LifeWise
Health Plan of Washington

PHARMACY / MEDICAL POLICY – 5.01.540

Miscellaneous Oncology Drugs

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Introduction

Chemotherapy, often called chemo, is cancer treatment that uses drugs. Radiation and surgery treat one area of cancer. But chemo usually travels through the bloodstream to treat the whole body. Treating the whole body is called a systemic treatment. The goal of chemo is to either treat cancer or ease its symptoms. Treating cancer can be to cure it, decrease the chance it will return, or stop or slow its growth. Easing cancer symptoms without trying to cure the cancer is called palliative therapy. Chemotherapy drugs can be used in many different ways. Chemo can make a tumor smaller before surgery or radiation, destroy cancer cells that surgery or radiation didn't treat, help other treatments work better, or kill cancer cells that have come back or spread. Chemotherapy is given in different ways. This includes by mouth (oral), through a vein (intravenous), by a shot (injection), or with a cream rubbed onto the skin (topical). In some cases, chemo is injected between the layers of tissue covering the brain and spinal cord (intrathecal), is given into the belly area (intraperitoneal), or is injected into an artery (intra-arterial). This policy gives information about many different types of chemo drugs and the criteria for when they may be medically necessary.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

Policy Coverage Criteria

Drug	Medical Necessity
Oral Drugs	
Hedgehog Pathway Inhibitors	
Erivedge (vismodegib) oral	**Erivedge (vismodegib) may be considered medically necessary for adult individuals with ANY of the following:** • Metastatic basal cell carcinoma (BCC) **OR** • Locally advanced BCC that has recurred following surgery **OR** • Locally advanced BCC in individuals who are not candidates for surgery or radiation therapy **AND** • The dose is limited to 150 mg per day
Odomzo (sonidegib) oral	**Odomzo (sonidegib) may be considered medically necessary for adult individuals with ANY of the following:** • Locally advanced basal cell carcinoma (BCC) that has recurred following surgery or radiation therapy **OR** • Locally advanced BCC in individuals who are not candidates for surgery or radiation therapy **AND** • The dose is limited to 200 mg per day
Drugs Targeting Acute Myeloid Leukemia (AML)	
Idhifa (enasidenib) oral	**Idhifa (enasidenib) may be considered medically necessary for:** • Treatment of relapsed or refractory acute myeloid leukemia (AML) in adult individuals with an isocitrate dehydrogenase-2 (**IDH2**) mutation
Tabloid (thioguanine) oral	**Tabloid (thioguanine) may be considered medically necessary for the treatment of acute myeloid leukemia when all of the following are met:**

Drug	Medical Necessity
Oral Drugs	
	• The individual has been diagnosed with acute myeloid leukemia **AND** • Tabloid (thioguanine) will be used for remission induction or remission consolidation therapy **AND** • The dose is limited to 3 mg/kg per day
Tibsovo (ivosidenib) oral	**Tibsovo (ivosidenib) may be considered medically necessary for use in combination with azacitidine or as monotherapy for the treatment of adult individuals with newly-diagnosed acute myeloid leukemia (AML) with a susceptible isocitrate dehydrogenase-1 (IDH1) mutation who are ≥ 75 years old or who have comorbidities that preclude use of intensive induction chemotherapy.** **Tibsovo (ivosidenib) may be considered medically necessary for the treatment of relapsed or refractory acute myeloid leukemia (AML) in adult individuals with a susceptible IDH1 mutation.** **Tibsovo (ivosidenib) may be considered medically necessary for the treatment of adult individuals with previously treated, locally advanced or metastatic cholangiocarcinoma with a susceptible IDH1 mutation.** **Tibsovo (ivosidenib) may be considered medically necessary for the treatment of adult individuals with relapsed or refractory myelodysplastic syndromes with a susceptible IDH1 mutation.**
Daurismo (glasdegib) oral	**Daurismo (glasdegib), in combination with low-dose cytarabine, may be considered medically necessary for newly-diagnosed acute myeloid leukemia (AML) in:** • Adult individuals who are ≥75 years old

Drug	Medical Necessity
Oral Drugs	
	OR • Who have comorbidities that preclude use of intensive induction chemotherapy
Poly (ADP-ribose) Polymerase (PARP) Inhibitors	

Lynparza (olaparib) oral	**Lynparza (olaparib) may be considered medically necessary for the maintenance treatment of adult individuals with advanced epithelial ovarian, fallopian tube or primary peritoneal cancer when ALL the following are true:**
	• Individual has a deleterious or suspected deleterious BRCA mutation (as confirmed by genetic testing)
	AND
	• Individual is in complete or partial response to first-line platinum-based chemotherapy
	
	Lynparza (olaparib) may be considered medically necessary in combination with bevacizumab for the maintenance treatment of adult individuals with advanced epithelial ovarian, fallopian tube or primary peritoneal cancer when ALL the following are true:
	• Individual is in complete or partial response to first-line platinum-based chemotherapy
	AND
	• The cancer is associated with homologous recombination deficiency (HRD)-positive status defined by:
	  ○ A deleterious or suspected deleterious BRCA mutation (as confirmed by genetic testing)
	  AND/OR
	  ○ Microsatellite instability or SNP analysis (loss of heterozygosity)
	
	Lynparza (olaparib) may be considered medically necessary for the maintenance treatment of adult individuals with recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer,

Drug	Medical Necessity
Oral Drugs	
	who are in a complete or partial response to platinum-based chemotherapy. **Lynparza (olaparib) may be considered medically necessary for the treatment of adult individuals with advanced ovarian cancer unresponsive to platinum-based chemotherapy when ALL the following are true:** • Individual has a deleterious or suspected deleterious **germline** BRCA-mutation (gBRCAm) (as confirmed by genetic testing) **AND** • Individual has been treated with 3+ prior lines of chemotherapy **Lynparza (olaparib) may be considered medically necessary for the adjuvant treatment of adult individuals with high risk early breast cancer when ALL the following are true:** • Individual has a deleterious or suspected deleterious BRCA-mutation or a PALB2 mutation (as confirmed by genetic testing) **AND** • Individual has HER2-negative high risk early breast cancer **AND** • Individual has been treated with chemotherapy in the neoadjuvant or adjuvant setting **Note:** Early breast cancer is distinguished from locally advanced and metastatic disease. Early breast cancer includes Stages 0 to IIB or T0 to T2 and N0 to N1. Locally advanced breast cancer includes stages IIIA to IIIC or T3N0 and Tx N2-3. Metastatic breast cancer is Tx Nx M1 or Stage IV. **Lynparza (olaparib) may be considered medically necessary for the treatment of adult individuals with metastatic breast cancer when ALL the following are true:**

Drug	Medical Necessity
Oral Drugs	
	• Individual has a deleterious or suspected deleterious BRCA mutation or a PALB2 mutation (as confirmed by genetic testing) **AND** • Individual has HER2-negative metastatic breast cancer **AND** • Individual has been treated with chemotherapy in the neoadjuvant, adjuvant or metastatic setting **AND** • If hormone receptor (HR)-positive, individual should have been treated with a prior endocrine therapy or be considered inappropriate for endocrine therapy **Lynparza (olaparib) may be considered medically necessary for the maintenance treatment of adult individuals with metastatic pancreatic adenocarcinoma when ALL the following are true:** • Individual has a deleterious or suspected deleterious **germline** BRCA-mutation (gBRCAm) (as confirmed by genetic testing) **AND** • The disease has not progressed on at least 16 weeks of a first-line platinum-based chemotherapy regimen **Lynparza (olaparib) may be considered medically necessary for the treatment of adult individuals:** • For the treatment of deleterious or suspected deleterious germline or somatic homologous recombination repair (HRR) gene-mutated (see **Appendix** for biomarker testing) metastatic castration-resistant prostate cancer (mCRPC) who have progressed following prior treatment with Xtandi (enzalutamide) or abiraterone.

Drug	Medical Necessity
Oral Drugs	
	• In combination with abiraterone and prednisone or prednisolone, for the treatment of deleterious or suspected deleterious BRCA-mutated (BRCAm) (see **Appendix** for biomarker testing) metastatic castration-resistant prostate cancer (mCRPC).
Rubraca (rucaparib) oral	**Rubraca (rucaparib) may be considered medically necessary for the treatment of adult individuals with:** • BRCA mutations (germline and/or somatic) associated epithelial ovarian, fallopian tube, or primary peritoneal cancer who have been treated with two or more chemotherapies (as confirmed by genetic testing) **OR** • Recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy as maintenance treatment **OR** • BRCA mutations (germline and/or somatic) associated metastatic castration-resistant prostate cancer (mCRPC) who have been treated with androgen receptor-directed therapy and a taxane-based chemotherapy (as confirmed by genetic testing)
Talzenna (talazoparib) oral	**Talzenna (talazoparib) may be considered medically necessary for adult individuals when:** • As a single agent, for the treatment of germline BRCA-mutated, HER2-negative locally advanced or metastatic breast cancer (as confirmed by genetic testing) • In combination with enzalutamide, for the treatment of HRR gene-mutated metastatic castration-resistant prostate cancer (mCRPC) (see **Appendix**)
Zejula (niraparib) oral	**Zejula (niraparib) may be considered medically necessary for the treatment of adult individuals with epithelial ovarian, fallopian tube, or primary peritoneal cancer if all the following are met:**

Drug	Medical Necessity
Oral Drugs	
	• Individual is 18 years of age or older **AND** • Used as a maintenance component of first-line platinum-based chemotherapy in an individual who has had a complete response or partial response to platinum-based initial chemotherapy **OR** • Used as maintenance component of treatment for individuals with recurrent disease who have achieved a complete response or partial response after second-line platinum-based chemotherapy **AND** • Individual has a known or suspected deleterious BRCA mutation
Cyclin-Dependent Kinases 4 and 6 (CDK4/6) Inhibitors	
Ibrance (palbociclib) oral	**Ibrance (palbociclib) may be considered medically necessary for the treatment of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer in combination with:** • An aromatase inhibitor as initial endocrine based therapy **OR** • Faslodex (fulvestrant) in individuals with disease progression following endocrine therapy
Kisqali (ribociclib) oral	**Kisqali (ribociclib) may be considered medically necessary in individuals 18 years and older when:** • Used in combination with an aromatase inhibitor as initial endocrine-based therapy for the treatment of premenopausal or postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer **OR**

Drug	Medical Necessity
Oral Drugs	
	• Used for initial treatment or following disease progression on endocrine therapy, for postmenopausal with HR+, HER2- advanced or metastatic breast cancer, in combination with Faslodex (fulvestrant) **Use as maintenance therapy following response to chemotherapy regimens is considered not medically necessary.**
Kisqali Femara Co-Pack (ribociclib – letrozole) oral	**Kisqali Femara Co-Pack (ribociclib – letrozole) may be considered medically necessary in individuals 18 years and older when:** • Used for the treatment of premenopausal or postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer **Use as maintenance therapy following response to chemotherapy regimens is considered not medically necessary.**
Verzenio (abemaciclib) oral	**Verzenio (abemaciclib) may be considered clinically necessary for the treatment of postmenopausal women, or pre/perimenopausal women whose estrogen levels are suppressed on GnRH (gonadotrophin releasing hormone) therapy, who meet ONE of the following indications:** • In combination with endocrine therapy (tamoxifen or an aromatase inhibitor) for the adjuvant treatment of adult individuals with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, node-positive, early breast cancer at high risk of recurrence **OR** • In combination with an aromatase inhibitor as initial endocrine-based therapy for the treatment of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer **OR**

Drug	Medical Necessity
Oral Drugs	
	• In combination with Faslodex (fulvestrant) for the treatment of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer in women with disease progression following endocrine therapy **OR** • As monotherapy for the treatment of HR-positive, HER2 – negative advanced or metastatic breast cancer in individuals with disease progression following endocrine therapy and prior chemotherapy in the metastatic setting
Nuclear Export Inhibitors	
Xpovio (selinexor) oral	**Xpovio (selinexor), in combination with bortezomib and dexamethasone, may be considered medically necessary for treatment of adult individuals with multiple myeloma who have received at least one prior therapy.** **Xpovio (selinexor) in combination with dexamethasone may be considered medically necessary for treatment of adult individuals with relapsed or refractory multiple myeloma (RRMM) who have received at least four prior therapies and whose disease is refractory to:** • At least two proteasome inhibitors (e.g., bortezomib, carfilzomib) **AND** • At least two immunomodulatory agents (e.g., lenalidomide, pomalidomide) **AND** • An anti-CD-38 monoclonal antibody (e.g., daratumumab, isatuximab-irfc) **Xpovio (selinexor) may be considered medically necessary for treatment of adult individuals with relapsed or refractory**

Drug	Medical Necessity
Oral Drugs	
	diffuse large B-cell lymphoma (DLBCL), not otherwise specified, including DLBCL arising from follicular lymphoma, after at least 2 lines of systemic therapy.
Inhibitor of Tropomyosin Receptor Tyrosine Kinases	
Rozlytrek (entrectinib) oral	**Rozlytrek (entrectinib) may be considered medically necessary for the treatment of:** • Adult individuals with metastatic non-small cell lung cancer (NSCLC) whose tumors are *ROS1*-positive **OR** • Adult and pediatric individuals 12 years of age and older with solid tumors that: ○ Have a neurotrophic tyrosine receptor kinase (NTRK) gene fusion without a known acquired resistance mutation **AND** ○ Are metastatic or where surgical resection is likely to result in severe morbidity **AND** ○ Have no satisfactory alternative treatments or that have progressed following treatment
Vitrakvi (larotrectinib) oral	**Vitrakvi (larotrectinib) may be considered medically necessary for the treatment of adult and pediatric individuals with solid tumors that:** • Have a neurotrophic receptor tyrosine kinase (*NTRK*) gene fusion without a known acquired resistance mutation **AND** • Are metastatic or where surgical resection is likely to result in severe morbidity **AND** • Have no satisfactory alternative treatments or that have progressed following treatment
Nitrosoureas	
Gleostine (lomustine) oral	**Gleostine (lomustine) may be considered medically necessary for the treatment of individuals with any of the following:**

Drug	Medical Necessity
Oral Drugs	
	• Primary and metastatic brain tumors following appropriate surgical and/or radiotherapeutic procedures • Hodgkin's lymphoma whose disease has progressed following initial chemotherapy when used as a component of combination chemotherapy
Janus-Associated Kinase Inhibitors	
Jakafi (ruxolitinib) oral	**Jakafi (ruxolitinib) may be considered medically necessary for:** • Myelofibrosis in adults 18 years of age or older • Polycythemia vera in adults 18 years of age or older, after trial and failure of hydroxyurea • Steroid-refractory acute graft-versus-host disease in adult and pediatric individuals 12 years and older • Chronic graft-versus-host disease after failure of one or two lines of systemic therapy in adult and pediatric individuals 12 years and older
Ojjaara (momelotinib) oral	**Ojjaara (momelotinib) may be considered medically necessary for adults when all of the following are met:** • The individual is 18 years or older **AND** • The individual has been diagnosed with intermediate or high-risk myelofibrosis (MF), including primary MF or secondary MF (post-polycythemia vera and post-essential thrombocythemia) **AND** • The individual has been diagnosed with transfusion-dependent anemia associated with MF **AND** • The dose is limited to 200 mg daily
Vonjo (pacritinib) oral	**Vonjo (pacritinib) may be considered medically necessary for:** • Adults with intermediate or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) myelofibrosis with a platelet count below 50 × 10^9/L **AND**

Drug	Medical Necessity
Oral Drugs	
	• The dose is limited to 400 mg per day (taken as 200 my twice daily) **Note:** Documentation for intermediate or high-risk primary myelofibrosis should include a statement about risk stratification and/or genetically inspired prognostic scoring system (GIPSS) of >2 or a GIPSS of 1-2 plus MIPPS70 of >4. Documentation of intermediate or high-risk secondary myelofibrosis should include a statement about risk stratification and record of post-polycythemia vera or post-essential thrombocythemia.
RET Inhibitors	
Gavreto (pralsetinib) oral	**Gavreto (pralsetinib) may be considered medically necessary for:** • Adult individuals with metastatic RET fusion-positive non-small cell lung cancer (NSCLC) • Adult and pediatric individuals 12 years of age and older with advanced or metastatic RET fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate) **AND** • The dose (for all indications) is limited to 400 mg once daily
Retevmo (selpercatinib) oral	**Retevmo (selpercatinib) may be considered medically necessary for:** • Adult individuals with metastatic RET fusion-positive non-small cell lung cancer (NSCLC) • Adult and pediatric individuals 12 years of age and older with advanced or metastatic RET-mutant medullary thyroid cancer (MTC) who require systemic therapy • Adult and pediatric individuals 12 years of age and older with advanced or metastatic RET fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate) • Adult individuals with locally advanced or metastatic RET fusion-positive solid tumors that have progressed on or

Drug	Medical Necessity
Oral Drugs	

	following prior systemic treatment or who have no satisfactory alternative treatment options
	AND
	• The dose (for all indications) is limited to:
	  ○ 240 mg per day (taken as 120 mg twice daily) if < 50 kg
	  ○ 320 mg per day (taken as 160 mg twice daily) if ≥ 50 kg

Nucleoside Metabolic Inhibitors	
Onureg (azacitidine) oral	**Onureg (azacitidine) may be considered medically necessary for the treatment of:** • Adult individuals with acute myeloid leukemia (AML) who achieved first complete remission (CR) or complete remission with incomplete blood count recovery (CRi) following intensive induction chemotherapy and are not able to complete intensive curative therapy. **AND** • The dose is limited to 300 mg once daily for 14 consecutive days followed by 14 days off therapy in 28-day cycles
Purixan (mercaptopurine) oral	**Purixan (mercaptopurine) may be considered medically necessary for the treatment of individuals with acute lymphoblastic leukemia (ALL) as part of a combination chemotherapy maintenance regimen.**
Hypoxia-Inducible Factor Inhibitor	

Welireg (belzutifan) oral	**Welireg (belzutifan) may be considered medically necessary for the treatment of adult individuals with von Hippel-Lindau (VHL) disease when all of the following are met:**
	• The individual is 18 years or older
	AND
	• The individual has ≥ 1 of the following associated with VHL disease:
	  ○ Renal cell carcinoma (RCC)
	  ○ Central nervous system (CNS) hemangioblastomas
	  ○ Pancreatic neuroendocrine tumors (pNET)
	AND

Drug	Medical Necessity
Oral Drugs	
	• The individual is not requiring immediate surgery **AND** • The diagnosis of VHL disease is confirmed by a germline alteration in the VHL gene **AND** • The dose is limited to 120 mg once daily **Welireg (belzutifan) may be considered medically necessary for the treatment of adult individuals with advanced renal cell carcinoma (RCC) when all of the following are met:** • The individual is 18 years or older **AND** • The individual has been diagnosed with advanced RCC **AND** • The individual has been previously treated with a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor **AND** • The individual has been previously treated with a vascular endothelial growth factor (VEGF) tyrosine kinase inhibitor **AND** • The dose is limited to 120 mg once daily
Isocitrate Dehydrogenase-1 (IDH1) Inhibitor	
Rezlidhia (olutasidenib) oral	**Rezlidhia (olutasidenib) may be considered medically necessary for the treatment of adult individuals with relapsed or refractory acute myeloid leukemia (AML) with a susceptible isocitrate dehydrogenase-1 (IDH1) mutation.**
Miscellaneous Oral Agents	
Balversa (erdafitinib) oral	**Balversa (erdafitinib) may be considered medically necessary for treatment of adult individuals with locally advanced or metastatic urothelial carcinoma (mUC) that has:** • Susceptible FGFR3 (fibroblast growth factor receptor) genetic alterations

