: lower toxicity profile
  - Favors docetaxel:- treatment duration
- mCRPC- treatment decisions are stratified based on presence or absence of visceral metastases
  - No visceral metastases-abiraterone, enzalutamide or docetaxel (all category 1)
    - ASCO: Abiraterone, enzalutamide and docetaxel are all associated with improved survival and quality of life (QOL); docetaxel is associated with a moderate toxicity risk
  - Visceral metastases-docetaxel or enzalutamide (category 1), abiraterone (category 2A)
  - Abiraterone and enzalutamide are effective in both the pre-docetaxel and post-docetaxel settings
  - Recommendations regarding sequencing of abiraterone and enzalutamide are not present in the guidelines and optimal sequencing of these agents are still under investigation
    - Response rate to enzalutamide after abiraterone is ~ 15% to 30%
    - Response rate to abiraterone after treatment with enzalutamide is likely < 10%

Oncology, Oral- Prostate – Guidelines

- NCCN Prostate Cancer Guidelines

Oncology, Oral- Prostate – Guidelines, Selected References

- Morris MJ, Rumble RB, Basch E, et al. Optimizing Anticancer Therapy in Metastatic Non-Castrate Prostate Cancer: American Society of Clinical Oncology Clinical Practice Guideline. Available at: http://ascopubs.org/doi/pdf/10.1200/JCO.2018.78.0619 Accessed February 6, 2019
- Sweeney CJ, Chen YH, Carducci M, et al: Chemohormonal therapy in metastatic hormone sensitive prostate cancer. N Engl J Med 2015; 373: 737-746,
- James ND, Sydes MR, Clarke NW, et al: Addition of docetaxel, zoledronic acid, or both to first line long-term hormone therapy in prostate cancer

(STAMPEDE): Survival results from an adaptive, multiarm, multistage, platform randomised controlled trial. Lancet 2016;387:1163-1177

- James ND, de Bono JS, Spears MR, et al: Abiraterone for prostate cancer not previously treated with hormone therapy. N Engl J Med 2017;377: 338-351
- Fizazi K, Tran N, Fein L, et al: Abiraterone plus prednisone in metastatic, castration-sensitive prostate cancer. N Engl J Med 2017; 377: 352-360
- Smith M, Saad F, Chowdhury S, et al. Apalutamide treatment and metastasis-free survival in prostate cancer. N Engl J Med. 2018; 378:1408-18
- Hussain M, Fizazi K, Saad F, et al Enzalutamide in Men with Nonmetastatic, Castration-Resistant Prostate Cancer N Engl J Med 2018;378:2465-2474
- Antiandrogen Therapies for Nonmetastatic Castration-Resistant Prostate Cancer: Effectiveness and Value: Final Evidence Report Institute for Clinical and Economic Review. Available at: https://icer-review.org/wp-content/uploads/2018/02/ICER_Prostate_Cancer_Final_Evidence_Report_100418.pdf Accessed February 4, 2019

Washington State Health Care Authority

Antineoplastics and Adjunctive Therapy, Oral Agents, Prostate Cancer

Ryan Pistoresi, PharmD, MS
Assistant Chief Pharmacy Officer
Clinical Quality & Care Transformation
February 20, 2019

Antineoplastics and Adjunctive Therapy, Oral Agents, Abbreviations

Abbreviation	Term
FDA	Food and Drug Administration
LHRH	Luteinizing hormone-releasing hormone
mCRPC	Metastatic castration-resistant prostate cancer
mCSPC	Metastatic castration-sensitive prostate cancer
nm-CRPC	Non-metastatic castration-resistant prostate cancer

Antineoplastics and Adjunctive Therapy, Oral Agents, Prostate Cancer

Drug name (Brand Nane)	Mechanism of Action	FDA Approval
abiraterone acetate (Zytiga®)	Antiandrogen	2011
abiraterone acetate (Yonsa®)	Antiandrogen	2011
apalutamide (Erleada®)	Antiandrogen	2018
bicalutamide (Casodex®)	Antiandrogen	1995
enzalutamide (Xtandi®)	Antiandrogen	2012
estramustine (Emcyt®)	Estrogen / Nitrogen Mustard	1981
flutamide*	Antiandrogen	1989
nilutamide (Nilandron®)*	Antiandrogen	1996

*Generic available

Antineoplastics and Adjunctive Therapy, Oral Agents, Prostate Cancer

Initial request:

- Diagnosis that is listed in FDA-approved label **OR** in compendia recognized by Medicaid (defined in Section 1927 of the Social Security Act); **AND**
- If an FDA-approved companion diagnostic test for the requested agent exists, documentation that the test was performed to confirm the diagnosis; **AND**
- If a test with adequate ability to confirm a disease mutation exists, documentation that the test was performed to confirm the diagnosis; **AND**
- If not indicated as a first line agent, documentation of all previous therapies; **AND**
- Must be used in combination with other chemotherapeutic or adjuvant agents or interventional procedure according to the FDA approved prescribing information; **AND**

Antineoplastics and Adjunctive Therapy, Oral Agents, Prostate Cancer

Initial request (continued):

- Prescribed by, or in consultation with, a specialist in oncology or hematology; **AND**
- The patient does not have any contraindications to the requested oral oncology medication; **AND**
- The prescribed quantity and dosing regimen falls within the manufacturer's published dosing guidelines and is appropriate for the patient's age; **AND**
- Documentation from the provider on what measure they'll use to determine whether the patient has had a positive clinical response

Antineoplastics and Adjunctive Therapy, Oral Agents, Prostate Cancer

Reauthorization criteria:

- Documentation from the provider that the patient has had a positive clinical response and is able to tolerate therapy

Antineoplastics and Adjunctive Therapy, Oral Agents, Prostate Cancer

abiraterone acetate (Zytiga)

- In combination with prednisone for the treatment of patients with metastatic castration-resistant prostate cancer (mCRPC) or metastatic high-risk castration-sensitive prostate cancer (mCSPC)

abiraterone acetate (Yonsa)

- In combination with methylprednisolone for the treatment of patients with mCRPC

apalutamide (Erleada)

- Treatment of patients with non-metastatic, castration-resistant prostate cancer (NM-CRPC)

bicalutamide (Casodex)

- In combination therapy with a luteinizing hormone-releasing hormone (LHRH) analog for the treatment of stage D2 metastatic carcinoma of the prostate

Antineoplastics and Adjunctive Therapy, Oral Agents, Prostate Cancer

enzalutamide (Xtandi)

- Treatment of patients with mCRPC

estramustine (Emcyt)

- Palliative treatment of metastatic and/or progressive carcinoma of the prostate

flutamide

- In combination with LHRH agonists for the management of locally confined stage B2-C and Stage D2 metastatic carcinoma of the prostate

nilutamide (Nilandron)

- In combination with surgical castration for the treatment of metastatic prostate cancer (stage D2).

Antineoplastics and Adjunctive Therapy, Oral Agents, Prostate Cancer

Motion:

- "I move that the Apple Health Medicaid Program implement the clinical criteria listed on slides 54-56 as recommended. The prostate oncology drugs listed on slide 53 are considered safe and efficacious for their respective FDA indications. One drug of each active ingredient should be preferred for their FDA labeled indications. Estramustine should be non-preferred on the AH PDL."

  - Motion: Flatebo
  - 2nd: Park

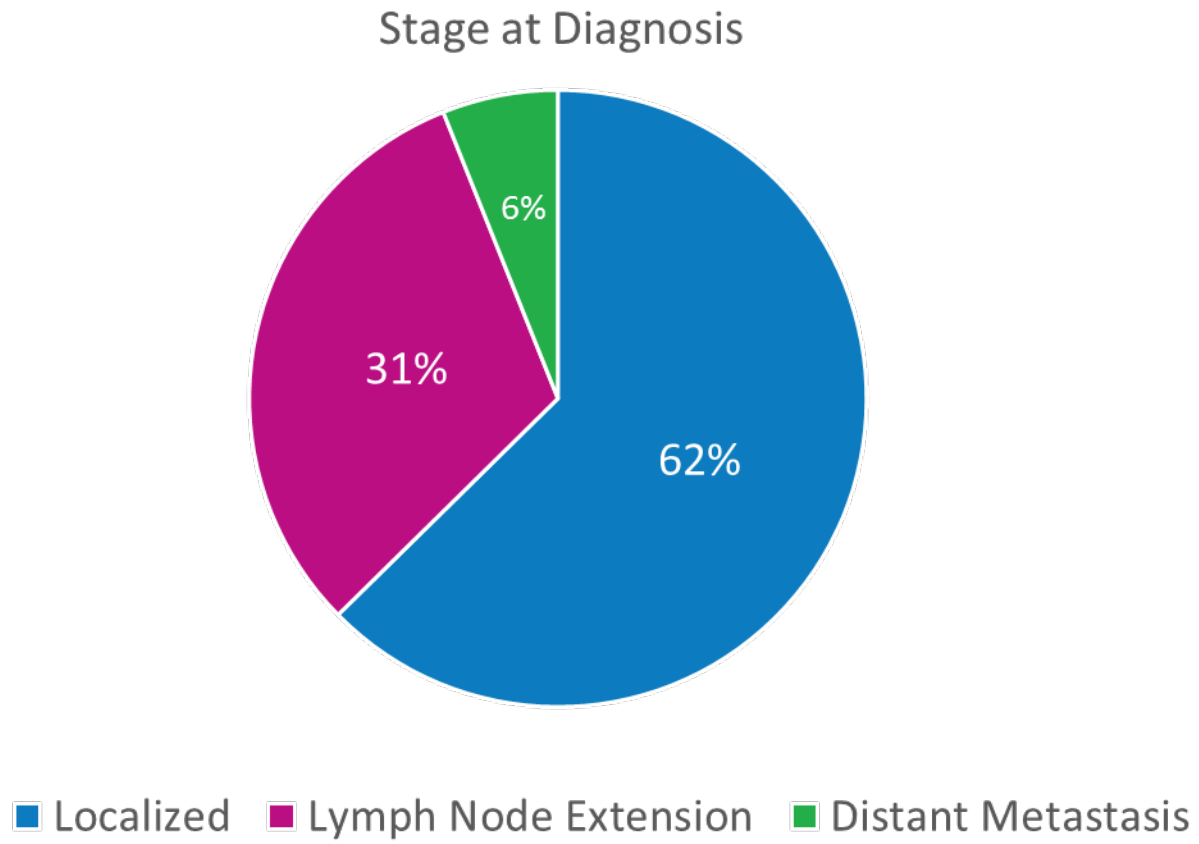
Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Oncology, Oral- Breast Cancer

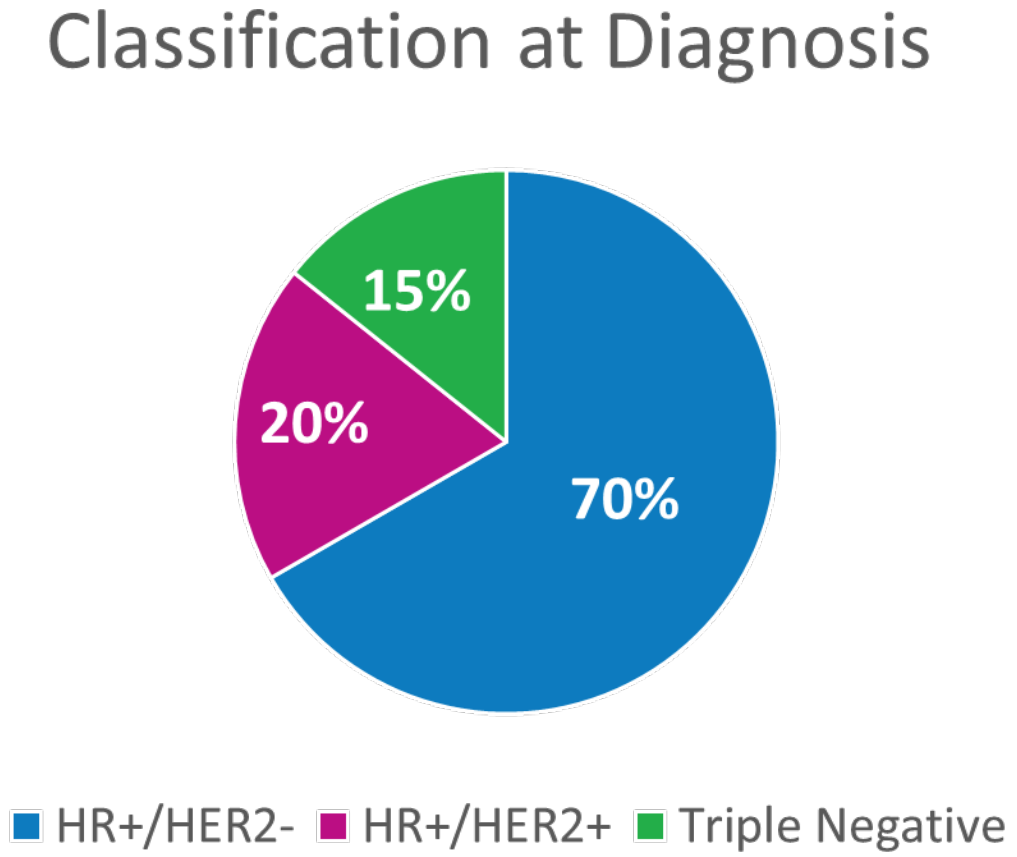
Overview of Disease State – Oncology, Oral- Breast Cancer

