LifeWise
Health Plan of Washington

MEDICAL POLICY – 5.01.650
Bispecific Antibodies

Effective Date:	Sep. 1, 2026	RELATED MEDICAL POLICIES:
Last Revised:	Aug. 11, 2026	N/A
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Introduction

Bispecific antibody drugs are a type of immunotherapy. Immunotherapy drugs work with the immune system and make it stronger. These drugs help the cells in the immune system find and kill cancer cells more effectively. This policy describes when certain bispecific antibody drugs may be considered 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
Bizengri (zenocutuzumab-zbco) IV	**Bizengri (zenocutuzumab-zbco) may be considered medically necessary for the treatment of adults when all the following are met:** • The individual is aged 18 years or older **AND**

Drug	Medical Necessity

	• Meets 1 of the following:
	  ○ Has been diagnosed with advanced, unresectable, or metastatic pancreatic adenocarcinoma
	OR
	  ○ Has been diagnosed with advanced, unresectable, or metastatic non-small cell lung cancer (NSCLC)
	OR
	  ○ Has been diagnosed with advanced, unresectable, or metastatic cholangiocarcinoma
	AND
	• Is harboring a neuregulin 1 (*NRG1*) gene fusion
	AND
	• Bizengri (zenocutuzumab-zbco) will be administered as monotherapy
	AND
	• Has experienced disease progression on or after prior systemic therapy
	AND
	• Dose is limited to 750 mg every 2 weeks

Blincyto (blinatumomab) IV	**Blincyto (blinatumomab) may be considered medically necessary for the treatment of individuals when all the following are met:**
	• The individual is aged 1 month or older
	AND
	• Meets 1 of the following:
	  ○ CD19-positive 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%
	OR
	  ○ Relapsed or refractory CD-19-positive B-cell precursor ALL
	OR
	  ○ CD19-positive B-cell precursor ALL in the consolidation phase of multiphase chemotherapy
	OR
	  ○ Standard or high-risk B-cell ALL in individuals aged less than 18 years

Drug	Medical Necessity
Columvi (glofitamab-gxbm) IV	**Columvi (glofitamab-gxbm) may be considered medically necessary for the treatment of relapsed or refractory diffuse large B-cell lymphoma, not otherwise specified (DLBCL, NOS) or large B-cell lymphoma (LBCL) arising from follicular lymphoma when all the following criteria are met:** • The individual is aged 18 years or older **AND** • Has been diagnosed with relapsed or refractory DLBCL, NOS or LBCL arising from follicular lymphoma **AND** • Has had an inadequate response to 2 or more lines of systemic therapy **AND** • Documentation of pretreatment with a single 1,000 mg dose of obinutuzumab intravenously 7 days before initiation of Columvi

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:**
	• The individual is aged 18 years or older
	AND
	• Has been diagnosed with relapsed or refractory multiple myeloma
	AND
	• Has received at least 4 prior lines of therapy including:
	  ○ A proteasome inhibitor (e.g., bortezomib, carfilzomib, ixazomib)
	  ○ An immunomodulatory agent (e.g., lenalidomide, pomalidomide, thalidomide)
	  ○ An anti-CD38 monoclonal antibody (e.g., daratumumab, isatuximab-irfc)

Epkinly (epcoritamab-bysp) SC	**Epkinly (epcoritamab-bysp) may be considered medically necessary for the treatment of relapsed or refractory diffuse large B-cell lymphoma (DLBCL) when all the following criteria are met:** • The individual is aged 18 years and older **AND**

Drug	Medical Necessity

	• Has been diagnosed with relapsed or refractory DLBCL, not otherwise specified, including DLBCL arising from indolent lymphoma, and high-grade B-cell lymphoma
	AND
	• Has received two or more lines of systemic therapy
	
	Epkinly (epcoritamab-bysp) may be considered medically necessary for the treatment of relapsed and refractory follicular lymphoma (FL) when all the following criteria are met:
	• The individual is aged 18 years or older
	AND
	• Has been diagnosed with relapsed and refractory FL
	AND
	• Meets 1 of the following:
	  ○ Epkinly (epcoritamab-bysp) is used in combination with lenalidomide and rituximab
	  OR
	  ○ Used as monotherapy after 2 or more lines of systemic therapy

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 aged 18 years or older **AND** • Has been diagnosed with relapsed or refractory ES-SCLC **AND** • Has had progression on or after treatment with platinum-based chemotherapy (e.g., cisplatin and carboplatin) **AND** • Imdelltra (tarlatamab-dlle) is prescribed by or in consultation with an oncologist
Lynozyfic (linvoseltamab-gcpt) IV	**Lynozyfic (linvoseltamab-gcpt) may be considered medically necessary for the treatment of relapsed or refractory multiple myeloma when all the following criteria are met:** • The individual is aged 18 years or older

Drug	Medical Necessity

	AND
	• Has been diagnosed with relapsed or refractory multiple myeloma
	AND
	• Has received at least 4 prior lines of therapy including:
	  ○ A proteasome inhibitor (e.g., bortezomib, carfilzomib, ixazomib)
	  ○ An immunomodulatory agent (e.g., lenalidomide, pomalidomide, thalidomide)
	  ○ An anti-CD38 monoclonal antibody (e.g., daratumumab, isatuximab-irfc)

