Medical Policy

BlueCross BlueShield of Kansas
An Independent Licensee of the Blue Cross and Blue Shield Association

Title: Self Administered Oncology Agents

Prior Authorization Form:
http://www.bcbsks.com/CustomerService/Forms/pdf/PriorAuth_6106KS_OralOncology.pdf
Prime Therapeutics will review Prior Authorization requests.

For information concerning Prior Authorization Prescription Drugs:
http://www.bcbsks.com/CustomerService/PrescriptionDrugs/prior_authorization.htm

Link to Drug List (Formulary):
http://www.bcbsks.com/CustomerService/PrescriptionDrugs/drug_list.htm

Professional
Original Effective Date: January 1, 2011
Revision Date(s): February 1, 2012; July 1, 2012; March 1, 2013; September 1, 2013; February 28, 2014; August 28, 2014
Current Effective Date: August 28, 2014

Institutional
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State and Federal mandates and health plan member contract language, including specific provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. To verify a member's benefits, contact Blue Cross and Blue Shield of Kansas Customer Service.

The BCBSKS Medical Policies contained herein are for informational purposes and apply only to members who have health insurance through BCBSKS or who are covered by a self-insured group plan administered by BCBSKS. Medical Policy for FEP members is subject to FEP medical policy which may differ from BCBSKS Medical Policy.

The medical policies do not constitute medical advice or medical care. Treating health care providers are independent contractors and are neither employees nor agents of Blue Cross and Blue Shield of Kansas and are solely responsible for diagnosis, treatment and medical advice.

If your patient is covered under a different Blue Cross and Blue Shield plan, please refer to the Medical Policies of that plan.

DESCRIPTION

The intent of the Self Administered Oncology Agents Prior Authorization (PA) program is to ensure appropriate selection of patients for treatment according to product labeling and/or clinical studies and/or clinical guidelines. Patients currently prescribed therapy with one of these agents will be able to continue their established therapy. Pharmaceutical compendia [National Comprehensive Cancer Network (NCCN) Drugs & Biologics Compendium, American Hospital Formulary Service (AHFS) Drug Information, DrugDex, and Clinical Pharmacology] may be consulted to evaluate for medically accepted off-label use. Since off-label, medically accepted indications will change as new clinical information becomes available, the PA criteria will not attempt to list all off-label, medically accepted indications, but will include FDA labeled indications only. Compendia and other peer-reviewed medical literature will be consulted to evaluate off-label, medically accepted indications when evidence supporting an intended use is submitted by the prescriber. Requests for self-administered oncology agents will be reviewed when patient-specific documentation is provided.

FDA Approved Indications[1-40]

Medication	Indication	Dosing
Afinitor/Afinitor Disperz (everolimus)	• HR+BC* • RCC* • Angiomyolipoma with TSC • SEGA • PNET	**Advanced HR+BC, PNET, RCC, renal angiomyolipoma with TSC**: 10 mg once daily **^SEGA and TSC**: 4.5 mg/m^2 once daily, adjusted to attain trough concentrations of 5-15 ng/mL ^Administration with strong CYP3A4 inducer requires dose of 9 mg/m^2.
Bosulif (bosutinib)	• CML chronic, accelerated or blast phase Ph+*	**CML**: 500 mg orally once daily until disease progression. Consider increasing to 600 mg daily incomplete response.
Caprelsa (vandetanib)	• MTC	**MTC**: 300 mg once daily
Cometriq (cabozantinib)	• MTC	**MTC:** 140 mg orally once daily
Erivedge (vismodegib)	• BCC	**BCC**: 150 mg orally once daily
Gilotrif (afatinib)	• NSCLC^{GT}	**NSCLS:** 40 mg orally once daily
Gleevec (imatinib)	• CML • CML blast crisis, accelerated phase, chronic phase* • ALL, Ph+ pediatric ALL • MDS/MPD • ASM • HES • CEL • DFSP • GIST	**CML**: 400 mg/day in chronic phase; 600 mg/day in accelerated phase or blast crisis **ALL**: 600 mg/day; pediatrics 340 mg/m^2/day **MDS/MPD**: 400mg/day **GIST**: 400 mg/day **ASM, HES/CEL**: 100-400 mg/day **DFSP**: 800 mg/day
Hexalen (altretamine)	• OC*	**OC**: 260 mg/m^2/day in 4 divided doses for 14 or 21 consecutive days in a 28 day cycle
Hycamtin (topotecan)	• SCLC	**SCLC**: 2.3mg/m^2/day for 5 days, repeated every 21 days