- Breast cancer is the most common site of cancer and the 2nd leading cause of death in U.S. women
- 2019: Estimated 268,600 cases diagnosed and 41,760 deaths will occur in U.S. due to breast cancer
- Death rates from breast cancer have steadily decreased since 1989 due to improvements in both early detection and improvements in treatment
  - > 50% of breast cancers in the U.S. are diagnosed on screening mammography



Overview of Disease State – Oncology, Oral- Breast Cancer

- Analysis of tumor markers- Defines appropriate breast cancer treatment options for both the adjuvant setting as well as treatment of advanced/metastatic disease
- Breast Cancer can be divided into 3 main subtypes:
  1. **Hormone receptor (HR)- positive/HER2-negative**
     - Hormone receptor includes both estrogen receptor (ER) and progesterone receptor (PR)
     - Expression of either ER or PR in ≥ 1% of tumor cells is considered HR+
  2. **Hormone receptor (HR)- positive/HER2- positive**
     - HER2 is a transmembrane receptor tyrosine kinase in the epidermal growth factor receptor family
  3. **Triple negative**
     - lack of expression of HR or HER2 molecular targets



Overview of Disease State – Oncology, Oral- Breast Cancer

- 5 year prognosis is excellent for patients with non-metastatic disease
  - HR+/HER2: 99%
  - HR+/HER2+: 94%
  - Triple Negative: 85%
- However, median survival for metastatic disease is much poorer
  - HR+/HER2-: 4-5 years
  - HR+/HER2+: 5 years
  - Triple Negative: 10-13 months

Overview of Disease State – Oncology, Oral- Breast Cancer Pharmacologic Classes

Antiestrogen
• fulvestrant (Faslodex)
• tamoxifen
• toremifene (Fareston)
Aromatase Inhibitors
• anastrozole (Arimidex)
• exemestane (Aromasin)
• letrozole (Femara)
HER2-directed
• lapatinib (Tykerb)
• neratinib (Nerlynx)
CDK 4/6 Inhibitors
• abemaciclib (Verzenio)
• palbociclib (Ibrance)
• ribociclib (Kisqali)
Traditional cytotoxics
• capecitabine (Xeloda)
• cyclophosphamide

Note: There are a variety of other drugs utilized in the treatment of breast cancer but these are parenteral drugs billed under the medical benefit and will not be included in this review

Oncology, Oral- Breast Cancer – Indications

Drugs	Generic	Indications
abemaciclib (Verzenio)	---	▪ In combination with an aromatase inhibitor (AI) as initial endocrine-based therapy for the treatment of postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer ▪ In combination with fulvestrant for the treatment of women with hormone receptor HR-positive, HER2-negative advanced or metastatic breast cancer with disease progression following endocrine therapy ▪ Monotherapy for the treatment of adult patients with HR-positive, HER2-negative advanced or metastatic breast cancer with disease progression following endocrine therapy and prior chemotherapy in the metastatic setting
anastrozole (Arimidex)	X	▪ Adjuvant treatment of postmenopausal women with HR-positive early breast cancer ▪ First-line treatment of postmenopausal women with HR-positive or receptor unknown locally advanced or metastatic breast cancer ▪ Treatment of advanced breast cancer in postmenopausal women with disease progression following tamoxifen therapy; patients with estrogen receptor (ER)-negative disease and patients who did not respond to previous tamoxifen therapy rarely respond to anastrozole
capecitabine (Xeloda)	X	▪ In combination with docetaxel after failure of prior anthracycline-containing therapy for metastatic breast cancer ▪ As monotherapy for metastatic breast cancer in patients who are resistant to both paclitaxel and an anthracycline-containing regimen ▪ Adjuvant treatment of colon cancer (Dukes' C) ▪ First-line monotherapy for metastatic colorectal cancer when treatment with fluoropyrimidine therapy alone is preferred
cyclophosphamide	X	▪ Lymphomas: Hodgkin's disease, lymphocytic lymphoma, mixed-cell type lymphoma, histiocytic lymphoma, Burkitt's lymphoma ▪ Other malignant diseases: multiple myeloma, leukemias, mycosis fungoides, neuroblastoma, adenocarcinoma of ovary, retinoblastoma, breast carcinoma ▪ Nephrotic syndrome: biopsy proven minimal change nephrotic syndrome in pediatric patients who failed to adequately respond to or are unable to tolerate adrenocorticosteroid therapy
exemestane (Aromasin)	X	▪ Adjuvant treatment of postmenopausal women with ER-positive early breast cancer who have received 2 to 3 years of tamoxifen and are switched to exemestane for completion of a total of 5 consecutive years of adjuvant hormonal therapy ▪ Treatment of advanced breast cancer in postmenopausal women whose disease has progressed following tamoxifen therapy

Oncology, Oral- Breast Cancer – Indications

Drugs	Generic	Indications
fulvestrant (Faslodex)	---	▪ Treatment of HR-positive, HER2-negative advanced breast cancer in postmenopausal women not previously treated with endocrine therapy ▪ Treatment of HR-positive advanced breast cancer in postmenopausal women whose disease has progressed following endocrine therapy ▪ Treatment of HR-positive, HER2-negative advanced or metastatic breast cancer in combination with palbociclib or abemaciclib in women with disease progression after endocrine therapy
lapatinib (Tykerb)	---	▪ In combination with capecitabine (Xeloda), for the treatment of patients with advanced or metastatic breast cancer whose tumors over express HER2 and who have received prior therapy including an anthracycline, a taxane, and trastuzumab (Herceptin)† ▪ In combination with letrozole (Femara), for the treatment of postmenopausal women with hormone receptor-positive metastatic breast cancer that over expresses the HER2 receptor for whom hormonal therapy is indicated‡
letrozole (Femara)	**X**	▪ Adjuvant treatment of postmenopausal women with HR-positive early breast cancer ▪ Extended adjuvant treatment of early breast cancer in postmenopausal women who have received prior adjuvant tamoxifen therapy ▪ First- and second-line treatment of postmenopausal women HR-positive or unknown advanced breast cancer
neratinib (Nerlynx)	---	▪ Extended adjuvant treatment of adults with early stage HER-2 overexpressed/amplified breast cancer following adjuvant trastuzumab therapy
palbociclib (Ibrance)	---	▪ Treatment of ER)-positive, HER2-negative advanced or metastatic breast cancer in combination with an AI as initial endocrine-based therapy for postmenopausal women ▪ Treatment of ER-positive, HER2-negative advanced or metastatic breast cancer in combination with fulvestrant (Faslodex) in women with disease progression following endocrine therapy
ribociclib (Kisqali)	---	▪ Treatment of pre/perimenopausal or postmenopausal women with HR-positive, HER2-negative advanced or metastatic breast cancer, as initial endocrine-based therapy, in combination with an AI ▪ Treatment of postmenopausal women with HR-positive, HER2-negative advanced or metastatic breast cancer as initial endocrine-based therapy or following disease progression on endocrine therapy, in combination with fulvestrant (Faslodex)
ribociclib/letrozole (Kisqali Femara Co-Pack)	---	▪ Treatment of postmenopausal women with HR-positive, HER2-negative advanced or metastatic breast cancer as initial endocrine-based therapy

Oncology, Oral- Breast Cancer – Indications

Drugs	Generic	Indications
tamoxifen citrate	**X**	▪ Adjuvant therapy for breast cancer in women following total mastectomy or segmental mastectomy, axillary dissection, and breast irradiation to decrease the incidence of contralateral breast cancer ▪ Treatment of metastatic breast cancer in men and pre-and post-menopausal women ▪ Treatment of ductal carcinoma in situ (DCIS) following breast surgery and radiation therapy to reduce the risk of invasive breast cancer in pre-and post-menopausal women ▪ Breast cancer prophylaxis in women who are at high risk (5-year risk ≥ 1.67%) for developing the disease
toremifene (Fareston)	**---**	▪ Treatment of metastatic breast cancer in postmenopausal women with ER-positive or unknown tumors

Oncology, Oral- Breast Cancer – Dosing and Availability

Drug	Adjuvant Therapy	Advanced or Metastatic Disease	DCIS	Prophylaxis	Duration	Other Indications	Administration	Dosage Forms
abemaciclib (Verzenio)	---	-200 mg twice daily if monotherapy -150 mg twice daily if used with an AI, refer to the dosing of selected AI If used with fulvestrant, give fulvestrant on days 1, 15, 29, and once monthly thereafter; pre/perimenopausal women should also receive a GnRH agonist	---	---	Continue until disease progression or unacceptable toxicity	---	Take orally at the same time each day with or without food Swallow whole; do not crush or cut tablets	Tablet: 50 mg, 100 mg, 150 mg, 200 mg
anastrozole (Arimidex)	1 mg once daily	1 mg once daily	---	---	For adjuvant therapy; optimal duration is unknown; no data to support more than 5 years of therapy For advanced disease, continue until tumor progression	---	Same time each day with or without food	Tablet: 1 mg
capecitabine (Xeloda)	---	Monotherapy or in combination with docetaxel: 1,250 mg/m2 twice daily for 2 weeks followed by a 1 week rest period for a 3-week cycle	---	---	Adjuvant for Dukes C CRC: 6 months (8 total 3 week cycles) for advanced breast cancer until disease progression or unacceptable toxicity	Monotherapy for metastatic colorectal cancer (CRC) or adjuvant monotherapy for CRC: 1,250 mg/m2 twice daily for 2 weeks followed by a 1 week rest period for a 3-week cycle	Swallow whole with water within 30 minutes after a meal; do not crush or cut tablets; dose is calculated according to body surface area (BSA)	Tablet: 150 mg, 500 mg

Oncology, Oral- Breast Cancer – Dosing and Availability

Drug	Adjuvant Therapy	Advanced or Metastatic Disease	DCIS	Prophylaxis	Duration	Other Indications	Administration	Dosage Forms
cyclophosphamide	100 mg/m2 by mouth days 1 through 14 of a 28-day cycle when given as part of the CMF	100 mg/m2 by mouth days 1 through 14 of a 28-day cycle when given as part of either the CMF or the CAF regimen; OR 50 mg orally daily on days 1 through 21 every 28 days as a single agent	---	---	For adjuvant therapy with CMF: given for 6 cycles For metastatic disease: given until disease progression or unacceptable toxicity	Nephrotic syndrome: 2 mg/kg daily for 8 to 12 weeks (maximum cumulative dose 168 mg/kg)	Tablets should not be opened, chewed or crushed	Tablet: 25 mg, 50 mg
exemestane (Aromasin)	25 mg once daily	25 mg once daily	---	---	Adjuvant therapy: 5 years OR Complete a total of 5 consecutive years after 2 to 3 years of tamoxifen Advanced disease: until disease progression or unacceptable toxicity	---	Take after a meal	Tablet: 25 mg
fulvestrant (Faslodex)	---	Monotherapy: 500 mg IM days 1, 15, and 29 and monthly thereafter Combination therapy with abemaciclib or palbociclib: 500 mg IM on days 1, 15, and 29 and once monthly thereafter	---	---	Until disease progression or unacceptable toxicity	---	Deep IM injection into buttock (gluteal area) slowly (1 to 2 minutes per injection) as two 5 mL injections, 1 into each buttock	Injection: 250 mg/ 5 mL
lapatinib (Tykerb)	---	HER2+: 1,250 mg once daily for days 1 through 21 when given in conjunction with capecitabine (Xeloda) HER2+, HR+: 1,500 mg once daily when given in conjunction with letrozole (Femara)	---	---	Until disease progression or unacceptable toxicity	---	Take at least 1 hour before or 1 hour after food	Tablet: 250 mg

Oncology, Oral- Breast Cancer – Dosing and Availability

Drug	Adjuvant Therapy	Advanced or Metastatic Disease	DCIS	Prophylaxis	Duration	Other Indications	Administration	Dosage Forms
letrozole (Femara)	2.5 mg once daily	2. 5 mg once daily In combination with palbociclib: 2.5 mg taken once daily throughout the 28-day cycle	---	---	Adjuvant: optimal duration of treatment is unknown; no data to support use beyond 5 years; treatment should be discontinued at relapse Advanced: until tumor progression is evident or unacceptable toxicity	---	Can be taken without regard to food	Tablet: 2.5 mg
neratinib (Nerlynx)	240 mg (6 tablets) once daily	---	---	---	One year	---	Take with food; swallow tablets whole; tablets should not be chewed, crushed or split prior to swallowing Loperamide should be initiated with the first dose of neratinib and continue during first 2 cycles of treatment	Tablet: 40 mg
palbociclib (Ibrance)	---	For combination therapy with either letrozole or fulvestrant: 125 mg once daily for 21 consecutive days followed by 7 days off, to complete a 28-day cycle	---	---	Until disease progression or unacceptable toxicity	---	Take with food; capsules should be swallowed whole without chewing, crushing, or opening them prior to swallowing When given in combination with letrozole, letrozole dose is 2.5 mg once daily given continuously throughout the 28-day cycle When given in combination with fulvestrant, fulvestrant dose is 500 mg IM on days 1, 15, and 29 and then monthly thereafter	Capsule: 75 mg, 100 mg, 125 mg