Drug	Medical Necessity
Oral Drugs	
	AND • Progressed during or following at least one line of prior systemic therapy
Casodex (bicalutamide) oral	**Casodex (bicalutamide) may be considered medically necessary for the treatment of adults with metastatic carcinoma of the prostate when all the following are met:** • The individual is 18 years of age or older **AND** • The individual has been diagnosed with metastatic carcinoma of the prostate **AND** • Casodex (bicalutamide) will be used in combination with gonadotropin releasing hormone (GnRH) analogs (e.g., leuprolide or goserelin) **AND** • The individual has tried and had an inadequate response or intolerance to generic bicalutamide **AND** • The dose is limited to 50 mg daily
Eulexin (flutamide) oral	**Eulexin (flutamide) may be considered medically necessary for the treatment of adults with locally confined or metastatic carcinoma of the prostate when all the following are met:** • The individual is 18 years of age or older **AND** • The individual has been diagnosed with locally confined or metastatic carcinoma of the prostate **AND** • Eulexin (flutamide) will be used in combination with gonadotropin releasing hormone (GnRH) analogs (e.g., leuprolide or goserelin) **AND** • The individual has tried and had an inadequate response or intolerance to generic bicalutamide

Drug	Medical Necessity
Oral Drugs	
	AND • The dose is limited to 750 mg daily
Inqovi (decitabine and cedazuridine) oral	**Inqovi (decitabine and cedazuridine) may be considered medically necessary for treatment of adult individuals with myelodysplastic syndromes (MDS), including previously treated and untreated, de novo and secondary MDS.**
Inrebic (fedratinib) oral	**Inrebic (fedratinib) may be considered medically necessary for treatment of adult individuals with intermediate-2 or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) myelofibrosis (MF).** **Note:** Documentation for intermediate-2 or high-risk primary myelofibrosis should include a statement about risk stratification and/or genetically inspired prognostic scoring system (GIPSS) of ≥2. Documentation of intermediate-2 or high-risk secondary myelofibrosis should include a statement about risk stratification and record of post-polycythemia vera or post-essential thrombocythemia.
Iwilfin (eflornithine) oral	**Iwilfin (eflornithine) may be considered medically necessary for the treatment of adult and pediatric individuals with high-risk neuroblastoma when all of the following are met:** • The individual is diagnosed with high-risk neuroblastoma **AND** • The individual has demonstrated at least a partial response to prior multiagent, multimodality therapy including anti-GD2 immunotherapy (e.g., naxitamab-gqgk or dinutuximab) **AND** • The dose is limited to 768 mg twice daily
Krazati (adagrasib) oral	**Krazati (adagrasib) may be considered medically necessary for the treatment of:** • Adult individuals with KRAS G12C-mutated locally advanced or metastatic non-small cell lung cancer (NSCLC) who have received at least one prior systemic therapy **AND**

Drug	Medical Necessity
Oral Drugs	
	• The dose is limited to 1,200 mg per day (taken as 600 mg twice daily)
Lonsurf (trifluridine and tipiracil) oral	**Lonsurf (trifluridine and tipiracil) may be considered medically necessary for treatment of adult individuals with metastatic colorectal cancer as a single agent or in combination with bevacizumab in those who have been:** • Previously treated with fluoropyrimidine, oxaliplatin, and irinotecan-based chemotherapy **AND** • Previously treated with an anti-VEGF biological therapy **AND** • If the tumor is RAS wild-type, previously treated with an anti-EGFR therapy **Lonsurf (trifluridine and tipiracil) may be considered medically necessary for treatment of adult individuals with metastatic gastric or gastroesophageal junction adenocarcinoma who have been:** • Treated with at least two prior lines of chemotherapy that included a fluoropyrimidine, a platinum, either a taxane or irinotecan **AND** • If appropriate, HER2/neu-targeted therapy* **Note:** *Individuals with HER2/neu-positive tumors must have received prior HER2/neu-targeted therapy. Example of HER2/neu-targeted therapy is Herceptin (trastuzumab).
Lumakras (sotorasib) oral	**Lumakras (sotorasib) may be considered medically necessary for the treatment of:** • Adult individuals with KRAS G12C-mutated locally advanced or metastatic non-small cell lung cancer (NSCLC), as determined by an FDA-approved test, who have received at least one prior systemic therapy

Drug	Medical Necessity
Oral Drugs	
	AND • The dose is limited to 960 mg per day
Lysodren (mitotane) oral	**Lysodren (mitotane) may be considered medically necessary for the treatment of inoperable, functional or nonfunctional, adrenal cortical carcinoma.**
Lytgobi (futibatinib) oral	**Lytgobi (futibatinib) may be considered medically necessary for the treatment of:** • Adult individuals with previously treated, unresectable, locally advanced or metastatic intrahepatic cholangiocarcinoma harboring fibroblast growth factor receptor 2 (FGFR2) gene fusions or other rearrangements **AND** • The dose is limited to 20 mg per day
Matulane (procarbazine hydrochloride) oral	**Matulane (procarbazine hydrochloride) may be considered medically necessary for the treatment of stage III and IV Hodgkin's disease, when used in combination with other anticancer drugs.**
• **Nilandron (nilutamide) oral** • **Generic nilutamide oral**	**Nilandron (nilutamide) may be considered medically necessary for the treatment of adults with metastatic prostate cancer when all the following are met:** • The individual is 18 years of age or older **AND** • The individual has been diagnosed with metastatic prostate cancer **AND** • Nilandron (nilutamide) will be used in combination with a bilateral orchiectomy **AND** • The individual has tried and had an inadequate response or intolerance to generic bicalutamide **AND** • The dose is limited to 300 mg daily for 30 days followed by 150 mg daily

Drug	Medical Necessity
Oral Drugs	
Ninlaro (ixazomib) oral	**Ninlaro (ixazomib) may be considered medically necessary when used in combination with Revlimid (lenalidomide) and dexamethasone for the treatment of individuals with multiple myeloma who have received at least one prior therapy.**
Ogsiveo (nirogacestat) oral	**Ogsiveo (nirogacestat) may be considered medically necessary when all of the following are met:** • The individual is 18 years or older **AND** • The individual is diagnosed with progressing desmoid tumors that require systemic treatment **AND** • The individual has tried and had an inadequate response or intolerance to generic sorafenib **AND** • The dose is limited to 150 mg twice daily
Pemazyre (pemigatinib) oral	**Pemazyre (pemigatinib) may be considered medically necessary for the treatment of:** • Adults with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or other rearrangement as detected by an FDA-approved test **AND** • The dose is limited to 13.5 mg once daily for 14 consecutive days followed by 7 days off therapy in 21-day cycles **Pemazyre (pemigatinib) may be considered medically necessary for the treatment of:** • Adults with relapsed or refractory myeloid/lymphoid neoplasms (MLNs) with fibroblast growth factor receptor 1 (FGFR1) rearrangement **AND** • The dose is limited to 13.5 mg once daily

Drug	Medical Necessity
Oral Drugs	
Rydapt (midostaurin) oral	**Rydapt (midostaurin) may be considered medically necessary for the treatment of adult individuals with:** • Newly diagnosed acute myeloid leukemia (AML) that is FLT3 mutation-positive as detected by an FDA-approved test, in combination with standard cytarabine and daunorubicin induction and cytarabine consolidation ○ Documentation of genetic testing is required for coverage consideration • Aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated hematological neoplasm (SM-AHN), or mast cell leukemia (MCL) **Note:** Rydapt is not indicated as a single-agent induction therapy for the treatment of individuals with AML
Generic temozolamide oral	**Generic temozolamide may be considered medically necessary for the treatment of adult individuals with:** • Newly diagnosed glioblastoma concomitantly with radiotherapy, and then as maintenance treatment • Refractory anaplastic astrocytoma, where individual has experienced disease progression on a drug regimen containing nitrosourea and procarbazine
Tazverik (tazemetostat) oral	**Tazverik (tazemetostat) may be considered medically necessary for the treatment of:** • Adult and pediatric individuals aged 16 years and older with metastatic or locally advanced epithelioid sarcoma not eligible for complete resection **AND** • Have previously tried and failed chemotherapy or radiation treatment **OR** • Adult individuals with relapsed or refractory follicular lymphoma whose tumors are positive for an EZH2 (enhancer of zeste homolog 2 protein) mutation as detected by an FDA-

Drug	Medical Necessity
Oral Drugs	
	approved test and who have received at least 2 prior systemic therapies. **OR** • Adult individuals with relapsed or refractory follicular lymphoma who have no satisfactory alternative treatment options. **AND** • The quantity prescribed is limited to 240 tablets per 30 days (4 x 200 mg taken orally twice daily)
Temodar (temozolomide) oral	**Temodar (temozolamide) may be considered medically necessary for the treatment of adult individuals when all of the following are met:** • The individual is 18 years or older **AND** • The individual is newly diagnosed with glioblastoma and Temodar (temozolomide) will be used concomitantly with radiotherapy, and then as maintenance treatment **OR** • The individual is newly diagnosed with anaplastic astrocytoma **OR** • The individual is diagnosed with refractory anaplastic astrocytoma, where individual has experienced disease progression on a drug regimen containing nitrosourea and procarbazine **AND** • The individual has tried and failed generic temozolomide
Generic temozolomide oral	**Generic temozolomide may be considered medically necessary for the treatment of adult individuals when all of the following are met:** • The individual is 18 years or older **AND**

Drug	Medical Necessity
Oral Drugs	
	• The individual is newly diagnosed with glioblastoma and Temodar (temozolomide) will be used concomitantly with radiotherapy, and then as maintenance treatment **OR** • The individual is newly diagnosed with anaplastic astrocytoma **OR** • The individual is diagnosed with refractory anaplastic astrocytoma, where individual has experienced disease progression on a drug regimen containing nitrosourea and procarbazine
Thalomid (thalidomide) oral	**Thalomid (thalidomide) may be considered medically necessary for the treatment of individuals with:** • Newly diagnosed multiple myeloma when used in combination with dexamethasone • Cutaneous manifestations of moderate to severe erythema nodosum leprosum (ENL)
Vistogard (uridine triacetate) oral	**Vistogard (uridine triacetate) may be considered medically necessary for the emergency treatment of adult and pediatric individuals:** • Fluorouracil or capecitabine overdose regardless of the presence of symptoms **OR** • Early-onset, severe or life-threatening toxicity affecting cardiac or central nervous system OR early-onset, unusually severe adverse reactions (e.g., gastrointestinal toxicity or neutropenia) within 96 hours (4 days) following the end of fluorouracil or capecitabine administration
Vitrakvi (larotrectinib) oral	**Vitrakvi (larotrectinib) may be considered medically necessary for the treatment of adult and pediatric individuals with solid tumors that:** • Have a neurotrophic receptor tyrosine kinase (*NTRK*) gene fusion without a known acquired resistance mutation **AND**

Drug	Medical Necessity
Oral Drugs	
	• Are metastatic or where surgical resection is likely to result in severe morbidity **AND** • Have no satisfactory alternative treatments or that have progressed following treatment

Drug	Medical Necessity
Interferon Agents	
Intron A (interferon alfa-2b) IL, IM, IV, SC	**Intron A (interferon alfa-2b) may be considered medically necessary for the treatment of individuals with:** • Hairy cell leukemia and are 18 years of age or older (route is IM, SC) • Malignant melanoma as adjuvant to surgical treatment in individuals 18 years of age or older who are free of disease but at high risk for systemic recurrence within 56 days of surgery (route is IV, SC) • Clinically aggressive follicular Non-Hodgkin's Lymphoma in conjunction with anthracycline-containing combination chemotherapy in individuals 18 years of age or older (route is SC) • Condylomata acuminata involving external surfaces of the genital and perianal areas for intralesional treatment of individuals 18 years of age or older (route is intralesional [IL]) • AIDS Related Kaposi's Sarcoma in individuals 18 years of age or older (route is IM, SC) • Chronic hepatitis C in individuals 18 years of age or older with compensated liver disease who have a history of blood or blood-product exposure and/or are HCV antibody positive (route is IM, SC) • Chronic hepatitis C, when used in combination with ribavirin, in individuals 3 years of age and older with compensated liver disease previously untreated with alpha interferon therapy and

Drug	Medical Necessity
	in individuals 18 years of age and older who have relapsed following alpha interferon therapy (route is IM, SC) • Chronic hepatitis B in individuals 1 year of age or older with compensated liver disease and who have been serum HBsAg positive for at least 6 months and have evidence of HBV replication (serum HBeAg positive) with elevated serum ALT (route is IM, SC)
Sylatron (peginterferon alfa-2b) SC	**Sylatron (peginterferon alfa-2b) may be considered medically necessary for the treatment of adult individuals for:** • The adjuvant treatment of melanoma with microscopic or gross nodal involvement within 84 days of definitive surgical resection including complete lymphadenectomy

Drug	Medical Necessity
Miscellaneous Intramuscular/Intravenous/Subcutaneous Agents	
• **Abraxane (paclitaxel protein-bound particles) IV** • **Brand paclitaxel protein-bound particles (American Regent-unbranded) IV** • **Brand paclitaxel protein-bound particles (Teva-unbranded) IV**	**Abraxane (paclitaxel protein-bound particles), brand paclitaxel protein-bound particles (American Regent – unbranded), and brand paclitaxel protein-bound particles (Teva – unbranded) may be considered medically necessary for the treatment of individuals with:** • Metastatic breast cancer, after failure of combination chemotherapy for metastatic disease or relapse within 6 months of adjuvant chemotherapy. Prior therapy must include an anthracycline (e.g., daunorubicin, doxorubicin, epirubicin, idarubicin, valrubicin) unless clinically contraindicated • Locally advanced or metastatic non-small cell lung cancer (NSCLC), as first-line treatment in combination with carboplatin, in individuals who are not candidates for curative surgery or radiation therapy • Metastatic adenocarcinoma of the pancreas as first-line treatment, in combination with gemcitabine

Drug	Medical Necessity
Miscellaneous Intramuscular/Intravenous/Subcutaneous Agents	
Amtagvi (lifileucel) IV	**Amtagvi (lifileucel) may be considered medically necessary for the treatment of individuals with unresectable or metastatic melanoma when all the following are met:** • The individual is 18 years of age or older **AND** • The individual has been diagnosed with unresectable or metastatic melanoma **AND** • The individual has been treated with a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) blocking antibody such as pembrolizumab, nivolumab, or atezolizumab **AND** • If the individual is *BRAF* V600 mutation-positive, the individual has been treated with a BRAF inhibitor with or without a MEK inhibitor **AND** • The individual has not been previously treated with Amtagvi (lifileucel) **AND** • Amtagvi (lifileucel) is prescribed by or in consultation with an oncologist
Aphexda (motixafortide) SC	**Aphexda (motixafortide) may be considered medically necessary to mobilize hematopoietic stem cells for collection and subsequent autologous transplantation in individuals with multiple myeloma when all the following are met:** • The individual has been histologically diagnosed with multiple myeloma **AND** • The individual is eligible for autologous hematopoietic stem cell transplant **AND**

Drug	Medical Necessity
Miscellaneous Intramuscular/Intravenous/Subcutaneous Agents	
	• Documentation of a valid medical rationale is provided for why the individual is not able to use generic plerixafor
Arranon (nelarabine) IV, Generic nelarabine IV	**Arranon (nelarabine) and generic nelarabine may be considered medically necessary for the treatment of individuals with T-cell acute lymphoblastic leukemia (T-ALL) and T-cell lymphoblastic lymphoma (T-LBL) in adult and pediatric individuals age 1 year and older whose disease has not responded to or has relapsed following treatment with at least two chemotherapy regimens OR as first-line therapy when added to the ABFM (augmented Berlin-Frankfurter Muenster) regimen in intermediate to high-risk individuals or ABFM regimen induction failures.** **Note**: The ABFM induction therapy consists of vincristine, daunorubicin, prednisone, asparaginase, intrathecal cytarabine, and intrathecal methotrexate.
Asparlas (calaspargase pegol - mknl) IV	**Asparlas (calaspargase pegol - mknl) may be considered medically necessary as a component of a multi-agent chemotherapeutic regimen for the treatment of:** • Acute lymphoblastic leukemia in pediatric and young adult individuals age 1 month to 21 years
Blincyto (blinatumomab) IV	**Blincyto (blinatumomab) may be considered medically necessary for the treatment of adults and children with:** • B-cell precursor acute lymphoblastic leukemia (ALL) in first or second complete remission with minimal residual disease (MRD) greater than or equal to 0.1% • Relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL)
Cosela (trilaciclib) IV	**Cosela (trilaciclib) may be considered medically necessary to decrease the incidence of chemotherapy-induced myelosuppression in adult individuals when administered prior to a platinum (e.g., cisplatin, carboplatin,**

Drug	Medical Necessity
Miscellaneous Intramuscular/Intravenous/Subcutaneous Agents	
	oxaliplatin)/etoposide-containing regimen or topotecan containing regimen for extensive-stage small cell lung cancer.
Dacogen (decitabine) IV	**Dacogen (decitabine) may be considered medically necessary for the treatment of adults with myelodysplastic syndromes (MDS) when all the following are met:** • The individual is 18 years of age or older **AND** • The individual has been diagnosed with MDS* **AND** • The individual has tried and had an inadequate response to generic decitabine Note: Including previously treated and untreated, de novo and secondary MDS of all French-American-British subtypes (refractory anemia, refractory anemia with ringed sideroblasts, refractory anemia with excess blasts, refractory anemia with excess blasts in transformation, and chronic myelomonocytic leukemia) and intermediate-1, intermediate-2, and high-risk International Prognostic Scoring System groups
Danyelza (naxitamab-gqgk) IV	**Danyelza (naxitamab-gqgk), in combination with GM-CSF (e.g., sargramostim), may be considered medically necessary for the treatment of pediatric individuals 1 year of age and older and adult individuals with relapsed or refractory high-risk neuroblastoma in the bone or bone marrow who have demonstrated a partial response, minor response, or stable disease to prior therapy.**
Darzalex (daratumumab) IV	**Darzalex (daratumumab) may be considered medically necessary for the treatment of adult individuals with multiple myeloma when used:** • In combination with lenalidomide and dexamethasone as first-line therapy and in individuals with relapsed or refractory multiple myeloma who have received at least one prior therapy • In combination with bortezomib, melphalan and prednisone as first-line therapy

Drug	Medical Necessity
Miscellaneous Intramuscular/Intravenous/Subcutaneous Agents	
	• In combination with bortezomib, thalidomide, and dexamethasone as first-line therapy in individuals who are eligible for autologous stem cell transplant • In combination with bortezomib and dexamethasone in individuals who have received at least one prior therapy • In combination with Kyprolis (carfilzomib) and dexamethasone in individuals with relapsed or refractory multiple myeloma who have received one to three prior lines of therapy • In combination with pomalidomide and dexamethasone in individuals who have received at least two prior therapies including lenalidomide and a proteasome inhibitor (e.g., bortezomib, carfilzomib, ixazomib) • As monotherapy, in individuals who have received at least three prior lines of therapy including a proteasome inhibitor (PI) (e.g., bortezomib, carfilzomib, ixazomib) and an immunomodulatory agent (e.g., thalidomide, pomalidomide, lenalidomide) or who are refractory to a PI and an immunomodulatory agent
Darzalex Faspro (daratumumab and hyaluronidase-fihj) SC	**Darzalex Faspro (daratumumab and hyaluronidase-fihj) may be considered medically necessary for the treatment of adult individuals with multiple myeloma when used:** • In combination with Revlimid (lenalidomide) and dexamethasone as first-line therapy and in individuals with relapsed or refractory multiple myeloma who have received at least one prior therapy • In combination with bortezomib, melphalan and prednisone as first-line therapy • In combination with bortezomib, thalidomide, and dexamethasone as first-line therapy in individuals who are eligible for autologous stem cell transplant • In combination with bortezomib and dexamethasone in individuals who have received at least one prior therapy • In combination with Pomalyst (pomalidomide) and dexamethasone in individuals who have received at least one