Medication	Indication	Dosing
Iclusig (ponatinib)	• CML, Ph+ ALL	**CML & Ph+ ALL**: 45 mg orally one daily until disease progression.
Imbruvica (ibrutinib)	• MCL*, CLL	**MCL**: 560 mg orally once daily. CLL: 420 mg orally once daily.
Inlyta (axitinib)	• RCC*	**RCC**: 5 mg orally twice daily. Max dose 10 mg twice daily
Jakafi (ruxolitinib)	• Myelofibrosis	**Myelofibrosis**: ~~1~~5-20 mg orally twice daily depending on platelet count. Max dose is 25 mg twice daily.
Lysodren (mitotane)	• ACC	**ACC**: 2-6 g/day in 3-4 divided doses titrated up to 9-10 g/day as tolerated. May be titrated higher as tolerated.
Matulane (procarbazine)	• HD	**HD** *MOPP Regimen*: 100 mg/m^2 daily for 14 days **HD** *single agent*: 2-4 mg/kg/day for 1 week, then 4-6mg/kg/day until max response/hematologic toxicity. At max response, maintain 1-2 mg/kg/day.
Mekinist (trametinib)	• Metastatic Melanoma[GT]	**Metastatic melanoma:** 2 mg orally once daily as single agent and in combination with dabrafenib
Nexavar (sorafenib)	• RCC • HCC • DTC	**HCC, ~~or~~ RCC, DTC**: 400 mg orally twice daily
Oforta (fludarabine)	• CLM	**CLL**: 40 mg/m^2 daily for 5 consecutive days every 28 days
Pomalyst (pomalidomide)	• MM**	**MM**: 4 mg once daily on days 1-21 of a repeated 28 day cycle. May be used as monotherapy or in combination with dexamethasone.
Revlimid (lenalidomide)	• MM* • MDS • MCL	**MM, MCL**: 25 mg once daily on days 1-21 of repeated 28 day cycles (MM – used in combination with dexamethasone) **MDS**: 10 mg once daily
Sprycel (dasatinib)	• CML, chronic phase • CML, chronic, accelerated, myeloid or lymphoid blast* • ALL	**CML**: 100 mg/day in chronic phase **ALL, CML accelerated, myeloid, or lymphoid blast phase**: 140 mg once daily
Stivarga (regorafenib)	• mCRC* • GIST**	**GIST or mCRC**: 160 mg once daily for the first 21 days of a 28 day cycle.
Sutent (sunitinib)	• RCC • GIST* • PNET	**GIST or RCC**: 50 mg/day; regimen should be 4 weeks on followed by 2 weeks off **PNET**: 37.5 mg/day continuously with no off period
Sylatron (peginterferon alfa-2b)	• Melanoma	**Melanoma**: 6 mcg/kg/week SC for 8 doses followed by 3 mcg/kg/week SC for up to 5 years
Tafinlar (dabrafenib)	• Metastatic melanoma[GT]	**Metastatic melanoma:** 150 mg orally twice daily
Tarceva (erlotinib)	• NSCLC, first line for EGFR deletion of exon 19 or exon 21 substitutions • NSCLC, maintenance* • NSCLC, treatment* • PC	**NSCLC**: 150 mg daily **PC**: 100 mg daily
Targretin (bexarotene)	• CTCL*	**CTCL**: 300 mg/m^2/day
Tasigna (nilotinib)	• CML chronic phase • CML accelerated phase*	**CML** *newly diagnosed*: 300 mg twice daily **CML** *resistant or intolerant to imatinib*: 400 mg twice daily

Medication	Indication	Dosing
Temodar[a] (temozolomide)	• GBM • AA*	**GBM**: 75 mg/m^2 for 42 days with focal radiotherapy, then maintenance dose of 150 mg/m^2 once daily for days 1-5 of a 28 day cycle for 6 cycles. **AA**: 150 mg/m^2 once daily for 5 consecutive days per 28-day cycle
Thalomid (thalidomide)	• MM • ENL, acute treatment and maintenance therapy for prevention	**MM**: 200 mg once daily in 28 treatment cycles in combination with dexamethasone **ENL**: 100-300mg/day for an episode. Up to 400mg/day for severe cutaneous ENL
Tretinoin, oral	• APL*	**APL**: 45 mg/m^2/day as two divided doses until 30 days after complete remission or 90 days total treatment, whichever occurs first
Tykerb (lapatinib)	• HER2+Metastatic BC** • HR+HER2+Metastatic BC	**BC**: 1,250 mg daily on days 1-21 of each cycle **BC HER2+ positive**: 1,500 mg once daily
Votrient (pazopanib)	• RCC • Soft tissue sarcoma*	**RCC, soft tissue sarcoma**: 800 mg/day
Xalkori (crizotinib)	• NSCLC[GT]	**NSCLC**: 250 mg orally twice daily.
Xeloda (capecitabine)	• Metastatic BC* • CC, adjuvant and metastatic	**BC, CC**: 1,250 mg/m^2 twice daily for two weeks, then one week rest period, in 3-week cycles
Xtandi (enzalutamide)	• CRPC*	**CRPC**: 160 mg orally once daily
Zelboraf (vemurafenib)	• Metastatic melanoma[GT]	**Metastatic melanoma**: 960 mg orally twice daily
Zolinza (vorinostat)	• CTCL**	**CTCL**: 400 mg once daily
Zykadia (ceritinib)	• NSCLC*	**NSCLC:** 750 mg once daily
Zytiga (abiraterone)	• CRPC	**CRPC**: 1000 mg once daily (in combination with prednisone 5 mg twice daily)