Oncology, Oral- Breast Cancer – Dosing and Availability

Drug	Adjuvant Therapy	Advanced or Metastatic Disease	DCIS	Prophylaxis	Duration	Other Indications	Administration	Dosage Forms
ribociclib (Kisqali)	---	600 mg (three 200 mg tablets) once daily for 21 consecutive days followed by 7 days off treatment to complete a 28-day cycle	---	---	Until disease progression or unacceptable toxicity	---	Coadminister with A (see individual product labeling for dose) or fulvestrant 500 mg IM on days 1, 15, and 29, and once monthly thereafter Pre/perimenopausal women should be treated with a luteinizing hormone-releasing hormone (LHRH) agonist according to current clinical practice standards Take ribociclib with or without food at the same time each day, preferably in the morning	200 mg tablets
ribociclib/ letrozole (Kisqali Femara Co-Pack)	---	ribociclib: 600 mg (three 200 mg tablets) once daily for 21 consecutive days followed by 7 days off letrozole: 2.5 mg once daily continuously for a 28-day cycle	---	---	Until disease progression or unacceptable toxicity	---	May be administered with or without food; tablets should be swallowed whole and not chewed, crushed or split prior to swallowing.	200 mg-2.5 mg co-pack tablets 400 mg-2.5 mg co-pack tablets 600 mg-2.5 mg co-pack tablets (all doses of ribociclib are provided using 200 mg tablets)
tamoxifen	20 mg to 40 mg daily	20 mg to 40 mg daily	20 mg daily	20 mg daily	Adjuvant: 5 to 10 years or 2 to 6 years followed by 2 to 3 years of an AI DCIS & prophylaxis: 5 years	---	May be administered with or without food There is no evidence that doses > 20 mg/day are more effective; 10 mg twice daily is the most common dose used in clinical practice, doses greater than 20 mg/day should be given in divided doses (morning and evening)	10 mg, 20 mg tablets 10 mg/5 mL solution (under trade name Soltamox)
toremifene (Fareston)	---	60 mg once daily	---	---	Until disease progression	---	Without regard to food	60 mg tablet

Oncology, Oral- Breast Cancer – Guidelines

- Principles of Adjuvant Drug Therapy:
  - The need for adjuvant drug therapy is based primarily on the risk of recurrence
  - Some patients will not require adjuvant drug therapy
  - If the tumor is HR+ and the risk of recurrence is sufficiently high, adjuvant endocrine therapy will be utilized, either following systemic chemotherapy or alone
  - No established role for fulvestrant endocrine therapy in the adjuvant setting
  - Neratinib is the only HER2-directed therapy in this review with a role in adjuvant setting
  - Oral cyclophosphamide is infrequently utilized as part of an adjuvant chemotherapy regimen
  - Capecitabine has a recently established role in the adjuvant setting
- Adjuvant Endocrine Therapy:
  - **Original Standard of Care: tamoxifen x 5 years**
    - Early Breast Cancer Trialists' Collaborative Group (EBCTCG):
      - 2011: Meta-analysis of 20 trials (n >21K patients) found that 5 years of tamoxifen versus control reduced the risk of recurrence by 50% at 5 years
  - **Current Standard of Care: Inclusion of an aromatase inhibitor (AI)**
    - Early Breast Cancer Trialists' Collaborative Group (EBCTCG):
      - 2015: Meta-analysis (n=31,920 postmenopausal women) of tamoxifen versus AI x 5 years: 10 year breast cancer mortality was 15% lower with AI vs tamoxifen
  - **Duration of Adjuvant Endocrine Therapy:**
    - **ASCO systematic review-11/18:**
      - Use of an AI beyond 5 years significantly reduces risk of breast cancer recurrence and development of contralateral breast cancer compared to placebo despite no improvement seen in overall survival. Bone related adverse events are more common with extended AI therapy

Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Relevance of breast cancer hormone receptors and other factors to the efficacy of adjuvant tamoxifen: patient-level meta-analysis of randomized trials Lancet. 2011; 378(9793):771-84

Early Breast Cancer Trialists' Collaborative Group, et al. Aromatase inhibitors versus tamoxifen in early breast cancer: patient-level meta-analysis of the randomized trials. Lancet. 2015. 386:1341-52

Burstein HJ, Lacchetti C, Anderson Het al. American Society of Clinical Oncology Clinical Practice Guideline: Adjuvant Endocrine Therapy for Women with Hormone Receptor-Positive Breast Cancer: ASCO Clinical Practice Guideline Focused Update Available at: https://www.asco.org/practice-guidelines/quality-guidelines/guidelines/breast-cancer#/9326. Accessed January 31, 2019.

Oncology, Oral- Breast Cancer – Guidelines

American Society of Clinical Oncology Clinical Practice Guidelines –Adjuvant Endocrine Therapy

- Postmenopausal women with HR+ breast cancer-most recent update November 2018:
  - Include AI therapy at some point during adjuvant treatment either as up-front therapy or as sequential treatment after tamoxifen
  - All of the following options reduce the risk of breast cancer recurrence compared to 5 years of tamoxifen alone:
    - AI as initial endocrine therapy
    - Sequential therapy, using both tamoxifen and an AI in either order
    - Extended AI treatment after 5 years of tamoxifen
  - Tamoxifen and AIs differ in their adverse effect profile and these differences may inform treatment preferences
  - Node-positive patients should be offered extended AI therapy for up to a total of 10 years of adjuvant endocrine therapy
  - Node-negative patients may be offered extended AI therapy for up to total of 10 years
- Premenopausal women with HR+ breast cancer-Most recent update February 2016
  - Ovarian suppression + endocrine therapy should be given to women with Stage 2 or 3 disease
  - Ovarian suppression + endocrine therapy may be considered in lower risk group women although women with Stage 1 breast cancer not warranting chemotherapy should not receive ovarian suppression with their endocrine therapy nor should women with tumors ≤ 1 cm and who are node-negative
  - Ovarian suppression may be administered with either tamoxifen or an AI
  - Clinicians should discuss potential benefits and risk profiles with their patients

Burstein HJ, Lacchetti C, Anderson Het al. American Society of Clinical Oncology Clinical Practice Guideline: Adjuvant Endocrine Therapy for Women with Hormone Receptor-Positive Breast Cancer: ASCO Clinical Practice Guideline Focused Update Available at: https://www.asco.org/practice-guidelines/quality-guidelines/guidelines/breast-cancer#/9326. Accessed January 31, 2019.

Oncology, Oral- Breast Cancer – Guidelines

American Society of Clinical Oncology Clinical Practice Guidelines –Adjuvant Therapy

- Optimal Adjuvant Chemotherapy and Targeted Therapy for Early Breast Cancer-Most recent update May 2018
  - Capecitabine: Patients with HER2-negative disease and pathologic invasive residual disease at time of surgery following standard anthracycline and taxane-based preoperative therapy may be offered up to 6 to 8 cycles of adjuvant capecitabine (moderate)
    - Based on the CREATE-X trial (n=910) in stages I to IIIB HER2-negative breast cancer
      - DFS @ 5 years =74.1% vs 67.6% (HR=0.7; p=0.01), OS was 89.2% vs 83.6% (HR=0.59, p=0.01) favoring capecitabine over control
      - In TNBC, DFS was 69.8% vs 56.1% (HR=0.58), OS=78.8% vs 70.3% (HR=0.52)
    - The ASCO expert panel preferentially supports the use of adjuvant capecitabine in TNBC
  - Neratinib: Extended adjuvant therapy with neratinib may be used in patients with early-stage HER1-positive breast cancer (moderate)
    - Based on the ExteNET trial (n=2,840) which demonstrated an iDFS of 94.2% at 2 years vs 91.9% (HR=0.66, p=0.008) favoring neratinib
    - Extended follow up of the ExteNET trial with 2.117 of the original 2.840 patients showed a 5 year iDFS of 90.2% vs 87.7% (HR=0.73)
    - No OS benefit has been demonstrated to date
    - There are no data on the added benefit of neratinib in patients who also received pertuzumab in the neoadjuvant or adjuvant setting
    - Neratinib causes substantial diarrhea and diarrhea prophylaxis must be utilized
    - The ASCO expert panel preferentially supports the use of neratinib in HR-positive, node-positive patients

Masuda N, Lee SJ, Ohtani S, et al. Adjuvant Capecitabine for Breast Cancer after Preoperative Chemotherapy N Engl J Med 2017;376:2147-2159

Chan A, Delaloge S, Holmes FA, et al. Neratinib after trastuzumab-based adjuvant therapy in patients with HER2-positive breast cancer (ExteNET): a multicenter, randomized, double blind, placebo-controlled phase 3 trial. Lancet Oncol. 2016;17:367-7

Martin M, Holmes FA, Ejlertsen B, et al for the ExteNET Study Group. Neratinib after trastuzumab-based adjuvant therapy in HER2-positive breast cancer (ExteNET): 5-year analysis of a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Oncol. 2017;18(12):1688-1700

Denduluri N, Chavez-MacGregor M, Telli ML, et al. Selection of Optimal Adjuvant Chemotherapy and Targeted Therapy for Early Breast Cancer: ASCO Clinical Practice Guideline Focused Update. Available at: https://www.asco.org/practice-guidelines/quality-guidelines/guidelines/breast-cancer#/11081 Accessed January 31, 2019

Oncology, Oral- Breast Cancer – Guidelines
Metastatic/Advanced Breast Cancer

- Principles of Therapy for Advanced/Metastatic Breast Cancer
  - For HR-positive, HER2-negative disease, endocrine therapy is recommended as 1st line in nearly all patients (exception: patients with symptomatic visceral disease may be considered for chemotherapy)
  - For HR-positive, HER2-negative patients, NCCN guidelines preferentially recommend fulvestrant ± a CDK4/6 inhibitor or and AI with the addition of a CDK4/6 inhibitor for patients with no prior endocrine therapy in the last year
  - Recommendations for premenopausal women with HR-positive, HER2-negative disease mimic those for postmenopausal women with the addition of ovarian suppression
  - Endocrine therapy may be utilized in HR-positive, HER2-positive patients with metastatic/advanced breast cancer who have not received prior endocrine therapy in the last year, the CDK4/6 inhibitors are not recommended in HER2-positive patients
  - In the past it was recommended that patients progress through 3 lines of endocrine therapy before moving on to systemic chemotherapy but this has changed somewhat in the era of CDK4/6 inhibitors being utilized in the front line setting of metastatic/advanced breast cancer
  - If there is disease progression while on a CDK4/6 inhibitor therapy, there are no data to support an additional line of therapy with another CDK4/6-containing regimen
  - Lapatinib, with or without capecitabine, is an option for patients with HER2-positive disease but is considered a 3rd line agent after the use of other parenteral HER2-directed therapies

Rugo HS, Rumble B, Macrae E, et al. American Society of Clinical Oncology Clinical Practice Guideline. Endocrine Therapy for Hormone Receptor-Positive Metastatic Breast Cancer. Available at: https://www.asco.org/practice-guidelines/quality-guidelines/guidelines/breast-cancer#/11751 Accessed February 1, 2019

Giordano, SH Temin S, Chandarlapaty S, et al. Systemic therapy for patients with advanced human epidermal growth factor receptor 2-positive breast cancer: ASCO clinical practice guideline update. Available at: http://ascopubs.org/doi/pdf/10.1200/JCO.2018.79.2697 Accessed February 1, 2019

Oncology, Oral- Breast Cancer – Guidelines

- NCCN Breast Cancer Guidelines V3.2018

Washington State Health Care Authority

Antineoplastics and Adjunctive Therapy, Oral Agents, Breast Cancer

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Clinical Quality & Care Transformation
February 20, 2019

Antineoplastics and Adjunctive Therapy, Oral Agents, Abbreviations

Abbreviation	Term
AI	Aromatase Inhibitor
EGFR	Epidermal Growth Factor Receptor
ER	estrogen receptor
FDA	Food and Drug Administration
HER2	Human Epidermal Growth Factor Receptor 2
HR	hormone receptor
mTOR	Mammalian Target of Rapamycin
PARP	Poly (ADP-ribose) polymerase
VEGF	Vascular Endothelial Growth Factor

Antineoplastics and Adjunctive Therapy, Oral Agents, Breast Cancer

Drug name (Brand Nane)	Mechanism of Action	FDA Approval
abemaciclib (Verzenio™)	Cyclin-Dependent Kinase Inhibitor	2017
anastrozole (Arimidex®)*	Aromatase Inhibitor	1995
capecitabine (Xeloda®)*	Pyrimidine Analog	1998
cyclophosphamide*	Nitrogen Mustard	1959
everolimus (Afinitor®)	mTOR Inhibitor	2009
exemestane (Aromasin®)*	Aromatase Inhibitor	1999
fulvestrant (Faslodex®)*	Antiestrogen	2002
lapatinib (Tykerb®)	EGFR Tyrosine Kinase Inhibitor	2007
letrozole (Femara®)*	Aromatase Inhibitor	1997

