Corporate Medical Policy: Preferred Injectable Oncology Program

Restricted Product(s):

- Alymsys® (bevacizumab-maly) intravenous infusion for administration by a healthcare professional
- Avastin® (bevacizumab) intravenous infusion for administration by a healthcare professional
- Avzivi® (bevacizumab-tnjn) intravenous infusion for administration by a healthcare professional
- Herceptin® (trastuzumab) intravenous infusion for administration by a healthcare professional
- Herceptin Hylecta™ (trastuzumab and hyaluronidase-oysk) subcutaneous injection for administration by a healthcare professional
- Herzuma® (trastuzumab-pkrb) intravenous infusion for administration by a healthcare professional
- Ogivri™ (trastuzumab-dkst) intravenous infusion for administration by a healthcare professional
- Ontruzant™ (trastuzumab-dttb) intravenous infusion for administration by a healthcare professional
- Riabni® (rituximab-arrx) intravenous infusion for administration by a healthcare professional
- Rituxan® (rituximab) intravenous infusion for administration by a healthcare professional
- Rituxan Hycela® (rituximab and hyaluronidase) subcutaneous injection for administration by a healthcare professional
- Vegzelma® (bevacizumab-adcd) intravenous infusion for administration by a healthcare professional

Preferred Bevacizumab Containing Agent(s) (Unrestricted)	**Non-Preferred Bevacizumab Containing Agent(s)**
Mvasi® (bevacizumab-awwb) Zirabev® (bevacizumab-bvzr)	Avastin® (bevacizumab) Alymsys® (bevacizumab-maly) Avzivi® (bevacizumab-tnjn) Vegzelma® (bevacizumab-adcd)

Preferred Rituximab Containing Agent(s) (Unrestricted)	**Non-Preferred Rituximab Containing Agent(s)**
*Ruxience® (rituximab-pvvr) *Truxima® (rituximab-abbs)	Rituxan® (rituximab) Riabni® (rituximab-arrx) Rituxan Hycela® (rituximab and hyaluronidase)

Preferred Trastuzumab Containing Agent(s) (Unrestricted)	**Non-Preferred Trastuzumab Containing Agent(s)**

Kanjinti™ (trastuzumab-anns) Trazimera™ (trastuzumab-qyyp)	Herceptin® (trastuzumab) Herzuma® (trastuzumab-pkrb) Ogivri™ (trastuzumab-dkst) Ontruzant™ (trastuzumab-dttb) Herceptin Hylecta™ (trastuzumab and hyaluronidase-oysk)

*These products may require authorization for non-oncology related indications; please refer to our Prior Review and Limitations Page https://www.bluecrossnc.com/understanding-health-insurance/how-drug-benefits-work/getting-your-prescriptions-approved

FDA Approved Use:

- Alymsys® (bevacizumab-maly)
  - For treatment of metastatic colorectal cancer, in combination with intravenous fluorouracil-based chemotherapy for first- or second-line treatment
  - For treatment of metastatic colorectal cancer, in combination with fluoropyrimidine-irinotecan- or fluoropyrimidine-oxaliplatin-based chemotherapy for second-line treatment in patients who have progressed on a first-line bevacizumab product-containing regimen
    - Limitations of use: Not for adjuvant treatment of colon cancer
  - For treatment of unresectable, locally advanced, recurrent or metastatic non-squamous non-small cell lung cancer, in combination with carboplatin and paclitaxel for first-line treatment
  - For treatment of recurrent glioblastoma in adults
  - For treatment of metastatic renal cell carcinoma in combination with interferon alfa
  - For treatment of persistent, recurrent, or metastatic cervical cancer, in combination with paclitaxel and cisplatin, or paclitaxel and topotecan
  - For treatment of epithelial ovarian, fallopian tube, or primary peritoneal cancer in combination with paclitaxel, pegylated liposomal doxorubicin, or topotecan for platinum-resistant recurrent disease who received no more than 2 prior chemotherapy regimens