Lunsumio (mosunetuzumab-axgb) IV	**Lunsumio (mosunetuzumab-axgb) may be considered medically necessary for the treatment of relapsed or refractory follicular lymphoma (FL) when all the following criteria are met:** • The individual is aged 18 years or older **AND** • Has been diagnosed with relapsed or refractory FL **AND** • Has had an inadequate response or intolerance to 2 or more lines of systemic therapy
Lunsumio Velo (mosunetuzumab-axgb) SC	**Lunsumio Velo (mosunetuzumab-axgb) may be considered medically necessary for the treatment of relapsed or refractory follicular lymphoma (FL) when all the following criteria are met:** • The individual is aged 18 years or older **AND** • Has been diagnosed with relapsed or refractory FL **AND** • Has had an inadequate response or intolerance to 2 or more lines of systemic therapy
Rybrevant (amivantamab-vmjw) IV	**Rybrevant (amivantamab-vmjw) may be considered medically necessary for non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 20 insertion mutations when all the following criteria are met:** • The individual is aged 18 years or older **AND**

Drug	Medical Necessity

	• Has been diagnosed with locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations
	AND
	• Meets 1 of the following:
	  ○ Disease has progressed on or after platinum-based (e.g., cisplatin, carboplatin, oxaliplatin) chemotherapy, and Rybrevant (amivantamab-vmjw) is given as a single agent
	  OR
	  ○ Rybrevant (amivantamab-vmjw) will be first-line treatment used in combination with carboplatin and pemetrexed
	AND
	• The maintenance dose is limited to:
	  ○ 1,400 mg every 2 weeks if given as a single agent
	  ○ 2,100 mg every 3 weeks if given in combination with chemotherapy
	
	Rybrevant (amivantamab-vmjw) may be considered medically necessary for non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R substitution mutations when all the following criteria are met:
	• The individual is aged 18 years or older
	AND
	• Has been diagnosed with locally advanced or metastatic NSCLC with EGFR exon 19 deletions or exon 21 L858R substitution mutations
	AND
	• Meets 1 of the following:
	  ○ Disease has progressed on or after treatment with an EGFR tyrosine kinase inhibitor and Rybrevant (amivantamab-vmjw) will be used in combination with carboplatin and pemetrexed
	  OR
	  ○ Rybrevant (amivantamab-vmjw) will be used as first-line treatment in combination with Lazcluze (lazertinib)
	AND

Drug	Medical Necessity

	• The maintenance dose is limited to:
	  ○ 1,400 mg every 2 weeks if given in combination with Lazcluze (lazertinib)
	  ○ 2,100 mg every 3 weeks if given in combination with chemotherapy

Rybrevant Faspro (amivantamab and hyaluronidase-lpuj) SC	**Rybrevant Faspro (amivantamab and hyaluronidase-lpuj) may be considered medically necessary for non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 20 insertion mutations when all the following criteria are met:**
	• The individual is aged 18 years or older
	AND
	• Has been diagnosed with locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations
	AND
	• Meets 1 of the following:
	  ○ Disease has progressed on or after platinum-based (e.g., cisplatin, carboplatin, oxaliplatin) chemotherapy, and Rybrevant Faspro (amivantamab and hyaluronidase-lpuj) will be used as a single agent
	  OR
	  ○ Rybrevant Faspro (amivantamab and hyaluronidase-lpuj) will be first-line treatment used in combination with carboplatin and pemetrexed
	AND
	• The maintenance dose is limited to:
	  ○ 2,240 mg amivantamab every 2 weeks or 4,640 mg amivantamab every 4 weeks if given as a single agent
	  ○ 3,360 mg amivantamab every 3 weeks if given in combination with chemotherapy
	
	Rybrevant Faspro (amivantamab and hyaluronidase-lpuj) may be considered medically necessary for non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R substitution mutations when all the following criteria are met:
	• The individual is aged 18 years or older

Drug	Medical Necessity

	AND
	• Has been diagnosed with locally advanced or metastatic NSCLC with EGFR exon 19 deletions or exon 21 L858R substitution mutations
	AND
	• Meets 1 of the following:
	  ○ Disease has progressed on or after treatment with an EGFR tyrosine kinase inhibitor and Rybrevant Faspro (amivantamab and hyaluronidase-lpuj) will be used in combination with carboplatin and pemetrexed
	  OR
	  ○ Rybrevant Faspro (amivantamab and hyaluronidase-lpuj) will be used as first-line treatment in combination with Lazcluze (lazertinib)
	AND
	• The maintenance dose is limited to:
	  ○ 2,240 mg amivantamab every 2 weeks or 4,640 mg amivantamab every 4 weeks if given in combination with Lazcluze (lazertinib)
	  ○ 3,360 mg amivantamab every 3 weeks if given in combination with chemotherapy

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:**
	• The individual is aged 18 years or older
	AND
	• Has been diagnosed with relapsed or refractory multiple myeloma
	AND
	• Has received at least 4 prior lines of therapy including:
	  ○ A proteasome inhibitor (e.g., bortezomib, carfilzomib, ixazomib)
	  ○ An immunomodulatory agent (e.g., lenalidomide, pomalidomide, thalidomide)
	  ○ An anti-CD38 monoclonal antibody (e.g., daratumumab, isatuximab-irfc)