*Generic available

Antineoplastics and Adjunctive Therapy, Oral Agents, Breast Cancer

Drug name (Brand Nane)	Mechanism of Action	FDA Approval
neratinib (Nerlynx®)	EGFR Tyrosine Kinase Inhibitor	2017
olaparib (Lynparza®)	PARP Enzymes Inhibitor	2014
palbociclib (Ibrance®)	Cyclin-Dependent Kinase Inhibitor	2015
ribociclib (Kisqali®)	Cyclin-Dependent Kinase Inhibitor	2017
ribociclib/letrozole (Kisqali Femara Co-Pack®)	Cyclin-Dependent Kinase Inhibitor / Aromatase Inhibitor	2017
talazoparib (Talzenna)	PARP Enzymes Inhibitor	2018
tamoxifen citrate*	Antiestrogen	1977
toremifene (Fareston®)	Antiestrogen	1997

*Generic available

Antineoplastics and Adjunctive Therapy, Oral Agents, Breast Cancer

Initial request:

- Diagnosis that is listed in FDA-approved label **OR** in compendia recognized by Medicaid (defined in Section 1927 of the Social Security Act); **AND**
- If an FDA-approved companion diagnostic test for the requested agent exists, documentation that the test was performed to confirm the diagnosis; **AND**
- If a test with adequate ability to confirm a disease mutation exists, documentation that the test was performed to confirm the diagnosis; **AND**
- If not indicated as a first line agent, documentation of all previous therapies; **AND**
- Must be used in combination with other chemotherapeutic or adjuvant agents according to the FDA approved prescribing information; **AND**

Antineoplastics and Adjunctive Therapy, Oral Agents, Breast Cancer

Initial request (continued):

- Prescribed by, or in consultation with, a specialist in oncology or hematology; **AND**
- The patient does not have any contraindications to the requested oral oncology medication; **AND**
- The prescribed quantity and dosing regimen falls within the manufacturer's published dosing guidelines and is appropriate for the patient's age; **AND**
- Documentation from the provider on what measure they'll use to determine whether the patient has had a positive clinical response

Antineoplastics and Adjunctive Therapy, Oral Agents, Breast Cancer

Reauthorization criteria:

- Documentation from the provider that the patient has had a positive clinical response and is able to tolerate therapy

Antineoplastics and Adjunctive Therapy, Oral Agents, Breast Cancer

abemaciclib (Verzenio)

- In combination with an aromatase inhibitor (AI) as initial endocrine-based therapy for the treatment of postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer
- In combination with fulvestrant for the treatment of women with hormone receptor HR-positive, HER2-negative advanced or metastatic breast cancer with disease progression following endocrine therapy
- Monotherapy for the treatment of adult patients with HR-positive, HER2-negative advanced or metastatic breast cancer with disease progression following endocrine therapy and prior chemotherapy in the metastatic setting

Antineoplastics and Adjunctive Therapy, Oral Agents, Breast Cancer

anastrozole (Arimidex)

- Adjuvant treatment of postmenopausal women with HR-positive early breast cancer
- First-line treatment of postmenopausal women with HR-positive or receptor unknown locally advanced or metastatic breast cancer
- Treatment of advanced breast cancer in postmenopausal women with disease progression following tamoxifen therapy; patients with estrogen receptor (ER)-negative disease and patients who did not respond to previous tamoxifen therapy rarely respond to anastrozole

capecitabine (Xeloda)

- In combination with docetaxel after failure of prior anthracycline-containing therapy for metastatic breast cancer
- As monotherapy for metastatic breast cancer in patients who are resistant to both paclitaxel and an anthracycline-containing regimen
- Adjuvant treatment of colon cancer (Dukes' C)
- First-line monotherapy for metastatic colorectal cancer when treatment with fluoropyrimidine therapy alone is preferred

Antineoplastics and Adjunctive Therapy, Oral Agents, Breast Cancer

cyclophosphamide

- Lymphomas: Hodgkin's disease, lymphocytic lymphoma, mixed-cell type lymphoma, histiocytic lymphoma, Burkitt's lymphoma
- Other malignant diseases: multiple myeloma, leukemias, mycosis fungoides, neuroblastoma, adenocarcinoma of ovary, retinoblastoma, breast carcinoma
- Nephrotic syndrome: biopsy proven minimal change nephrotic syndrome in pediatric patients who failed to adequately respond to or are unable to tolerate adrenocorticosteroid therapy

exemestane (Aromasin)

- Adjuvant treatment of postmenopausal women with ER-positive early breast cancer who have received 2 to 3 years of tamoxifen and are switched to exemestane for completion of a total of 5 consecutive years of adjuvant hormonal therapy
- Treatment of advanced breast cancer in postmenopausal women whose disease has progressed following tamoxifen therapy

Antineoplastics and Adjunctive Therapy, Oral Agents, Breast Cancer

everolimus (Afinitor)

- Adults with advanced renal cell carcinoma (RCC) after failure of treatment with sunitinib or sorafenib
- Pediatric and adult patients with subependymal giant cell astrocytoma (SEGA) associated with tuberous sclerosis complex (TSC) that requires therapeutic intervention but cannot be curatively resected
- Adults with progressive neuroendocrine tumors (NET) of pancreatic origin that are unresctable, locally advanced, or metastatic and adults with progressive, well-differentiated, non-functional NET of gastrointenstinal or lung origin that are unresectable, locally advanced, or metastatic
- Adults with renal angiomyolipoma and TSC, not requiring immediate surgery
- Postmenopausal women with advanced hormone receptor-positive, HER2-negative breast cancer (advanced HR+ BC) in combination with exemestane after failure of treatment with letrozole or anastrozole

Antineoplastics and Adjunctive Therapy, Oral Agents, Breast Cancer

fulvestrant (Faslodex)

- Treatment of HR-positive, HER2-negative advanced breast cancer in postmenopausal women not previously treated with endocrine therapy
- Treatment of HR-positive advanced breast cancer in postmenopausal women whose disease has progressed following endocrine therapy
- Treatment of HR-positive, HER2-negative advanced or metastatic breast cancer in combination with palbociclib or abemaciclib in women with disease progression after endocrine therapy

lapatinib (Tykerb)

- In combination with capecitabine (Xeloda), for the treatment of patients with advanced or metastatic breast cancer whose tumors over express HER2 and who have received prior therapy including an anthracycline, a taxane, and trastuzumab (Herceptin)
- In combination with letrozole (Femara), for the treatment of postmenopausal women with hormone receptor-positive metastatic breast cancer that over expresses the HER2 receptor for whom hormonal therapy is indicated

Antineoplastics and Adjunctive Therapy, Oral Agents, Breast Cancer

letrozole (Femara)

- Adjuvant treatment of postmenopausal women with HR-positive early breast cancer
- Extended adjuvant treatment of early breast cancer in postmenopausal women who have received prior adjuvant tamoxifen therapy
- First- and second-line treatment of postmenopausal women HR-positive or unknown advanced breast cancer

neratinib (Nerlynx)

- Extended adjuvant treatment of adults with early stage HER-2 overexpressed/amplified breast cancer following adjuvant trastuzumab therapy

palbociclib (Ibrance)

- Treatment of ER)-positive, HER2-negative advanced or metastatic breast cancer in combination with an AI as initial endocrine-based therapy for postmenopausal women
- Treatment of ER-positive, HER2-negative advanced or metastatic breast cancer in combination with fulvestrant (Faslodex) in women with disease progression following endocrine therapy

Antineoplastics and Adjunctive Therapy, Oral Agents, Breast Cancer

olaparib (Lynparza)

- Monotherapy in patients with deleterious or suspected deleterious germline BRCA-mutated (gBRCAm) advanced ovarian cancer as detected by an FDA-approved test who have been treated with 3 or more prior lines of chemotherapy
- Maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer, who are in a complete or patient response to platinum-based chemotherapy
- Patients with deleterious or suspsected deleterious gBRCAm, human epidermal growth factor receptor 2 (HER2)-negative metastatic breast cancer who have been treated with chemotherapy in the neoadjuvant, adjuvant, or metastatic setting; patients with hormone receptor (HR)-positive breast cancer should have been treated with prior endocrine therapy or be considered inappropriate for endocrine therapy, and patients should be selected for treatment based on the FDA-approved companion diagnostic

Antineoplastics and Adjunctive Therapy, Oral Agents, Breast Cancer

ribociclib (Kisqali)

- Treatment of pre/perimenopausal or postmenopausal women with HR-positive, HER2-negative advanced or metastatic breast cancer, as initial endocrine-based therapy, in combination with an AI
- Treatment of postmenopausal women with HR-positive, HER2-negative advanced or metastatic breast cancer as initial endocrine-based therapy or following disease progression on endocrine therapy, in combination with fulvestrant (Faslodex)

ribociclib/letrozole (Kisqali Femara Co-Pack)

- Treatment of postmenopausal women with HR-positive, HER2-negative advanced or metastatic breast cancer as initial endocrine-based therapy

talazoparib (Talzenna)

- treatment of adult patients with deleterious or suspected deleterious germline BRCA-mutated, HER2-negative locally advanced or metastatic breast cancer. Patient selection is based on confirmation of germline BRCA-mutated status via an FDA-approved companion diagnostic

Antineoplastics and Adjunctive Therapy, Oral Agents, Breast Cancer

tamoxifen citrate

- Adjuvant therapy for breast cancer in women following total mastectomy or segmental mastectomy, axillary dissection, and breast irradiation to decrease the incidence of contralateral breast cancer
- Treatment of metastatic breast cancer in men and pre-and post-menopausal women
- Treatment of ductal carcinoma in situ (DCIS) following breast surgery and radiation therapy to reduce the risk of invasive breast cancer in pre-and post-menopausal women
- Breast cancer prophylaxis in women who are at high risk (5-year risk ≥ 1.67%) for developing the disease

toremifene (Fareston)

- Treatment of metastatic breast cancer in postmenopausal women with ER-positive or unknown tumors

Antineoplastics and Adjunctive Therapy, Oral Agents, Breast Cancer

Motion:

- "I move that the Apple Health Medicaid Program implement the clinical criteria listed on slides 81-83 as recommended. The breast oncology drugs listed on slides 79-80 are considered safe and efficacious for their respective FDA indications. All drugs are preferred for their FDA labeled indications."

  - Motion: Schwilke
  - 2nd: Storhaug

Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Oncology, Oral- Renal Cell Carcinoma

Overview of Disease State – Oncology, Oral- Renal Cell Carcinoma

- In 2019, predicted 73,820 diagnosed cases and 14,770 deaths associated with cancer of the kidney and renal pelvis
- ~ 90% of all kidney tumors are renal cell carcinoma (RCC) and 70% of those are clear cell carcinomas, the most common histology
- Smoking, obesity and hypertension are known risk factors for the development of RCC
- A genetic disorder, von Hippel-Lindau (VHL) disease predisposed patients to developing RCC
- Median age at diagnosis is 64 years and the incidence in men is more than twice that of women
- Presenting symptoms include hematuria, flank mass and flank pain, however more than half of all RCC are diagnosed based on incidental finding associated with routine imaging
- Surgery involving a partial or radical nephrectomy is usually performed, particularly in patients without metastatic disease
- RCC demonstrates a poor response rate (4%-6%) to traditional cytotoxic agents
  - Early immunotherapy agents (interferon and interleukin-2 were the previous standard of care)
- Targeted therapies are now used in the first line and second line setting of advanced RCC
- First approval for a targeted therapy used in the adjuvant setting post-nephrectomy for high risk patients was granted in late 2017

Oncology, Oral- Renal Cell Carcinoma – Indications

Drugs	Generic	Indications
axitinib (Inlyta)	---	▪ Treatment of advanced renal cell carcinoma (RCC) in adults after failure of 1 prior systemic therapy
cabozantinib (Cabometyx)	---	▪ Treatment of advanced RCC
everolimus (Afinitor)	---	▪ Adults with advanced RCC after failure of treatment with sunitinib (Sutent) or sorafenib (Nexavar) ▪ Pediatric and adult patients with subependymal giant cell astrocytoma (SEGA) associated with tuberous sclerosis complex (TSC) that requires therapeutic intervention but cannot be curatively resected. ▪ Adults with progressive neuroendocrine tumors (PNET) of pancreatic origin that are unresectable, locally advanced, or metastatic and adults with progressive, well-differentiated, non-functional neuroendocrine tumors (NET) of gastrointestinal (GI) or lung origin that are unresectable, locally advanced, or metastatic ▪ Adults with renal angiomyolipoma and tuberous sclerosis complex (TSC), not requiring immediate surgery ▪ Postmenopausal women with advanced hormone receptor-positive, HER2-negative breast cancer (advanced HR+ BC) in combination with exemestane after failure of treatment with letrozole or anastrozole
everolimus (Afinitor Disperz)	---	▪ Adult and pediatric patients with SEGA associated with TSC requiring therapeutic intervention but cannot be curatively resected ▪ Adjunctive treatment of patients aged 2 years and older with Tuberous Sclerosis Complex (TSC) associated partial-onset seizures