- Avastin® (bevacizumab)
  - For treatment of metastatic colorectal cancer, in combination with intravenous fluorouracil-based chemotherapy for first- or second-line treatment

- For treatment of metastatic colorectal cancer, in combination with fluoropyrimidine-irinotecan- or fluoropyrimidine-oxaliplatin-based chemotherapy for second-line treatment in patients who have progressed on a first-line bevacizumab product-containing regimen
  - Limitations of use: Not for adjuvant treatment of colon cancer
- For treatment of unresectable, locally advanced, recurrent or metastatic non-squamous non-small cell lung cancer, in combination with carboplatin and paclitaxel for first-line treatment
- For treatment of recurrent glioblastoma in adults
- For treatment of metastatic renal cell carcinoma in combination with interferon alfa
- For treatment of persistent, recurrent, or metastatic cervical cancer, in combination with paclitaxel and cisplatin, or paclitaxel and topotecan
- For treatment of epithelial ovarian, fallopian tube, or primary peritoneal cancer in the following situations:
  - In combination with carboplatin and paclitaxel, followed by a bevacizumab product as a single agent, for stage III or IV disease following initial surgical resection
  - In combination with paclitaxel, pegylated liposomal doxorubicin, or topotecan for platinum-resistant recurrent disease who received no more than 2 prior chemotherapy regimens
  - In combination with carboplatin and paclitaxel or carboplatin and gemcitabine, followed by a bevacizumab product as a single agent, for platinum-sensitive recurrent disease
- For treatment of hepatocellular carcinoma (HCC), in combination with atezolizumab for the treatment of patients with unresectable or metastatic HCC who have not received prior systemic therapy

- Avzivi® (bevacizumab-tnjn)
  - For treatment of metastatic colorectal cancer, in combination with intravenous fluorouracil-based chemotherapy for first- or second-line treatment
  - For treatment of metastatic colorectal cancer, in combination with fluoropyrimidine-irinotecan- or fluoropyrimidine-oxaliplatin-based chemotherapy for second-line treatment in patients who have progressed on a first-line bevacizumab product-containing regimen
    - Limitations of use: Not for adjuvant treatment of colon cancer
  - For treatment of unresectable, locally advanced, recurrent or metastatic non-squamous non-small cell lung cancer, in combination with carboplatin and paclitaxel for first-line treatment
  - For treatment of recurrent glioblastoma in adults
  - For treatment of metastatic renal cell carcinoma in combination with interferon alfa
  - For treatment of persistent, recurrent, or metastatic cervical cancer, in combination with paclitaxel and cisplatin, or paclitaxel and topotecan

  - For treatment of epithelial ovarian, fallopian tube, or primary peritoneal cancer in combination with paclitaxel, pegylated liposomal doxorubicin, or topotecan for platinum-resistant recurrent disease who received no more than 2 prior chemotherapy regimens

- Herceptin® (trastuzumab)
  - For treatment of HER2-overexpressing breast cancer
  - For treatment of HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma
  - Patient selection for therapy is based on an FDA-approved companion diagnostic for Herceptin. Assessment of HER2 protein overexpression and/or HER2 gene amplification should be performed using FDA-approved tests specific for breast or gastric cancers by laboratories with demonstrated proficiency

- Herceptin Hylecta™ (trastuzumab and hyaluronidase-oysk)
  - For treatment of HER2-overexpressing breast cancer
  - Patient selection for therapy is based on an FDA-approved companion diagnostic for trastuzumab. Assessment of HER2 protein overexpression and/or HER2 gene amplification should be performed using FDA-approved tests specific for breast cancers by laboratories with demonstrated proficiency

- Herzuma® (trastuzumab-pkrb)
  - For treatment of HER2-overexpressing breast cancer
  - For treatment of HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma
  - Patient selection for therapy is based on an FDA-approved companion diagnostic for a trastuzumab product. Assessment of HER2 protein overexpression and/or HER2 gene amplification should be performed using FDA-approved tests specific for breast or gastric cancers by laboratories with demonstrated proficiency