AA-anaplastic astrocytoma, ACC-adrenal cortical carcinoma, ALL-acute lymphoblastic leukemia, APL-acute promyelocytic leukemia, ASM-aggressive systemic mastocytosis, BC-breast cancer, BCC–basal cell carcinoma, CC–colorectal cancer, CEL-chronic eosinophilic leukemia, CLL-chronic lymphocytic leukemia, CML-chronic myelogenous leukemia, CRPC-castration-resistant prostate cancer, CTCL-cutaneous T-cell lymphoma, DTC–differentiated thyroid carcinoma, DFSP-dermatofibrosarcoma protuberans, ENL-Erythema nodosum leprosum, HR+BC-hormone receptor positive breast cancer, HES-hyperosinophilic syndrome, HR+ hormone receptor positive, GBM-glioblastoma multiforme, GIST-gastrointestinal stromal tumor, HCC-hepatocellular carcinoma, HL-Hodgkin's Disease, mCRC–metastatic colorectal cancer, MCL-mantle cell lymphoma, MDS–myelodysplastic syndrome, MDS/MPD-myelodysplastic/myeloproliferative disease, MM-multiple myeloma, MTC-medullary thyroid cancer, NSCLC-non small cell lung cancer, OC-ovarian cancer, PC-pancreatic cancer, PNET-pancreatic neuroendocrine tumors, RCC-renal cell carcinoma, SCLC-small cell lung cancer, SEGA-subependymal giant cell astrocytoma, TS-tuberous sclerosis complex

*Following one previous therapy based on FDA label **Following two previous therapies based on FDA label

[a]generic available [GT]Genetic test required based on FDA label

POLICY
Prior Authorization Criteria for Approval

A **Target Agent** will be approved when ONE of the following is met:

1. There is documentation that the patient is currently receiving the target agent
   OR
2. The prescribing physician states the patient is using the target agent AND is at risk if therapy is changed
   OR
3. ALL of the following:
   a. ONE of the following:
      i. The patient has an FDA approved diagnosis for the target agent (evidence of a paid claim within the past 180 days, or patient is new to the claim system within the past 120 days and a statement by the physician that patient is currently taking the requested medication in the past 180 days)
         OR
      ii. Meets the off-labeled use of an FDA approved prescription drug for cancer treatment “if the prescription drug is recognized for treatment of the indication in one of the standard reference compendia or in substantially accepted peer reviewed medical literature. The prescribing physician shall submit to the insurer documentation supporting the proposed off-label use or uses if requested by the insurer."
      (State mandate 40-2, 168 article 2 General Provisions) (History: L. 1999, ch. 128, § 2; May 6.)
      AND
   b. ALL of the following:
      i. Genetic testing* has been completed (if applicable) using an FDA approved genetic test if required for therapy with the target agent and results indicate therapy with target agent is appropriate
         AND
      ii. The patient does NOT have any FDA labeled contraindication(s)
      AND
   c. ONE of the following:
      i. The patient has tried and failed the first line agent for the intended indication (if applicable)
         OR
      ii. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to the first line agent
      AND
   d. The patient does not have any FDA labeled limitations of use

Length of Approval: 1 month for dose titration requests
12 months for all other requests

Agent	FDA Labeled Limitation of Use
Gilotrif (afatinib)	Efficacy and safety not established in NSCLC with EGFR mutation other than exon 19 deletions or exon 21 (L858R) substitutions
Mekinist (trametinib)	Not indicated in patients with prior BRAF-inhibitor therapy
Tafinlar (dabrafenib)	Not indicated in patients with wild type BRAF melanoma
Tarceva (erlotinib)	Not recommended in combination with platinum-based chemotherapy. Efficacy and safety not established in NSCLC with EGFR mutation other than exon 19 deletions or exon 21 (L858R) substitutions
Votrient (pazopanib)	Efficacy in adipocytic soft tissue sarcoma or gastrointestinal stromal tumors has not been demonstrated
Zelboraf (vemurafenib)	Not indicated in patients with wild type BRAF melanoma

***Genetic Testing**

Agent	FDA Approved Genetic Test	Required Result
Gilotrif (afatinib)	See website below for FDA approved tests	Positive mutation detection
Mekinist (trametinib)	See website below for FDA approved tests	Positive mutation detection
Tafinlar (dabrafenib)	See website below for FDA approved tests	Positive mutation detection
Tarceva (erlotinib)	Cobas EGFR Mutation Test	Positive mutation detection
Zelboraf (vemurafenib)	Cobas 4800 BRAF V600 Mutation Test	Positive mutation detection
Xalkori (crizotinib)	Vysi ALK Break Apart FISH Probe Kit	Positive gene expression

FDA Companion Diagnostics:
http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/InVitroDiagnostics/ucm301431.htm

RATIONALE

Approved therapy is based not only on labeling but on evidence in clinical guidelines / compendia including NCCN Compendia evidence level 1A, 2A, or 2B, AHFS, DrugDex, or Clinical Pharmacology.