Drug	Medical Necessity
Tecvayli (teclistamab-cqyv) SC	**Tecvayli (teclistamab-cqyv) may be considered medically necessary for the treatment of relapsed or refractory multiple myeloma when all the following criteria are met:** • The individual is aged 18 years or older **AND** • Has been diagnosed with relapsed or refractory multiple myeloma **AND** • Meets 1 of the following: ○ Have received at least 1 prior line of therapy including a proteasome inhibitor (e.g., bortezomib, carfilzomib, ixazomib) and an immunomodulatory agent (e.g., lenalidomide, pomalidomide, thalidomide), and Tecvayli (teclistamab-cqyv) is used in combination with daratumumab hyaluronidase-fihj **OR** ○ Has received at least 4 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), and Tecvayli (teclistamab-cqyv) is given as monotherapy
Ziihera (zanidatamab-hrii) IV	**Ziihera (zanidatamab-hrii) may be considered medically necessary for the treatment of adults with biliary tract cancer (BTC) when all the following are met:** • The individual is aged 18 years or older **AND** • Has been diagnosed with unresectable or metastatic HER2-positive (IHC 3+ or ISH+) BTC **AND** • Has been previously treated **AND** • Ziihera (zanidatamab-hrii) will be administered as monotherapy **AND** • Ziihera (zanidatamab-hrii) is prescribed by or in consultation with an oncologist **AND**

Drug	Medical Necessity
	• Dose is limited to 20 mg/kg every 2 weeks

Drug	Investigational
As listed	**Use of Rybrevant (amivantamab-vmjw) to treat other types of solid tumors and hematological malignancies not listed above is considered investigational.** **All other uses of the medications listed in this policy are considered investigational.** **The medications listed in this policy are subject to the product's US Food and Drug Administration (FDA) dosage and administration prescribing information.**

Length of Approval	
Approval	**Criteria**
Initial authorization	**All drugs listed in the policy may be approved up to 6 months.**
Re-authorization criteria	**All drugs listed in the 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	

Code	Description
C9307	Injection, linvosel tamab-gcpt, 1 mg (code termed 04/01/26)
J1323	Injection, elranatamab-bcmm (Elrexfio), 1 mg
J3055	Injection, talquetamab-tgvs (Talvey), 0.25 mg
J9026	Injection, tarlatamab-dlle (Imdelltra), 1 mg
J9039	Injection, blinatumomab (Blincyto), 1 mcg
J9061	Injection, amivantamab-vmjw, (Rybrevant), 2 mg
J9062	Injection, amivantamab 5 mg and hyaluronidase-lpuj (Rybrevant Faspro) (new code effective 07/01/26)
J9276	Injection, zanidatamab-hrii (Ziihera), 2 mg
J9286	Injection, glofitamab-gxbm (Columvi), 2.5 mg
J9321	Injection, epcoritamab-bysp (Epkinly), 0.16 mg
J9350	Injection, mosunetuzumab-axgb (Lunsumio, Lunsumio Velo), 1 mg
J9380	Injection, teclistamab-cqyv (Tecvayli), 0.5 mg
J9382	Injection, zenocutuzumab-zbco (Bizengri), 1 mg
J9601	Injection, linvoseltamab-gcpt, (Lynozyfic), 1 mg (new code effective 04/01/26)
J9999	Not otherwise classified, antineoplastic drugs (use to report: Rybrevant Faspro)

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 FDA-approved indications, where applicable.

Benefit Application

The drugs in this policy are managed through the medical benefit.

Evidence Review

Bizengri (zenocutuzumab-zbco)

Bizengri's approval is supported by results from the Phase 1/2 eNRGy trial (NCT02912949), a multicenter, open-label study that included 64 individuals with NRG1+ non-small cell lung cancer (NSCLC) and 30 individuals with NRG1+ PDAC. All study participants had disease progression following standard-of-care (SOC) treatment. Trial results demonstrated a 33% overall response rate (ORR) in individuals with NSCLC and 40% in individuals with pancreatic adenocarcinoma (PDAC), with a median duration of response (DOR) of 7.4 months in NSCLC and a range of 3.7 to 16.6 months in PDAC. In the pooled safety population, the most common adverse reactions (ARs) (≥10%) were diarrhea, musculoskeletal pain, fatigue, nausea, infusion-related reactions, dyspnea, rash, constipation, vomiting, abdominal pain, and edema. The most common Grade 3 or 4 laboratory abnormalities (≥10%) were increased gamma-glutamyl transferase, decreased hemoglobin, decreased sodium, and decreased platelets. The prescribing information includes a Boxed Warning for embryo-fetal toxicity.

The efficacy of Bizengri was evaluated in the eNRGy study (NCT02912949), a multicenter, open-label, multi-cohort clinical study. The study enrolled adult individuals with advanced, unresectable or metastatic NRG1 fusion-positive cholangiocarcinoma. Identification of an NRG1 gene fusion was prospectively determined in local laboratories using next generation sequencing (NGS). Individuals received Bizengri as an intravenous infusion, 750 mg every 2 weeks, until unacceptable toxicity or disease progression. Tumor assessments were performed every 8 weeks. The major efficacy outcome measures were overall response rate (ORR) and duration of response (DOR), and individuals in the trial achieved an ORR of 36.8% and a DOR ranging from 2.8 to 12.9 months. Serious side effects associated with Bizengri include infusion-related reactions, interstitial lung disease/pneumonitis, and left ventricular dysfunction.