- Ogivri™ (trastuzumab-dkst)
  - For treatment of HER2-overexpressing breast cancer
  - For treatment of HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma
  - Patient selection for therapy is based on an FDA-approved companion diagnostic for a trastuzumab product. Assessment of HER2 protein overexpression and/or HER2 gene amplification should be performed using FDA-approved tests specific for breast or gastric cancers by laboratories with demonstrated proficiency

- Ontruzant™ (trastuzumab-dttb)
  - For treatment of HER2-overexpressing breast cancer
  - For treatment of HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma

- Patient selection for therapy is based on an FDA-approved companion diagnostic for a trastuzumab product. Assessment of HER2 protein overexpression and/or HER2 gene amplification should be performed using FDA-approved tests specific for breast or gastric cancers by laboratories with demonstrated proficiency

- Riabni® (rituximab-arrx)
  - For treatment of adults with non-Hodgkin's lymphoma in the following situations:
    - Relapsed or refractory, low grade or follicular, CD20-positive B-cell NHL as a single agent
    - Previously untreated follicular, CD20-positive, B-cell NHL in combination with first line chemotherapy and, in patients achieving a complete or partial response to a rituximab product in combination with chemotherapy, as single-agent maintenance therapy
    - Non-progressing (including stable disease), low-grade, CD20-positive, B-cell NHL as a single agent after first-line cyclophosphamide, vincristine, and prednisone (CVP) chemotherapy
    - Previously untreated diffuse large B-cell, CD20-positive NHL in combination with cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) or other anthracycline-based chemotherapy regimens
  - For treatment of previously untreated and previously treated CD20-positive chronic lymphocytic leukemia (CLL) in adults, in combination with fludarabine and cyclophosphamide (FC)

- Rituxan® (rituximab)
  - For treatment of adults with non-Hodgkin's lymphoma in the following situations:
    - Relapsed or refractory, low grade or follicular, CD20-positive B-cell NHL as a single agent
    - Previously untreated follicular, CD20-positive, B-cell NHL in combination with first line chemotherapy and, in patients achieving a complete or partial response to a rituximab product in combination with chemotherapy, as single-agent maintenance therapy
    - Non-progressing (including stable disease), low-grade, CD20-positive, B-cell NHL as a single agent after first-line cyclophosphamide, vincristine, and prednisone (CVP) chemotherapy
    - Previously untreated diffuse large B-cell, CD20-positive NHL in combination with cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) or other anthracycline-based chemotherapy regimens
  - For treatment of pediatric patients aged 6 months and older with mature B-cell NHL and mature B-cell acute leukemia (B-AL):
    - Previously untreated, advanced stage, CD20-positive, diffuse large B-cell lymphoma (DLBCL), Burkitt lymphoma (BL), Burkitt-like lymphoma (BLL) or mature B-cell acute leukemia (B-AL) in combination with chemotherapy
  - For treatment of previously untreated and previously treated CD20-positive chronic lymphocytic leukemia (CLL) in adults, in combination with fludarabine and cyclophosphamide (FC)

- Rituxan Hycela® (rituximab and hyaluronidase)
  - For treatment of adults with follicular lymphoma (FL) in the following situations:
    - Relapsed or refractory, follicular lymphoma as a single agent
    - Previously untreated follicular lymphoma in combination with first-line chemotherapy and, in patients achieving a complete or partial response to rituximab in combination with chemotherapy, as single-agent maintenance therapy
    - Non-progressing (including stable disease), follicular lymphoma as a single agent after first-line cyclophosphamide, vincristine, and prednisone (CVP) chemotherapy
  - For treatment of previously untreated diffuse large B-cell lymphoma in combination with cyclophosphamide, doxorubicin, vincristine, prednisone (CHOP) or other anthracycline-based chemotherapy regimens
  - For treatment of previously untreated and previously treated chronic lymphocytic leukemia (CLL) in combination with fludarabine and cyclophosphamide (FC)
  - Limitations of use:
    - Treatment should be initiated only after patients have received at least one full dose of a rituximab product by intravenous infusion
    - Not indicated for treatment of non-malignant conditions