Drug	Medical Necessity
Miscellaneous Intramuscular/Intravenous/Subcutaneous Agents	
	prior line of therapy including Revlimid (lenalidomide) and a proteasome inhibitor (PI) (e.g., bortezomib, carfilzomib, ixazomib) • In combination with Kyprolis (carfilzomib) and dexamethasone in individuals with relapsed or refractory multiple myeloma who have received one to three prior lines of therapy • As monotherapy, in individuals who have received at least three prior lines of therapy including a proteasome inhibitor (PI) (e.g., bortezomib, carfilzomib, ixazomib) and an immunomodulatory agent (e.g., thalidomide, pomalidomide, lenalidomide) or who are refractory to a PI and an immunomodulatory agent **Darzalex Faspro (daratumumab and hyaluronidase-fihj) may be considered medically necessary for the treatment of adult individuals with light chain (AL) amyloidosis when used:** • In combination with bortezomib, cyclophosphamide, and dexamethasone as first-line therapy
Generic decitabine IV	**Generic decitabine may be considered medically necessary for the treatment of adults with myelodysplastic syndromes (MDS) when all the following are met:** • The individual is 18 years of age or older **AND** • The individual has been diagnosed with MDS* Note: Including previously treated and untreated, de novo and secondary MDS of all French-American-British subtypes (refractory anemia, refractory anemia with ringed sideroblasts, refractory anemia with excess blasts, refractory anemia with excess blasts in transformation, and chronic myelomonocytic leukemia) and intermediate-1, intermediate-2, and high-risk International Prognostic Scoring System groups
Elitek (rasburicase) IV	**Elitek (rasburicase) may be considered medically necessary for the initial management of plasma uric acid levels in individuals with leukemia, lymphoma, or solid tumor malignancies who**

Drug	Medical Necessity
Miscellaneous Intramuscular/Intravenous/Subcutaneous Agents	
	are receiving anticancer therapy expected to result in tumor lysis and subsequent elevation of plasma uric acid
Elrexfio (elranatamab-bcmm) SC	**Elrexfio (elranatamab-bcmm) may be considered medically necessary for the treatment of relapsed or refractory multiple myeloma when all the following criteria are met:** • Individual is 18 years of age or older **AND** • Individual has received at least four prior therapies including a proteasome inhibitor (e.g., bortezomib, carfilzomib, ixazomib), an immunomodulatory agent (e.g., lenalidomide, pomalidomide, thalidomide), and an anti-CD38 monoclonal antibody (e.g., daratumumab, isatuximab-irfc)
Elzonris (tagraxofusp-erzs) IV	**Elzonris (tagraxofusp-erzs) may be considered medically necessary for the treatment of blastic plasmacytoid dendritic cell neoplasm (BPDCN) in adults and in pediatric individuals 2 years and older.**
Empliciti (elotuzumab) IV	**Empliciti (elotuzumab) may be considered medically necessary:** • In combination with Revlimid (lenalidomide) and dexamethasone for the treatment of adult individuals with multiple myeloma who have received one to three prior therapies • In combination with Pomalyst (pomalidomide) and dexamethasone for the treatment of adult individuals with multiple myeloma who have received at least two prior therapies including Revlimid (lenalidomide) and a proteasome inhibitor (e.g., Velcade [bortezomib], Kyprolis [carfilzomib], Ninlaro [ixazomib])
Epkinly (epocoritamab-bysp) SQ	**Epkinly (epocoritamab-bysp) may be considered medically necessary for adult individuals with:** • Relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, including DLBCL arising from indolent lymphoma, and high-grade B-cell lymphoma after two or more lines of systemic therapy

Drug	Medical Necessity
Miscellaneous Intramuscular/Intravenous/Subcutaneous Agents	
Erwinaze (asparaginase *Erwinia chrysanthemi*) IM, IV	**Erwinaze (asparaginase *Erwinia chrysanthemi*) may be considered medically necessary as a component of a multi-agent chemotherapeutic regimen for the treatment of individuals with acute lymphoblastic leukemia (ALL) who have developed hypersensitivity to *E. coli*-derived asparaginase (e.g., Oncaspar [pegaspargase], Asparlas [calaspargase pegol – mknl])**
Gazyva (obinutuzumab) IV	**Gazyva (obinutuzumab) may be considered medically necessary:** • In combination with chlorambucil, for previously untreated chronic lymphocytic leukemia (CLL) • In combination with bendamustine followed by Gazyva monotherapy, for relapsed or refractory follicular lymphoma, following a rituximab-containing regimen • In combination with chemotherapy followed by Gazyva monotherapy in individuals achieving at least a partial remission, for the treatment of adult individuals with previously untreated stage II bulky, III or IV follicular lymphoma • In combination with zanubrutinib in adults diagnosed with relapsed or refractory follicular lymphoma who have received two or more lines of systemic therapy
Halaven (eribulin mesylate) IV	**Halaven (eribulin mesylate) may be considered medically necessary for the treatment of individuals with:** • Metastatic breast cancer who have previously received at least two chemotherapeutic regimens for the treatment of metastatic disease. Unless clinically contraindicated prior therapy must include an anthracycline (e.g., daunorubicin, doxorubicin, epirubicin, idarubicin, valrubicin) and a taxane (e.g., docetaxel, paclitaxel) in either the adjuvant or metastatic setting • Unresectable or metastatic liposarcoma who have received a prior anthracycline (e.g., daunorubicin, doxorubicin, epirubicin, idarubicin, valrubicin) containing regimen

Drug	Medical Necessity
Miscellaneous Intramuscular/Intravenous/Subcutaneous Agents	
Hepzato Kit (melphalan hepatic delivery system) intra-arterial	**Hepzato Kit (melphalan hepatic delivery system) may be considered medically necessary if all of the following are met:** • The individual is 18 years of age or older **AND** • The individual has a diagnosis of unresectable or metastatic uveal melanoma **AND** • The individual has histologically or cytologically-proven ocular melanoma metastases affecting less than 50% of the parenchyma of the liver **AND** • The individual has disease that is limited to the bone, lymph, nodes, subcutaneous tissues, or lung and is amenable to resection or radiation **AND** • The individual has an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1 **AND** • The individual has ≥100,000 platelets/μL at the time of treatment **AND** • The individual has an absolute neutrophil count (ANC) of ≥1,500 cells/μL at the time of treatment **AND** • The individual has not received more than six treatments
Imdelltra (tarlatamab-dlle) IV	**Imdelltra (tarlatamab-dlle) may be considered medically necessary for the treatment of adults with extensive stage small cell lung cancer (ES-SCLC) when all the following are met:** • The individual is 18 years or older **AND** • The individual has relapsed or refractory ES-SCLC **AND**

Drug	Medical Necessity
Miscellaneous Intramuscular/Intravenous/Subcutaneous Agents	
	• The individual has had progression on or after treatment with platinum-based chemotherapy (e.g., cisplatin and carboplatin) **AND** • The individual has an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1 **AND** • Imdelltra (tarlatamab-dlle) is prescribed by or in consultation with an oncologist
Jelmyto (mitomycin) vial	**Jelmyto (mitomycin) may be considered medically necessary for the treatment of adult individuals with low-grade upper tract urothelial cancer (LG-UTUC).**
Kimmtrak (tebentafusp-tebn) IV	**Kimmtrak (tebentafusp-tebn) may be considered medically necessary for the treatment of HLA-A*02:01-positive adult individuals with unresectable or metastatic uveal melanoma.**
Kyprolis (carfilzomib) IV	**Kyprolis (carfilzomib) may be considered medically necessary for the treatment of adult individuals when used:** • In combination with dexamethasone, Revlimid (lenalidomide) plus dexamethasone, Darzalex (daratumumab) plus dexamethasone, or Darzalex Faspro (daratumumab and hyaluronidase-fihj) plus dexamethasone for the treatment of individuals with relapsed or refractory multiple myeloma who have received one to three lines of therapy • As a single agent for the treatment of individuals with relapsed or refractory multiple myeloma who have received one or more lines of therapy
Leukine (sargramostim) IV, SC	**Leukine (sargramostim) may be considered medically necessary for:** • Acute myeloid leukemia following induction chemotherapy • Mobilization and following transplantation of autologous peripheral blood progenitor cells • Myeloid reconstitution after (allogenic or autologous) bone marrow transplantation

Drug	Medical Necessity
Miscellaneous Intramuscular/Intravenous/Subcutaneous Agents	
	• Bone marrow transplantation (allogenic or autologous) failure or engraftment delay • Exposure to myelosuppressive doses of radiation (Hematopoietic Syndrome of Acute Radiation Syndrome) • In combination with Danyelza (naxitamab-gqgk) for the treatment of pediatric individuals 1 year of age and older and adult individuals with relapsed or refractory high-risk neuroblastoma in the bone or bone marrow who have demonstrated a partial response, minor response, or stable disease to prior therapy) • In combination with Unituxin, for the treatment of pediatric individuals with high-risk neuroblastoma who achieve at least a partial response to prior first-line multiagent, multimodality therapy **Leukine (sargramostim) may be considered medically necessary as second-line therapy for the treated of individuals taking myelosuppressive anti-cancer regimens, at risk of severe febrile neutropenia** to decrease the incidence of infection when documentation for one of the following is provided:** • Granix (tbo-filgrastim) or Nivestym (filgrastim-aafi) has been tried and failed **OR** • There is a contraindication to the use of Granix (tbo-filgrastim) and Nivestym (filgrastim-aafi) ****The following types of individuals are considered to be at risk of severe febrile neutropenia:** 1. Individuals that have experienced febrile neutropenia during a previous cycle of treatment with the current chemotherapy regimen

Drug	Medical Necessity
Miscellaneous Intramuscular/Intravenous/Subcutaneous Agents	
	OR 2. Individuals receiving chemotherapy regimen that is expected to result in a 20 % or higher incidence of FN, based on guidelines from the American Society of Clinical Oncology **OR** 3. Individuals with bone marrow impairment **OR** 4. Individuals that have received 2 or more prior chemotherapy regimens or extensive radiation **OR** 5. Individuals with other serious comorbidities (reviewed on a case basis)
Onivyde (irinotecan liposome injection) IV	**Onivyde (irinotecan liposome injection) may be considered medically necessary for the treatment of adults with:** • Metastatic adenocarcinoma of the pancreas when combined with fluorouracil and leucovorin following disease progression on gemcitabine-based therapy • Metastatic adenocarcinoma of the pancreas when combined with oxaliplatin, fluorouracil, and leucovorin as first-line treatment • Metastatic cholangiocarcinoma when combined with fluorouracil and leucovorin following disease progression on gemcitabine plus cisplatin
Rylaze (asparaginase erwinia chrysanthemi (recombinant)-rywn) IM	**Rylaze (asparaginase erwinia chrysanthemi (recombinant)-rywn) may be considered medically necessary as a component of a multi-agent chemotherapeutic regimen for the treatment of acute lymphoblastic leukemia (ALL) and lymphoblastic lymphoma (LBL) in individuals who have developed hypersensitivity to *E. coli*-derived asparaginase (e.g., Oncaspar [pegaspargase], Asparlas [calaspargase pegol – mknl])**
Sarclisa (isatuximab-irfc) IV	**Sarclisa (isatuximab-irfc) may be considered medically necessary for the treatment of multiple myeloma when all the following criteria are met:**

Drug	Medical Necessity
Miscellaneous Intramuscular/Intravenous/Subcutaneous Agents	
	• Individual is 18 years of age or older **AND** • Sarclisa (isatuximab-irfc) is given in in combination with Pomalyst (pomalidomide) and dexamethasone and the individual has received at least two prior therapies including lenalidomide and a proteasome inhibitor (e.g., Velcade [bortezomib], Kyprolis [carfilzomib], Ninlaro [ixazomib]) **OR** • Sarclisa (isatuximab-irfc) is given in combination with Kyprolis (carfilzomib) and dexamethasone and the individual has received 1 to 3 prior lines of therapy
Talvey (talquetamab-tgvs) SC	**Talvey (talquetamab-tgvs) may be considered medically necessary for the treatment of relapsed or refractory multiple myeloma when all the following criteria are met:** • Individual is 18 years of age or older **AND** • Individual has received at least four prior therapies including a proteasome inhibitor (e.g., bortezomib, carfilzomib, ixazomib), an immunomodulatory agent (e.g., lenalidomide, pomalidomide, thalidomide), and an anti-CD38 monoclonal antibody (e.g., daratumumab, isatuximab-irfc)
Tecvayli (teclistamab-cqyv) SC	**Tecvayli (teclistamab-cqyv) may be considered medically necessary for the treatment of adult individuals with relapsed or refractory multiple myeloma who have received at least four prior lines of therapy, including a proteasome inhibitor (e.g., bortezomib, carfilzomib, ixazomib), an immunomodulatory agent (e.g., lenalidomide, pomalidomide, thalidomide), and an anti-CD38 monoclonal antibody (e.g., daratumumab, isatuximab-irfc).**
Temodar (temozolomide) IV	**Temodar (temozolamide) may be considered medically necessary for the treatment of adult individuals when all of the following are met:** • The individual is 18 years or older

Drug	Medical Necessity
Miscellaneous Intramuscular/Intravenous/Subcutaneous Agents	
	AND • The individual is newly diagnosed with glioblastoma and Temodar (temozolomide) will be used concomitantly with radiotherapy, and then as maintenance treatment **OR** • The individual is newly diagnosed with anaplastic astrocytoma **OR** • The individual is diagnosed with refractory anaplastic astrocytoma, where individual has experienced disease progression on a drug regimen containing nitrosourea and procarbazine
Trodelvy (sacituzumab govitecan-hziy) IV	**Trodelvy (sacituzumab govitecan-hziy) may be considered medically necessary for the treatment of adult individuals with:** • Unresectable locally advanced or metastatic triple-negative breast cancer (mTNBC) who have received two or more prior systemic therapies, at least one of them for metastatic disease • Unresectable locally advanced or metastatic hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative (IHC 0, IHC 1+ or IHC 2+/ISH–) breast cancer who have received endocrine-based therapy and at least two additional systemic therapies in the metastatic setting • Locally advanced or metastatic urothelial cancer (mUC) who have previously received a platinum-containing chemotherapy and either programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor
Unituxin (dinutuximab) IV	**Unituxin (dinutuximab) may be considered medically necessary for the treatment of high-risk neuroblastoma in pediatric individuals when:** • Individual is using Unituxin in combination with granulocyte-macrophage colony-stimulating factor (GM-CSF), interleukin-2 (IL-2), and 13-cis-retinoic acid (RA) **AND**

Drug	Medical Necessity
Miscellaneous Intramuscular/Intravenous/Subcutaneous Agents	
	• Individual has achieved at least a partial response to prior first-line multiagent, multimodality therapy
Velcade (bortezomib) IV, Generic bortezomib IV, Brand bortezomib IV	**Generic bortezomib, brand bortezomib, and Velcade (bortezomib) may be considered medically necessary for the treatment of adult individuals with any of the following:** • Multiple myeloma • Mantle cell lymphoma
Yondelis (trabectedin) IV	**Yondelis (trabectedin) may be considered medically necessary for the treatment of individuals with unresectable or metastatic liposarcoma or leiomyosarcoma who received a prior anthracycline (e.g., daunorubicin, doxorubicin, epirubicin, idarubicin, valrubicin) containing regimen.**
Xgeva (denosumab) SC	**Xgeva (denosumab) may be considered medically necessary for the prevention of skeletal-related events in an individual with bone metastases from solid tumors when:** • There is a documented inadequate response or intolerance to intravenous 4 mg zoledronic acid **AND** • For treatment of breast cancer, the individual has an expected survival of 3 months or greater **OR** • For the treatment of prostate cancer, the individual has castration recurrent disease **Xgeva (denosumab) may be considered medically necessary when there is a documented inadequate response or intolerance to intravenous 4 mg zoledronic acid:** • When used for the prevention of skeletal-related events in individuals with multiple myeloma **OR** • When used to treat hypercalcemia of malignancy

Drug	Medical Necessity
Miscellaneous Intramuscular/Intravenous/Subcutaneous Agents	
	Xgeva (denosumab) may be considered medically necessary when used to treat giant cell tumor of the bone
Zepzelca (lurbinectedin) IV	**Zepzelca (lurbinectedin) may be considered medically necessary for the treatment of adult individuals with metastatic small cell lung cancer (SCLC) with disease progression on or after platinum-based chemotherapy.**

Drug	Investigational
As listed	**All other uses of the medications listed in this policy are considered investigational.**

Length of Approval	
Approval	**Criteria**
Initial authorization	**Oral administered drugs listed in policy may be approved up to 3 months.** **Intravenous, intramuscular, intralesional, and subcutaneous administered drugs listed in policy may be approved up to 6 months.**
Re-authorization criteria	**Future re-authorization of all drugs listed in policy may be approved up to 12 months as long as the drug-specific coverage criteria are met and chart notes demonstrate that the individual continues to show a positive clinical response to therapy.**

Documentation Requirements
The individual's medical records submitted for review for all conditions should document that medical necessity criteria are met. The record should include the following: • Office visit notes that contain the diagnosis, relevant history, physical evaluation and medication history

Coding

Code	Description
HCPCS	
C9148	Injection, teclistamab-cqyv (Tecvayli), 0.5 mg
C9163	Injection, talquetamab-tgvs,(Talvey), 0.25 mg ~~(new code effective 1/1/2024)~~ (code termed effective 4/1/2024)
C9165	Injection, elranatamab-bcmm, (Elrexfio) 1 mg ~~(new code effective 1/1/2024)~~ (code termed effective 4/1/2024)
C9399	Unspecified drugs or biologicals (used to report Hepzato and Imdelltra)
J0894	Injection, decitabine (Dacogen), 1 mg
J0897	Injection, denosumab (Xgeva), 1 mg
J1246	Injection, dinutuximab (Unitruxin), 0.1 mg (new code effective 1/1/2024)
J1323	Injection, elranatamab-bcmm (Elrexfio), 1 mg (new code effective 4/1/2024)
J1448	Injection, trilaciclib, (Cosela)1 mg
J2277	Injection, motixafortide (Aphexda), 0.25 mg (new code effective 4/1/2024)
J2783	Injection, rasburicase (Elitek), 0.5 mg
J2820	Injection, sargramostim (GM-CSF), (Leukine) 50 mcg
J3055	Injection, talquetamab-tgvs (Talvey), 0.25 mg (new code effective 4/1/2024)
J3590	Unclassified biologics (use to report Amtagvi, Sylatron and Tecvayli)
J9019	Injection, asparaginase (Erwinaze),1,000 IU
J9021	Injection, asparaginase, recombinant, (Rylaze), 0.1 mg)
J9039	Injection, blinatumomab, (Blincyto) 1 mcg
J9041	Injection, bortezomib (Velcade), 0.1 mg
J9046	Injection, bortezomib (Dr. Reddy's), not therapeutically equivalent to J9041, 0.1 mg

Code	Description
J9047	Injection, carfilzomib (Kyprolis), 1 mg
J9048	Injection, bortezomib (Fresenius Kabi), not therapeutically equivalent to J9041, 0.1 mg
J9049	Injection, bortezomib (Hospira), not therapeutically equivalent to J9041, 0.1 mg
J9051	Injection, bortezomib (maia), not therapeutically equivalent to J9041, 0.1 mg (new code effective 09/14/23)
J9118	Injection, calaspargase pegol-mknl (Asparlas), 10 units
J9144	Injection, daratumumab, 10 mg and hyaluronidase-fihj (Darzalex Faspro)
J9145	Injection, daratumumab (Darzalex), 10 mg
J9176	Injection, elotuzumab, (Empliciti)1 mg
J9179	Injection, eribulin mesylate, (Halaven) 0.1 mg
J9205	Injection, irinotecan liposome (Onivyde), 1 mg
J9214	Injection, interferon, alfa-2b, recombinant (Intron A), 1 million units
J9223	Injection, lurbinectedin, (Zepzelca) 0.1 mg
J9227	Injection, isatuximab-irfc, (Sarclisa) 10 mg
J9248	Injection, melphalan (Hepzato), 1 mg (new code effective 4/1/2024)
J9258	Injection, paclitaxel protein-bound particles (Teva), not therapeutically equivalent to J9264, 1 mg (new code effective 1/1/2024)
J9259	Injection, paclitaxel protein-bound particles (American Regent) not therapeutically equivalent to J9264, 1 mg
J9261	Injection, nelarabine (Arranon), 50 mg
J9264	Injection, paclitaxel protein-bound particles, (Abraxane)1 mg
J9269	Injection, tagraxofusp-erzs (Elzonris), 10 mcg
J9274	Injection, tebentafusp-tebn (Kimmtrak), 1 mcg
J9281	Mitomycin pyelocalyceal instillation, (Jelmyto) 1 mg
J9301	Injection, obinutuzumab (Gazyva), 10 mg
J9317	Injection, sacituzumab govitecan-hziy (Trodelvy), 2.5 mg

Code	Description
J9321	Injection, epcoritamab-bysp (Epkinly), 0.16 mg (new code effective 1/1/2024)
J9328	Injection, temozolomide (Temodar), 1 mg
J9348	Injection, naxitamab-gqgk (Danyelza),1 mg
J9352	Injection, trabectedin, (Yondelis) 0.1 mg
J9380	Injection, teclistamab-cqyv, (Tzield), 0.5 mg
J9999	Not otherwise classified, antineoplastic drugs (used to report Hepzato)

Note: CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). HCPCS codes, descriptions and materials are copyrighted by Centers for Medicare Services (CMS).