Oncology, Oral- Renal Cell Carcinoma – Indications

Drugs	Generic	Indications
lenvatinib (Lenvima)	---	▪ In combination with everolimus for patients with advanced RCC following 1 prior anti-angiogenic therapy ▪ Treatment of differentiated thyroid cancer (DTC) in patients with locally recurrent or metastatic, progressive radioactive iodine-refractory DTC
pazopanib (Votrient)	---	▪ Treatment of advanced RCC ▪ Advanced soft tissue sarcoma in patients who have received prior chemotherapy
sorafenib (Nexavar)	---	▪ Unresectable hepatocellular carcinoma (HCC) ▪ Advanced RCC ▪ Locally recurrent or metastatic progressive, differentiated thyroid carcinoma (DTC) refractory to radioactive iodine treatment
sunitinib malate (Sutent)	---	▪ Gastrointestinal stromal tumors (GIST) after disease progression on or intolerance to imatinib mesylate ▪ Advanced RCC ▪ Adjuvant treatment of RCC at high risk of recurrence following nephrectomy ▪ Progressive well-differentiated pancreatic neuroendocrine tumors (PNET) in patients with unresectable, locally advanced, or metastatic disease

Oncology, Oral- Renal Cell Carcinoma – Dosing and Availability

Drugs	Dose	Administration Comments	Availability
axitinib (Inlyta)	RCC: 5 mg twice daily	Take with or without food; swallow whole with a glass of water	1 mg, 5 mg tablets
cabozantinib (Cabometyx)	RCC: 60 mg daily	Do not administer with food; patients should not eat for 2 hours before and at least 1 hour after taking dose; swallow tablets whole, do not crush tablets	20 mg, 40 mg, 60 mg tablets
everolimus (Afinitor, Afinitor Disperz)	RCC: 10 mg daily SEGA: 4.5 mg/m2 once daily. Subsequent titration to trough concentrations of 5 to 15 ng/mL Advanced NET: 10 mg daily PNET: 10 mg daily Renal angiomyolipoma with TSC: 10 mg daily Advanced HR+ Breast Cancer: 10 mg daily TSC-Associated Partial-Onset Seizures: 5 mg/m2 once daily until disease progression or unacceptable toxicity	Tablets: May be taken consistently with or without food and should be swallowed whole with a glass of water Afinitor Disperz: Administer suspension immediately after preparation in either an oral syringe or small drinking glass; prepare suspension in water only; discard suspension if not administered within 60 minutes after preparation; Administer consistently at the same time every day consistently with or consistently without food; gloves should be worn to avoid possible contact with everolimus (Afinitor) when preparing suspensions of Afinitor Disperz for another person	2.5 mg, 5 mg, 7.5 mg, 10 mg tablets Afinitor Disperz tablets for oral suspension: 2 mg, 3 mg, 5 mg tablets for oral suspension Do not combine the 2 dosage forms (Afinitor tablets and Afinitor Disperz tablets for suspension) to achieve desired total dose; use 1 dosage form or the other

Oncology, Oral- Renal Cell Carcinoma – Dosing and Availability

Drugs	Dose	Administration Comments	Availability
lenvatinib (Lenvima)	DTC: 24 mg daily RCC: 18 mg daily in combination with everolimus 5 mg once daily	Take with or without food; capsules should be swallowed whole or the whole capsule can be dissolved in a small glass of water or apple juice	4 mg, 10 mg capsules in packages containing total daily doses of 8 mg, 10 mg, 14 mg, 18 mg, 20 mg, and 24 mg
pazopanib (Votrient)	RCC: 800 mg daily Soft tissue sarcoma: 800 mg daily	Give at least 1 hour before or 2 hours after a meal; do not crush tablets; If a dose is missed, it should not be taken if it is less than 12 hours until the next dose	200 mg tablets
sorafenib (Nexavar)	RCC: 400 mg twice daily HCC: 400 mg twice daily DTC: 400 mg twice daily	Take without food (at least 1 hour before or 2 hours after a meal)	200 mg tablets
sunitinib (Sutent)	RCC: 50 mg daily; 4 weeks on therapy, 2 weeks off therapy RCC, adjuvant treatment: 50 mg daily; 4 weeks on therapy, 2 weeks off therapy for nine 6-week cycles GIST: 50 mg daily; 4 weeks on therapy, 2 weeks off therapy PNET: 37.5 mg once daily, continuously without a scheduled off-treatment period	May be taken with or without food	12.5 mg, 25 mg, 37.5 mg, 50 mg capsules

Oncology, Oral- Renal Cell Carcinoma – Guidelines

- NCCN Kidney Cancer Guidelines

Oncology, Oral- Renal Cell Carcinoma – Guidelines, Selected References

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Washington State Health Care Authority

Antineoplastics and Adjunctive Therapy, Oral Agents, Renal Cancers

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Clinical Quality & Care Transformation
February 20, 2019

Antineoplastics and Adjunctive Therapy, Oral Agents, Abbreviations

Abbreviation	Term
DTC	Differentiated Thyroid Cancer
FDA	Food and Drug Administration
HCC	Hepatocellular Carcinoma
HER2	Human Epidermal Growth Factor Receptor 2
mTOR	Mammalian Target of Rapamycin
RCC	Renal Cell Carcinoma
SEGA	Subependymal Giant Cell Astrocytoma
TSC	Tuberous Sclerosis Complex
VEGF	Vascular Endothelial Growth Factor

Antineoplastics and Adjunctive Therapy, Oral Agents, Renal Cancers

Drug name (Brand Nane)	Mechanism of Action	FDA Approval
axitinib (Inlyta®)	VEGF Tyrosine Kinase Inhibitor	2012
cabozantinib (Cabometyx®)	VEGF Tyrosine Kinase Inhibitor	2012
everolimus (Afinitor®)	mTOR Inhibitor	2009
everolimus (Afinitor Disperz®)	mTOR Inhibitor	2009
lenvatinib (Lenvima®)	VEGF Tyrosine Kinase Inhibitor	2015
pazopanib (Votrient®)	VEGF Tyrosine Kinase Inhibitor	2009
sorafenib (Nexavar®)	Multikinase Inhibitor	2005
sunitinib malate (Sutent®)	VEGF Tyrosine Kinase Inhibitor	2006

Antineoplastics and Adjunctive Therapy, Oral Agents, Renal Cancers

Initial request:

- Diagnosis that is listed in FDA-approved label **OR** in compendia recognized by Medicaid (defined in Section 1927 of the Social Security Act); **AND**
- If an FDA-approved companion diagnostic test for the requested agent exists, documentation that the test was performed to confirm the diagnosis; **AND**
- If a test with adequate ability to confirm a disease mutation exists, documentation that the test was performed to confirm the diagnosis; **AND**
- If not indicated as a first line agent, documentation of all previous therapies; **AND**
- Must be used in combination with other chemotherapeutic or adjuvant agents according to the FDA approved prescribing information; **AND**

Antineoplastics and Adjunctive Therapy, Oral Agents, Renal Cancers

Initial request (continued):

- Prescribed by, or in consultation with, a specialist in oncology or hematology; **AND**
- The patient does not have any contraindications to the requested oral oncology medication; **AND**
- The prescribed quantity and dosing regimen falls within the manufacturer's published dosing guidelines and is appropriate for the patient's age; **AND**
- Documentation from the provider on what measure they'll use to determine whether the patient has had a positive clinical response

Antineoplastics and Adjunctive Therapy, Oral Agents, Renal Cancers

Reauthorization criteria:

- Documentation from the provider that the patient has had a positive clinical response and is able to tolerate therapy

Antineoplastics and Adjunctive Therapy, Oral Agents, Renal Cancers

everolimus (Afinitor)

- Adults with advanced renal cell carcinoma (RCC) after failure of treatment with sunitinib or sorafenib
- Pediatric and adult patients with subependymal giant cell astrocytoma (SEGA) associated with tuberous sclerosis complex (TSC) that requires therapeutic intervention but cannot be curatively resected
- Adults with progressive neuroendocrine tumors (NET) of pancreatic origin that are unresctable, locally advanced, or metastatic and adults with progressive, well-differentiated, non-functional NET of gastrointenstinal or lung origin that are unresectable, locally advanced, or metastatic
- Adults with renal angiomyolipoma and TSC, not requiring immediate surgery
- Postmenopausal women with advanced hormone receptor-positive, HER2-negative breast cancer (advanced HR+ BC) in combination with exemestane after failure of treatment with letrozole or anastrozole

Antineoplastics and Adjunctive Therapy, Oral Agents, Renal Cancers

everolimus (Afinitor Disperz)

- Adult and pediatric patients with SEGA associated with TSC requiring therapeutic intervention but cannot be curatively resected
- Adjunctive treatment of patients aged 2 years and older with TSC associated partial-onset seizures

axitinib (Inlyta)

- Treatment of advanced RCC in adults after failure of 1 prior systemic therapy

cabozantinib (Cabometyx)

- Treatment of advanced RCC

Antineoplastics and Adjunctive Therapy, Oral Agents, Renal Cancers

lenvatinib (Lenvima)

- In combination with everolimus for patients with advanced RCC following 1 prior anti-androgenic therapy
- Treatment of differentiated thyroid cancer (DTC) in patients with locally recurrent or metastatic, progressive radioactive iodine-refractory DTC

pazopanib (Votrient)

- Treatment of advanced RCC
- Advanced soft tissue sarcoma in patients who have received prior chemotherapy

sorafenib (Nexavar)

- Locally recurrent or metastatic progressive, DTC refractory to radioactive iodine treatment
- Unresctable hepatocellular carcinoma (HCC)
- Advanced RCC

Antineoplastics and Adjunctive Therapy, Oral Agents, Renal Cancers

sunitinib (Sutent)

- Gastrointestinal stromal tumors (GIST) after disease progression on or intolerance to imatinib
- Advanced RCC
- Adjuvant treatment of RCC at high risk of recurrence following nephrectomy
- Progressive well-differentiated pancreatic neuroendocrine tumors (PNET) in patients with unresectable, locally advanced, or metastatic disease

Antineoplastics and Adjunctive Therapy, Oral Agents, Renal Cancers

Motion:

- "I move that the Apple Health Medicaid Program implement the clinical criteria listed on slides 105-107 as recommended. The renal oncology drugs listed on slide 104 are considered safe and efficacious for their respective FDA indications. All drugs are preferred for their FDA labeled indications."

  - Motion: Figueroa
  - 2nd: Flatebo

Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Oncology, Oral- Lung

Overview of Disease State – Oncology, Oral- Lung

- Lung cancer is the leading cause of cancer death in both men and women in the U.S.
- In 2019, there will be an estimated 228,150 cases diagnosed and 142,670 deaths in the U.S. due to lung cancer
- As a direct result of the decline in tobacco smoking rates, there was a 45% decline in the lung cancer death rate for men between 1993 and 2015 and a 19% decline between 2002 and 2015 for women
- Between 10% and 25% of lung cancer cases are diagnosed in patients who have never smoked
- Lung cancer is divided into 2 major subtypes
  - Non-small cell lung cancer (NSCLC)- 80% of all cases
    - Histologic subtypes include squamous cell and nonsquamous cell (includes adenocarcinoma which is the most common type)
  - Small cell lung cancer (SCLC)
- Treatment of lung cancer may involve surgery, radiation, chemotherapy, targeted therapy or immunotherapy
- Genomic profiling now allows further classification of NSCLC based on the presence of specific oncogenes
  - Occur much more commonly in adenocarcinoma but may been seen in squamous cell histology, particularly in never smokers
  - Epidermal growth factor receptor (EGFR) sensitizing mutations occur in ~ 10% of Caucasians, may be as high as 50% for East Asians
  - Anaplastic lymphoma kinase (ALK) translocations-2% to 7% of cases
  - ROS proto-oncogene 1 (ROS1)-1% to 2% of cases
  - EGFR, ALK, ROS1 all occur more commonly in non-smokers
  - Tyrosine kinase inhibitors (TKIs) aimed at these specific oncogenes are now considered standard of care for these patients
  - Development of resistance usually occurs with these agents; thee intervals vary but are in the neighborhood of 1 year