- Vegzelma® (bevacizumab-adcd)
  - For treatment of metastatic colorectal cancer, in combination with intravenous fluorouracil-based chemotherapy for first- or second-line treatment
  - For treatment of metastatic colorectal cancer, in combination with fluoropyrimidine-irinotecan- or fluoropyrimidine-oxaliplatin-based chemotherapy for second-line treatment in patients who have progressed on a first-line bevacizumab product-containing regimen
    - Limitations of use: Not for adjuvant treatment of colon cancer
  - For treatment of unresectable, locally advanced, recurrent or metastatic non-squamous non-small cell lung cancer, in combination with carboplatin and paclitaxel for first-line treatment
  - For treatment of recurrent glioblastoma in adults
  - For treatment of metastatic renal cell carcinoma in combination with interferon alfa
  - For treatment of persistent, recurrent, or metastatic cervical cancer, in combination with paclitaxel and cisplatin, or paclitaxel and topotecan
  - For treatment of epithelial ovarian, fallopian tube, or primary peritoneal cancer in the following situations:
    - In combination with carboplatin and paclitaxel, followed by a bevacizumab product as a single agent, for stage III or IV disease following initial surgical resection

- In combination with paclitaxel, pegylated liposomal doxorubicin, or topotecan for platinum-resistant recurrent disease who received no more than 2 prior chemotherapy regimens
- In combination with carboplatin and paclitaxel or carboplatin and gemcitabine, followed by a bevacizumab product as a single agent, for platinum-sensitive recurrent disease

Criteria for Medical Necessity:

The restricted product(s) may be considered medically necessary when the following criteria are met:

Initial Criteria for Approval:

1. ONE of the following:
    a. The patient is currently being treated with the requested agent and has been stable on therapy for at least 180 days; **OR**
    b. The patient has been treated with the requested agent within the past 180 days AND is at risk if therapy is changed; **OR**

2. The patient has an FDA labeled indication for the requested agent and route of administration; **AND**
    a. ONE of the following:
        i. The requested indication does NOT require genetic/specific diagnostic testing (e.g., ALK, EGFR, HER2, KRAS) in FDA labeling; **OR**
        ii. The requested indication requires genetic/specific diagnostic testing in FDA labeling AND both of the following:
            1. Genetic/specific diagnostic testing has been performed; **AND**
            2. The results of the genetic/specific diagnostic testing indicate therapy with the requested agent is appropriate in FDA labeling; **AND**
    b. ONE of the following:
        i. The requested agent will be used as a first-line agent AND is FDA labeled as a first-line agent for the requested indication, including any genomic aberrations (e.g., EGFR, ALK) and/or tumor expression factors [e.g., PD-L1 Tumor Proportion Score (TPS) values]; **OR**
        ii. The patient has used the appropriate number and type(s) of prerequisite agent(s) listed in the FDA labeling for the requested indication, including any genomic aberrations (e.g., EGFR, ALK) and/or tumor expression factors [e.g., PD-L1 Tumor Proportion Score (TPS) values]; **OR**
        iii. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to ALL of the required prerequisite agent(s) listed in the FDA labeling for the requested indication, indication including any genomic aberrations (e.g., EGFR, ALK) and/or tumor expression factors [e.g., PD-L1 Tumor Proportion Score (TPS) values]; **AND**

c. ONE of the following:
    i. The requested agent is being used as monotherapy AND is approved for use as monotherapy in the FDA labeling for the requested indication, including any genomic aberrations (e.g., EGFR, ALK) and/or tumor expression factors [e.g., PD-L1 Tumor Proportion Score (TPS) values]; **OR**
    ii. The requested agent will be used in combination as combination therapy with all agent(s) and/or treatments (e.g., radiation) listed for concomitant use in the FDA labeling for the requested indication; **AND**
d. ONE of the following:
    i. The FDA label does NOT include a performance status requirement; **OR**
    ii. The patient meets the performance status requirement in the FDA labeling; **OR**