Efficacy

See individual package inserts for pivotal clinical trials or NCCN Compendium for recommendations of efficacy.

Safety[1-40]

Agent	Toxicities, Side Effects, Warnings, Precautions	Contraindications/ Boxed Warnings
Afinitor (everolimus)	Stomatitis, diarrhea, nausea, vomiting, asthenia, fatigue, peripheral edema, cough, dyspnea, rash, headache, non-infectious pneumonitis, infections, oral ulceration	CI: Hypersensitivity to everolimus, to other rapamycin derivatives, or to any of the excipients
Bosulif (bosutinib)	Gastrointestinal toxicity, myelosuppression, hepatotoxicity, fluid retention, embryofetal toxicity, diarrhea, nausea, thrombocytopenia, vomiting, abdominal pain, rash, anemia, pyrexia, fatigue	CI: Hypersensitivity to bosutinib
Caprelsa (vandetanib)	Diarrhea, rash, acne, nausea, hypotension, fatigue, headache, decreased appetite, abdominal pain; contraindicated in patients with congenital long QT syndrome; avoid concomitant use w/ strong CYP3A4 inducers or agents that may prolong the QT interval	CI: Congenital long QT syndrome BW: QT prolongation, torsades de points, sudden death
Cometriq (cabozantinib)	Diarrhea, stomatitis, palmar-plantar erythrodysesthesia syndrome (PPES), decreased weight, decreased appetite, nausea, fatigue, oral pain, hair color changes, dysgeusia, hypertension, abdominal pain, constipation, increased AST/ALT, lymphopenia, increased alkaline phosphatase, hypocalcemia, neutropenia, thrombocytopenia, hypophosphatemia, and hyperbilirubinemia	CI: None BW: gastrointestinal perforations and fistulas and hemorrhage
Erivedge (vismodegib)	Muscle spasms, alopecia, dysgeusia, weight loss, fatigue, nausea, diarrhea, decreased appetite, constipation, arthralgias, vomiting, and ageusia	CI: None BW: embryo-fetal death and severe birth defects
Gilotrif (afatinib)	Diarrhea, rash/dermatitis acneiform, stomatitis, paronychia, dry skin, decreased appetite, pruritus.	CI: None BW: None
Gleevec (imatinib)	Fluid retention and edema, nausea and vomiting, muscle cramps, musculoskeletal pain, diarrhea, rash; cytopenias; severe congestive heart failure, left ventricular dysfunction, hepatotoxicity, hemorrhage, gastrointestinal disorders, hypereosinophilic cardiac toxicity, dermatologic toxicities, hypothyroidism, fetal harm to pregnant women, growth retardation in children and pre-adolescents, tumor lysis syndrome, driving and using machinery	None
Hexalen (altretamine)	Nausea, vomiting, neuropathy, leucopenia, thrombocytopenia, anemia; myelosuppression and neurotoxicity; no concomitant administration with MAOI's	CI: Hypersensitivity to altretamine, Bone marrow suppression, neurological disease BW: peripheral blood counts should be monitored monthly
Hycamtin (topotecan	Anemia, nausea, diarrhea, vomiting, fatigue, anorexia, asthenia, pyrexia; bone marrow suppression, interstitial lung disease; avoid concomitant use of P-glycoprotein inhibitors	CI: Bone marrow suppression, hypersensitivity to topotecan or its ingredients BW: Bone marrow suppression