Related Information

Consideration of Age

Age limits specified in this policy are determined according to the US Food and Drug Administration (FDA) -approved indications, where applicable.

Benefit Application

The drugs in this policy that are administered orally are managed through the pharmacy benefit. Drugs administered via IV infusion are managed through the medical benefit.

Evidence Review

Amtagvi (lifileucel)

The approval of Amtagvi was based on results from the prospective, interventional multicenter Phase 2 C-144- 01 trial. Among the primary efficacy analysis set of 73 individuals in Cohort 4 who received Amtagvi at the recommended dose, the objective response rate (ORR) was 31.5% and the median duration of response (DOR) was not reached at 18.6 months follow-up. Among a pooled efficacy set of 153 patients from Cohorts 2 and 4 who received the recommended Amtagvi dose, the ORR was 31.4% and the median DOR was not reached at 21.5 months follow-up. The prescribing information for Amtagvi includes a Boxed Warning regarding the risk of treatment-related mortality, prolonged severe cytopenia, severe infection, and cardiopulmonary and renal impairment.

Balversa (erdafitinib)

Balversa (erdafitinib) a kinase inhibitor that binds to and inhibits enzymatic activity of FGFR1, FGFR2, FGFR3 and FGFR4 based on *in vitro* data. Balversa also binds to RET, CSF1R, PDGFRA, PDGFRB, FLT4, KIT, and VEGFR2. Balversa inhibited FGFR phosphorylation and signaling and decreased cell viability in cell lines expressing FGFR genetic alterations, including point mutations, amplifications, and fusions. Balversa is the first targeted therapy for metastatic bladder cancer approved by the FDA. This drug is currently fulfilling a previous unmet space in therapy for the most common type of bladder cancer; transitional cell carcinoma (urothelial carcinoma). The overall response rate of the participants in the clinical trial was 32.2% with 2.3% having a complete response. Warning and precautions regarding Balversa includes ocular disorders (central serous retinopathy/retinal pigment epithelial detachment) resulting in visual defects and hyperphosphatemia (76% in treated individuals).

Darzalex (daratumumab)

Darzalex (daratumumab) is a CD38-directed cytolytic antibody indicated for the treatment of adult individuals with multiple myeloma. When used in combination treatment with lenalidomide and dexamethasone (DRd) in individuals ineligible for autologous stem cell transplant daratumumab demonstrated an improvement in Progression Free Survival (PFS) in the DRd arm as compared to the lenalidomide and low-dose dexamethasone (Rd) arm; the

median PFS had not been reached in the DRd arm and was 31.9 months in the Rd arm (hazard ratio [HR]=0.56; 95% CI: 0.43, 0.73; p<0.0001), representing 44% reduction in the risk of disease progression or death in individuals treated with DRd. When used in combination treatment with bortezomib, melphalan and prednisone (VMP) in individuals ineligible for autologous stem cell transplant daratumumab demonstrated an improvement in PFS in the D-VMP arm as compared to the VMP arm; the median PFS had not been reached in the D-VMP arm and was 18.1 months (95% CI:16.53, 19.91) in the VMP arm (HR=0.5; 95% CI: 0.38, 0.65; p<0.0001), representing 50% reduction in the risk of disease progression or death in individuals treated with D-VMP. The most frequently reported adverse reactions (incidence ≥20%) were infusion reactions, neutropenia, thrombocytopenia, fatigue, asthenia, nausea, diarrhea, constipation, decreased appetite, vomiting, muscle spasms, arthralgia, back pain, pyrexia, chills, dizziness, insomnia, cough, dyspnea, peripheral edema, peripheral sensory neuropathy, bronchitis, pneumonia and upper respiratory tract infection.

Elrexfio (elranatamab-bcmm)

Elrexfio is an antibody that binds bispecific B-cell maturation antigen (BCMA) on plasma cells, plasmablasts, multiple myeloma (MM) cells, and CD3 on T-cells leading to proinflammatory cytokine release and eventually cytolysis of the BCMA-expressing cells.

The efficacy of Elrexfio monotherapy was evaluated in an open-label, single-arm, multi-center study (MagnetisMM-3) with 123 individuals receiving Elrexfio once weekly post initial titration. After 24 weeks, individuals who achieved an IMWG response category of partial response or better for a duration of at least 2 months changed dosing interval from weekly to biweekly. The objective response rate, calculated as a total of stringent complete response, complete response, very good partial response, and partial response, was achieved in 57.7% (47.3-67.7%) of BCMA-directed therapy naïve individuals and 33.3% (22-46.3%) of individuals who had previously tried BCMA-directed therapy.

Serious adverse reactions occurred in 68% of individuals receiving Elrexfio, with those occurring in at least 2% of individuals being pneumonia (25%), sepsis (13%), cytokine release syndrome (CRS) (13%), upper respiratory tract infection (URTI) (4.4%), acute kidney injury (3.8%), urinary tract infection (3.3%), COVID-19 (3.3%), encephalopathy (3.3%), pyrexia (2.2%), and febrile neutropenia (2.2%). Fatal adverse reactions occurred in 10% of individuals, including pneumonia, sepsis, acute respiratory distress syndrome, cardio-respiratory arrest, cardiogenic shock,

cardiopulmonary failure, COVID-19, failure to thrive, and pulmonary embolism. Permanent discontinuation of Elrexfio due to adverse reactions occurred in 17% of individuals and dosage interruptions due to adverse reactions occurred in 73% of individuals. The most common adverse events (at least 20%) were CRS, fatigue, injection site reaction, diarrhea, URTI, musculoskeletal pain, pneumonia, decreased appetite, rash, cough, nausea, and pyrexia. The most common Grade 3 to 4 laboratory abnormalities (at least 30%) were decreases in lymphocyte, neutrophil, hemoglobin, white blood cell, and platelet counts.

Epkinly (epcoritamab-bysp)

Epkinly (epcoritamab-bysp) is a T-cell engaging bispecific antibody that binds to the CD3 receptor on the T-cell and CD20 receptor on the lymphoma cells and healthy B-lineage cells. Once Epkinly binds to T-cell, T-cell gets activated which in turn releases the proinflammatory cytokines and induces B-cells lysis. Epkinly received an accelerated approval based on the response rate and durability of the response. Epkinly should be administered by the healthcare providers in the well-hydrated individuals and premedicated individuals. Epkinly should be administered subcutaneously following the dosing regimen. Due to the risk of severe reactions such as cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS), the individual should be hospitalized for 24 hours after administration of Cycle 1 Day 15 dosage of 48 mg.

The efficacy and safety of Epkinly was evaluated in an open label, multicenter, single-arm, multi-cohort trial "EPCORE NHL-1", where 157 individuals with relapsed or refractory large B-cell lymphoma (LBCL) after two or more lines of systemic therapy received Epkinly as a subcutaneous injection following 28-day dosage schedule. The individuals received Epkinly until disease progression or unacceptable toxicity. The primary efficacy endpoint was the overall response rate (ORR) determined by Lugano 2014 criteria, and duration of response (DOR). The ORR was in 61% individuals (n = 90), where 38% (n = 56) individuals had a complete response, and 23% (n = 34) individuals had a partial response. The median duration of response was 15.6 months.

The most common adverse events in the clinical trial were cytokine release syndrome, fatigue, musculoskeletal pain, injection site reactions, pyrexia, abdominal pain, nausea, and diarrhea. More than 10% individuals experienced Grade 3 to 4 laboratory abnormalities, such as, reduced level of lymphocyte count, neutrophil count, white blood cell count, hemoglobin, and platelets.

Erivedge (vismodegib)

Erivedge (vismodegib) is a Hedgehog pathway inhibitor. It binds to and inhibits Smoothened, a trans-membrane protein involved in Hedgehog signal transduction. The evidence of efficacy was established in the pivotal Phase II open label trial of vismodegib 150mg once daily. This study demonstrated a statistically significant single-agent activity for both locally advanced (42.9% response rate; $p<0.0001$) and metastatic (30.3% response rate; $p=0.0011$) basal cell carcinoma (laBCC and mBCC respectively). Overall median duration of treatment for the combined cohorts ($n=104$) was 9.7 months (range 1.1 to 18.7 months). The median duration of response was 7.6 months and median progression free survival (PFS) was 9.5 months for both groups (independently). This data is pending press in the New England Journal of Medicine and is currently only available from the manufacturer. Published efficacy data is only available from the extension of the open label Phase I study currently ongoing. As of January 2010, there were 2 individuals who achieved complete remission and 17 who achieved partial response from the original 33 individuals enrolled in the study who had aBCC (overall response of 57%).

Gazyva (obinutuzumab)

Gazyva (obinutuzumab) targets the CD20 antigen expressed on the surfaces of pre-B and mature B-lymphocytes. After binding, obinutuzumab mediates B-cell lysis by engaging immune effector cells, directly activating direct cell death pathways, and/or activating the complement cascade. The immune effector cell mechanisms include antibody-dependent cellular cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis.

Clinical trials explored the safety of Gazyva (obinutuzumab) in previously untreated individuals with CLL. Individuals were treated with chlorambucil alone, obinutuzumab + chlorambucil, or rituximab + chlorambucil. Adverse reactions included infusion reactions, neutropenia, thrombocytopenia, leukopenia, pyrexia, diarrhea, constipation, nasopharyngitis, and urinary tract infections. These adverse reactions are consistent with those seen comparing obinutuzumab + chlorambucil to chlorambucil alone except back pain (5% vs. 2%), anemia (12% vs. 10%) and cough (10% vs. 7%), which were observed at a higher incidence in the obinutuzumab treated individuals. The incidence of Grade 3-4 back pain (<1% vs. 0%), cough (0% vs. <1%) and anemia (5% vs. 4%) was similar in both treatment arms.

Obinutuzumab was approved on the basis of an improvement in progression-free survival (PFS) in a randomized, open-label, multicenter trial in individuals with Follicular Lymphoma, which is a type of the Non-Hodgkin Lymphoma, with no response or who have progressed within 6 months of a rituximab-containing regimen. These individuals were randomized to bendamustine alone (n = 166) or bendamustine + obinutuzumab (n = 155) for six 28-day cycles. Individuals in the combination arm who had a complete response (CR), partial response (PR), or stable disease (SD) at the end continued obinutuzumab monotherapy for two years. The primary endpoints included PFS. The median PFS in the combination arm was not reported, whereas the bendamustine arm was 13.8 months. The best overall response was 78.7% for obinutuzumab combination and 74.7% for bendamustine alone, which was defined as the best CR/PR within 12 months of initiating therapy. The most common adverse reactions (≥ 10%) were infusion reactions, neutropenia, nausea, fatigue, cough, diarrhea, constipation, pyrexia, thrombocytopenia, vomiting, upper respiratory tract infection, decreased appetite, arthralgia, sinusitis, anemia, asthenia, and urinary tract infections. The most common grade 3-4 reactions (≥ 10%) were neutropenia, thrombocytopenia, and infusion reactions. The safety profile was consistent with the overall indolent non-Hodgkin lymphoma population.

Ibrance (palbociclib)

Ibrance (palbociclib) is an orally active selective and reversible inhibitor of CDK 4/6. The agent halts the progression of the cell cycle at G1 via its selective inhibition of CDK 4/6, thereby preventing cellular proliferation. Palbociclib is indicated in combination with letrozole for the treatment of postmenopausal women with ER+/HER2- advanced breast cancer as initial endocrine-based therapy for metastatic disease.

This indication was approved under accelerated approval based on PFS and continued approval may be contingent upon verification and description of clinical benefit in a confirmatory trial. The current approval was based on data from an international, randomized, double-blind, placebo-controlled, clinical trial (PALOMA-2) that randomized 666 postmenopausal women (2:1) to palbociclib plus letrozole or placebo plus letrozole. Palbociclib 125 mg or placebo was administered orally once daily for 21 consecutive days, followed by 7 days off. Letrozole 2.5 mg was administered orally once daily. Treatment continued until disease progression or unacceptable toxicity. The median progression-free survival (PFS) was 24.8 months in the palbociclib plus letrozole arm and 14.5 months in the placebo plus letrozole arm (HR=0.576, 95% CI: 0.463, 0.718, p<0.0001). Overall survival data are immature.

Safety data was evaluated in 444 individuals who received palbociclib plus letrozole. Neutropenia was the most frequently reported adverse reaction in PALOMA-2 with an incidence of 80%. The most common adverse reactions observed in 10% or more of individuals taking palbociclib were neutropenia, infections, leukopenia, fatigue, nausea, alopecia, stomatitis, diarrhea, anemia, rash, asthenia, thrombocytopenia, vomiting, decreased appetite, dry skin, pyrexia, and dysgeusia. The most frequently reported grade 3 or greater adverse reactions in individuals receiving palbociclib plus letrozole were neutropenia, leukopenia, infections, and anemia.

Idhifa (enasidenib)

The efficacy of Idhifa (enasidenib) 100 mg was evaluated in an open-label, single-arm, multicenter, two-cohort clinical trial of 199 individuals with relapsed or refractory AML and an IDH2 mutation. IDH2 mutations were identified by a local diagnostic test and retrospectively confirmed by the Abbott RealTime IDH2 assay or prospectively identified by the Abbott RealTime IDH2 assay. Efficacy was based off of the rate of complete response (CR)/complete response with partial hematologic recovery (CR/CRh), the duration of CR/CRh, and the rate of conversion from transfusion dependence to transfusion independence. For individuals who achieved a CR/CRh, the median time to first response was 1.9 months and the median time to best response was 3.7 months. Of the 157 individuals who were dependent on red blood cell and/or platelet transfusions at baseline, 34% became independent of transfusions during any 56-day post baseline period.

Imdelltra (tarlatamab-dlle)

The accelerated approval was based on overall response rate (ORR) and duration of response (DOR) observed in the Phase 2 DeLLphi-301 trial, which evaluated Imdelltra in individuals with small cell lung cancer (SCLC) who had failed two or more prior lines of treatment, and who had received the 10 mg every-2-weeks (Q2W) dosing regimen. Results from the DeLLphi-301 trial demonstrated an ORR of 40% and a median DOR of 9.7 months. The median overall survival (OS) was 14.3 months. The prescribing information for Imdelltra includes a Boxed Warning regarding cytokine release syndrome (CRS) and neurologic toxicity, including immune effector

cell–associated neurotoxicity syndrome (ICANS). Accordingly, the approved dosage of Imdelltra is based on a step-up dosing schedule to reduce the incidence of CRS.

Iwilfin (eflornithine)

Approval of Iwilfin was based on findings from an externally controlled trial comparing outcomes from Study 3b (investigational arm) and Study ANBL0032 (clinical trial-derived external control arm).

In Study 3b (NCT02395666), eligible individuals with high-risk neuroblastoma (HRNB) received Iwilfin orally twice daily, with dosage based on body surface area (BSA), until disease progression, unacceptable toxicity, or for a maximum of 2 years. The external control arm included individuals in the experimental arm of Study ANBL0032, which evaluated dinutuximab, granulocyte-macrophage colony-stimulating factor, interleukin-2, and cis-retinoic acid compared to cis-retinoic acid alone in pediatric individuals with HRNB.

Individuals who met the criteria for the comparative analysis of Study 3b and Study ANBL0032, with complete data for specified clinical covariates, were matched (1:3) using propensity scores. Results showed that, in the protocol-specified primary analysis, the event-free survival (EFS) hazard ratio (HR) was 0.48 and overall survival (OS) HR was 0.32. Supplementary analyses in subpopulations or using alternative statistical methods were performed because of the externally controlled study design. In these analyses, the EFS HR ranged from 0.43 to 0.59 and the OS HR ranged from 0.29 to 0.45.

Kisqali (ribociclib)

Kisqali (ribociclib) offers a favorable overall response rate of 52.7% versus 37.1% in the ribociclib plus letrozole versus the placebo plus letrozole, respectively, and a median duration of response hazard ratio of 0.59 (95% CI: 0.41,0.85, P=.002). The evidence supporting efficacy are limited to the completed placebo-controlled and ongoing dose expansion-crossover Phase 3 trials, it does however present in favor of ribociclib when used in combination with letrozole. This drug is conveniently dosed in an oral, film-coated tablet has a diverse adverse effect profile with an increased risk of QT prolongation, hepatobiliary toxicity, neutropenia, embryo-fetal toxicity, and a warning for avoidance of the use in pregnancy. Post-marketing surveillance and close-monitoring will be critical.

Lartruvo (olaratumab)

Lartruvo (olaratumab) is a human IgG1 antibody that binds platelet-derived growth factor receptor alpha (PDGFR- α). PDGFR- α is a receptor tyrosine kinase expressed on cells of mesenchymal origin. Signaling through this receptor plays a role in cell growth, chemotaxis, and mesenchymal stem cell differentiation. The receptor has also been detected on some tumor and stromal cells, including sarcomas, where signaling can contribute to cancer cell proliferation, metastasis, and maintenance of the tumor microenvironment. The interaction between olaratumab and PDGFR- α prevents binding of the receptor by the PDGF-AA and –BB ligands as well as PDGF-AA, -BB, and –CC-induced receptor activation and downstream PDGFR- α pathway signaling. Olaratumab exhibits in vitro and in vivo anti-tumor activity against selected sarcoma cell lines and disrupted the PDFGR- α signaling pathway in vivo tumor implant models.