3. The patient has an indication that is supported by ALL requirements in NCCN 1 or 2A recommended use for the requested agent [i.e., the indication must be supported by ALL requirements in the NCCN "Recommended Use" box (e.g., performance status, disease severity, previous failures, monotherapy vs combination therapy)] **[medical record documentation required]**; **AND**

4. If the request is for **bevacizumab (Avastin)** or **non-preferred bevacizumab biosimilars** [e.g., bevacizumab-maly (Alymsys), bevacizumab-tnjn (Avzivi), bevacizumab-adcd (Vegzelma)], then both of the following criteria are met:
    a. The patient has a documented serious adverse event that required medical intervention to both preferred bevacizumab biosimilar products [i.e., bevacizumab-awwb (Mvasi), bevacizumab-bvzr (Zirabev)] that is not anticipated with the requested product; **AND**
    b. The prescriber has completed and submitted an FDA MedWatch Adverse Event Reporting Form **[medical record documentation required]**; **AND**
5. If the request is for **rituximab (Rituxan)**, **rituximab and hyaluronidase (Rituxan Hycela)**, or **non-preferred rituximab biosimilars** [e.g., rituximab-arrx (Riabni)], then both of the following criteria are met:
    a. The patient has a documented serious adverse event that required medical intervention to both preferred rituximab biosimilar products [i.e., rituximab-abbs (Truxima), rituximab-pvvr (Ruxience)] that is not anticipated with the requested product; **AND**
    b. The prescriber has completed and submitted an FDA MedWatch Adverse Event Reporting Form **[medical record documentation required]**; **AND**
6. If the request is for **trastuzumab (Herceptin)**, **trastuzumab and hyaluronidase-oysk (Herceptin Hylecta)**, or **non-preferred trastuzumab biosimilars** [e.g., trastuzumab-pkrb (Herzuma), trastuzumab-dkst (Ogivri), trastuzumab-dttb (Ontruzant)], then both of the following criteria are met:
    a. The patient has a documented serious adverse event that required medical intervention to both preferred trastuzumab biosimilar products [i.e., trastuzumab-anns (Kanjinti), trastuzumab-qyyp (Trazimera)] that is not anticipated with the requested product; **AND**
    b. The prescriber has completed and submitted an FDA MedWatch Adverse Event Reporting Form **[medical record documentation required]**; **AND**

7. The patient has not experienced disease progression or unacceptable toxicity on the same treatment as the requested agent or during treatment with another agent from the same drug class in a prior line of therapy (e.g., PD-L1/PD-1 inhibitors) unless there is acceptable supporting literature for use beyond progression in a different combination regimen; **AND**
8. ONE of the following:
    a. The patient's age is within FDA labeling for the requested indication or NCCN 1 or 2A compendia supported recommendation for the requested agent; **OR**
    b. The prescriber has provided information in support of using the requested agent for the patient's age; **AND**
9. The patient does NOT have any FDA labeled contraindications to the requested agent; **AND**
10. The requested quantity (dose) and treatment duration (and maximum units) is within FDA labeled dosing for the requested indication or NCCN 1 or 2A compendia supported dosing for the requested indication.