Agent	Toxicities, Side Effects, Warnings, Precautions	Contraindications/ Boxed Warnings
Iclusig (ponatinib)	Non-hematological include hypertension, rash, abdominal pain, fatigue, headache, dry skin, constipation, arthralgia, nausea, and pyrexia. Hematologic include thrombocytopenia, anemia, neutropenia, lymphopenia, and leukopenia.	BW: arterial thrombosis (cardiovascular, cerebrovascular, peripheral, and fatal MI and stroke), hepatotoxicity including liver failure and death CI: None
Imbruvica (ibrutnib)	Thrombocytopenia, diarrhea, neutropenia, anemia, fatigue, musculoskeletal pain, peripheral edema, upper respiratory tract infection, nausea, bruising, dyspnea, constipation, rash, abdominal pain, vomiting and decreased appetite	BW: None CI: None
Inlyta (axitinib)	Diarrhea, hypertension, fatigue, decreased appetite, nausea, dysphonia, hand-foot syndrome, decreased weight, vomiting, asthenia and constipation	None
Jakafi (ruxolitinib)	Thrombocytopenia, anemia, neutropenia, bruising, dizziness and headache. Dose reductions recommended for thrombocytopenia.	None
Lysodren (mitotane)	Anorexia, nausea, vomiting, diarrhea, lethargy, somnolence, dizziness, vertigo, skin rash; temporarily D/C following shock/trauma	CI: Hypersensitivity to mitotane
Matulane (procarbazine)	Leukopenia, anemia, thrombocytopenia, nausea and vomiting; do not use with other CNS depressants, disulfiram-like reaction with alcohol consumption, exhibits MAOI activity so avoid drugs/food with high tyramine content, stomatitis, hemorrhage, CNS symptoms,	CI: Bone marrow suppression, known hypersensitivity to procarbazine
Mekinist (trametinib)	Rash, diarrhea, lymphedema, cardiomyopathy, retinal pigment epithelial detachment, retinal vein occlusion, interstitial lung disease, serious skin toxicity, embryofetal toxicity	CI: None
Nexavar (sorafenib)	Fatigue, weight loss, rash, pruritus, hand-foot skin reactions, SJS, diarrhea, anorexia, abdominal pain; hypertension; incidence of cardiac ischemia/infarction higher compared with placebo in clinical trial, bleeding, hypertension, GI perforation, QT prolongation, drug-induced hepatitis, fetal harm to pregnant women	CI: Known hypersensitivity to sorafenib or its components, use in combination with carboplatin and paclitaxel in patients with squamous cell lung cancer
Oforta (fludarabine)	Fever, infection, asthenia, cough, nausea, diarrhea, anorexia, abdominal pain; dose dependent severe neurologic effects (blindness, coma and death), life-threatening autoimmune hemolytic anemia, pulmonary toxicity	CI: None BW: CNS toxicity, hemolytic anemia, and pulmonary toxicity
Pomalyst (pomalidomide)	Fatigue and asthenia, neutropenia, anemia, constipation, nausea, diarrhea, dyspnea, upper-respiratory tract infections, back pain and pyrexia	CI: Pregnancy BW: fetal risk, venous thromboembolism
Revlimid (lenalidomide)	Teratogenicity, fatigue, hematologic toxicity, DVT, PE, allergic reactions (SJS, TEN, angioedema), TLS, tumor flare, secondary primary malignancies, neutropenia, constipation, diarrhea, muscle cramp anemia, pyrexia, peripheral edema, nausea, back pain, upper respiratory tract infection, dyspnea, dizziness, thrombocytopenia, tremor and rash	CI: Pregnancy, hypersensitivity to lenalidomide BW: fetal risk, hematologic toxicity, DVT and PE

Agent	Toxicities, Side Effects, Warnings, Precautions	Contraindications/ Boxed Warnings
Sprycel (dasatinib)	Fluid retention, diarrhea, headache, skin rash, nausea, hemorrhage, fatigue, dyspnea; myelosuppression, bleeding related events, QT prolongation, pulmonary arterial hypertension, congestive heart failure, left ventricular dysfunction and myocardial infarction, fetal harm in pregnancy	None
Stivarga (regorafenib)	Asthenia/fatigue, decreased appetite and food intake, hand-foot skin reaction (SFSR) [palmar-plantar erythrodysesthesia (PPE)], diarrhea, mucositis, weight loss, infection, hypertension, and dysphonia	CI: None BW: Severe, sometimes fatal hepatotoxicity
Sutent (sunitinib)	Fatigue, asthenia, diarrhea, nausea, mucositis/stomatitis, vomiting, dyspepsia, abdominal pain, constipation, hypertension, rash, hand-foot syndrome, skin discoloration, altered taste, anorexia, bleeding; cardiotoxicity, may prolong QT interval; discontinue if congestive heart failure is manifested, serious infection, myopathy, rhabdomyolysis, thrombotic microangiopathy, proteinuria/nephrotic syndrome, hyperthyroidism, hepatotoxicity, fetal harm during pregnancy, hemorrhagic events, osteonecrosis of the jaw, tumor lysis syndrome adrenal hemorrhage	CI: None BW: hepatotoxicity
Sylatron (peginterferon alfa-2b)	Fatigue, increased ALT, increased AST, pyrexia, headache, anorexia, myalgia, nausea, chills, and injection site reactions, significant or unstable cardiac disease, retinal disorders, hypothyroidism, hyperthyroidism, hyperglycemia	CI: Autoimmune hepatitis, hepatic decompensation (Child-Pugh score >6, Blass B and C), hypersensitivity to peginterferon alfa-2a or peginterfon alfa-2b BW: depression and other neuropsychiatric disorders
Tafinlar (dabrafenib)	Hyperkeratosis, headache, pyrexia, arthralgia, papilloma, alopecia, and palmar-plantar erythrodysesthesia syndrome	CI: None
Tarceva (erlotinib)	Rash, diarrhea, anorexia, fatigue, dyspnea, cough, nausea and vomiting; infrequent reports of serious interstitial lung disease-like events, renal failure, hepatotoxicity, gastrointestinal perforation, ocular disorders, bullous and exfoliative skin disorders, myocardial infarction/ischemia, cerebrovascular events, microangiopathic hemolytic anemia, elevated INR, potential bleeding events, fetal harm in pregnancy	None
Targretin (bexarotene)	Hyperlipidemia, hypercholesterolemia, headache, hypothyroidism, asthenia, rash, leukopenia, nausea, peripheral edema, infection, abdominal pain, pancreatitis, liver function test abnormalities, hepatic insufficiency, thyroid axis alterations, cataracts, photosensitivity	CI: Pregnancy
Tasigna (nilotinib)	Rash, pruritus, nausea, fatigue, headache, constipation, diarrhea, and vomiting; thrombocytopenia, neutropeniaavoid concomitant use with strong CYP3A4 inhibitors or inducer, myelosuppression, QT prolongation, sudden deaths, elevated serum lipase, liver function abnormality, electrolyte abnormalities, hepatic impairment, tumor lysis syndrome, food effects (increase blood levels of Tasigna), fetal harm during pregnancy	CI: Hypokalemia, hypomagnesemia, QT prolongation BW: QT prolongation and sudden deaths
Temodar (temozolomide)	Fatigue, headache, anorexia, nausea, vomiting; myelosuppression, myelodysplastic syndrome, erythema multiforme, toxic epidermal necrosis, Steven-Johnson Syndrome, hepatotoxicity, fetal harm in pregnancy	CI: Hypersensitivity to dacarbazine (DTIC) or Temodar component