The efficacy of Lartruvo (olaratumab) was demonstrated in Trial 1, an open-label, randomized, active-controlled study. Eligible individuals were required to have soft tissue sarcoma not amenable to curative treatment with surgery or radiotherapy, a histologic type of sarcoma for which an anthracycline-containing regimen was appropriate but had not been administered, ECOG PS of 0-2, and tumor specimen available for assessment of PDGFR-α expression by an investigational use assay. Individuals were randomized (1:1) to receive olaratumab in combination with doxorubicin or doxorubicin as a single agent. PDGFR-α expression (positive versus negative), number of previous lines of treatment (0 versus 1 or more), histological tumor type (leiomyosarcoma versus synovial sarcoma versus all others), and ECOG PS (0 or 1 versus 2) were used to allocate individuals in the randomization. olaratumab was administered at 15 mg/kg as an intravenous infusion on Days 1 and 8 of each 21-day cycle until disease progression or unacceptable toxicity. All individuals received doxorubicin 75 mg/m^2 as an intravenous infusion on Day 1 of each 21-day cycle for a maximum of eight cycles and were permitted to receive dexrazoxane prior to doxorubicin in Cycles 5 to 8. Individuals randomized to receive doxorubicin as a single agent were offered olaratumab at the time of disease progression. The efficacy outcome measures were overall survival (OS), and progression-free survival (PFS) and objective response rate (ORR) as assessed by investigator and by independent review according to RECIST v1.1. A total of 133 individuals were randomized, 66 individuals to the LARTRUVO plus doxorubicin arm and 67 individuals to the doxorubicin arm. Baseline demographics and disease characteristics were: median age of 58 years (range 22 to 86); 44% men; 86% White, 8% Black, 3% Asian, and 2% Other; 56% ECOG PS 0 and 39% ECOG PS 1; 65%

no prior chemotherapy (excluding adjuvant and neoadjuvant therapy); 38% leiomyosarcoma, 1.5% synovial sarcoma, and 61% other histologies [17% liposarcoma (8% dedifferentiated, 4% myxoid, 3% well-differentiated, 1.5% pleomorphic, 1% liposarcoma not otherwise specified (NOS)), 11% undifferentiated pleomorphic sarcoma, 5% angiosarcoma, 5% undifferentiated sarcoma NOS, 3% extraskeletal myxoid chondrosarcoma, 2% malignant peripheral nerve sheath tumor, 2% myxofibrosarcoma, 2% malignant solitary fibrous tumor, 2% endometrial stromal sarcoma, 1.5% chondrosarcoma, 1.5% epithelioid sarcoma, 1.5% fibrosarcoma, 1.5% low-grade fibromyxoid sarcoma, and 5% other histologies with one individual each]. All individuals had metastatic disease and were enrolled at US sites. Among individuals randomized to doxorubicin, 30 (45%) individuals received LARTRUVO as a single agent at the time of disease progression. Trial 1 demonstrated a significant improvement in overall survival.

Lonsurf (trifluridine and tipiracil)

Lonsurf is a combination of trifluridine, a nucleoside metabolic inhibitor, and tipiracil, a thymidine phosphorylase inhibitor. Inclusion of tipiracil increases trifluridine exposure by inhibiting its metabolism by thymidine phosphorylase. Following uptake into cancer cells, trifluridine is incorporated into DNA, interferes with DNA synthesis and inhibits cell proliferation. Trifluridine/tipiracil demonstrated anti-tumor activity against KRAS wild-type and mutant human colorectal cancer xenografts in mice.

The clinical efficacy and safety of Lonsurf (trifluridine and tipiracil) were evaluated in an international, randomized, double-blind, placebo-controlled study conducted in individuals with previously treated metastatic colorectal cancer (CRC).

A total of 800 individuals were randomized 2:1 to receive Lonsurf (N=534) plus best supportive care (BSC) or matching placebo (N=266) plus BSC. Randomization was stratified by KRAS status (wild-type vs. mutant), time since diagnosis of first metastasis (<18 months vs. ≥ 18 months), and region (Japan vs. US, Europe and Australia). Key eligibility criteria included prior treatment with at least 2 lines of standard chemotherapy for metastatic CRC, ECOG 0-1, absence of brain metastasis, and absence of ascites requiring drainage in the past four weeks. Individuals received 35 mg/m2 Lonsurf or matching placebo orally twice daily after meals on Days 1 - 5 and 8 – 12 of each 28-day cycle until disease progression or unacceptable toxicity. The major efficacy outcome measure was overall survival (OS), and an additional efficacy outcome measure was progression-free survival (PFS). The median age was 63 years, 61% were male, 58% and 35%

were White and Asian respectively, and all individuals had baseline ECOG Performance Status (PS) of 0 or 1. The primary site of disease was colon (62%) or rectum (38%). KRAS status was wild-type (49%) or mutant (51%) at study entry. All individuals received prior treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy. All but one individual received bevacizumab, and all but two individuals with KRAS wild-type tumors received panitumumab or cetuximab. A statistically significant improvement in overall survival and progression-free survival were demonstrated in individuals in the Lonsurf plus BSC arm compared to those who received placebo plus BSC.

Lynparza (olaparib)

There is limited evidence from a non-randomized open-label study in individuals with deleterious or suspected deleterious gBRCAm-associated advanced ovarian cancer. All individuals (N=193) were treated with Lynparza (olaparib) with an objective response rate of 31% and a median duration of response of 7.4 months.[5] In the subgroup of individuals who had 3 or more lines of prior chemotherapy (n=137), ORR was 34%, mostly classified as partial response (CR 2%, PR 32%). Median duration of response was 7.9 months. A separate randomized open-label study showed similar progression free survival (8.8 vs. 7.1 months) and objective response rate (31% vs. 18%, NS) after treatment with olaparib or pegylated liposomal doxorubicin, respectively, in 97 gBRCAm individuals. Over half of the individuals had received 3 or more prior chemotherapy regimens.[9] The use of olaparib as a maintenance agent following objective response to chemotherapy was not well supported by current evidence and not approved by the FDA. No evidence of real-world effectiveness was found at the time of review. An indirect comparison of response rates for olaparib (from the single pivotal trial) to historically reported response rates of other therapeutic agents in heavily pretreated advanced ovarian cancer individuals was performed by the FDA. Estimated response rate to 4th- line alternative chemotherapy regimens is 10-20%,[2] but it is expected gBRCAm individuals would have a higher response rate. Olaparib appears to provide at least a similar to a more favorable response rate in this heavily pretreated population, with a response rate of 34% from the pivotal trial.

The incidence of myelodysplastic syndrome and/or acute myeloid leukemia (MDS/AML) in olaparib clinical trials is higher than that reported generally in ovarian cancer individuals, 0.8% to 3.1% vs. 0.0033% respectively.[2] Seventeen of the 22 cases found in olaparib clinical trials were fatal. Post-marketing surveillance and monthly monitoring of complete blood count is warranted. Other serious concerns include potential development of secondary malignancy and

pneumonitis. Common adverse events include mostly gastrointestinal complaints and fatigue. Anemia is the most frequently reported serious adverse event. In the comparative trial against liposomal doxorubicin, olaparib is associated with numerically less serious adverse events than liposomal doxorubicin. The most reported serious adverse events were anemia for olaparib and palmar-plantar erythrodysesthesia syndrome for liposomal doxorubicin.

Ovarian cancer (OC) is the leading cause of death in women with gynecological cancer and is the 5th most common cause of cancer mortality in women. Most individuals are diagnosed at advanced stage (stage III or above) with a median age of diagnosis at 63. Epithelial ovarian cancer accounts for the majority (90%) of OC cases. The incidence rate for ovarian cancer between 2006 and 2010 was 12.5 cases per 100,000 women. Women with a family history of ovarian cancer, such as first-degree family members with ovarian cancer and BRCA1 or BRCA2 mutation, are at increased risk of developing advanced OC. Other risk factors for ovarian cancer include nulliparity, older age at pregnancy and first birth, hormone therapy, pelvic inflammatory disease, etc.

Possible causes of OC include incessant ovulation, increasing age and hormonal exposure. Epithelial OC comprises the majority of primary OC. Histologically, serous tumors account for the majority and are typically associated with a poorer prognosis. Due to deleterious mutations of a tumor suppressor BRCA genes, about 10-15% of epithelial OC and up to 50% of high-grade serous tumors are affected by homologous DNA repair defects. The enzymes poly (ADP-ribose) polymerase (PARP) are required for efficient DNA repair. Inhibition of PARP ensures that DNA breaks cannot be repaired and thus results in cell death. Lynparza (olaparib) is an inhibitor of PARP enzymes, including PARP1, PARP2, and PARP3. PARP enzymes are involved in normal cellular homeostasis, such as DNA transcription, cell cycle regulation, and most notably DNA repair. Olaparib disrupts cellular homeostasis and induces cell death by inhibiting PARP enzymatic activity. In the presence of deleterious BRCA mutation, DNA single strand breaks occur which would require PARP enzymes for repair. PARP inhibitors disable this repair pathway rendering cell death.

Current standard treatment for advanced OC include cytoreductive surgery followed by chemotherapy with platinum and taxane based agents. However, there is a high risk for recurrence and developing drug resistance. Individuals who relapse within 6 months after initial chemotherapy are termed platinum-resistant. Platinum resistance is associated with lower subsequent response rate to subsequent regimens and lower survival.

The efficacy and safety of Lynparza in combination with abiraterone and prednisone or prednisolone in individuals with mCRPC was evaluated in a randomized, double-blind, placebo-controlled, multi-center trial "PROpel". In this trial, 796 individuals with mCRPC were randomized 1:1 to receive either Lynparza and abiraterone or placebo and abiraterone. All individuals received either prednisone or prednisolone, a GnRH analog or prior bilateral orchiectomy. The major efficacy endpoint was Radiological Progression-Free Survival (rPFS) and Overall Survival (OS). In the individuals with BRCAm, rPFS was 30% in the treatment group compared to 74% in the placebo group, with the hazard ratio of 0.24 (0.12, 0.45). The overall survival was 28% in the treatment group compared to 66% in the placebo group, with the hazard ratio of 0.30 (0.15, 0.59).

Lysodren (mitotane)

Lysodren is an adrenal cytotoxic agent which is indicated for the treatment of inoperable, functional or nonfunctional, adrenal cortical carcinoma. The mechanism of action of mitotane is unknown. Mitotane modifies the peripheral metabolism of steroid and directly suppresses the adrenal cortex.

The most common adverse reactions are nausea, vomiting, diarrhea, anorexia, dizziness, depression, vertigo and rash.

Ninlaro (ixazomib)

Ninlaro (ixazomib) is a reversible proteasome inhibitor. It preferentially binds and inhibits the chymotrypsin-like activity of the beta 5 subunit of the 20S proteasome. Lxazomib induced apoptosis of multiple myeloma cell lines in vitro. It demonstrated in vitro cytotoxicity against myeloma cells from individuals who had relapsed after multiple prior therapies, including bortezomib, lenalidomide, and dexamethasone. The combination of ixazomib and lenalidomide demonstrated synergistic cytotoxic effects in multiple myeloma cell lines. In vivo, ixazomib demonstrated antitumor activity in a mouse multiple myeloma tumor xenograft model.

The efficacy and safety of Ninlaro in combination with lenalidomide and dexamethasone was evaluated in a randomized, double-blind, placebo-controlled, multicenter study in individuals with relapsed and/or refractory multiple myeloma who had received at least one prior line of

therapy. Individuals who were refractory to lenalidomide or proteasome inhibitors were excluded from the study. A total of 722 individuals were randomized in a 1:1 ratio to receive either the combination of Ninlaro, lenalidomide and dexamethasone (N=360; Ninlaro regimen) or the combination of placebo, lenalidomide and dexamethasone (N=362; placebo regimen) until disease progression or unacceptable toxicity. Randomization was stratified according to number of prior lines of therapy (1 versus 2 or 3), myeloma International Staging System (ISS) (stage I or II versus III), and previous therapy with a proteasome inhibitor (exposed or naïve). Twenty three percent (N=166) of the individuals had light chain disease and 12% (N=87) of individuals had free light chain-measurable only disease. Thromboprophylaxis was recommended for all individuals in both treatment groups according to the lenalidomide prescribing information. Antiemetics were used in 19% of individuals in the Ninlaro regimen and 12% of individuals in the placebo regimen; antivirals in 64% and 60%, respectively, and antihistamines in 27% and 19%, respectively. These medications were given to individuals at the physician's discretion as prophylaxis and/or management of symptoms. Individuals received Ninlaro 4 mg or placebo on Days 1, 8, and 15 plus lenalidomide (25 mg) on Days 1 through 21 and dexamethasone (40 mg) on Days 1, 8, 15, and 22 of a 28-day cycle. Individuals with renal impairment received a starting dose of lenalidomide according to its prescribing information. Treatment continued until disease progression or unacceptable toxicities. The efficacy of Ninlaro was evaluated by progression-free survival (PFS) according to the 2011 International Myeloma Working Group (IMWG) Consensus Uniform Response Criteria as assessed by a blinded independent review committee (IRC) based on central lab results. Response was assessed every four weeks until disease progression.

The approval of Ninlaro was based upon a statistically significant improvement in PFS of the Ninlaro regimen compared to the placebo regimen. The median time to response was 1.1 months in the NINLARO regimen and 1.9 months in the placebo regimen. The median duration of response was 20.5 months in the Ninlaro regimen and 15 months in the placebo regimen for responders in the response evaluable population. A non-inferential PFS analysis was conducted at a median follow up of 23 months with 372 PFS events. Hazard ratio of PFS was 0.82 (95% confidence interval [0.67, 1.0]) for Ninlaro regimen versus placebo regimen, and estimated median PFS was 20 months in the Ninlaro regimen and 15.9 months in the placebo regimen. At the same time, a planned interim OS analysis was conducted with 35% of the required number of deaths for final OS analysis; there were 81 deaths in the Ninlaro regimen and 90 deaths in the placebo regimen. An OS benefit was not demonstrated.

Odomzo (sonidegib)

The safety of Odomzo was evaluated in Study 1, a randomized, double-blind, multiple cohort trial in which 229 individuals received Odomzo at either 200 mg (n=79) or 800 mg (n=150) daily. The frequency of common adverse reactions including muscle spasms, alopecia, dysgeusia, fatigue, nausea, decreased weight, decreased appetite, myalgia, pain, and vomiting was greater in individuals treated with Odomzo 800 mg as compared to 200 mg. The data described below reflect exposure to Odomzo 200 mg daily in 79 individuals with locally advanced BCC (laBCC; n=66) or metastatic BCC (mBCC; n=13) enrolled in Study 1. Individuals were followed for at least 18 months unless discontinued earlier. The median duration of treatment with Odomzo was 11.0 months (range 1.3 to 33.5 months). The study population characteristics were: median age of 67 years (range 25 to 92; 59% were ≥65 years), 61% male, and 90% white. The majority of individuals had prior surgery (75%), radiotherapy (24%), systemic chemotherapy (4%), or topical or photodynamic therapies (18%) for treatment of BCC. No individual had prior exposure to a hedgehog pathway inhibitor. Odomzo was permanently discontinued in 34% of individuals or temporarily interrupted in 20% of individuals for adverse reactions. Adverse reactions reported in at least two individuals that led to discontinuation of the drug were: muscle spasms and dysgeusia (each 5%), asthenia, increased lipase, and nausea (each 4%), fatigue, decreased appetite, alopecia, and decreased weight (each 3%). Serious adverse reactions occurred in 18% of individuals. The most common adverse reactions occurring in ≥10% of individuals treated with Odomzo 200 mg were muscle spasms, alopecia, dysgeusia, fatigue, nausea, musculoskeletal pain, diarrhea, decreased weight, decreased appetite, myalgia, abdominal pain, headache, pain, vomiting, and pruritus.

Ojjaara (momelotinib)

The approval is based on results from the Phase 3 MOMENTUM study (NCT04173494) and a subpopulation of adult individuals with myelofibrosis (MF) and anemia from the Phase 3 SIMPLIFY-1 trial (NCT01969838). MOMENTUM compared Ojjaara with danazol in 195 individuals with MF and anemia who had previously used a JAK inhibitor. The trial met all primary and key secondary endpoints, demonstrating statistically significant response in terms of symptoms, splenic improvement, and transfusion independence. In the SIMPLIFY-1 trial, which included 432 JAK inhibitor-naïve individuals with MF, a numerically lower percentage of individuals treated

with Ojjaara (25%) achieved a Total Symptom Score reduction of 50% or more at Week 24 compared with Incyte's Jakafi (ruxolitinib) (36%).

Purixan (mercaptopurine)

Purixan (mercaptopurine) is an oral purine analog that undergoes intracellular transport and activation to form metabolites including thioguanine nucleotides. Incorporation of thioguanine nucleotides into DNA or RNA results in cell-cycle arrest and cell death. Thioguanine nucleotides and other mercaptopurine metabolites are also inhibitors of de novo purine synthesis and purine nucleotide interconversions. Mercaptopurine was cytotoxic to proliferating cancer cells in in vitro and had antitumor activity in mouse tumor models. It is not known which of the biochemical effects of mercaptopurine and its metabolites are directly or predominantly responsible for cell death.

Rozlytrek (entrectinib)

Rozlytrek (entrectinib) is an oral inhibitor of the tyrosine kinases TRKA, TRKB, TRKC, ROS1, and ALK. Pooled analyses of ALKA-372-001, STARTRK-1, and STARTRK-2 demonstrated that entrectinib was efficacious in adult individuals with neurotrophic tropomyosin receptor kinase (NTRK) fusion-positive tumors and adult individuals with ROS1-positive non-small cell lung cancer (NSCLC). The overall response rate (ORR) of 77.4% in the latter, however, was more compelling than the ORR in the former. The 57.4% ORR rate in individuals with NTRK fusion-positive tumors, along with uncertainty about which cancer types would benefit in a larger individual sample, results in less certainty regarding the efficacy of entrectinib in this individual population. Although overall response rates (ORR) were similar in individuals with and without central nervous system (CNS) disease at baseline, which support findings of the ability of entrectinib to cross the blood-brain barrier (BBB), the median duration of response (DOR) and progression-free survival (PFS) were shorter for individuals with CNS disease. In the STARTRK-NG study of primarily pediatric individuals, entrectinib demonstrated efficacy in individuals with NTRK and ROS1 fusion-positive tumors. These findings further demonstrate its efficacy in individuals with NTRK and ROS1 gene fusions, especially in those with high-grade CNS tumors and extracranial tumors. Among individuals with neuroblastoma (n=15), however, only one individual (ALK fusion-positive) achieved complete response (CR).

Rubraca (rucaparib)

Rubraca (rucaparib) is an inhibitor of poly (ADP-ribose) polymerase (PARP) enzymes, including PARP-1, PARP-2, and PARP-3, which play a role in DNA repair. In vitro studies have shown that rucaparib-induced cytotoxicity may involve inhibition of PARP enzymatic activity and increased formation of PARP-DNA complexes resulting in DNA damage, apoptosis, and cell death. Increased rucaparib-induced cytotoxicity was observed in tumor cell lines with deficiencies in BRCA1/2 and other DNA repair genes. Rucaparib has been shown to decrease tumor growth in mouse xenograft models of human cancer with or without deficiencies in BRCA.

Rubraca (rucaparib) 600mg twice daily as monotherapy has been studied in 377 individuals with ovarian cancer treated in two open label, single arm trials. In these individuals, the median age was 62 years (range 31 to 86), 100% had an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1, 38% had BRCA-mutated ovarian cancer, 45% had received 3 or more prior lines of chemotherapy, and the median time since ovarian cancer diagnosis was 43 months (range 6 to 197). Adverse reactions led to dose reduction or interruption in 62% of individuals, most frequently from anemia (27%), and fatigue/asthenia (22%). Adverse reactions led to dose discontinuation in 10% of individuals, most frequently from fatigue/asthenia (2%). The median duration of treatment was 5.5 months (range 0.1 to 28.0).