Columvi (glofitamab-gxbm)

The efficacy of Columvi (glofitamab-gxbm) was evaluated in an open-label, multicenter, multicohort, single-arm clinical trial which included 132 individuals with relapsed or refractory large B-cell lymphoma (LBCL) after two or more lines of systemic therapy. The inclusion criteria required individuals to have ECOG performance status of 0 or 1, absolute neutrophil count greater than or equal to 1500/µL, platelet count greater than or equal to 75,000 /µL independent of transfusion, serum creatinine less than or equal to 1.5 x ULN or CLcr greater than or equal to 50 ml/min, hepatic transaminases less than or equal to 3 x ULN. The individuals required to have pretreatment with Obinutuzumab on Cycle 1 Day 1.

The primary efficacy endpoint was objective response rate (ORR) and duration of response (DOR). The overall response rate was 56% for the Columvi group, where 43% individuals had complete response and 13% individuals had partial response. Out of 74 individuals with overall response, median duration of response was 18.4 months.

The most common adverse effects included cytokine release syndrome, musculoskeletal pain, rash and fatigue. The most common Grade 3 to 4 laboratory abnormalities are reduced lymphocyte counts, reduced phosphate level, reduced neutrophil count, increased uric acid and reduced fibrinogen. Treatment related adverse events which led to permanent discontinuation in the Columvi group included infection, delirium, neutropenia, and CRS. Also, adverse events which led to dose interruption included neutropenia and thrombocytopenia.

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)

The Phase 1/2 EPCORE NHL-1/Study GCT3013-01 (NCT03625037) trial was an open-label, multicohort, multicenter, single-arm study involving individuals with relapsed or refractory (R/R) B-cell lymphoma. The efficacy population included 148 individuals with DLBCL, not otherwise specified (NOS), including DLBCL arising from indolent lymphoma, and high-grade B-cell lymphoma. The study excluded individuals with central nervous system (CNS) involvement of lymphoma, allogeneic hematopoietic stem cell transplant (HSCT) or solid organ transplant, or ongoing active infection, and any individuals with known impaired T-cell immunity. Individuals received Epkinly subcutaneously (SC) with Cycle 1 step-up dosing consisting of a 0.16 mg priming dose once on Day 1, followed by an 0.8 mg intermediate dose once on Day 8, and subsequent full 48 mg doses once on Day 15 and Day 22. Cycles were every 28 days. On Cycles 2 and 3, individuals received 48 mg on Days 1, 8, 15, and 22. On Cycles 4–9, individuals received 48 mg on Days 1 and 15. From Cycle 10 and beyond, individuals received 48 mg once every 28 days. Individuals continued to receive Epkinly until disease progression or unacceptable toxicity. In the setting of a suspected tumor flare reaction, continued treatment was permitted. The primary efficacy measure of the study was the overall response rate (ORR) assessed according to the Lugano 2014 criteria by an independent review committee. The ORR was determined to be 61% (95% CI: 53, 69), with 38% of individuals achieving complete responses. Among responders, with a median follow-up of 9.8 months, the estimated median duration of response (DOR) was 15.6 months (95% confidence interval [CI]: 9.7, not reached). The median time to response was 1.4 months (range: 1.0 to 8.4 months). Among responders, the median follow-up for DOR was 9.8 months (range: 0.0 to 17.3 months). The prescribing information has a Boxed Warning for

serious or life-threatening cytokine release syndrome (CRS) and life-threatening or fatal immune effector cell-associated neurotoxicity syndrome (ICANS). Warnings and precautions include infections and cytopenias. In the full EPCORE NHL-1 clinical trial involving 157 individuals with R/R large B-cell lymphoma who received Epkinly at the recommended dose, CRS occurred in 51% of individuals, ICANS in 6%, and serious infections in 15%. It is emphasized that Epkinly should only be administered by a qualified healthcare professional with appropriate medical support to manage severe reactions such as CRS and ICANS. Due to the risk of these reactions, individuals should be hospitalized for 24 hours following the Cycle 1, Day 15 dosage of 48 mg. The most frequently reported adverse reactions associated with Epkinly include CRS, fatigue, musculoskeletal pain, injection site reactions, fever, abdominal pain, nausea, and diarrhea. The most common Grade 3 to 4 laboratory abnormalities observed were decreased lymphocyte count, decreased neutrophil count, decreased white blood cell count, decreased hemoglobin, and decreased platelets.