Agent	Toxicities, Side Effects, Warnings, Precautions	Contraindications/ Boxed Warnings
Thalomid (thalidomide)	Teratogenicity, somnolence, dizziness, orthostatic hypotension, constipation, sensory neuropathy, confusion, hypocalcemia, edema, dyspnea, thrombosis/embolism, and rash/desquamation, neutropenia, increased HIV viral load, bradycardia, SJS/TEN, seizures, TLS	CI: Pregnancy, thalidomide hypersensitivity BW: fetal risk and VTE events
Tretinoin (oral)	Headache, fever, skin/mucous membrane dryness, bone pain, nausea/vomiting, rash, mucositis, pruritus, increased sweating, visual disturbances, ocular disorders, alopecia, skin changes, changed visual acuity, and bone inflammation	CI: Paraben hypersensitivity, retinoid hypersensitivity BW: retinoic acid-APL syndrome
Tykerb (lapatinib)	Diarrhea, nausea and vomiting, dermatologic reactions, fatigue; has been reported to decrease left ventricular ejection fraction, hepatotoxicity, interstitial lung disease and QT prolongation have been associated with lapatinib, fetal harm in pregnancy	CI: Known hypersensitivity to lapatinib or Tykerb components BW: hepatotoxicity
Votrient (pazopanib)	Diarrhea, hair color changes, nausea, anorexia, vomiting, fatigue, asthenia, hepatotoxicity, increase serum transaminase levels, QT prolongation, hemorrhagic events, cardiac dysfunction, fatal hemorrhagic events, arterial thrombotic events, venous thrombotic events, gastrointestinal perforation, hypertension, reversible posterior leukoencephalopathy syndrome, hypothyroidism; may need to reduce dose if used with strong CYP3A4 inhibitors, avoid with CYP3A4 inducers, proteinuria, serious infections, fetal harm in pregnancy	CI: None BW: hepatotoxicity
Xalkori (crizotinib)	Hepatotoxicity, vision disorder, nausea, diarrhea, vomiting, edema, and constipation. QT prolongation and severe (including fatal) pneumonitis have been reported, fetal harm in pregnancy	None
Xeloda (capecitabine)	Diarrhea, coagulopathy, cardiotoxicity, hand-and-foot syndrome, nausea, vomiting, abdominal pain, fatigue/weakness, and hyperbilirubinemia, hematologic, fetal harm in pregnancy	CI: Dihydropyrimidine dehydrogenase (DPD) deficiency, severe renal failure, hypersensitivity to capecitabine or 5-fluorouracil BW: Xeloda-warfarin interaction
Xtandi (enzalutamide)	Seizure, asthenia/fatigue, back pain, diarrhea, arthralgia, hot flush, peripheral edema, musculoskeletal pain, headache, upper respiratory infection, muscular weakness, dizziness, insomnia, lower respiratory infection, spinal cord compression and cauda equina syndrome, hematuria, paresthesia, anxiety, and hypertension	CI: Pregnancy
Zelboraf (vemurafenib)	Arthralgia, rash, alopecia, fatigue, photosensitivity reaction, nausea, pruritus and skin papilloma, QT prolongation, severe hypersensitivity reactions (including anaphylaxis), severe dermatologic reactions (including Stevens-Johnson syndrome), cutaneous squamous cell carcinoma, new primary malignant melanomas, liver abnormalities, severe ophthalmologic reactions, fetal harm in pregnancy	None
Zolinza (vorinostat)	Pulmonary embolism, diarrhea, fatigue, nausea, anorexia and dysgeusia; severe thrombocytopenia and gastrointestinal bleeding have been reported with concomitant use other HDAC inhibitors (e.g. valproic acid), hyperglycemia, monitor platelet count, fetal	CI: Severe hepatic impairment