Duration of Approval: 365 days (1 year)

Continuation Criteria for Approval:

1. The patient was approved through Blue Cross NC initial criteria for approval; **OR**
2. The patient would have met initial criteria for approval at the time they started therapy; **AND**
3. The patient has continued clinical benefit while receiving the requested agent as demonstrated by tumor response or lack of disease progression, and an acceptable toxicity profile; **AND**
4. The requested quantity (dose) and treatment duration (and maximum units) is within FDA labeled dosing for the requested indication or NCCN 1 or 2A compendia supported dosing for the requested indication; **AND**
5. If the request is for **bevacizumab (Avastin)** or **non-preferred bevacizumab biosimilars** [e.g., bevacizumab-maly (Alymsys), bevacizumab-tnjn (Avzivi), bevacizumab-adcd (Vegzelma)], then both of the following criteria are met:
    a. The patient has a documented serious adverse event that required medical intervention to both preferred bevacizumab biosimilar products [i.e., bevacizumab-awwb (Mvasi), bevacizumab-bvzr (Zirabev)] that is not anticipated with the requested product ; **AND**
    b. The prescriber has completed and submitted an FDA MedWatch Adverse Event Reporting Form **[medical record documentation required]**; **AND**
6. If the request is for **rituximab (Rituxan)**, **rituximab and hyaluronidase (Rituxan Hycela)**, or **non-preferred rituximab biosimilars** [e.g., rituximab-arrx (Riabni)], then both of the following criteria are met:
    a. The patient has a documented serious adverse event that required medical intervention to both preferred rituximab biosimilar products [i.e., rituximab-abbs (Truxima), rituximab-pvvr (Ruxience)] that is not anticipated with the requested product; **AND**

   b. The prescriber has completed and submitted an FDA MedWatch Adverse Event Reporting Form **[medical record documentation required]**; **AND**
7. If the request is for **trastuzumab (Herceptin)**, **trastuzumab and hyaluronidase-oysk (Herceptin Hylecta)**, or **non-preferred trastuzumab biosimilars** [e.g., trastuzumab-pkrb (Herzuma), trastuzumab-dkst (Ogivri), trastuzumab-dttb (Ontruzant)], then both of the following criteria are met:
   a. The patient has a documented serious adverse event that required medical intervention to both preferred trastuzumab biosimilar products [i.e., trastuzumab-anns (Kanjinti), trastuzumab-qyyp (Trazimera)] that is not anticipated with the requested product; **AND**
   b. The prescriber has completed and submitted an FDA MedWatch Adverse Event Reporting Form **[medical record documentation required]**.

Duration of Approval: 365 days (1 year)

NOTE:

Use of injectable and healthcare administered oncology agents may be considered medically necessary for clinical indications not listed above when the drug is prescribed for the treatment of **cancer** either:

1. In accordance with FDA label when clinical benefit has been established, and it is not determined to be investigational as defined in the Blue Cross NC Corporate Medical Policy (CMP), "Investigational (Experimental) Services." [please refer to CMP "Investigational (Experimental) Services" for a summary of evidence standards from nationally recognized compendia]; **OR**
2. In accordance with specific strong endorsement or support by nationally recognized compendia (e.g., National Comprehensive Cancer Network, NCCN), when such recommendation is based on the highest level of evidence (Level 1, 2A), and/or uniform consensus of clinical appropriateness has been reached.

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units**

Alymsys® (bevacizumab-maly)
 	
intravenous (IV) infusion
	• Metastatic colorectal cancer
	  ○ in combination with IV fluorouracil-based chemotherapy for first- or second-line treatment
	  ○ in combination with fluoropyrimidine-irinotecan- or fluoropyrimidine-oxaliplatin-based chemotherapy for second-line treatment after progression on a first-line bevacizumab product-containing regimen
	
	• Unresectable, locally advanced, recurrent or metastatic non-squamous non-small cell lung cancer, in combination with carboplatin and paclitaxel, as first-line
	
	• Recurrent glioblastoma in adults
	
	• Metastatic renal cell carcinoma in combination with interferon alfa
	
	• Persistent, recurrent, or metastatic cervical cancer in combination with paclitaxel and cisplatin, or paclitaxel and topotecan
		• Metastatic colorectal cancer:
		  ○ 5 mg/kg every 2 weeks with bolus-IFL
		  ○ 10 mg/kg every 2 weeks with FOLFOX4
		  ○ 5 mg/ kg every 2 weeks or 7.5 mg/kg every 3 weeks with fluoropyrimidine-irinotecan- or fluoropyrimidine-oxaliplatin-based chemotherapy after progression on a first-line bevacizumab product containing regimen
		