The efficacy of EPKINLY in combination with lenalidomide and rituximab was evaluated in EPCORE FL-1 (Study M20-638; NCT05409066), an open-label, randomized, multicenter, global trial in individuals with relapsed or refractory FL after at least one line of systemic therapy. Individuals were randomized to receive EPKINLY in combination with lenalidomide and rituximab, or lenalidomide and rituximab alone. The study excluded individuals with known CNS involvement by lymphoma, prior allograft, and known active infection. Individuals received EPKINLY via subcutaneous injection in 28-day cycles for a total of 12 cycles or until disease progression or unacceptable toxicity, whichever occurred first. Efficacy was established based on progression free survival (PFS) and overall response rate (ORR) as assessed by Independent Review Committee (IRC) using Lugano 2014 criteria. Median progression-free survival (PFS) was not reached (NR) among individuals treated with EPKINLY plus lenalidomide and rituximab (95% CI: 21.9-NR) compared to 11.2 months for individuals treated with lenalidomide and rituximab (95% CI: 10.5-NR). Among individuals who were treated with EPKINLY plus lenalidomide and rituximab, 89% responded to treatment (n=216/243, 95% CI: 84-93, $p<0.0001$) and 74% achieved a complete response (CR) (n=181/243, 95% CI: 69-80). This is compared to a 74% overall response rate (n=181/245, 95% CI: 68-79) and 43% CR rate among individuals treated with lenalidomide and rituximab (n=106/245, 95% CI: 37-50). The most common (≥ 20%) adverse reactions in individuals who received EPKINLY plus lenalidomide and rituximab were rash, upper respiratory tract infections, fatigue, injection site reactions, constipation, diarrhea, cytokine release syndrome (CRS), pneumonia, COVID-19, and fever. The most common Grade 3 to 4 laboratory abnormalities (≥ 10%) were decreased neutrophil count, lymphocyte count, and platelets. CRS occurred in 24% of individuals at the recommended 3 step-up dosing schedule, and was primarily low grade (19% Grade 1, 5% Grade 2). A single event of immune effector cell-associated neurotoxicity syndrome (ICANS) occurred in one individual, grade 1 (0.8%). The

prescribing information has a Boxed Warning for serious or fatal CRS and ICANS. Warnings and precautions include infections, cytopenias, and embryo-fetal toxicity.

Imdelltra (tarlatamab-dlle)

The efficacy of IMDELLTRA was evaluated in DeLLphi-304 (NCT05740566), a multicenter, randomized, open-label trial. Eligible individuals were required to have SCLC with disease progression following treatment with platinum-based chemotherapy with or without an anti-PD-(L)1 antibody. Individuals were required to have an ECOG Performance Status of 0 or 1 and at least one measurable lesion per Response Evaluation Criteria in Solid Tumors (RECIST v1.1). Individuals with symptomatic brain metastases or active immunodeficiency were ineligible. The global Phase III DeLLphi-304 study met its primary endpoint, demonstrating that IMDELLTRA reduced the risk of death by 40% and significantly extended median overall survival (OS) by more than five months compared to standard of care (SOC) chemotherapy as a treatment for individuals with ES-SCLC who progressed on or after one line of platinum-based chemotherapy (median OS: 13.6 vs. 8.3 months; hazard ratio (HR), 0.60; 95% confidence interval (CI): 0.47, 0.77; $P < 0.001$). 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.

Lunsumio (mosunetuzumab-axgb)

Lunsumio (mosunetuzumab-axgb) is a T-cell engaging bispecific antibody that binds to the CD3 receptor expressed on the surface of T-cells and CD20 expressed on the surface of lymphoma cells and some healthy B-lineage cells. In vitro, mosunetuzumab-axgb activated T-cells, caused the release of proinflammatory cytokines, and induced lysis of B-cells.

The efficacy of Lunsumio (mosunetuzumab-axgb) was evaluated in an open-label, multicenter, multi-cohort study (GO29781, NCT02500407) in individuals with relapsed or refractory follicular lymphoma (FL) who had received at least two prior therapies, including an anti-CD20 monoclonal antibody and an alkylating agent. The study excluded individuals with active infections, history of autoimmune disease, prior allogeneic transplant, or any history of CNS lymphoma or CNS disorders.

Individuals received step-up doses of 1 mg on Cycle 1 Day 1 and 2 mg on Cycle 1 Day 8, followed by 60 mg on Cycle 1 Day 15, and 60 mg on Cycle 2 Day 1, then 30 mg every 3 weeks in

subsequent cycles. The treatment cycle was 21 days. Lunsumio was administered for 8 cycles unless individuals experienced progressive disease or unacceptable toxicity. After 8 cycles, individuals with a complete response discontinued therapy; individuals with a partial response or stable disease continued treatment up to 17 cycles, unless individuals experienced progressive disease or unacceptable toxicity.

Among the 90 individuals with relapsed or refractory FL, the median age was 60 years (range: 29 to 90 years), 33% were 65 years of age or older, 61% were male, 82% were White, 9% were Asian, 4% were Black or African American, and 8% were Hispanic or Latino. A total of 77% of individuals had Stage III-IV disease, 34% had bulky disease, and all individuals had an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1. The median number of prior therapies was 3 (range: 2 to 10), with 38% receiving 2 prior therapies, 31% receiving 3 prior therapies, and 31% receiving more than 3 prior therapies.

Seventy-nine percent of individuals were refractory to prior anti-CD20 monoclonal antibody therapy, 53% were refractory to both anti-CD20 monoclonal antibody and alkylator therapy, 9% received prior rituximab plus lenalidomide therapy, 21% received prior autologous stem cell transplant, and 3% received prior CAR T therapy. Fifty-two percent of individuals had progression of disease within 24 months of first systemic therapy.