Agent	Toxicities, Side Effects, Warnings, Precautions	Contraindications/ Boxed Warnings
	harm during pregnancy	
Zykadia (ceritinib)	Severe or persistent gastrointestinal toxicity (diarrhea, nausea, vomiting, abdominal pain), hepatotoxicity and elevated transaminases, interstitial lung disease/pneumonitis, QT interval prolongation, hyperglycemia, bradycardia, embryofetal toxicity, constipation, esophageal disorder, fatigue, decreased appetite, rash, neuropathy, vision disorder	None
Zytiga (abiraterone)	Mineralocorticoid excess, adrenocortical insufficiency, Joint swelling or discomfort, hyperkalemia, edema, muscle discomfort, hot flush, diarrhea, urinary tract infection, cough, hypertension, arrhythmia, urinary frequency, nocturia, dyspepsia, upper respiratory tract infection; avoid concomitant use with CYP2D6 substrates with narrow therapeutic indices if possible; monitor for hepatotoxicity, use with caution in patients with a history of cardiovascular disease, food effect (increase exposure if taken with meals)	CI: Pregnancy

BW- boxed warning, CI-contraindication

CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

J7527	Everolimus, oral, 0.25 mg
J8520	Capecitabine, oral, 150 mg
J8521	Capecitabine, oral, 500 mg
J8562	Fludarabine phosphate, oral, 10 mg
J8700	Temozolomide, oral, 5 mg
J8705	Topotecan, oral, 0.25 mg
J9351	Injection, topotecan, 0.1 mg
S0088	Imatinib, 100 mg
S0182	Procarbazine HCl, oral, 50 mg

There are no specific HCPCS codes for the remaining drugs listed in this policy.

REVISIONS

01-01-2011	Policy added to the bcbsks.com web site.
02-01-2012	Added the following Target Agents: Caprelsa (vandetanib), Hexalen (altretamine), Hycamtin (topotecan), Lysodren (mitotane), Matulane (procarbazine), Oforta (fludarabine), Targretin (bexarotene), Temodar (temozolomide), Tretinoin (oral), Xalkori (crizotinib), Xeloda (capecitabine), Zelboraf (vemurafenib), Zolinza (vorinostat),

	Zytiga (abiraterone)
	Updated description section
	In Policy section: ▪ Removed criteria for Afinitor (everolimus), Gleevec (imatinib),Nexavar (sorafenib), Sprycel (dasatinib), Sutent (sunitinib), Tarceva (erlotinib), Tasigna (nilotinib), Tykerb (lapatinib), Votrient (pazopanib) ▪ Added the following blanket criteria for all Target Agents listed in the policy: "A Target Agent will be approved when ONE of the following is met: 1. There is documentation that the patient is currently receiving the target agent OR 2. The prescribing physician states the patient is using the target agent AND is at risk if therapy is changed OR 3. BOTH of the following: a. ONE of the following: i. The patient has an FDA approved diagnosis for the target agent OR ii. The use of the target agent is for an indication that is supported by compendia. (NCCN Compendium™ level of evidence 1, 2A, or 2B, AHFS, DrugDex, Clinical Pharmacology) or the prescriber has submitted additional documentation supporting the requested therapeutic use (approval by the Clinical Review Pharmacist required) AND b. ALL of the following: i. Genetic testing* has been completed (if applicable) using an FDA approved genetic test if required for therapy with the target agent and results indicate therapy with target agent is appropriate AND ii. The patient does NOT have any FDA labeled contraindication(s) AND iii. The patient has tried and failed the first line agent for the intended indication (if applicable) ▪ Added the following Genetic Testing requirement for Zelboraf and Zalkori: Agent — FDA Approved Genetic Test — Required Result Zelboraf (vemurafenib) — Cobas 4800 BRAF V600 Mutation Test — Positive Mutation Detection Xalkori (crizotinib) — Vysi ALK Break Apart FISH Probe Kit — Positive Gene Expression
	References updated
07-01-2012	Title Changed from: "Oral Oncology Agents Prior Authorization Criteria" to: "Self Administered Oncology Agents Prior Authorization Criteria"
	Added the following target drugs: Erivedge™ (vismodegib), Inlyta® (axitinib, Jakafi™ (ruxolitinib, Revlimid® (lenalidomide), Sylatron (peginterferon alfa-2b), Thalomid® (thalidomide)
	In Policy section: ▪ Removed the following indication, "The prescribing physician states the patient is using the target agent AND is at risk if therapy is changed" ▪ Revised the Kansas Mandate wording from: "The use of the target agent is for an indication that is supported by compendia. (NCCN Compendium™ level of evidence 1, 2A, or 2B, AHFS, DrugDex, Clinical Pharmacology) or the prescriber has submitted additional documentation supporting the requested therapeutic use (approval by the Clinical Review Pharmacist required)" to: "Meets the off-labeled use of an FDA approved prescription drug for cancer treatment "if the prescription