		• First-line non-squamous non-small cell lung cancer: 15 mg/kg every 3 weeks with carboplatin and paclitaxel
		
		• Recurrent glioblastoma: 10 mg/kg every 2 weeks
		
		• Metastatic renal cell carcinoma: 10 mg/kg every 2 weeks with interferon alfa
		
		• Persistent, recurrent, or metastatic cervical cancer: 15 mg/kg every 3 weeks with paclitaxel and cisplatin, or paclitaxel and topotecan
			Q5126	9999

	• Epithelial ovarian, fallopian tube, or primary peritoneal cancer for platinum-resistant recurrent disease in patients who received no more than 2 prior chemotherapy regimens	• Platinum-resistant recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer: ○ 10 mg/kg every 2 weeks with paclitaxel, pegylated liposomal doxorubicin, or topotecan given every week ○ 15 mg/kg every 3 weeks with topotecan given every 3 weeks		
Avastin® (bevacizumab) intravenous (IV) infusion	• Metastatic colorectal cancer ○ in combination with IV fluorouracil-based chemotherapy for first- or second-line treatment ○ in combination with fluoropyrimidine-irinotecan- or fluoropyrimidine-oxaliplatin-based chemotherapy for second-line treatment after progression on a first-line bevacizumab product-containing regimen • Unresectable, locally advanced, recurrent or metastatic non-squamous non-small cell lung cancer, in combination with carboplatin and paclitaxel, as first-line	• Metastatic colorectal cancer: ○ 5 mg/kg every 2 weeks with bolus-IFL ○ 10 mg/kg every 2 weeks with FOLFOX4 ○ 5 mg/ kg every 2 weeks or 7.5 mg/kg every 3 weeks with fluoropyrimidine-irinotecan- or fluoropyrimidine-oxaliplatin-based chemotherapy after progression on a first-line bevacizumab product containing regimen • First-line non-squamous non-small cell lung cancer: 15 mg/kg every 3 weeks with carboplatin and paclitaxel	J9035	9999

	• Recurrent glioblastoma in adults	• Recurrent glioblastoma: 10 mg/kg every 2 weeks		
	• Metastatic renal cell carcinoma in combination with interferon alfa	• Metastatic renal cell carcinoma: 10 mg/kg every 2 weeks with interferon alfa		
	• Persistent, recurrent, or metastatic cervical cancer in combination with paclitaxel and cisplatin, or paclitaxel and topotecan	• Persistent, recurrent, or metastatic cervical cancer: 15 mg/kg every 3 weeks with paclitaxel and cisplatin, or paclitaxel and topotecan		
	• Epithelial ovarian, fallopian tube, or primary peritoneal cancer: ○ Stage III or IV disease following initial surgical resection	• Stage III or IV epithelial ovarian, fallopian tube, or primary peritoneal cancer following initial surgical resection: 15 mg/kg every 3 weeks with carboplatin and paclitaxel for up to 6 cycles, followed by 15 mg/kg every 3 weeks as a single agent, for a total of up to 22 cycles		
	○ Platinum-resistant recurrent disease in patients who received no more than 2 prior chemotherapy regimens	• Platinum-resistant recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer: ○ 10 mg/kg every 2 weeks with paclitaxel, pegylated liposomal doxorubicin, or topotecan given every week ○ 15 mg/kg every 3 weeks with topotecan given every 3 weeks		
	○ Platinum-sensitive recurrent disease			