Efficacy was established based on objective response rate (ORR) and duration of response (DOR) as assessed by an independent review facility according to standard criteria for NHL (Cheson 2007). The median follow-up for DOR was 14.9 months. The ORR was achieved in 80% (95% CI: 70%, 88%) of individuals and the median DOR was 22.8 months (95% CI: 10 months, not reached).

Lynozyfic (linvoseltamab-gcpt)

Lynozyfic (linvoseltamab-gcpt) is a bispecific T-cell engaging antibody that binds to the CD3 receptor expressed on the surface of T-cells and B-cell maturation antigen (BCMA) expressed on the surface of multiple myeloma cells and some healthy B-lineage cells. In vitro, Lynozyfic activated T-cells, caused the release of various proinflammatory cytokines, and resulted in the lysis of multiple myeloma cells.

Efficacy was evaluated in LINKER-MM1, an open-label, multi-center multicohort trial. The trial included individuals who had previously received at least 3 prior therapies, including a proteasome inhibitor (PI), an immunomodulatory agent, and an anti-CD38 monoclonal antibody. The trial excluded individuals with prior BCMA-directed bispecific antibody therapy, prior bispecific T-cell engaging therapy, or prior BCMA CAR-T cell therapy. The efficacy population

included 80 individuals who had received at least 4 prior lines of therapy, including a PI, an immunomodulatory agent, and an anti-CD38 monoclonal antibody. Efficacy was based on objective response rate (ORR) determined by a blinded independent review committee using International Myeloma Working Group criteria. The ORR was 70% (95% CI: 59, 80). With a median follow-up of 11.3 months among responders, the estimated duration of response (DOR) was 89% (95% CI: 77, 95) at 9 months and 72% (95% CI: 54, 84) at 12 months.

Due to the risks of cytokine release syndrome (CRS) and neurologic toxicity, including immune effector cell-associated neurotoxicity syndrome (ICANS), Lynozyfic is only available through the Lynozyfic Risk Evaluation and Mitigation Strategy (REMS). In the LINKER-MM1 trial, CRS occurred in 46% of individuals who received Lynozyfic, and neurologic toxicity, including ICANS, occurred in 54%. The most common adverse reactions (20%) are musculoskeletal pain, CRS, cough, upper respiratory tract infection, diarrhea, fatigue, pneumonia, nausea, headache, and dyspnea. The most common Grade 3 or 4 laboratory abnormalities (30%) are decreased lymphocyte count, decreased neutrophil count, decreased hemoglobin, and decreased white blood cell count.

Rybrevant (amivantamab-vmjw)

Rybrevant (amivantamab-vmjw) is a bispecific antibody that binds to the extracellular domains of EGFR and MET. In vitro and in vivo studies amivantamab-vmjw was able to disrupt EGFR and MET signaling functions through blocking ligand binding and, in exon 20 insertion mutation models, degradation of EGFR and MET. The presence of EGFR and MET on the surface of tumor cells also allows for targeting of these cells for destruction by immune effector cells, such as natural killer cells and macrophages, through antibody-dependent cellular cytotoxicity (ADCC) and trogocytosis mechanisms, respectively.

The efficacy of Rybrevant was evaluated in individuals with locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations in a multicenter, open-label, multi-cohort clinical trial (CHRYSALIS, NCT02609776). The study included individuals with locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations whose disease had progressed on or after platinum-based chemotherapy. Individuals with untreated brain metastases and individuals with a history of interstitial lung disease requiring treatment with prolonged steroids or other immunosuppressive agents within the last 2 years were not eligible for the study.

In the efficacy population, EGFR exon 20 insertion mutation status was determined by prospective local testing using tissue (94%) and/or plasma (6%) samples. Of the 81 individuals with EGFR exon 20 insertion mutations, plasma samples from 96% of individuals were tested

retrospectively using Guardant360 CDx. While 76% of individuals had an EGFR exon 20 insertion mutation identified in plasma specimen, 20% did not have an EGFR exon 20 insertion mutation identified in plasma specimen, and 3.7% did not have plasma samples for testing. The overall response rate was 40% with 3.7% of participants having a complete response and 36% of participants with a partial response.

The efficacy of Rybrevant in combination with carboplatin and pemetrexed was evaluated in individuals with locally advanced or metastatic NSCLC with EGFR exon 19 deletions or exon 21 L858 that progressed after receiving treatment with Tagrisso (osimertinib) in a randomized, open-label, multicenter trial (MARIPOSA-1). Individuals with asymptomatic or previously treated and stable intracranial metastases were eligible to enroll. A total of 394 individuals were randomized between the two arms, 131 to the Rybrevant in combination with carboplatin and pemetrexed arm and 263 to the carboplatin and pemetrexed arm.

In the efficacy population, 45% had history of brain metastasis, and 99.7% had Stage IV cancer at study enrollment. The trial demonstrated a statistically significant improvement in PFS for Rybrevant in combination with carboplatin and pemetrexed compared to carboplatin and pemetrexed. HR (95% CI); p-value: 0.48 (036,0.64); p<0.0001.