Oncology, Oral- Lung – Indications

Drugs	Generic	Indications
ALK Tyrosine Kinase Inhibitors		
alectinib (Alecensa)	---	▪ Treatment of patients with anaplastic lymphoma kinase (ALK)-positive, metastatic non-small cell lung cancer (NSCLC) as detected by an FDA approved test
brigatinib (Alunbrig)	---	▪ Treatment of ALK-positive metastatic NSCLC in patients who have progressed on or are intolerant to crizotinib
ceritinib (Zykadia)	---	▪ Treatment of ALK-positive metastatic NSCLC as detected by an FDA-approved test
crizotinib (Xalkori)	---	▪ Treatment of metastatic NSCLC in patients whose tumors are ALK-positive or ROS1-positive as detected by an FDA-approved test
loralatinib (Lobrena)	_	▪ Treatment of ALK-positive metastatic NSCLC after disease progression on crizotinib and at least 1 other ALK inhibitor for metastatic disease or alectinib as the first ALK inhibitor for metastatic disease or ceritinib as the first ALK inhibitor for metastatic disease
EGFR Tyrosine Kinase Inhibitors		
afatinib (Gilotrif)	---	▪ First-line treatment of metastatic NSCLC with nonresistant epidermal growth factor receptor (EGFR) mutations as detected by an FDA-approved test ▪ Treatment of metastatic, squamous NSCLC progressing after platinum-based therapy
dacomitinib (Vizimpro)	-	▪ First-line treatment of metastatic NSCLC with EGFR exon 19 deletion or exon 21 L858R substitution mutations as detected by and FDA-approved test
erlotinib (Tarceva)	---	▪ Treatment of patients with metastatic NSCLC whose tumors have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test who are receiving first-line, maintenance, or second- or greater-line treatment after progression following at least 1 prior chemotherapy regimen ▪ First-line treatment of patients with locally advanced, unresectable, or metastatic pancreatic cancer, in combination with gemcitabine
gefitinib (Iressa)	---	▪ First-line treatment of patients with NSCLC whose tumors have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test
osimertinib (Tagrisso)	---	▪ Treatment of patients with metastatic EGFR T790M mutation-positive NSCLC as detected by an FDA-approved test, who have progressed on or after EGFR tyrosine kinase inhibitor (TKI) therapy
Non-targeted Agents		
Topotecan (Hycamtin)	---	▪ Treatment of relapsed small cell lung cancer

Oncology, Oral- Lung – Dosing and Availability

Drugs	Dose	Administration	Available Strengths
ALK Tyrosine Kinase Inhibitors			
alectinib (Alecensa)	600 mg twice daily	Take with food; do not open or dissolve capsules	150 mg capsules
brigatinib (Alunbrig)	90 mg once daily for 7 days; may increase to 180 mg once daily as tolerated	Take with or without food; swallow tablets whole If therapy is interrupted for ≥ 14 days for reasons other than adverse reactions, resume treatment at 90 mg once daily for 7 days before increasing to the previously tolerated dose	30 mg, 90 mg, 180 mg tablets
ceritinib (Zykadia)	450 mg once daily	Take once daily with food	150 mg capsules
crizotinib (Xalkori)	250 mg twice daily	Take with or without food Swallow capsules whole	200 mg, 250 mg capsules
loralatinib (Lobrena)	100 mg once daily	Take with or without food Swallow tablets whole	25 mg, 100 mg tablets
EGFR Tyrosine Kinase Inhibitors			
afatinib (Gilotrif)	40 mg once daily	Take at least 1 hour before or 2 hours after a meal	20 mg, 30 mg, 40 mg tablets
dacomitinib (Vizimpro)	45 mg once daily	Take with or without food	15 mg, 30 mg, 45 mg tablets
erlotinib (Tarceva)	NSCLC: 150 mg daily Pancreatic cancer: 100 mg daily in combination with IV gemcitabine	Take on empty stomach 1 hour before or 2 hours after a meal	25 mg, 100 mg, 150 mg tablets

Oncology, Oral- Lung – Dosing and Availability

Drugs	Dose	Administration	Available Strengths
EGFR Tyrosine Kinase Inhibitors (Continued)			
gefitinib (Iressa)	250 mg once daily	Take with or without food For patients who have difficulty swallowing solids, tablets may be immersed in 4 to 8 ounces of water and stirred for approximately 15 minutes The patient should drink the mixture immediately or it may be administered through a naso-gastric (NG) tube immediately The container should be rinsed with 4 to 8 ounces of water and readministered	250 mg tablets
osimertinib (Tagrisso)	80 mg once daily	Take with or without food For patients who have difficulty swallowing solids, the tablet may be dispersed in approximately 60 mL of non-carbonated water only Stir until tablet is completely dispersed; rinse the container with 4 to 8 ounces of water and immediately drink Do not crush, heat, or ultrasonicate during preparation For administration through a nasogastric tube (NG), disperse tablet in 15 mL of non-carbonated water and then use an additional 15 mL of water to transfer any residues to the syringe; the resulting 30 mL should be administered per NG tube with appropriate water flushes (approximately 30 mL)	40 mg, 80 mg tablets
Non-targeted Agents			
topotecan (Hycamtin)	2.3 mg/m2/day for 5 consecutive days (cycle repeated every 21 days) Round dose to nearest 0.25 mg	Take with or without food, swallow capsules whole, do not chew, crush, or divide the capsules	0.25 mg, 1 mg capsules

Oncology, Oral- Lung – Guidelines

- ASCO has a clinical practice guideline regarding recommended molecular testing in order to facilitate appropriate selection of lung cancer patients who may be treated with TKIs
  - Biomarker testing should be performed in all tumors with an adenocarcinoma component, nonsquamous, non-small cell histology or any non-small cell histology when clinical features indicated a high probability of an oncogenic drive (e.g. young age [< 50 years], light or absent tobacco exposure)
- The ASCO guideline for the systemic treatment of stage 4 NSCLC is currently undergoing review for update
- NCCN NSCLC Guidelines

Oncology, Oral- Lung – Guidelines, Selected References

- Soria JC, Ohe Y, Vansteenkiste J, et al. Osimertinib in untreated EGFR-mutated advanced non-small cell lung cancer J Clin Onc 2018;378:113-125
- Peters S, Camidge DR, Shaw AT, Gadgeel S, Ahn JS, et al. Alectinib versus crizotinib in untreated ALK-positive non-small-cell lung cancer. N Engl J Med. 2017;377(9):829-838
- Shaw AT, Ou S, Bang Y, et al. Crizotinib in ROS1-Rearranged Non-Small Cell Lung Cancer N Engl J Med 2014;371:1963-71

Washington State Health Care Authority

Antineoplastics and Adjunctive Therapy, Oral Agents, Lung Cancer

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Clinical Quality & Care Transformation
February 20, 2019

Antineoplastics and Adjunctive Therapy, Oral Agents, Abbreviations

Abbreviation	Term
ALK	Anaplastic Lymphoma Kinase
BRAF	B-Raf proto-oncogene
DNA	deoxyribonucleic acid
EGFR	Epidermal Growth Factor Receptor
FDA	Food and Drug Administration
NSCLC	Non-small cell lung cancer

Antineoplastics and Adjunctive Therapy, Oral Agents, Lung Cancer

Drug name (Brand Nane)	Mechanism of Action	FDA Approval
afatinib (Gilotrif®)	EGFR Tyrosine Kinase Inhibitor	2013
alectinib (Alecensa®)	ALK Tyrosine Kinase Inhibitor	2015
brigatinib (Alunbrig™)	ALK Tyrosine Kinase Inhibitor	2017
ceritinib (Zykadia™)	ALK Tyrosine Kinase Inhibitor	2014
crizotinib (Xalkori®)	ALK Tyrosine Kinase Inhibitor	2011
dabrafenib (Tafinlar®)	BRAF Inhibitor	2013
dacomitinib (Vizimpro®)	EGFR Tyrosine Kinase Inhibitor	2018
erlotinib (Tarceva®)	EGFR Tyrosine Kinase Inhibitor	2004
gefitinib (Iressa®)	EGFR Tyrosine Kinase Inhibitor	2015
osimertinib (Tagrisso™)	EGFR Tyrosine Kinase Inhibitor	2015
topotecan (Hycamtin®)	DNA Topoisomerase Inhibitors	1996

Antineoplastics and Adjunctive Therapy, Oral Agents, Lung Cancer

Initial request:

- Diagnosis that is listed in FDA-approved label **OR** in compendia recognized by Medicaid (defined in Section 1927 of the Social Security Act); **AND**
- If an FDA-approved companion diagnostic test for the requested agent exists, documentation that the test was performed to confirm the diagnosis; **AND**
- If a test with adequate ability to confirm a disease mutation exists, documentation that the test was performed to confirm the diagnosis; **AND**
- If not indicated as a first line agent, documentation of all previous therapies; **AND**
- Must be used in combination with other chemotherapeutic or adjuvant agents according to the FDA approved prescribing information; **AND**

Antineoplastics and Adjunctive Therapy, Oral Agents, Lung Cancer

Initial request (continued):

- Prescribed by, or in consultation with, a specialist in oncology or hematology; **AND**
- The patient does not have any contraindications to the requested oral oncology medication; **AND**
- The prescribed quantity and dosing regimen falls within the manufacturer's published dosing guidelines and is appropriate for the patient's age; **AND**
- Documentation from the provider on what measure they'll use to determine whether the patient has had a positive clinical response

Antineoplastics and Adjunctive Therapy, Oral Agents, Lung Cancer

Reauthorization criteria:

- Documentation from the provider that the patient has had a positive clinical response and is able to tolerate therapy

Antineoplastics and Adjunctive Therapy, Oral Agents, Lung Cancer

afatinib (Gilotrif)

- First-line treatment of metastatic non-small cell lung cancer (NSCLC) with nonresistant epidermal growth factor receptor (EGFR) mutations as detected by an FDA-approved test
- Treatment of metastatic, squamous NSCLC progressing after platinum-based therapy

alectinib (Alecensa)

- Treatment of patients with ALK-positive, metastatic NSCLC as detected by an FDA approved test.

brigatinib (Alunbrig)

- Treatment of ALK-positive metastatic NSCLC in patients who have progressed on or are intolerant to crizotinib

ceritinib (Zykadia)

- Treatment of ALK-positive metastatic NSCLC as detected by an FDA-approved test

Antineoplastics and Adjunctive Therapy, Oral Agents, Lung Cancer

crizotinib (Xalkori)

- Treatment of metastatic NSCLC in patients whose tumors are ALK-positive or ROS1-positive as detected by an FDA-approved test

dabrafanib (Tafinlar)

- Treatment of patients with metastatic NSCLC with BRAF V600E mutation as detected by an FDA-approved test, in combination with trametinib

dacomitinib (Vizimpro)

- First-line treatment of metastatic NSCLC with EGFR exon 19 deletion or exon 21 L858R substitution mutations as detected by an FDA-approved test

Antineoplastics and Adjunctive Therapy, Oral Agents, Lung Cancer

erlotinib (Tarceva)

- Treatment of patients with metastatic NSCLC whose tumors have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test who are receiving first-line, maintenance, or second- or greater-line treatment after progression following at least 1 prior chemotherapy regiment
- First-line treatment of patients with locally advanced, unresectable, or metastatic pancreatic cancer, in combination with gemcitabine

gefitinib (Iressa)

- First-line treatment of patients with NSCLC whose tumors have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test

Antineoplastics and Adjunctive Therapy, Oral Agents, Lung Cancer

osimertinib (Tagrisso)

- Treatment of patients with metastatic EGFR T790M mutation-positive NSCLC as detected by an FDA approved test, who have progressed on or after EFGR tyrosine kinase inhibitor therapy

topotecan (Hycamtin)

- Treatment of relapsed small cell lung cancer

Antineoplastics and Adjunctive Therapy, Oral Agents, Lung Cancer

Motion:

- "I move that the Apple Health Medicaid Program implement the clinical criteria listed on slides 123-125 as recommended. The lung oncology drugs listed on Magellan slide 115 are considered safe and efficacious for their respective FDA indications. All drugs are preferred for their FDA labeled indications."

  - Motion: Huynh
  - 2nd: Brown

Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Oncology, Oral- Skin Cancer

Overview of Disease State – Oncology, Oral- Skin Cancer

- Largely divided into 2 groups- melanoma/non-melanoma skin cancer
  - Non-melanoma skin cancers= basal cell carcinoma (BCC) and squamous cell carcinoma (SCC)
  - Other cancers involving the skin include cutaneous lymphomas, some sarcomas and Merkel cell carcinoma
- Non-melanoma skin cancer:
  - Most common type of cancer diagnosed in U.S. (> 5 million cases/year) and account for 97% of all skin cancers
  - BCC is twice as common as SCC
- BCC:
  - Risk is increased by both exposure to both UV-A and UV-B radiation
  - Rarely metastasizes but can cause extensive local tissue destruction and potentially bone degradation
  - Surgery is the primary modality of treatment, preferably Moh's micrographic surgery
  - Other local therapy options include radiation, cryosurgery, photodynamic therapy, topical 5-fluorouracil or imiquimod
- Melanoma:
  - In 2019, the projected number of diagnoses will be 96,480 and a projected 7,230 deaths will be attributable to melanoma
  - Prognosis for cutaneous melanoma depends on stage at diagnosis, for localized disease 5-year survival is >90% but for distant metastatic disease is < 10%; recently immunotherapy has made long term remission a reality for select patients
  - BRAF mutations occur in ~ 50% of cases of metastatic cutaneous melanoma
  - For BRAF+ patients, monotherapy with BRAF inhibitors improves RR, PFS and OS compared to single agent chemotherapy
  - BRAF + MEK inhibitors improve RR, duration of response, PFS and OS compared to BRAF monotherapy and also results in a lower incidence of development of SCC and keratoacanthomas compared to monotherapy