Rydapt (midostaurin)

Rydapt (midostaurin) is approved for the first-line treatment of adults with FMS-like tyrosine kinase 3 mutation-positive (FLT3+) acute myeloid leukemia (AML) as detected by an FDA-approved test, in combination with chemotherapy. It is also approved to treat adults with aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated hematological neoplasm (SM-AHN) or mast cell leukemia (MCL). The recommended dose for AML is 50mg twice daily with food. For ASM, SM-AHN and MCL, the recommended dose is 100mg twice daily with food. It will be available through open distribution.

This is the first significant advance in treatment of a subset of AML individuals. AML is difficult to treat, with one year survival rates less than 50%.

The safety and efficacy of Rydapt for individuals with AML were studied in a randomized trial of 717 individuals who had not been treated previously for AML. In the trial, individuals who received Rydapt in combination with chemotherapy lived longer than individuals who received chemotherapy alone, although a specific median survival rate could not be reliably estimated. In addition, individuals who received Rydapt in combination with chemotherapy in the trial went longer (median 8.2 months) without certain complications (failure to achieve complete remission within 60 days of starting treatment, progression of leukemia or death) than individuals who received chemotherapy alone (median three months).

Common side effects of Rydapt in individuals with AML include low levels of white blood cells with fever (febrile neutropenia), nausea, inflammation of the mucous membranes (mucositis), vomiting, headache, spots on the skin due to bleeding (petechiae), musculoskeletal pain, nosebleeds (epistaxis), device-related infection, high blood sugar (hyperglycemia) and upper respiratory tract infection. Rydapt should not be used in individuals with hypersensitivity to midostaurin or other ingredients in Rydapt. Women who are pregnant or breastfeeding should not take Rydapt because it may cause harm to a developing fetus or a newborn baby. Individuals who experience signs or symptoms of lung damage (pulmonary toxicity) should stop using Rydapt.

Rydapt was also approved today for adults with certain types of rare blood disorders (aggressive systemic mastocytosis, systemic mastocytosis with associated hematological neoplasm or mast cell leukemia). Common side effects of Rydapt in these individuals include nausea, vomiting, diarrhea, swelling (edema), musculoskeletal pain, abdominal pain, fatigue, upper respiratory tract infection, constipation, fever, headache, and shortness of breath.

Talvey (talquetamab-tgvs)

Talvey binds to the CD3 receptor expressed on the surface of T-cells and G protein-coupled receptor class C group 5 member D (GPRC5D) expressed on the surface of multiple myeloma (MM) cells and non-malignant plasma cells, causing the release of proinflammatory cytokines that leads to the lysis of multiple myeloma cells.

The efficacy of Talvey monotherapy was evaluated in an open-label, single-arm, multicenter study (MonumenTAL-1) with 100 individuals receiving Talvey weekly (0.4 mg/kg) and 87 individuals receiving Talvey biweekly (0.8 mg/kg) until disease progression or unacceptable

toxicity. Overall response rate, calculated as a total of stringent complete response, complete response, very good partial response, and partial response, was observed in 73% (63.2-81.4%) of the weekly dosing group and 73.6% (63-82.4%) of the biweekly dosing group. The duration of exposure for each group was 5.9 months and 3.7 months, accordingly.

Serious adverse reactions were reported in 47% of individuals who received Talvey, with those occurring in at least 2% of individuals being cytokine release syndrome (CRS) (13%), bacterial infection (8%), pyrexia (4.7%), immune effector cell-associated neurotoxicity syndrome (ICAN) (3.8%), COVID-19 (2.7%), neutropenia (2.1%), and upper respiratory tract infection (URTI) (2.1%). Fatal adverse reactions occurred in 3.2% of individuals, including COVID-19, dyspnea, general health deterioration, bacterial infection, basilar artery occlusion, fungal infection, infection, and pulmonary embolism. Permanent discontinuation of Talvey occurred in 9% of individuals and dosage interruptions due to adverse reactions occurred in 56% of individuals. Most common adverse reactions (> 20%) were pyrexia, CRS, dysgeusia, nail disorder, musculoskeletal pain, skin disorder, rash, fatigue, weight loss, dry mouth, xerosis, dysphagia, URTI, diarrhea, hypotension, and headache. The most common Grade 3 or 4 laboratory abnormalities (at least 30%) were decreases in lymphocyte, neutrophil, white blood cell, and hemoglobin counts.

Talzenna (talazoparib)

Talzenna is a poly (ADP-ribose) polymerase (PARP) enzyme inhibitor, including PARP1 and PARP3, which play a role in DNR repair.

The safety and efficacy of Talzenna (talazoparib) was evaluated in Embraca study where 431 individuals with deleterious or suspected deleterious germline BRCA-mutated HER2-negative Locally Advanced or Metastatic Breast Cancer were randomized 2:1 to receive Talzenna 1 mg or healthcare provider's choice of chemotherapy (capecitabine, eribulin, gemcitabine or vinorelbine) until the disease progression or unacceptable toxicity.

The efficacy endpoint was progression-free survival (PFS) evaluated based on Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1. There was a statistically significant improvement in the PFS as there was 65% disease progression or death in the Talzenna group compared to 58% in the chemotherapy group, with p-value < 0.0001.

The efficacy of Talzenna in combination with combination with Xtandi was evaluated in TALAPRO-2 trial, which was randomized, double-blind, placebo-controlled, multi-cohort trial. In

this trial 399 individuals with HRR gene mutated (HRRm) mCRPC were randomized 1:1 to receive either enzalutamide 160 mg daily plus either Talzenna 0.5 mg or placebo daily until individual experiences unacceptable toxicity or progression. All the individuals received a GnRH analog or had prior bilateral orchiectomy and they were progressed on prior androgen deprivation therapy. Mutation in HRR gene was determined using either circulating tumor DNA based next generation sequencing assays or solid tumor tissue. The primary efficacy outcome was to evaluate radiographic progression-free survival (rPFS) and another efficacy outcome measure was overall survival. The number of rPFS events were in 33% individual in the treatment group versus 52% in the placebo group with p-value < 0.0001.

Tazverik (tazemetostat)

Tazemetostat is an inhibitor of the methyltransferase, enhancer of zeste homolog 2 (EZH2), and some EZH2 gain-of-function mutations including Y646X and A687V. EZH2 is a methyltransferase associated with inhibition of apoptosis and increased cellular proliferation that is mutated or overexpressed in a variety of solid and hematological cancers. Epithelioid sarcoma (ES) is a rare type (≤1%) of soft tissue sarcoma (STS), a solid malignancy arising from connective tissue that comprises approximately 1% of all cancers. Two subtypes of ES, classic (distal type) which typically affects the distal upper extremity of adolescents and young adults and the less common and more aggressive proximal variant that affects young to middle-aged adults. The efficacy of tazemetostat was evaluated in an open-label, single-arm cohort (Cohort 5) of a multi-center study (Study EZH-202) in individuals with histologically confirmed, metastatic or locally advanced epithelioid sarcoma. Individuals were required to have INI1 loss, detected using local tests, and an Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 0-2. Individuals received tazemetostat 800 mg orally twice daily until disease progression or unacceptable toxicity. Tumor response assessments were performed every 8 weeks. The major efficacy outcome measures were confirmed overall response rate (ORR) according to Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 as assessed by blinded independent central review (BICR) and duration of response (DOR). Median duration of follow-up was 14 months (range 0.4 to 31). In study EZH-202 the overall response rate (95% CI) for tazemetostat was 15% (7%, 26%).

Temodar (temozolomide)

Temodar (temozolamide) is an alkylating drug indication for the treatment of adult individuals with either newly diagnosed glioblastoma concomitantly with radiotherapy and then as maintenance treatment, or for refractory anaplastic astrocytoma who have experienced disease progression on a drug regimen containing nitrosourea and procarbazine. Temozolomide goes through rapid nonenzymatic conversion at physiologic pH to the reactive compound 5- (3-methyltriazen-1-yl)-imidazole-4-carboxamide (MTIC).

The efficacy and safety of Temodar in the individuals with newly diagnosed glioblastoma was evaluated in a randomized, multicenter, and open-label trial. In this trial, 573 individuals were randomized to receive either radiation therapy alone (n = 286) or Temodar along with the radiation (n = 287) for total of 42 days. The primary efficacy endpoint was the overall survival. The treatment group (Temodar plus radiotherapy) achieved statistically significant improvement in the overall survival compared to the placebo group (radiotherapy alone), with p-value < 0.0001. Also, the median survival increased by 2.5 months in the treatment group.

The efficacy and safety of Temodar in individuals with refractory anaplastic astrocytoma was studied in a single-arm, multicenter trial. In this trial, 54 individuals with anaplastic astrocytoma and Karnofsky performance status (KPS) of 70 or greater were included. These individuals had previously received radiation therapy and may also have previously received nitrosourea with or without other chemotherapy. The primary efficacy endpoints were overall response rate and median duration of response. Other efficacy endpoints also evaluated the progression free survival at 6 months and 12 months. The overall response rate in Temodar group was 22%, where 9% individuals had complete response. The median duration of response was 50 weeks. The progression-free survival at 6 months was 45% and at 12 months was 29%.

The most common adverse reactions are alopecia, nausea, vomiting, fatigue, headache, constipation, anorexia, and convulsions. Some individuals with anaplastic astrocytoma ($\geq$10% incidence) experienced Grade 3 to 4 hematologic laboratory abnormalities including reduced level of lymphocytes, platelets, neutrophils, and leukocytes.

Tibsovo (ivosidenib)

Tibsovo (ivosidenib) is the first approved oral therapy that targets mutant IDH1 in AML IDH1 is one of three known driver mutations with poor prognosis in AML. The efficacy of ivosidenib was

evaluated in a Phase I, multicenter, open-label, dose-escalation and expansion clinical study of orally administered AG-120 in subjects with advanced hematologic malignancies with an IDH1 mutation. The first portion of the study is a dose-escalation to find the highest tolerable dose of the combination of ivosidenib that can be given to individuals with relapsed or refractory AML with IDH1 mutation. The second part of the study or dose expansion found the highest tolerable dose of ivosidenib that can help to control the disease.

In the dose-escalation and expansion clinical trial of ivosidenib, the primary outcome was an objective response rate (ORR) of 41.6%. Ivosidenib induced a complete response (CR) or a CR with a partial hematologic recovery (CPh) in 30.4% of the study population. The secondary outcome was a median duration of response of 9.3 months for individuals who achieved a CR, 8.2 months for those who achieved a CR/CRh, and 6.5 months for all responders. The median time to first response was 1.9 months, median time to CR was 2.8 months, and the median time to CR/CRh was 2.7 months.

The safety of ivosidenib was evaluated in the Phase I dose-escalation and dose expansion study mentioned above. The most common adverse events were diarrhea (33.3%), elevated levels of white blood cells (30.2%), nausea (29.5%), fatigue (28.7%), and febrile neutropenia (25.2%); 10 (8%) of 125 individuals had grade 3 QT prolongation. Ivosidenib was reduced in one individual and held in five individuals (for any grade of QT prolongation), and no cases were Grade 4 or fatal. The prevalence of differentiation syndrome (DS) was observed in 11.2% of individuals, but no instances of DS leading to permanent treatment discontinuation or death.

Unituxin (dinutuximab)

Unituxin (dinutuximab) is a glycolipid GD2-binding monoclonal antibody. Glycolipid GD2 is expressed on neuroblastoma cells and on the normal cells of neuroectodermal origin, including the central nervous system and peripheral nerves. Dinutuximab works by biding to cell surface GD2 and inducing the cell lysis of GD2-expressing cells through antibody-dependent cell-mediated cytotoxicity (ADCC) and complement-dependent cytotoxicity (CDC).

The safety and efficacy of Unituxin was evaluated in a randomized, open-label, multicenter trial where 226 pediatric individuals with high-risk neuroblastoma were randomized to receive Unituxin treatment (n = 113) or RA treatment (n = 113). All individuals had previously received therapies including induction combination chemotherapy, maximum feasible surgical resection,

myeloablative consolidation chemotherapy followed by autologous stem cell transplant, and radiation therapy to residual soft tissue disease. Individuals needed to have at least a partial response prior to autologous stem cell transplantation and have no evidence of disease progression following completion of front-line multimodality therapy, and individuals have adequate pulmonary, hepatic, cardiac and renal functions.

Individuals in the Unituxin group received up to 5 cycles of Unituxin in combination with granulocyte-macrophage colony-stimulating factor (GM-CSF) or interleukin-2 (IL-2) plus 13-cis-retinoic acid (RA), followed by 1 cycle of RA alone. Meanwhile, individuals in the RA group received 6 cycles of RA. The individuals received Unituxin at a dose of 17.5 mg/m^2/day on 4 consecutive days. Individuals in both arms received 6 cycles of RA at a dose of 160 mg/m^2/day (individual's weight > 12kg) or 5.33 mg/kg/day (individual's weight $\leq$ 12 kg) in divided doses for 14 consecutive days.

The primary efficacy endpoint was investigator-assessed event-free survival (EFS), which is defined as the time from randomization to the first occurrence of relapse, progressive disease, secondary malignancy, or death. The efficacy outcome also evaluated the overall survival.

At the end of the study, the EFS was 29% in Unituxin/RA group compared to 44% in the RA group, with p- value of 0.01. Similarly the OS was 27% in Unituxin/RA arm compared to 42% in the RA arm, with hazard ratio of 0.58 (0.37, 0.91).

Verzenio (abemaciclib)

Verzenio (abemaciclib) selectively inhibits cyclin-dependent kinases (CDK) 4 and 6 (CDK 4/6). It blocks retinoblastoma tumor suppressor protein phosphorylation and prevents progression through the cell cycle, resulting in arrest at the G1 phase.

The efficacy of Verzenio (abemaciclib) in combination with Faslodex (fulvestrant) was evaluated in the Monarch 2 trial. Monarch 2 was a randomized, placebo-controlled, multicenter study in 669 women with HR-positive, HER2-negative metastatic breast cancer in individuals with disease progression on endocrine therapy. The primary endpoint was progression-free survival. The median extended progression free survival duration for abemaciclib plus fulvestrant vs. fulvestrant alone was 16.4 months vs. 9.3 months. The efficacy of Verzenio as monotherapy was evaluated in the Monarch 1 trial. Monarch 1 was a single-arm, open-label, multicenter study in 132 women with measurable HR-positive, HER2-negative metastatic breast cancer whose

disease progressed during endocrine therapy, had received taxane in any setting, and who received 1 or 2 prior chemotherapy regimens in the metastatic setting. The primary objective of Monarch 1 was investigator-assessed objective response rate. Other endpoints were clinical benefit rate, progression-free survival, and overall survival. At the 12-month final analysis, the confirmed objective response rate was 19.7%, median progression-free survival was 6 months and median overall survival was 17.7 months.

Vistogard (uridine triacetate)

Vistogard is a pyrimidine analog. Uridine triacetate is an acetylated pro-drug of uridine. Once the uridine triacetate is deacetylated in the body via nonspecific esterases, the end product uridine is yielded in the circulation. The uridine competitively inhibits the cell damage and cell death caused by fluorouracil.

The efficacy and safety of Vistogard was evaluated in two open-label trials, where 135 individuals with either fluorouracil or capecitabine overdose, or individuals with severe or life-threatening toxicities within 96 hours following the end of fluorouracil or capecitabine administration. The Vistogard was administered at dose of 10 grams orally every 6 hours for total of 20 doses or 6.2 grams/m^2/dose for total of 20 doses for individuals between the age of 1 to 7 years old.

The primary efficacy endpoint was individual's survival at 30 days or until the resumption of chemotherapy if prior to 30 days. Overall, out of 135 individuals, 96% (n = 130) achieved the primary endpoint of either survival at 30 days or the resumption of chemotherapy if prior to 30 days. Death occurred in 5 individuals with fluorouracil or capecitabine overdose.

The most common adverse reactions in individuals who received Vistogard included vomiting, nausea, and diarrhea.

Xgeva (denosumab)

Clinical data from the pivotal Xgeva multiple myeloma '482 study demonstrated that Xgeva is non-inferior to zoledronic acid in delaying time to first on-study skeletal-related events (SREs). The median time to first on-study SRE was 22.83 months for Xgeva vs 23.98 months for

zoledronic acid. Xgeva delayed the time to first SRE following randomization as compared to zoledronic acid in individuals with breast or castration-resistant prostate cancer (CRPC). In individuals with bone metastasis due to other solid tumors, Xgeva was noninferior to zoledronic acid in delaying the time to first SRE following randomization. Overall survival and progression-free survival were similar between arms in all three trials.

Xpovio (selinexor)

Xpovio (selinexor) is a first-in-class, oral selective inhibitor of nuclear export (SINE) protein XPO1. This leads to accumulation of tumor suppressor proteins in the cell nucleus and selective induction of apoptosis in cancer cells. Selinexor has been granted Orphan Drug designation in multiple myeloma (MM) and Fast Tract approval in combination with dexamethasone (DEX) for the treatment of individuals with relapsed/refractory (R/R) MM who have received ≥4 prior therapies and whose disease is triple therapeutic class refractory (i.e., preteosome inhibitor, immunomodulatory agent, and anti-CD38 monoclonal antibody), based upon the STORM study. A pivotal, randomized, open-label, Phase III trial (BOSTON) of selinexor in combination with bortezomib (VELCADE) and DEX in individuals with R/R MM is ongoing. The FDA extended the review period for selinexor from April to July 2019 in order to also review data from the BOSTON trial.

Zejula (niraparib)

Zejula (niraparib) offers a significant increase in PFS in individuals with platinum sensitive recurrent epithelial ovarian cancer. This is also the first PARPi to demonstrate efficacy in this population irrespective of BRCA mutation status. This is useful in that the individual will not be required to undergo expensive genetic testing prior to therapy.

The evidence supporting Zejula's efficacy is sufficient and was demonstrated in the multi-center, randomized, double-blind, placebo-controlled ENGOT-OV16/NOVA trial that included 553 individuals. The once-daily dosing and oral dosage form are also aspects which increase ease of use. Zejula has an extremely diverse adverse effect profile including an increased risk in MDS/AML and a warning for fetal toxicity. Post-marketing surveillance and individual reporting will be critical.

2013 Update

Policy was updated to reflect new NCCN guidelines which recommend abiraterone as an initial therapy for metastatic castrate-resistant prostate cancer.

2014 Update

A literature search from 7/1/12 to 10/31/14 found no new evidence requiring changes to this policy.

2015 Update

A literature search from 1/1/14 to 3/31/15 found no new evidence requiring changes to the Erivedge (vismodegib) policy. Added criteria for two recently approved drugs: Opdivo (nivolumab) and Lynparza (olaparib). Added criteria for recently approved drug: Ibrance (palbociclib).

2016 Update

A literature search and review were conducted focusing on recently FDA-approved indications for use of Opdivo (nivolumab) and Keytruda (pembrolizumab) in non-small cell lung cancer, and for nivolumab in renal cell carcinoma. We also reviewed this evidence for combined use of nivolumab and ipilimumab in unresectable or metastatic melanoma. Medical necessity language was updated per new product labels.

Reasonable evidence exists to support the use of ipilimumab, nivolumab, the combination of ipilimumab + nivolumab and Keytruda (pembrolizumab) in the treatment of advanced and metastatic melanoma. Median survival benefits seem to fall in the range of 3-4 months, with the combination PD-1/CTLA-4 inhibition yielding slightly longer survival. To date the evidence is spotty and lacking in head-to-head comparisons. NCCN guidelines do not rate one option over

others. Given the number of different molecular targets now available (PD-1, CTLA-4, BRAF V600, MEK) it is impossible to say at this point which is the best treatment sequence to follow.