The efficacy of Rybrevant in combination with Lazcluze (lazertinib) was evaluated in individuals with untreated locally advanced or metastatic NSCLC with either exon 19 deletions or exon 21 L858R substitution EGFR mutations was evaluated in a multicenter, randomized, active-controlled trial (MARIPOSA-2). The study also included individuals with asymptomatic or previously treated and stable intracranial metastases. A total of 858 individuals were randomized between the two study arms, 429 to the Rybrevant in combination with Lazertinib and 429 to the Osimertinib monotherapy arm.

In the efficacy population, 60% of individuals had tumors harboring exon 19 deletions and the remaining 40% had exon 21 L858R substitution mutations, 41% had prior brain metastases; and 89% had Stage IV cancer at initial diagnosis. The trial demonstrated a statistically significant improvement in progression-free survival (PFS) for Rybrevant in combination with lazertinib compared to Osimertinib. HR (95% CI); p-value: 0.70 (0.58, 0.85); p=0.0002.

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 lead 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.

Ziihera (zanidatamab-hrii)

The FDA approval of Ziihera is based on results from the Phase 2b HERIZON-BTC-01 (NCT04466891) trial, which evaluated the drug as a single agent in previously treated, HER2-positive BTC (as determined by Roche Diagnostics' PATHWAY anti-HER-2/neu (4B5) Rabbit Monoclonal Primary Antibody companion diagnostic). The trial achieved its primary endpoint of confirmed ORR (cORR) by independent central review (ICR). Individuals with HER2-amplified, locally advanced unresectable or metastatic BTC (including GBC, ICC, and ECC) were enrolled and assigned into cohorts based on tumor IHC score by central assessment: Cohort 1 included individuals who were IHC 2+ or 3+ (HER2 positive) and Cohort 2 included individuals who were IHC 0 or 1+ (HER2 negative and HER2 low, respectively). The trial evaluated Ziihera at a dose of 20 mg/kg, administered intravenously every 2 weeks in individuals who had received at least one prior gemcitabine-based systemic chemotherapy regimen and had adequate cardiac function (defined as left ventricular ejection fraction [LVEF] ≥50%). No responses were observed in Cohort 2 (IHC 0 or 1+), while significant clinical benefit was demonstrated in Cohort 1. Among the 62 individuals evaluated with HER2-positive (IHC 3+) BTC, Ziihera demonstrated an ORR of

52% (95% CI: 39, 65) with an estimated median DOR of 14.9 months (95% CI: 7.4−not estimable) by ICR. The safety profile of Ziihera was evaluated in 80 individuals in the HERIZON-BTC-01 trial. Serious adverse reactions (SARs) occurred in 53% of individuals who received Ziihera. The most common adverse reactions (ARs) in individuals who received Ziihera (≥20%) were diarrhea, infusion-related reaction (IRR), abdominal pain, and fatigue. SARs in >2% of individuals included biliary obstruction (15%), biliary tract infection (8%), sepsis (8%), pneumonia (5%), diarrhea (3.8%), gastric obstruction (3.8%), and fatigue (2.5%). A fatal adverse reaction of hepatic failure occurred in one individual who received Ziihera. Permanent discontinuation due to an adverse reaction occurred in 2.5% of individuals who received Ziihera.

References

1. Bizengri (zenocutuzumab-zbco). Prescribing information. Lexington, MA; Partner Therapeutics, Inc. Revised May 2026.
2. Blincyto (blinatumomab). Prescribing information. Thousand Oaks, CA; Amgen Inc. Revised October 2025.
3. Columvi (glofitamab-gxbm). Prescribing Information. South San Francisco, CA; Genentech, Inc. Revised October 2025.
4. Elrexfio (elranatamab-bcmm). Prescribing information. New York, NY; Pfizer Inc. Revised February 2026.
5. Epkinly (epcoritamab-bysp). Prescribing Information. Plainsboro, NJ; Genmab US, Inc. Revised November 2025.
6. Imdelltra (tarlatamab-dlle). Prescribing information. Thousand Oaks, CA; Amgen, Inc. Revised November 2025.
7. Lunsumio (mosunetuzumab-axgb). Prescribing Information. South San Francisco, CA. Genentech, Inc. Revised December 2025.
8. Lunsumio Velo (mosunetuzumab-axgb). Prescribing Information. South San Francisco, CA. Genentech, Inc. Revised December 2025.
9. Lynozyfic (linvoseltamab-gcpt). Prescribing Information. Tarrytown, NY; Regeneron Pharmaceuticals, Inc. Revised July 2025.
10. Rybrevant (amivantamab-vmjw). Prescribing Information. Horsham, PA: Janssen Biotech, Inc; Revised November 2025.
11. Rybrevant Faspro (amivantamab and hyaluronidase-lpuj). Prescribing Information. Janssen Biotech, Inc.; Horsham, PA. Revised February 2026.
12. Talvey (talquetamab-tgvs). Prescribing information. Horsham, PA; Janssen Biotech. Revised October 2025.
13. Tecvayli (teclistamab-cqyv). Prescribing information. Horsham, PA; Janssen Biotech, Inc. Revised March 2026.
14. Ziihera (zanidatamab-hrii). Prescribing information. Palo Alto, CA; Jazz Pharmaceuticals, Inc. Revised November 2024.
15. Falchi L, et al. Epcoritamab, lenalidomide, and rituximab versus lenalidomide and rituximab for relapsed or refractory follicular lymphoma (EPCORE FL-1): a global, open-label, randomised, phase 3 trial. Lancet. 2025 Dec 7:S0140-6736(25)02360-8. doi: 10.1016/S0140-6736(25)02360-8.
16. Mountzios G, et al. Tarlatamab in Small-Cell Lung Cancer after Platinum-Based Chemotherapy. N Engl J Med. 2025 Jul 24;393(4):349-361. doi: 10.1056/NEJMoa2502099. Epub 2025 Jun 2.