Oncology, Oral- Skin Cancer – Indications

Drugs	Generic	Indications
binimetinib (Mektovi)	---	▪ In combination with encorafenib for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation, as detected by an FDA-approved test
cobimetinib (Cotellic)	---	▪ Treatment of unresectable or metastatic melanoma with a BRAF V600E or V600K mutation, in combination with vemurafenib (Zelboraf)
dabrafenib (Tafinlar)	---	▪ As a single agent for patients with unresectable or metastatic melanoma with BRAF V600E mutation as detected by an FDA-approved test ▪ In combination with trametinib (Mekinist) for patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test ▪ In combination with trametinib (Mekinist) for the treatment of metastatic non-small cell lung cancer (NSCLC) with BRAF V600E mutation as detected by an FDA-approved test ▪ In combination with trametinib for the adjuvant treatment of melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test and involvement of lymph node(s), following complete resection ▪ In combination with trametinib for the treatment of locally advanced or metastatic anaplastic thyroid cancer (ATC) with BRAF V600E mutation and with no satisfactory locoregional treatment options
encorafenib (Braftovi)	---	▪ In combination with binimetinib for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation, as detected by an FDA-approved test

Oncology, Oral- Skin Cancer – Indications

Drugs	Generic	Indications
sonidegib (Odomzo)	---	▪ Treatment of locally advanced basal cell carcinoma (BCC) that has recurred following surgery or radiation therapy, or for those who are not candidates for surgery or radiation therapy
trametinib (Mekinist)	---	▪ As a single agent or in combination with dabrafenib (Tafinlar) for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test ▪ In combination with dabrafenib (Tafinlar)for the treatment of metastatic NSCLC with BRAF V600E mutation as detected by an FDA-approved test* ▪ In combination with dabrafenib for the adjuvant treatment of melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test and involvement of lymph node(s), following complete resection ▪ In combination with dabrafenib for the treatment of locally advanced or metastatic ATC with BRAF V600E mutation and with no satisfactory locoregional treatment options
vemurafenib (Zelboraf)	---	▪ Treatment of unresectable or metastatic melanoma with BRAF V600E mutation as detected by an FDA-approved test ▪ Treatment of patients with Erdheim-Chester Disease (ECD) with BRAF V600 mutation
vismodegib (Erivedge)	---	▪ Treatment of adults with metastatic basal cell carcinoma (BCC), or with locally advanced BCC that has recurred following surgery or who are not candidates for surgery and who are not candidates for radiation

Oncology, Oral- Skin Cancer – Dosing and Availability

Drug	Melanoma	Basal Cell Carcinoma	Non-Small Cell Lung Cancer	Other Indications	Administration Comments	Available Strengths
binimetinib (Mektovi)	In combination with encorafenib (Braftovi): 45 mg twice daily	---	---	---	---	15 mg tablets
cobimetinib (Cotellic)	In combination with vemurafenib (Zelboraf): 60 mg (three 20 mg tablets) orally once daily for the first 21 days of each 28-day cycle	---	---	---	---	20 mg tablets
dabrafenib (Tafinlar)	As a single agent: 150 mg every 12 hours In combination with trametinib (Mekinist): 150 mg every 12 hours	---	In combination with trametinib: 150 mg twice daily	Anaplastic Thyroid Carcinoma 150 mg twice daily in combination with trametinib	Do not open, crush or break capsules; take at least 1 hour before or 2 hours after a meal	50 mg, 75 mg capsules
encorafenib (Braftovi)	In combination with binimetinib (Mektovi): 450 mg twice daily	---	---	---	---	50 mg, 75 mg capsules

Oncology, Oral- Skin Cancer – Dosing and Availability

Drug	Melanoma	Basal Cell Carcinoma	Non-Small Cell Lung Cancer	Other Indications	Administration Comments	Available Strengths
sonidegib (Odomzo)	---	200 mg orally once daily	---	---	Take on an empty stomach, at least 1 hour before or 2 hours after a meal	200 mg capsule
trametinib (Mekinist)	As a single agent: 2 mg once daily In combination with dabrafenib (Tafinlar): 2 mg once daily	---	In combination with dabrafenib: 2 mg once daily	Anaplastic Thyroid Carcinoma: 2 mg once daily in combination with dabrafenib	Take 1 hour before or 2 hours after a meal	0. 5 mg, 2 mg tablets
vemurafenib (Zelboraf)	960 mg (four 240 mg tablets) twice daily (12 hours apart)	---	---	Erdheim-Chester Disease: 960 mg (four 240 mg tablets) every 12 hours	May be taken with or without food; swallow capsules whole with water; do not crush or chew tablets	240 mg tablets
vismodegib (Erivedge)	---	150 mg once daily	---	---	May be taken with or without food; swallow capsules whole	150 mg capsule

Oncology, Oral- Skin Cancer – Guidelines

- NCCN Cutaneous Melanoma Guidelines
- The only ASCO guideline regarding melanoma is related to sentinel lymph node biopsy
- The American Academy of Dermatology published melanoma guidelines in January 2019 which correspond to the NCCN guidelines (https://www.aad.org/practicecenter/quality/clinical-guidelines/melanoma)

- Basal Cell Skin Cancer NCCN guidelines

Oncology, Oral- Skin Cancer – Guidelines, Selected References

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Washington State Health Care Authority

Antineoplastics and Adjunctive Therapy, Oral Agents, Skin Cancers

Ryan Pistoresi, PharmD, MS
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Clinical Quality & Care Transformation
February 20, 2019

Antineoplastics and Adjunctive Therapy, Oral Agents, Abbreviations

Abbreviation	Term
ATC	Anaplastic Thyroid Cancer
BCC	Basal Cell Carcinoma
BRAF	B-Raf proto-oncogene
FDA	Food and Drug Administration
NSCLC	Non-small cell lung cancer

Antineoplastics and Adjunctive Therapy, Oral Agents, Skin Cancers

Drug name (Brand Nane)	Mechanism of Action	FDA Approval
binimetinib (Mektovi®)	MEK Inhibitor	2018
cobimetinib (Cotellic®)	MEK Inhibitor	2015
dabrafenib (Tafinlar®)	BRAF Inhibitor	2013
encorafenib (Braftovi™)	BRAF Inhibitor	2018
sonidegib (Odomzo®)	Hedgehog Pathway Inhibitor	2015

Antineoplastics and Adjunctive Therapy, Oral Agents, Skin Cancers

Initial request:

- Diagnosis that is listed in FDA-approved label **OR** in compendia recognized by Medicaid (defined in Section 1927 of the Social Security Act); **AND**
- If an FDA-approved companion diagnostic test for the requested agent exists, documentation that the test was performed to confirm the diagnosis; **AND**
- If a test with adequate ability to confirm a disease mutation exists, documentation that the test was performed to confirm the diagnosis; **AND**
- If not indicated as a first line agent, documentation of all previous therapies; **AND**
- Must be used in combination with other chemotherapeutic or adjuvant agents according to the FDA approved prescribing information; **AND**

Antineoplastics and Adjunctive Therapy, Oral Agents, Skin Cancers

Initial request (continued):

- Prescribed by, or in consultation with, a specialist in oncology or hematology; **AND**
- The patient does not have any contraindications to the requested oral oncology medication; **AND**
- The prescribed quantity and dosing regimen falls within the manufacturer's published dosing guidelines and is appropriate for the patient's age; **AND**
- Documentation from the provider on what measure they'll use to determine whether the patient has had a positive clinical response

Antineoplastics and Adjunctive Therapy, Oral Agents, Skin Cancers

Reauthorization criteria:

- Documentation from the provider that the patient has had a positive clinical response and is able to tolerate therapy

Antineoplastics and Adjunctive Therapy, Oral Agents, Skin Cancers

binimetinib (Mektovi)

- In combination with encorafenib for the treatment of patients with unresctable or metastatic melanoma with a BRAF V600E or V600K mutation, as detected by an FDA-approved test
- (Note: not indicated for treatment of patients with wild-type BRAF melanoma)

cobimetinib (Cotellic)

- Treatment of unresectable or metastatic melanoma with a BRAF V600E or V600K mutation, in combination with vemurafenib (Zelboraf)

Antineoplastics and Adjunctive Therapy, Oral Agents, Skin Cancers

dabrafenib (Tafinlar)

- As a single agent for patients with unresctable or metastatic melanoma with BRAF V600E mutation as detected by an FDA-approved test
- In combination with trametinib (Mekinist) for:
  - patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test
  - treatment of metastatic non-small cell lung cancer (NSCLC) with BRAF V600E mutation as detected by an FDA-approved test
  - adjuvant treatment of melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test and involvement of lymph node(s) following complete resection
  - treatment of locally advanced or metastatic anaplastic thyroid cancer (ATC) with BRAF V600E mutation and no satisfactory locoregional treatment options
    - (Note: not indicated for wild-type BRAF melanoma or wild-type BRAF NSCLC)

Antineoplastics and Adjunctive Therapy, Oral Agents, Skin Cancers

encorafenib (Braftovi)

- In combination with binimetinib (Mektovi) for the treatment of patients with unresctable or metastatic melanoma with a BRAF V600E or V600K mutation, as detected by an FDA-approved test
  - (Note: not indicated for treatment of patients with wild-type BRAF melanoma)

sonidegib (Odomzo)

- Treatment of locally advanced basal cell carcinoma (BCC) that has recurred following surgery or radiation therapy, or for those who are not candidates for surgery or radiation therapy

Antineoplastics and Adjunctive Therapy, Oral Agents, Skin Cancers

Motion:

- "I move that the Apple Health Medicaid Program implement the clinical criteria listed on slides 142-144 as recommended. The skin oncology drugs listed on Magellan slides 133-134 are considered safe and efficacious for their respective FDA indications. All drugs are preferred for their FDA labeled indications."

  - Motion: Flatebo
  - 2nd: Buccola

Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Oncology, Oral- Other

Overview of Disease State – Oncology, Oral- Other

- Agents in this TCR are indicated for a wide variety of solid tumors including CNS malignancies such as glioblastoma and anaplastic astrocytoma, colorectal cancer, gastrointestinal stromal tumor (GIST), hepatocellular carcinoma, medullary thyroid carcinoma and ovarian cancer
- Agents in this review include traditional cytotoxics (4) as well as targeted therapies (6)
- In many of these disease states, these agents have a limited role
  - Primary focus will be the 3 poly ADP-ribose polymerase (PARP) inhibitors and there role in the treatment of ovarian cancer
- Ovarian cancer is the 5th most common cause of cancer-related death in U.S. women with 22,530 cases projected to be diagnosed in 2019 and 13,980 deaths
- >70% of ovarian cancer patients present with advanced stage disease and < 40% are cured
- There is a genetic association between BRCA1 and BRCA2 genotypes and the risk of developing ovarian cancer but these genetic predispositions only account for 15% of all ovarian cancers
- Primary treatment of advanced ovarian cancer usually begins with cytoreductive surgery and adjuvant therapy is usually recommended
- PARP inhibitors prevent normal base excision repairs in single-stranded DNA breaks and appear to have increased cytotoxicity in BRCA-mutated cells
  - Original PARP inhibitor approvals in ovarian CA were in BRCA-mutated (germline or somatic) patients but now all 3 are approved for maintenance therapy regardless of BRCA status in patients who have had a CR or PR to platinum-based therapy

Oncology, Oral- Other – Indications

Drugs	Generic	Indications
altretamine (Hexalen)	---	▪ As a single agent in the palliative treatment of patients with persistent or recurrent ovarian cancer following first-line therapy with a cisplatin and/or alkylating agent-based combination
cabozantinib (Cometriq)	---	▪ Treatment of progressive, metastatic medullary thyroid cancer
lomustine (Gleostine)	---	▪ Brain tumors, primary and metastatic, following appropriate surgical and/or radiotherapeutic procedures ▪ Hodgkin's lymphoma in combination with other chemotherapies, following disease progression with initial chemotherapy
niraparib (Zejula)	---	▪ Maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy
olaparib (Lynparza)	---	▪ Monotherapy in patients with deleterious or suspected deleterious germline BRCA-mutated (gBRCAm) advanced ovarian cancer, as detected by an FDA-approved test, who have been treated with 3 or more prior lines of chemotherapy ▪ Maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer, who are in a complete or partial response to platinum-based chemotherapy ▪ Patients with deleterious or suspected deleterious gBRCAm, human epidermal growth factor receptor 2 (HER2)-negative metastatic breast cancer who have been treated with chemotherapy in the neoadjuvant, adjuvant, or metastatic setting; patients with hormone receptor (HR)-positive breast cancer should have been treated with a prior endocrine therapy or be considered inappropriate for endocrine therapy, and patients should be selected for treatment based on the FDA-approved companion diagnostic
regorafenib (Stivarga)	---	▪ Treatment of metastatic colorectal cancer (CRC) patients who have been previously treated with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy, anti-VEGF therapy, and, if RAS wild type, an anti-EGFR therapy ▪ Treatment of patients with locally advanced, unresectable, or metastatic gastrointestinal stromal tumor (GIST) who have been previously treated with imatinib mesylate and sunitinib malate ▪ Treatment of hepatocellular carcinoma (HCC) in patients who have been previously treated with sorafenib
rucaparib (Rubraca)	---	▪ Maintenance treatment of adult patients with recurrent ovarian cancer, epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy ▪ Treatment of patients with deleterious, BRCA mutation (germline and/or somatic) associated epithelial ovarian, fallopian tube, or primary peritoneal cancer who have been treated with 2 or more chemotherapies. Patients should be selected for treatment based on the FDA-approved companion diagnostic