Tecentriq's label criteria was added to the policy, along with description and rationale sections for this drug. Keytruda recently got a new recommendation for use in NSCLC as a first-line agent. Added criteria (along with description and rationale) for recently approved drugs: Lonsurf, Ninlaro, and Lartruvo. Tecentriq's recent approval in the setting of NSCLC was also added to the policy.

Added criteria per label for Rubraca (rucaparib), along with the drug description and clinical trials rationale.

2017 Update

Added two new indications for Opdivo (nivolumab). Added four new indications for Keytruda (pembrolizumab) and included their references.

2018 Update

Added Paloma-2 study for Ibrance (palbociclib) and Rydapt (midostaurin) safety and efficacy study in drug description.

2019 Update

Reviewed prescribing information for all drugs and updated Tibsovo (ivosidenib) coverage criteria. No new evidence was identified that would require changes to other drugs listed in this policy. Added coverage criteria for the new drug Balversa (erdafitinib).

2021 Update

Reviewed prescribing information for all drugs in policy and no new evidence was identified from prescribing information that would require changes to the drugs listed in this policy.

Added trial and failure with Ibrance (palbociclib) or Verzenio (abemaciclib) requirement to Kisqali (ribociclib) and Kisqali Femara Co-Pack (letrozole-ribociclib).

2022 Update

Reviewed prescribing information for all drugs in policy. Removed Aliqopa (copanlisib) as coverage criteria for Aliqopa are captured under Policy 5.01.592. Added to Darzalex (daratumumab) coverage for use in combination with carfilzomib and dexamethasone in individuals with relapsed or refractory multiple myeloma who have received one to three prior lines of therapy. Added a new indication to Tibsovo (ivosidenib) for use in combination with azacitidine or as monotherapy for the treatment of newly diagnosed acute myeloid leukemia. Added coverage for Leukine (sargramostim) as second-line therapy for the treated of individuals taking myelosuppressive anti-cancer regimens, at risk of severe febrile neutropenia.

2023 Update

Reviewed prescribing information for all drugs in policy. Updated Zejula criteria to indicate coverage for the maintenance treatment of adult individuals is limited to those with deleterious or suspected deleterious germline *BRCA*-mutated recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy. Updated Verzenio criteria to indicate coverage in combination with endocrine therapy for the adjuvant treatment of adult individuals with HR-positive, HER2-negative, node-positive early breast cancer at high risk of recurrence without requiring a Ki-67 score of 20 or greater. Added coverage criteria for Xgeva (denosumab). Added coverage criteria for Unituxin (dinutuximab). Unituxin in combination with granulocyte-macrophage colony-stimulating factor (GM-CSF), interleukin-2 (IL-2), and 13-cis-retinoic acid (RA), for the treatment of pediatric individuals with high-risk neuroblastoma who achieve at least a partial response to prior first-line multiagent, multimodality therapy. Added coverage criteria for Epkinly (epcoritamab-bysp) for the treatment of adult individuals with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, including DLBCL arising from indolent lymphoma, and high-grade B-cell lymphoma after two or more lines of systemic therapy. Added coverage criteria for Lynparza (olaparib) for the treatment of adult individuals with deleterious or suspected deleterious BRCA-mutated (BRCAm) metastatic castration-resistant prostate cancer (mCRPC)

when used in combination with abiraterone and prednisone or prednisolone. Added coverage criteria for Talzenna, when used in combination with enzalutamide, for the treatment of adult individuals with HRR gene- mutated metastatic castration-resistant prostate cancer (mCRPC). Added generic bortezomib to the criteria of Velcade (bortezomib). Added coverage criteria for Vistogard for the emergency treatment of fluorouracil or capecitabine overdose, or severe or life-threatening toxicity within 96 hours following the end of fluorouracil or capecitabine administration. Removed Gavreto's indication of adult and pediatric individuals 12 years of age and older with advanced or metastatic RET-mutant medullary thyroid cancer (MTC) who require systemic therapy per FDA label changes. Added coverage for Leukine for the treatment of pediatric individuals with high-risk neuroblastoma who achieve at least a partial response to prior first-line multiagent, multimodality therapy. Added Brand paclitaxel protein- bound particles (american regent-unbranded) IV to Abraxane criteria. Added criteria for Lysodren (mitotane) for the treatment of adrenal cortical carcinoma when the tumor is inoperable. Added criteria for Matulane (procarbazine hydrochloride) for the treatment of stage III and IV Hodgkin's disease when used in combination with other anticancer drugs. Added coverage criteria for Temodar (temozolomide) and generic temozolomide for the treatment of adult individuals with newly diagnosed glioblastoma concomitantly with radiotherapy and then as maintenance treatment, or for refractory anaplastic astrocytoma who have experienced disease progression on a drug regimen containing nitrosourea and procarbazine. 90 days notification is required for Temodar IV and Unituxin IV. Removed generic temozolomide IV criteria and added generic temozolomide oral criteria. Added Talvey and Elrexfio for the treatment of adult individuals with relapsed or refractory multiple myeloma where individual has tried at least four lines of prior therapies. Added coverage criteria for Purixan (mercaptopurine) for the treatment of acute lymphoblastic leukemia as part of a combination chemotherapy maintenance regimen.

2024 Update

Reviewed prescribing information for all drugs in policy. Added coverage criteria for Lonsurf (trifluridine and tipiracil) for the treatment of certain adult individuals with metastatic colorectal cancer in combination with bevacizumab. Added coverage criteria for Hepzato Kit (melphalan hepatic delivery system) for the treatment of certain adult individuals with unresectable or metastatic uveal melanoma. Added coverage criteria for Ogsiveo (nirogacestat) for the treatment of certain adult individuals with progressing desmoid tumors. Added coverage criteria for Tabloid (thioguanine) for the treatment of certain individuals with acute myeloid leukemia.

Added coverage criteria for Iwilfin (eflornithine) for the treatment of certain individuals with high-risk neuroblastoma. Added coverage criteria for oral Temodar (temozolomide) and oral generic temozolomide for the treatment of certain adult individuals with glioblastoma or anaplastic astrocytoma. Updated coverage criteria for IV Temodar (temozolomide) to include the treatment of certain adult individuals with newly diagnosed anaplastic astrocytoma. Updated coverage criteria for Tibsovo (ivosidenib) to include the treatment of certain adult individuals with myelodysplastic syndromes. Updated coverage criteria for Welireg (belzutifan) to include the treatment of certain adult individuals with renal cell carcinoma. Removed Truseltiq (infigratinib) coverage criteria as the product has been withdrawn from the market. Updated coverage criteria for Balversa (erdafitinib) to remove coverage criteria for the treatment of locally advanced or metastatic urothelial carcinoma with susceptible FGFR2 genetic alterations and broaden step therapy requirement from prior platinum-containing chemotherapy to prior systemic therapy. Added coverage criteria for Ojjaara (momelotinib) for the treatment of certain adults with myelofibrosis. Added coverage criteria for Thalomid (thalidomide). Added coverage criteria for Aphexda (motixafortide). Updated Onivyde (irinotecan) to include coverage criteria for the first-line treatment of certain adults with metastatic pancreatic adenocarcinoma. Updated Onivyde (irinotecan) to clarify that all coverage criteria is limited to adults. Updated Ogsiveo (nirogacestat) coverage criteria to include a requirement to try generic sorafenib first. Added coverage criteria for Amtagvi (lifileucel) for the treatment of certain individuals with unresectable or metastatic melanoma. Added coverage criteria for brand paclitaxel protein-bound particles (Teva – unbranded). Updated Gazyva (obinutuzumab) coverage criteria to include treatment of certain adults with follicular lymphoma in combination with zanubrutinib. Added coverage criteria for Imdelltra (tarlatamab-dlle) for the treatment of certain individuals with extensive-stage small cell lung cancer (ES-SCLC). Added coverage criteria for Dacogen (decitabine) and generic decitabine for the treatment of certain individuals with myelodysplastic syndrome. Added coverage criteria for Elitek (rasburicase) for the treatment of certain individuals with leukemia, lymphoma, or solid tumor malignancies who are receiving anticancer therapy expected to result in tumor lysis. Added coverage criteria for Casodex (bicalutamide), Eulexin (flutamide), Nilandron (nilutamide), and generic nilutamide for the treatment of certain adults with prostate cancer.

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64. Iwilfin (eflornithine) [prescribing information]. Louisville, KY; USWM, LLC. Revised December 2023.
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67. Ojjaara (momelotinib) [prescribing information]. Durham, NC; GlaxoSmithKline. Revised September 2023.
68. Thalomid (thalidomide) [prescribing information]. Princeton, NJ; Bristol Myers Squibb. Revised March 2023.
69. Aphexda (motixafortide) [prescribing information]. Waltham, MA; BioLineRx. Revised September 2023.

70. Amtagvi (lifileucel) [prescribing information]. Philadelphia, PA; Iovance Biotherapeutics, Inc. Revised February 2024.
71. Imdelltra (tarlatamab-dlle) [prescribing information]. Thousand Oaks, CA; Amgen, Inc. Revised May 2024.
72. Dacogen (decitabine) [prescribing information]. Dublin, CA; Otsuka America Pharmaceutical, Inc. Revised June 2020.
73. Elitek (rasburicase) [prescribing information]. Bridgewater, NJ; Sanofi-Aventis U.S. LLC. Revised December 2022.
74. Casodex (bicalutamide) [prescribing information]. Baudette, MN; ANI Pharmaceuticals, Inc. Revised December 2023.
75. Eulexin (flutamide) [prescribing information]. Wixom, MI; Waylis Therapeutics LLC. Revised January 2022.
76. Nilandron (nilutamide) [prescribing information]. Dublin, Ireland; Concordia Pharmaceuticals Inc. Revised July 2022.

Appendix

Biomarker Testing For Lynparza Individual Selection

Indication	Biomarker	Sample type		
		Tumor	Blood	Plasma (ctDNA)
Germline or somatic HRR gene-mutated metastatic castration-resistant prostate cancer	ATMm, BRCA1m, BRCA2m, BARD1m, BRIP1m, CDK12m, CHEK1m, CHEK2m, FANCLm, PALB2m, RAD51Bm, RAD51Cm, RAD51Dm, RAD54Lm	X		
	gBRCA1m, gBRCA2m		X	
	ATMm, BRCA1m, BRCA2m			X
BRCA-mutated metastatic castration-resistant prostate cancer in combination with abiraterone and	BRCA1m, BRCA2m	X	X	X

prednisone or prednisolone				

Homologous recombination repair (HRR) Gene mutation

HRR gene mutations can be found in 23% of metastatic castration-resistant prostate cancer. The most frequent gene mutations are found on breast cancer susceptibility gene (BRCA)2, ataxia-telangiectasia mutated (ATM), checkpoint kinase 2 (CHECK2), and BRCA1 genes.

Select individuals for the treatment of HRR gene-mutated mCRPC with Talzenna based on the following HRR gene mutations: ATM, ATR, BRCA1, BRCA2, CDK12, CHEK2, FANCA, MLH1, MRE11A, NBN, PALB2, or RAD51C.

The FDA approved test to detect HRR gene mutation for use with Talzenna is not available currently.

History

Date	Comments
06/12/12	New policy, add to Prescription Drug section. Reviewed by Pharmacy & Therapeutics Committee, June 2012.
07/08/13	Minor Update – Clarification was added to the policy that it is managed through the member's pharmacy benefit; this is now listed in the header and within the coding section.
10/14/13	Replace policy. Policy updated to reflect new NCCN guidelines which recommend abiraterone as an initial therapy for metastatic castrate-resistant prostate cancer.
11/11/13	Replace policy. Policy section updated with the removal of *Zytiga (abiraterone)*; Rationale section updated in accordance with this change. (See policy 5.01.544 for coverage on Zytiga).
12/08/14	Annual Review. Policy updated with literature review; no change in policy statement.
05/27/15	Annual Review. Policy updated with literature review. Title changed to match the scope of the policy which is no longer limited to oral medications. New policy statements added: nivolumab and olaparib may be considered medically necessary; Opdivo for

Date	Comments
	treatment metastatic squamous non-small cell lung cancer with progression on or after platinum-based chemotherapy may be considered medically necessary; all other uses of Erivedge, Lynparza or Opdivo are considered investigational. Rationale section updated in accordance with this change and new references added. The word "oral" removed from the title to match the scope of the policy.
07/14/15	Interim Update. Added new policy statements for newly approved drug palbociclib.
01/19/16	Coding update. New HCPCS codes J3380 and J9299 – effective 1/1/16 – added to policy.
01/29/16	Minor update. Removed code J3380.
04/01/16	Annual Review, approved March 8, 2016. Policy updated to reflect current labeling indications.
05/26/16	Coding update. J9271 added, effective 1/1/16.
10/01/16	Interim Review, approved September 13, 2016: inclusion of a new indication for Opdivo and Keytruda. Addition of length of approval as 3 months. Inclusion of Gazyva criteria, and rationale for Yervoy.
11/01/16	Interim Review, approved October 11, 2016. Tecentriq criteria and description added to the policy.
12/01/16	Interim Review, approved November 8, 2016. Keytruda's criteria was updated to reflect first-line use in NSCLC. Also, Lonsurf, Ninlaro, and Lartruvo criteria was added to the policy. Tecentriq's newest indication for NSCLC was also added to the policy.
01/01/17	Interim Review, approved December 13, 2016. Minor clarifications made to the criteria language. Also, Yervoy's criteria has been expanded based on NCCN guidelines.
02/01/17	Annual Review, approved January 10, 2017. Added rupacarib's labeled criteria, as well as drug description and clinical trials rationale. References section has been updated accordingly.
03/01/17	Interim Review, approved February 14, 2017. Added two new indications for nivolumab (recurrent or metastatic squamous cell carcinoma of the head and neck; urothelial carcinoma).
04/01/17	Interim Review, approved March 14, 2017. Updated criteria for Lartruvo.
06/01/17	Interim Review, approved May 16, 2017. Updated an indication for Tecentriq. Updated criteria for Ibrance to include any aromatase inhibitor therapy. Fixed minor grammatical/formatting errors. Added coverage criteria for Odomzo (sonidegib).
07/01/17	Interim Review, approved June 13, 2017. Added coverage criteria for Kisqali, Zejula, Bavencio, Rydapt, and Imfinzi.

Date	Comments
09/01/17	Minor update; updated title of related policy 5.01.543.
10/01/17	Interim Review, approved September 21, 2017. Added coverage criteria for Idhifa.
11/01/17	Interim Review, approved October 19, 2017. Added coverage criteria for Verzenio.
12/01/17	Interim Review, approved November 14, 2017. Added new indications for Keytruda and its new references. Added new indication for Lynparza.
01/01/18	Coding update, added HCPCS codes J9022, J9023, and J9285 (new codes effective 1/1/18).
02/01/18	Interim Review, approved January 16, 2018. Added coverage criteria for Aliqopa (copanlisib) and added new indication for Opdivo
03/01/18	Interim Review, approved February 27, 2018. Added new indication for Lynparza - deleterious or suspected deleterious germline BRCA-mutated (gBRCAm), human epidermal growth factor receptor 2 (HER2)-negative metastatic breast cancer who have been previously treated with chemotherapy either in the neoadjuvant, adjuvant or metastatic setting. Updated Opdivo and Imfinzi criteria to include all FDA approved indications.
06/01/18	Interim Review, approved May 3, 2018. Updated criteria for combination therapy with Opdivo and Yervoy as well as Rubraca to include newly approved FDA labeled indications.
07/01/18	Annual Review, approved June 22, 2018. Added Paloma-2 study for Ibrance and safety and efficacy study for Rydapt. Updated Keytruda criteria for clarity. Added general reauthorization criteria and documentation requirements.
11/01/18	Interim Review, approved October 26, 2018. Added Tibsovo (ivosidenib). Updated indications for all agents per labels. Added criteria for Talzenna (talazoparib). Organized by pharmacology. Moved immunotherapy drugs to new policy 5.01.591. Removed HCPCS codes J9022, J9228, J9271, and J9299.
01/01/19	Coding update, added new HCPCS code J9057 (new code effective 1/1/19).
02/01/19	Interim Review, approved January 8, 2019. Added coverage criteria for Daurismo (glasdegib) and Vitrakvi (larotrectinib) and added new indication for Lynparza (olaparib).
04/01/19	Interim Review, approved March 12, 2019. Updated criteria for Erivedge (vismodegib), Odomzo (sonidegib) and Lonsurf (trifluridine and tipiracil).
07/01/19	Interim Review, approved June 4, 2019. Updated criteria for Ibrance (palbociclib). Removed HCPCS code J3490.
08/01/19	Annual Review, approved July 9, 2019. Added coverage criteria for Balversa (erdafitinib). Updated criteria for Tibsovo (ivosidenib).

Date	Comments
10/01/19	Interim Review, approved September 10, 2019, effective January 3, 2020. Bavencio (avelumab) moved to policy 5.01.591 Immune Checkpoint Inhibitors. Added coverage criteria for Asparlas (calaspargase pegol-mknl), Intron A (interferon alfa-2b), and Sylatron (peginterferon alfa-2b). Removed HCPCS code J9023, added HCPCS codes J9118 (new code effective 10/1/19) and J9213.
12/01/19	Interim Review, approved November 12, 2019. Added coverage criteria for Piqray (alpelisib), Rozlytrek (entrectinib), Vitrakvi (larotrectinib), Xpovio (selinexor), and Kisqali Femara co-pack (ribociclib – letrozole).
02/01/20	Interim Review, approved January 14, 2020. Added criteria for Inrebic per August 2019 P&T. Removed HCPCS code J9213, added HCPCS code J9214.
03/01/20	Interim Review, approved February 11, 2020. Updated coverage criteria for Lynparza (olaparib) and Zejula (niraparib) effective for dates of service on or after March 1, 2020. Added coverage criteria for Darzalex (daratumumab) (HCPCS code J9145) which becomes effective for dates of service on or after June 5, 2020.
04/01/20	Interim Review, approved March 10, 2020. Added Padcev (enfortumab vedotin-ejfv) to policy with coverage criteria for urothelial cancer, effective for dates of service on or after July 2, 2020, after provider notification. Added Tazverik (tazemetostat) to policy with coverage criteria for epithelioid sarcoma; these criteria become effective April 1, 2020.
07/01/20	Annual Review, approved June 9, 2020, effective July 1, 2020. Added a dose limit of 200 mg per day to Odomzo (sonidegib). Added a dose limit of 150 mg per day to Erivedge (vismodegib). Added new indication to Zejula (niraparib) for the treatment of advanced ovarian cancer. Added new indications to Lynparza (olaparib) for the treatment of ovarian cancer when used in combination with bevacizumab and for the treatment of prostate cancer. Added new indication to Rubraca (rucaparib) for the treatment of prostate cancer. Added coverage criteria for Pemazyre (pemigatinib) for the treatment of cholangiocarcinoma. Added coverage criteria for Gleostine (lomustine) for the treatment of brain tumors and Hodgkin's lymphoma. Added coverage criteria for Sarclisa (isatuximab-irfc) for the treatment of multiple myeloma. Added coverage criteria for Trodelvy (sacituzumab govitecan-hziy) for the treatment of mTNBC. Removed Lartruvo (olaratumab) from policy as drug was withdrawn from the market on April 25, 2019. Changes to Kyprolis (carfilzomib) and Velcade (bortezomib) are effective for dates of service on or after October 2, 2020, following 90-day provider notification. Added coverage criteria for Velcade (bortezomib) for the treatment of multiple myeloma and mantle cell lymphoma. Added coverage criteria for Kyprolis (carfilzomib) for the treatment of multiple myeloma. Added J9177 effective 7/2/20. Added codes J9041 and J9047 effective 10/2/20. Removed code J9285 effective 7/1/20.