History

Date	Comments
05/01/25	New policy, approved April 8, 2025. Moved Rybrevant (amivantamab-vmjw) from policy 5.01.603 Epidermal Growth Factor Receptor (EGFR) Inhibitors to policy 5.01.650 Bispecific Antibodies. Moved Columvi (glofitamab-gxbm), Epkinly (epcoritamab-bysp), Lunsumio (mosunetuzumab-axgb) from policy 2.03.502 Monoclonal Antibodies for the Treatment of Lymphoma to policy 5.01.650 Bispecific Antibodies. Moved Blincyto (blinatumomab), Elrexfio (elranatamab-bcmm), Imdelltra (tarlatamab-dlle), Talvey (talquetamab-tgvs), and Tecvayli (teclistamab-cqyv) from policy 5.01.540 Miscellaneous Oncology Drugs to policy 5.01.650 Bispecific Antibodies. Added coverage criteria for Bizengri (zenocutuzumab-zbco). Added coverage criteria for Ziihera (zanidatamab-hrii). Updated Blincyto (blinatumomab) coverage criteria to include treatment of standard or high-risk B-cell ALL in pediatric individuals. Added HCPCS codes J1323, J3055, J9026, J9039, J9061, J9286, J9321, J9350, J9380, J9999.
07/01/25	Coding update. Added new HCPCS codes J9276 (Ziihera) and J9382 (Bizengri) due to quarterly coding update.
09/01/25	Interim Review, approved August 12, 2025. Added coverage criteria for Lynozyfic (linvoseltamab-gcpt) for the treatment of relapsed or refractory multiple myeloma. Added Unspecified HCPCS code J9999 for Lynozyfic.
01/01/26	Coding update. Added new HCPCS code C9307, effective January 1, 2026.
02/01/26	Interim Review, approved January 13, 2026. Updated coverage criteria for Epkinly with new indication in combination with lenalidomide and rituximab for the treatment of adult patients with relapsed or refractory follicular lymphoma (FL). Updated coverage criteria for Bizengri (zenocutuzumab-zbco) removing requirement for an ECOG performance status of 0 or 1. Updated coverage criteria for Ziihera (zanidatamab-hrii) for treatment of BTC HER2-positive (IHC 3+ or ISH+).
04/01/26	Annual Review, approved March 10, 2026. Added coverage criteria for Lunsumio Velo (mosunetuzumab-axgb) SC for the treatment of relapsed or refractory follicular lymphoma. Added coverage criteria for Rybrevant Faspro (amivantamab and hyaluronidase-lpuj) SC for the treatment of locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations, and the treatment of locally advanced or metastatic NSCLC with EGFR exon 19 deletions or exon 21 L858R substitution mutations when certain criteria are met. Updated criteria for Imdelltra (tarlatamab-dlle) and Ziihera (zanidatamab-hrii) removing requirement of Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1. Updated criteria for Rybrevant (amivantamab-vmjw) for treatment of NSCLC with EGFR exon 20 insertion and disease has progressed on or after platinum-based chemotherapy, adding Rybrevant will be used as a single

Date	Comments
	agent. Removed reference to non-formulary exception reviews. Added new HCPCS code J9601 and noted HCPCS code C9307 was terminated, effective April 1, 2026.
05/01/26	Interim Review, approved April 14, 2026. Updated criteria for Tecvayli (teclistamab-cqyv) indication for individuals who have received at least 4 prior lines of therapy clarifying Tecvayli is given as monotherapy, and added new indication for treatment of relapsed or refractory multiple myeloma in combination with daratumumab hyaluronidase-fihj in individuals who have received at least 1 prior line of therapy, including a proteasome inhibitor and an immunomodulatory agent. Updated criteria for Rybrevant Faspro (amivantamab and hyaluronidase-lpuj) maintenance dose limit when used as single agent or in combination with Lazcluze to include dose is limited to 4,640 mg every 4 weeks.
07/01/26	Coding update. Added new HCPCS code J9062 effective, July 1, 2026. Notated HCPCS code C9307 terminated effective April 1, 2026.
09/01/26	Interim Review, approved August 11, 2026. Updated Bizengri (zenocutuzumab-zbco) adding criteria for the treatment of adult individuals with advanced, unresectable, or metastatic cholangiocarcinoma harboring a neuregulin 1 (NRG1) gene fusion with disease progression on or after prior systemic therapy. Updated Blincyto (blinatumomab) removing reference to Philadelphia chromosome status from CD19-positive B-cell precursor ALL in the consolidation phase of multiphase chemotherapy.

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