	drug is recognized for treatment of the indication in one of the standard reference compendia or in substantially accepted peer reviewed medical literature. The prescribing physician shall submit to the insurer documentation supporting the proposed off-label use or uses if requested by the insurer." ▪ (State mandate 40-2, 168 article 2 General Provisions) (History: L. 1999, ch. 128, § 2; May 6.)"
	Rationale section added
	References updated
03-01-2013	Title revised from, "Self Administered Oncology Agents Prior Authorization Criteria" to, "Self Administered Oncology Agents"
	In Description section: Updated FDA Approved Indications chart to contain the following drugs: Afinitor (everolimus), Bosulif (bosutinib), Caprelsa (vandetanib), Erivedge (vismodegib), Gleevec (imatinib), Hexalen (altretamine), Hycamtin (topotecan), Inlyta (axitinib), Jakafi (ruxolitinib), Lysodren (mitotane), Matulane (procarbazine), Nexavar (sorafenib), Oforta (fludarabine), Revlimid (lenalidomide), Sprycel (dasatinib), Stivarga (regorafenib), Sutent (sunitinib), Sylatron (peginterferon alfa-2b), Tarceva (erlotinib), Targretin (bexarotene), Tasigna (nilotinib), Temodar (temozolomide), Thalomid (thalidomide), Tretinoin, oral, Tykerb (lapatinib), Votrient (pazopanib), Xalkori (crizotinib), Xeloda (capecitabine), Xtandi (enzalutamide), Zelboraf (vemurafenib), Zolinza (vorinostat), Zytiga (abiraterone)
	In Policy section: ▪ Added the following criteria, "2. The prescribing physician states the patient is using the target agent AND is at risk if therapy is changed, OR"
	Removed the Rationale narrative section and replaced with a Safety chart for the following drugs: Afinitor (everolimus), Bosulif (bosutinib), Caprelsa (vandetanib), Erivedge (vismodegib), Gleevec (imatinib), Hexalen (altretamine), Hycamtin (topotecan), Inlyta (axitinib), Jakafi (ruxolitinib), Lysodren (mitotane), Matulane (procarbazine), Nexavar (sorafenib), Oforta (fludarabine), Revlimid (lenalidomide), Sprycel (dasatinib), Stivarga (regorafenib), Sutent (sunitinib), Sylatron (peginterferon alfa-2b), Tarceva (erlotinib), Targretin (bexarotene), Tasigna (nilotinib), Temodar (temozolomide), Thalomid (thalidomide), Tretinoin, oral, Tykerb (lapatinib), Votrient (pazopanib), Xalkori (crizotinib), Xeloda (capecitabine), Xtandi (enzalutamide), Zelboraf (vemurafenib), Zolinza (vorinostat), Zytiga (abiraterone)
	References updated
09-01-2013	In Title Header ▪ Added under Prior Authorization Form link "Prime Therapeutics will review Prior Authorization requests."
	Description section updated ▪ Added the following agents to the FDA Approved Indications chart: Cometriq (cabozantinib), Iclusig (ponatinib), Pomalyst (pomalidomide)
	In Policy section ▪ Added Tarceva (erlotinib) to Genetic Testing chart
	Rationale section updated
	▪ Added Coding section to reflect HCPCS codes: J7527, J8520, J8521, J8562, J8700, J8705, S0088, S0182 ▪ Also added "There are no specific HCPCS codes for the remaining drugs listed in

	this policy."
	References updated
02-28-2014	Description section updated to include update to FDA Approved Indications chart.
	In Policy section: ▪ In Item 3 a i added Look-back period information. ▪ Moved the Kansas State Mandate information from being its own Item 4 to Item 3 a ii. ▪ Added in 3 c ii "The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to the first line agent" ▪ Updated Genetic Testing chart for required results.
	Rationale section updated to include updates to the Safety chart.
	In Coding section: ▪ HCPCS Code nomenclature correction: J8705 ▪ Added HCPCS code: J9351
	References updated
08-28-2014	In Description section: ▪ Added Zykadia (ceritinib) to the FDA Approved Indications chart ▪ Updated FDA Approved Indications chart for Imbruvica ((ibrutinib), Mekinist (trametinib), Nexavar (sorafenib), Revlimid (lenalidomide), Tykerb (lapatinib)
	In Policy section: ▪ Added Item 3 d "The patient does not have any FDA labeled limitations of use" ▪ Added to Length of Approval "1 month for dose titration requests" ▪ Added to Length of Approval "for all other requests" to read "12 months for all other requests" ▪ Added FDA Labeled Limitation of Use chart ▪ Updated Genetic Testing chart
	In Rationale section: ▪ Added Zykadia (ceritinib) to the Safety chart on Toxicities, Side Effects, Warnings, Precautions and Contraindications / Boxed Warnings
	Coding section reviewed
	References updated

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