Oncology, Oral- Other – Indications

Drugs	Generic	Indications
temozolomide (Temodar)	---	▪ Treatment of adult patients with newly diagnosed glioblastoma multiforme (GBM) concomitantly with radiotherapy and then as maintenance treatment ▪ Refractory anaplastic astrocytoma in adult patients who have experienced disease progression on a drug regimen containing a nitrosourea and procarbazine
trifluridine/ tipiracil (Lonsurf)	---	▪ Patients with metastatic colorectal cancer who have been previously treated with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy, an anti-VEGF biological therapy, and, if RAS wild-type, an anti-EGFR therapy
vandetanib (Caprelsa)	---	▪ Symptomatic or progressive medullary thyroid cancer in patients with unresectable locally advanced or metastatic disease

Oncology, Oral- Other – Dosing and Availability

Drugs	Medullary Thyroid Cancer	Colorectal Cancer	Ovarian Cancer	Other Diagnoses	Administration Comments	Dosage Forms
altretamine (Hexalen)	--	--	260 mg/m2/day given orally daily for 14 or 21 consecutive days in a 28 day cycle	--	The total daily dose should be given as 4 divided oral doses after meals and at bedtime	50 mg capsule
cabozantinib (Cometriq)	140 mg once daily	--	--	--	Take with 8 ounces of water; refrain from eating 2 hours before and 1 hour after daily dose; do not open capsules	20 mg, 80 mg capsules packaged as 60, 100, and 140 mg daily-dose cartons
lomustine (Gleostine)	--	--	--	Brain tumors/ Hodgkin's lymphoma: 130 mg/m2/day given as a single oral dose once every 6 weeks	Only a sufficient number of capsules for 1 dose should be dispensed and patients should be instructed that the dose will not be repeated for at least 6 weeks	5 mg, 10 mg, 40 mg, 100 mg capsules
niraparib (Zejula)	--	--	300 mg (three 100 mg capsules) once daily	--	Swallow capsules whole; may be taken with our without food; bedtime administration may be a potential method for managing nausea; start treatment no later than 8 weeks after most recent platinum-containing regimen	100 mg capsules
olaparib (Lynparza)	--	--	300 mg (two 150 mg tablets) twice daily	Breast cancer: 300 mg (two 150 mg tablets) twice daily	Swallow tablets or capsules whole; administer with or without food	50 mg hard capsules† 100 mg, 150 mg tablets
regorafenib (Stivarga)	--	160 mg (four 40 mg tablets) taken once daily for the first 21 days of each 28 day cycle	--	Hepatocellular carcinoma: 160 mg (four 40 mg tablets) taken once daily for the first 21 days of each 28-day cycle	Swallow tablet whole with water after a low-fat meal that contains less than 600 calories and less than 30% fat	40 mg tablets

Oncology, Oral- Other – Dosing and Availability

Drugs	Medullary Thyroid Cancer	Colorectal Cancer	Ovarian Cancer	Other Diagnoses	Administration Comments	Dosage Forms
rucaparib (Rubraca)	--	--	600 mg (two 300 mg tablets) twice daily	--	Take with or without food	200 mg, 250 mg, 300 mg tablets
temozolomide (Temodar)	--	--	--	Newly diagnosed GBM: 75 mg/m2 by mouth for 42 days concomitant with focal radiotherapy followed by initial maintenance dose of 150 mg/m2 by mouth once daily for Days 1-5 of a 28 day cycle for 6 cycles Refractory Anaplastic Astrocytoma: initial dose of 150 mg/m2 by mouth once daily for 5 consecutive days per 28-day treatment cycle	Handle per standard chemotherapy handling guidelines	5 mg, 20 mg, 100 mg, 140 mg, 180, mg and 250 mg capsules
trifluridine/tipiracil (Lonsurf)	--	35 mg/m2/dose orally twice daily on Days 1-5 and Days 8-12 of each 28-day cycle; Dose is based on trifluridine component; (Maximum single dose = 80 mg; round to nearest 5 mg increment)	--	--	Given within 1 hour of completion of morning and evening meals	15/6.14 mg, 20/8.19 mg tablets
vandetanib (Caprelsa)	300 mg orally once daily	--	--	--	Do not crush tablets; tablets may be dispersed in 2 ounces of water and may be administered through nasogastric or gastrostomy tubes	100 mg, 300 mg tablets

Oncology, Oral- Other – Guidelines

- NCCN Ovarian Cancer Guidelines

Oncology, Oral- Other – Guidelines, Selected References

- Mirza MR, Monk BJ, Herrstedt J, et al. Niraparib maintenance therapy in platinum-sensitive, recurrent ovarian cancer. N Engl J Med. 2016;375:2154-2164
- Kaufman B, Shapira-Frommer R, Schmutzler RK, et al. Olaparib monotherapy in patients with advanced cancer and a germline BRCA1/2 mutation. J Clin Oncol. 2015;33:244-50
- Domchek SM, Aghajanian C, Shapira-Frommer R, et al. Efficacy and safety of olaparib monotherapy in germline BRCA1/2 mutation carriers with advanced ovarian cancer and three or more lines of prior therapy. Gynecol Oncol. 2016;140:199-203
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Washington State Health Care Authority

Antineoplastics and Adjunctive Therapy, Oral Agents, Other Cancers

Ryan Pistoresi, PharmD, MS
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Clinical Quality & Care Transformation
February 20, 2019

Antineoplastics and Adjunctive Therapy, Oral Agents, Abbreviations

Abbreviation	Term
BRAF	B-Raf proto-oncogene
EGFR	Epidermal Growth Factor Receptor
FDA	Food and Drug Administration
HER2	Human Epidermal Growth Factor Receptor 2
HR	hormone receptor
PARP	Poly (ADP-ribose) polymerase
VEGF	Vascular Endothelial Growth Factor

Antineoplastics and Adjunctive Therapy, Oral Agents, Other Cancers

Drug name (Brand Nane)	Mechanism of Action	FDA Approval
altretamine (Hexalen®)*	Alkylating Agents (Methylmelamines)	1990
cabozantinib (Cometriq®)	VEGF Tyrosine Kinase Inhibitor	2012
dabrafenib (Tafinlar®)	BRAF Inhibitor	2013
lenvatinib (Lenvima®)	VEGF Tyrosine Kinase Inhibitor	2015
lomustine (Gleostine®)	Alkylating Agents (Nitrosoureas)	1976
niraparib (Zejula®)	PARP Enzymes Inhibitor	2017
olaparib (Lynparza®)	PARP Enzymes Inhibitor	2014
regorafenib (Stivarga®)	Multikinase Inhibitor	2012
rucaparib (Rubraca®)	PARP Enzymes Inhibitor	2016
sorafenib (Nexavar®)	VEGF Tyrosine Kinase Inhibitor	2005
temozolomide (Temodar®)**	Alkylating Agents (Triazene)	1999
trifluridine/ tipiracil (Lonsurf®)	Pyrimidine Analog / Thymidine Phosphorylase Inhibitor	2015
vandetanib (Caprelsa®)	Multikinase Inhibitor	2011

*Discontinued 9/30/2018 **Generic available

Antineoplastics and Adjunctive Therapy, Oral Agents, Other Cancers

Initial request:

- Diagnosis that is listed in FDA-approved label **OR** in compendia recognized by Medicaid (defined in Section 1927 of the Social Security Act); **AND**
- If an FDA-approved companion diagnostic test for the requested agent exists, documentation that the test was performed to confirm the diagnosis; **AND**
- If a test with adequate ability to confirm a disease mutation exists, documentation that the test was performed to confirm the diagnosis; **AND**
- If not indicated as a first line agent, documentation of all previous therapies; **AND**
- Must be used in combination with other chemotherapeutic or adjuvant agents according to the FDA approved prescribing information; **AND**

Antineoplastics and Adjunctive Therapy, Oral Agents, Other Cancers

Initial request (continued):

- Prescribed by, or in consultation with, a specialist in oncology or hematology; **AND**
- The patient does not have any contraindications to the requested oral oncology medication; **AND**
- The prescribed quantity and dosing regimen falls within the manufacturer's published dosing guidelines and is appropriate for the patient's age; **AND**
- Documentation from the provider on what measure they'll use to determine whether the patient has had a positive clinical response

Antineoplastics and Adjunctive Therapy, Oral Agents, Other Cancers

Reauthorization criteria:

- Documentation from the provider that the patient has had a positive clinical response and is able to tolerate therapy

Antineoplastics and Adjunctive Therapy, Oral Agents, Other Cancers

altretamine (Hexalen) [Discontinued as of 9/30/2018]

- As a single agent in the palliative treatment of patients with persistent or recurrent ovarian cancer following first-line therapy with a cisplatin and/or alkylating agent-based combination

cabozantinib (Cometriq)

- Treatment of progressive, metastatic medullary thyroid cancer

Antineoplastics and Adjunctive Therapy, Oral Agents, Other Cancers

dabrafenib (Tafinlar)

- As a single agent for patients with unresctable or metastatic melanoma with BRAF V600E mutation as detected by an FDA-approved test
- In combination with trametinib (Mekinist) for:
  - patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test
  - treatment of metastatic non-small cell lung cancer (NSCLC) with BRAF V600E mutation as detected by an FDA-approved test
  - adjuvant treatment of melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test and involvement of lymph node(s) following complete resection
  - treatment of locally advanced or metastatic anaplastic thyroid cancer (ATC) with BRAF V600E mutation and no satisfactory locoregional treatment options
    - (Note: not indicated for wild-type BRAF melanoma or wild-type BRAF NSCLC)

Antineoplastics and Adjunctive Therapy, Oral Agents, Other Cancers

lenvatinib (Lenvima)

- In combination with everolimus for patients with advanced RCC following 1 prior anti-androgenic therapy
- Treatment of differentiated thyroid cancer (DTC) in patients with locally recurrent or metastatic, progressive radioactive iodine-refractory DTC

lomustine (Gleostine)

- Brain tumors, primary and metastatic, following appropriate surgical and/or radiotherapeutic procedures
- Hodgkin's hymphoma in combination with other chemotherapies, following disease progression with initial chemotherapy

niraparib (Zejula)

- Maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy

Antineoplastics and Adjunctive Therapy, Oral Agents, Other Cancers

olaparib (Lynparza)

- Monotherapy in patients with deleterious or suspected deleterious germline BRCA-mutated (gBRCAm) advanced ovarian cancer as detected by an FDA-approved test who have been treated with 3 or more prior lines of chemotherapy
- Maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer, who are in a complete or patient response to platinum-based chemotherapy
- Patients with deleterious or suspsected deleterious gBRCAm, human epidermal growth factor receptor 2 (HER2)-negative metastatic breast cancer who have been treated with chemotherapy in the neoadjuvant, adjuvant, or metastatic setting; patients with hormone receptor (HR)-positive breast cancer should have been treated with prior endocrine therapy or be considered inappropriate for endocrine therapy, and patients should be selected for treatment based on the FDA-approved companion diagnostic

Antineoplastics and Adjunctive Therapy, Oral Agents, Other Cancers

regorafenib (Stivarga)

- Treatment of metastatic colorectal cancer (CRC) patients who have been previously treated with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy, anti-VEGF therapy, and if RAS wild type, an anti-EGFR therapy
- Treatment of patients with locally advanced, unresectable, or metastatic gastrointestinal stromal tumor (GIST) who have been previously treated with imatinib and sunitinib
- Treatment of hepatocellular carcinoma (HCC) in patients who have been previously treated with sorafenib

rucaparib (Rubraca)

- Maintanence treatment of adult patients with recurrent ovarian cancer, epitherlial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy
- Treatments of patients with deleterious, BRCA mutation (germline and/or somatic) associated epitherlial ovarian, fallopian tube, or primary peritoneal cancer who have been treated with 2 or more chemotherapies. Patients should be selected for treatment based on the FDA-approved companion diagnostic.

Antineoplastics and Adjunctive Therapy, Oral Agents, Other Cancers

sorafenib (Nexavar)

- Locally recurrent or metastatic progressive, DTC refractory to radioactive iodine treatment
- Unresctable hepatocellular carcinoma (HCC)
- Advanced RCC

temozolomide (Temodar)

- Treatment of adult patients with newly diagnosed glioblastoma multiforme (GBM) concomitantly with radiotherapy and then as maintenance treatment
- Refractory anaplastic astrocytoma in adult patients who have experienced disease progression on a drug regimen containing a nitrosourea and procarbazine

trifluridine / tipiracil (Lonsurf)

- Patients with metastatic colorectal cancer who have been previously treated with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy, an anti-VEGF biologic therapy, and, if RAS wild-type, an anti-EGFR therapy

vandetanib (Caprelsa)

- Symptomatic or progressive medullary thyroid cancer in patients with unresctable locally advanced or metastatic disease

Antineoplastics and Adjunctive Therapy, Oral Agents, Other Cancers

Motion:

- "I move that the Apple Health Medicaid Program implement the clinical criteria listed on slides 160-162 as recommended. The other oncology drugs listed on slide 159 are considered safe and efficacious for their respective FDA indications. All drugs are preferred for their FDA labeled indications."

  - Motion: Lee
  - 2nd: Park