Date	Comments
09/01/20	Interim Review, approved August 11, 2020, effective September 1, 2020. Added coverage criteria for Blenrep (belantamab mafodotin-blmf) for the treatment of multiple myeloma. Added coverage criteria for Darzalex Faspro (daratumumab and hyaluronidase-fihj) for the treatment of multiple myeloma. Added new indications to Tazverik (tazemetostat) for the treatment of follicular lymphoma. Added new indication to Xpovio (selinexor) for the treatment of diffuse large B-cell lymphoma. Added Blincyto (blinatumomab) to policy with coverage criteria for acute lymphoblastic leukemia (ALL) effective for dates of service on or after December 3, 2020, after provider notification. Added Leukine (sargramostim) to policy with coverage criteria for AML, progenitor cell mobilization, progenitor cell transplantation, BMT failure or engraftment delayed, and H-ARS effective for dates of service on or after December 3, 2020, after provider notification. Added HCPCS J2820 and J9039.
10/01/20	Coding update. Added HCPCS code J9227.
11/01/20	Interim Review, approved October 13, 2020. Added Jakafi (ruxolitinib) for the treatment of myelofibrosis, polycythemia vera, and acute GVHD. Added Zepzelca (lurbinectedin) for the treatment of metastatic SCLC. Added Inqovi (decitabine and cedazuridine) for the treatment of MDS. Added Retevmo (selpercatinib) for the treatment of NSCLC, MTC, and thyroid cancer. Added a dose limit to Pemazyre (pemigatinib). Added Zepzelca to J3590.
01/01/21	Interim Review, approved December 8, 2020. Updated Kyprolis (carfilzomib) criteria adding in combination with daratumumab plus dexamethasone for relapsed or refractory multiple myeloma. Added new HCPCS codes C9069, J9144, J9281, and J9317 - effective 1/1/21. Added HCPCS J9280 for Jelmyto. Added Jelmyto (mitomycin) to policy with coverage criteria for LG-UTUC effective for dates of service on or after April 7, 2021, after provider notification.
02/01/21	Interim Review, approved January 12, 2021. Added Gavreto (pralsetinib) for the treatment of NSCLC, MTC, and thyroid cancer. Added Danyelza (naxitamab-gqgk) for the treatment of relapsed or refractory high-risk neuroblastoma in the bone or bone marrow. Updated Leukine (sargramostim) criteria to include in combination with Danyelza (naxitamab-gqgk) for the treatment of relapsed or refractory high-risk neuroblastoma in the bone or bone marrow. Added Onureg (azacitidine) for the treatment of AML. Added new indication to Xpovio (selinexor) for treatment of MM in combination with bortezomib and dexamethasone. Added drug name Danyelza to HCPC code J3590.
04/01/21	Coding update. Added term date to HCPC C9069 and added new HCPC code J9037.
04/07/21	Coding update. Added HCPC code J9280.
06/01/21	Interim Review, approved May 11, 2021. Added Pepaxto (melphalan flufenamide) for the treatment of MM. Added Cosela (trilaciclib) to decrease the incidence of

Date	Comments
	chemotherapy-induced myelosuppression for extensive-stage SCLC. Added new indication to Sarclisa (isatuximab-irfc) for use in combination with Kyprolis (carfilzomib) and dexamethasone for MM. Added coverage for Darzalex Faspro (daratumumab and hyaluronidase-fihj) for use in combination with bortezomib, thalidomide, and dexamethasone as first-line therapy for MM. Added new indication to Darzalex Faspro for the treatment of light chain (AL) amyloidosis. Updated criteria for Trodelvy (sacituzumab govitecan-hziy) for treatment of TNBC to include unresectable locally advanced. Added new indication to Trodelvy (sacituzumab govitecan-hziy) for the treatment of urothelial cancer.
07/01/21	Annual Review, approved June 8, 2021. Added trial and failure with Ibrance (palbociclib) or Verzenio (abemaciclib) requirement to Kisqali (ribociclib) and Kisqali Femara Co-Pack (letrozole-ribociclib). Added HCPCS C9078, C9080 and J9348.
08/01/21	Interim Review, approved July 13, 2021. Added Empliciti (elotuzumab) for the treatment of multiple myeloma. Added Yondelis (trabectedin) for the treatment of unresectable or metastatic liposarcoma or leiomyosarcoma. Added Halaven (eribulin mesylate) for the treatment of metastatic breast cancer and unresectable or metastatic liposarcoma. Added Erwinaze (asparaginase *Erwinia chrysanthemi*) as a component of a multi-agent chemotherapeutic regimen for the treatment of ALL. Added Abraxane (paclitaxel protein-bound particles) for the treatment of metastatic breast cancer, locally advanced or metastatic NSCLC, and metastatic adenocarcinoma of the pancreas. Added Arranon (nelarabine) for the treatment of T-ALL and T-LBL. Added Rylaze (asparaginase erwinia chrysanthemi (recombinant)-rywn) as a component of a multi-agent chemotherapeutic regimen for the treatment of ALL and LBL. Added Lumakras (sotorasib) for the treatment of KRAS G12C-mutated locally advanced or metastatic NSCLC. Added Truseltiq (infigratinib) for the treatment of unresectable locally advanced or metastatic cholangiocarcinoma. Policy updates for Abraxane, Arranon, Empliciti, Erwinaze, Halaven, and Yondelis are effective for dates of service on or after November 5, 2021, after provider notification. Added HCPCS codes J9019, J9176, J9179, J9261, J9264 and J9352.
10/01/21	Interim Review, approved September 14, 2021. Added Welireg (belzutifan) for treatment of adult patients with von Hippel-Lindau disease who require therapy for associated RCC, CNS hemangioblastomas, or pNET. Added a new indication to Padcev (enfortumab vedotin-ejfv) for the treatment of UC for patients ineligible for cisplatin-containing chemotherapy who have previously received one or more prior lines of therapy. Added a new indication to Darzalex Faspro (daratumumab and hyaluronidase-fihj) for the treatment of multiple myeloma in combination with pomalidomide and dexamethasone. Added a new indication to Tibsovo (ivosidenib) for the treatment of cholangiocarcinoma with an IDH1 mutation. Updated Tibsovo criteria for newly diagnosed AML to require a susceptible IDH1 mutation. Removed effective date

Date	Comments
	10/1/2020 from HCPC code J9227. Added HCPC code J9281 for Jelmyto and removed HCPC code J9280. Added HCPCS J1448 and J9247.
01/01/22	Interim Review, approved December 14, 2021. Added a new indication to Jakafi (ruxolitinib) for the treatment of chronic graft-versus-host disease. Added a new indication to Verzenio (abemaciclib) for the treatment of early breast cancer at high risk of recurrence and a Ki-67 score ≥20%. Added a new indication to Darzalex Faspro (daratumumab and hyaluronidase-fihj) for the treatment of multiple myeloma in combination with Kyprolis (carfilzomib) and dexamethasone. Added a new indication to Kyprolis (carfilzomib) for the treatment of multiple myeloma in combination with Darzalex Faspro (daratumumab and hyaluronidase-fihj) and dexamethasone. Added generic nelarabine to policy with identical coverage criteria as brand Arranon (nelarabine). Removed Pepaxto (melphalan flufenamide) from policy as drug was withdrawn from the market on October 22, 2021. Moved Padcev (enfortumab vedotin-ejfv) from Policy 5.01.540 to Policy 5.01.582 with no changes to coverage criteria. Added HCPCS J9021. Removed HCPCS J9177.
06/01/22	Interim Review, approved May 10, 2022. Added Vonjo (pacritinib) for the treatment of adults with myelofibrosis . Added Kimmtrak (tebentafusp-tebn) for the treatment of adult patients with unresectable or metastatic uveal melanoma. Added a new indication to Lynparza (olaparib) for the adjuvent treatment of adult patients with high risk early breast cancer. Updated Lynparza indication for metastatic breast cancer to include PALB2 mutation and to require cancer is HER2-negative. Removed from Kisqali (ribociclib) and Kisqali Femara Co-Pack (ribociclib – letrozole) the requirement to have previously tried and failed Ibrance (palbociclib) or Verzenio (abemaciclib). Added a note to Inrebic (fedratinib) regarding documentation of intermediate-2 or high-risk MF. Removed HCPCS code C9069.
07/01/22	Annual Review, approved June 14, 2022. Added HCPCS code C9095. Removed HCPCS code J9057 and J9247. Removed Aliqopa (copanlisib) as coverage criteria for Aliqopa are captured under Policy 5.01.592. Moved Piqray (alpelisib) from Policy 5.01.540 to Policy 5.01.592 with no changes to coverage criteria. Added coverage for Leukine (sargramostim) as second-line therapy for the treated of patients taking myelosuppressive anti-cancer regimens, at risk of severe febrile neutropenia. Added to Darzalex (daratumumab) coverage for use in combination with carfilzomib and dexamethasone in patients with relapsed or refractory MM who have received one to three prior lines of therapy. Added a new indication to Tibsovo (ivosidenib) for use in combination with azacitidine or as monotherapy for the treatment of newly diagnosed AML.
10/01/22	Coding update. Added HCPCS code J9274.
11/01/22	Interim Review, approved October 11, 2022. Updated Pemazyre (pemigatinib) criteria to include coverage for relapsed or refractory myeloid/lymphoid neoplasms (MLNs)

Date	Comments
	with FGFR1 rearrangement. Removed from Zejula (niraparib) coverage for the treatment of advanced homologous recombination deficiency (HRD) positive ovarian cancer after > 3 lines of chemotherapy, as GSK voluntarily withdrew indication. Added coverage for Elzonris (tagraxofusp-erzs) for the treatment of blastic plasmacytoid dendritic cell neoplasm (BPDCN). Added coverage for Onivyde (irinotecan liposome injection) for treatment of metastatic adenocarcinoma of the pancreas and metastatic cholangiocarcinoma. Added a new indication to Retevmo (selpercatinib) for the treatment of locally advanced or metastatic RET fusion-positive solid tumors. Added coverage for Lytgobi (futibatinib) for the treatment of intrahepatic cholangiocarcinoma. Policy updates for Onivyde and Elzonris are effective for dates of service on or after February 3, 2023, after provider notification. Added HCPCS codes J9205 and J9269.
01/01/23	Interim Review, approved December 13, 2022. Added coverage for Rezlidhia (olutasidenib) for the treatment of adult individuals with relapsed or refractory AML with a susceptible IDH1 mutation. Added coverage for Tecvayli (teclistamab -cqyv) for the treatment of adult individuals with relapsed or refractory multiple myeloma. Removed Blenrep (belantamab mafodotin-blmf) from policy as drug is being withdrawn from market by the manufacturer due to lack of efficacy in follow-up trials. Added new HCPC codes J9046, J9048, J9049. Added name Tecvayli to HCPC J3590. Removed HCPC code J9037. Removed termed codes C9078 and C9080. Removed new code date from J9021.
03/01/23	Interim Review, approved February 14, 2023. Added coverage for Krazati (adagrasib) for the treatment of KRAS G12C-mutated locally advanced or metastatic NSCLC. Updated Ibrance (palbociclib) criteria when used in combination with an aromatase inhibitor as initial endocrine-based therapy removing the requirement individual is postmenopausal. Added a new indication to Trodelvy (sacituzumab govitecan-hziy) for the treatment of unresectable locally advanced or metastatic HR+, HER2-negative breast cancer. Removed new code effective date from HCPC code J9021.
04/01/23	Coding update. Added new HCPCS code C9148.
05/01/23	Annual Review, approved April 11, 2023. Changed the wording from "patient" to "individual" throughout the policy for standardization. Reviewed prescribing information for all drugs in policy. Updated Zejula criteria to indicate coverage for the maintenance treatment of adult individuals is limited to those with deleterious or suspected deleterious germline *BRCA*-mutated recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy. Updated Verzenio criteria to indicate coverage in combination with endocrine therapy for the adjuvant treatment of adult individuals with HR-positive, HER2-negative, node-positive early breast cancer at high risk of recurrence without requiring a Ki-67 score of 20 or greater. Added coverage criteria for

Date	Comments
	Xgeva (denosumab) effective for dates of service on or after August 4, 2023, following 90-day provider notification. Added HCPC code J0897 to report Xgeva.
07/01/23	Coding update. Termed HCPCS code C9148 and added new HCPCS code J9380.
09/01/23	Interim Review, approved August 8, 2023. Added coverage criteria for Epkinly (epcoritamab-bysp) for the treatment of adult individuals with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, including DLBCL arising from indolent lymphoma, and high-grade B-cell lymphoma after two or more lines of systemic therapy. Added coverage criteria for Lynparza (olaparib) for the treatment of adult individuals with deleterious or suspected deleterious BRCA-mutated (BRCAm) metastatic castration-resistant prostate cancer (mCRPC) when used in combination with abiraterone and prednisone or prednisolone. Added coverage criteria for Talzenna, when used in combination with enzalutamide, for the treatment of adult individuals with HRR gene- mutated metastatic castration-resistant prostate cancer (mCRPC). Added generic bortezomib to the criteria of Velcade (bortezomib). Added coverage criteria for Vistogard for the emergency treatment of fluorouracil or capecitabine overdose, or severe or life-threatening toxicity within 96 hours following the end of fluorouracil or capecitabine administration. Removed Gavreto's indication of adult and pediatric patients 12 years of age and older with advanced or metastatic RET-mutant medullary thyroid cancer (MTC) who require systemic therapy per FDA label changes. Added coverage for Leukine for the treatment of pediatric individuals with high-risk neuroblastoma who achieve at least a partial response to prior first-line multiagent, multimodality therapy. Added Brand paclitaxel protein- bound particles (american regent-unbranded) IV to Abraxane criteria. Added criteria for Lysodren (mitotane) for the treatment of adrenal cortical carcinoma when the tumor is inoperable. Added criteria for Matulane (procarbazine hydrochloride) for the treatment of stage III and IV Hodgkin's disease when used in combination with other anticancer drugs. Added coverage criteria for Temodar (temozolomide) IV and generic temozolomide oral for the treatment of adult individuals with newly diagnosed glioblastoma concomitantly with radiotherapy and then as maintenance treatment, or for refractory anaplastic astrocytoma who have experienced disease progression on a drug regimen containing nitrosourea and procarbazine. Added coverage criteria for Unituxin (dinutuximab). Unituxin in combination with granulocyte-macrophage colony-stimulating factor (GM-CSF), interleukin-2 (IL-2), and 13-cis-retinoic acid (RA), for the treatment of pediatric individuals with high-risk neuroblastoma who achieve at least a partial response to prior first-line multiagent, multimodality therapy. Policy changes to Temodar IV and Unituxin IV are effective December 7, 2023. Added HCPCS codes C9399, J9259 and J9328.
10/01/23	Coding update. Added new HCPCS codes C9155 and J9051.
11/01/23	Interim Review, approved October 10, 2023. Added Talvey and Elrexfio for the treatment of adult individuals with relapsed or refractory multiple myeloma where

Date	Comments
	individual has tried at least four lines of prior therapies. Updated coverage criteria for Arranon to be included as first-line treatment when added to the ABFM regimen in intermediate to high-risk individuals or ABFM regimen induction failures. Added brand bortezomib to policy with identical coverage criteria as generic bortezomib and Velcade (bortezomib).
01/01/24	Interim Review, approved December 12, 2023. Added coverage criteria for Purixan (mercaptopurine) for the treatment of acute lymphoblastic leukemia as part of a combination chemotherapy maintenance regimen. Removed HCPCS code C9155. Added new HCPCS codes C9163, C9165, J1246 and J9321.
02/01/24	Annual Review, approved January 9, 2024. Added coverage criteria for Lonsurf (trifluridine and tipiracil) for the treatment of certain adult individuals with metastatic colorectal cancer in combination with bevacizumab. Added coverage criteria for Hepzato Kit (melphalan hepatic delivery system) for the treatment of certain adult individuals with unresectable or metastatic uveal melanoma. Added coverage criteria for Ogsiveo (nirogacestat) for the treatment of certain adult individuals with progressing desmoid tumors. Added Hepzato to C9399 and added HCPC code J9999 for Hepzato.
03/01/24	Interim Review, approved February 13, 2024. Added coverage criteria for Tabloid (thioguanine) for the treatment of certain individuals with acute myeloid leukemia. Added coverage criteria for Iwilfin (eflornithine) for the treatment of certain individuals with high-risk neuroblastoma. Added coverage criteria for oral Temodar (temozolomide) and oral generic temozolomide for the treatment of certain adult individuals with glioblastoma or anaplastic astrocytoma. Updated coverage criteria for IV Temodar (temozolomide) to include the treatment of certain adult individuals with newly diagnosed anaplastic astrocytoma. Updated coverage criteria for Tibsovo (ivosidenib) to include the treatment of certain adult individuals with myelodysplastic syndromes. Updated coverage criteria for Welireg (belzutifan) to include the treatment of certain adult individuals with renal cell carcinoma. Removed Truseltiq (infigratinib) coverage criteria as the product has been withdrawn from the market. Updated coverage criteria for Balversa (erdafitinib) to remove coverage criteria for the treatment of locally advanced or metastatic urothelial carcinoma with susceptible FGFR2 genetic alterations and broaden step therapy requirement from prior platinum-containing chemotherapy to prior systemic therapy. Added coverage criteria for Ojjaara (momelotinib) for the treatment of certain adults with myelofibrosis.
04/01/24	Coding update. Added new HCPCS codes J1323, J3055, J9248. Termed HCPCS codes C9163 and C9165.
05/01/24	Interim Review, approved April 9, 2024. Added coverage criteria for Thalomid (thalidomide). Added coverage criteria for Aphexda (motixafortide). Updated Onivyde

Date	Comments
	(irinotecan) to include coverage criteria for the first-line treatment of certain adults with metastatic pancreatic adenocarcinoma. Updated Onivyde (irinotecan) to clarify that all coverage criteria is limited to adults. Updated Ogsiveo (nirogacestat) coverage criteria to include a requirement to try generic sorafenib first. Added HCPCS code J2277.
08/01/24	Interim Review, approved July 9, 2024. Added coverage criteria for Amtagvi (lifileucel) for the treatment of certain individuals with unresectable or metastatic melanoma. Added coverage criteria for brand paclitaxel protein-bound particles (Teva – unbranded). Updated Gazyva (obinutuzumab) coverage criteria to include treatment of certain adults with follicular lymphoma in combination with zanubrutinib. Added drug name Amtagvi to unlisted HCPCS code, J3590. Added new HCPCS code J9258.
09/01/24	Interim Review, approved August 13, 2024. Added coverage criteria for Imdelltra (tarlatamab-dlle) for the treatment of certain individuals with extensive-stage small cell lung cancer (ES-SCLC). Added coverage criteria for Dacogen (decitabine) and generic decitabine for the treatment of certain individuals with myelodysplastic syndrome. Added coverage criteria for Elitek (rasburicase) for the treatment of certain individuals with leukemia, lymphoma, or solid tumor malignancies who are receiving anticancer therapy expected to result in tumor lysis. Added coverage criteria for Casodex (bicalutamide), Eulexin (flutamide), Nilandron (nilutamide), and generic nilutamide for the treatment of certain adults with prostate cancer. Added HCPCS codes J0894 & J2783.

Scope: Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.

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Language Assistance

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ATENÇÃO: Se fala português, encontram-se disponíveis serviços linguísticos, grátis. Ligue para 800-817-3056 (TTY: 711).

ATTENZIONE: In caso la lingua parlata sia l'italiano, sono disponibili servizi di assistenza linguistica gratuiti. Chiamare il numero 800-817-3056 (TTY: 711).

توجه: اگر به زبان فارسی گفتگو می کنید، تسهیلات زبانی بصورت رایگان برای شما فراهم می باشد. با 800-817-3056 (TTY: 711) تماس بگیرید.