	• Unresectable or metastatic hepatocellular carcinoma (HCC), in combination with atezolizumab, in patients who have not received prior systemic therapy	• Platinum-sensitive recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer: ○ 15 mg/kg every 3 weeks with carboplatin and paclitaxel for 6-8 cycles, followed by 15 mg/kg every 3 weeks as a single agent ○ 15 mg/kg every 3 weeks with carboplatin and gemcitabine for 6-10 cycles, followed by 15 mg/kg every 3 weeks as a single agent HCC: 15 mg/kg (following 1,200 mg of atezolizumab) every 3 weeks		
Avzivi® (bevacizumab-tnjn) intravenous (IV) infusion	• Metastatic colorectal cancer ○ in combination with IV fluorouracil-based chemotherapy for first- or second-line treatment ○ in combination with fluoropyrimidine-irinotecan- or fluoropyrimidine-oxaliplatin-based chemotherapy for second-line treatment after progression on a first-line bevacizumab product-containing regimen	• Metastatic colorectal cancer: ○ 5 mg/kg every 2 weeks with bolus-IFL ○ 10 mg/kg every 2 weeks with FOLFOX4 ○ 5 mg/ kg every 2 weeks or 7.5 mg/kg every 3 weeks with fluoropyrimidine-irinotecan- or fluoropyrimidine-oxaliplatin-based chemotherapy after progression on a first-line bevacizumab product containing regimen	C9399** J3490** J3590** J9999**	9999

	• Unresectable, locally advanced, recurrent or metastatic non-squamous non-small cell lung cancer, in combination with carboplatin and paclitaxel, as first-line	• First-line non-squamous non-small cell lung cancer: 15 mg/kg every 3 weeks with carboplatin and paclitaxel		
	• Recurrent glioblastoma in adults	• Recurrent glioblastoma: 10 mg/kg every 2 weeks		
	• Metastatic renal cell carcinoma in combination with interferon alfa	• Metastatic renal cell carcinoma: 10 mg/kg every 2 weeks with interferon alfa		
	• Persistent, recurrent, or metastatic cervical cancer in combination with paclitaxel and cisplatin, or paclitaxel and topotecan	• Persistent, recurrent, or metastatic cervical cancer: 15 mg/kg every 3 weeks with paclitaxel and cisplatin, or paclitaxel and topotecan		
	• Epithelial ovarian, fallopian tube, or primary peritoneal cancer for platinum-resistant recurrent disease in patients who received no more than 2 prior chemotherapy regimens	• Platinum-resistant recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer: ○ 10 mg/kg every 2 weeks with paclitaxel, pegylated liposomal doxorubicin, or topotecan given every week ○ 15 mg/kg every 3 weeks with topotecan given every 3 weeks		

Herceptin® (trastuzumab)
 	
intravenous (IV) infusion
	• HER2-overexpressing breast cancer
	
	• HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma
		• Adjuvant treatment of HER2-overexpressing breast cancer
		  ○ Initial dose of 4 mg/kg IV, then 2 mg/kg weekly for 12 weeks (with paclitaxel or docetaxel) or 18 weeks (with docetaxel/carboplatin). One week after the last weekly dose, give 6 mg/kg every three weeks to complete a total of 52 weeks of therapy, or
		  ○ Initial dose of 8 mg/kg IV, then 6 mg/kg every three weeks for 52 weeks
		• Metastatic HER2-overexpressing breast cancer
		  ○ Initial dose of 4 mg/kg IV, followed by subsequent weekly doses of 2 mg/kg
		• Metastatic HER2-overexpressing gastric cancer
		  ○ Initial dose of 8 mg/kg IV, followed by 6 mg/kg every 3 weeks
		• Do not substitute for or with ado-trastuzumab emtansine
			J9355	9999

Herceptin Hylecta™ (trastuzumab and hyaluronidase-oysk) subcutaneous (SC) injection	• HER2-overexpressing breast cancer	• 600 mg/10,000 units (600 mg trastuzumab and 10,000 units hyaluronidase) SC over approximately 2-5 minutes once every three weeks • Do not administer IV and do not substitute for or with ado-trastuzumab emtansine	J9356	9999
Herzuma® (trastuzumab-pkrb) intravenous (IV) infusion	• HER2-overexpressing breast cancer • HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma	• Adjuvant treatment of HER2-overexpressing breast cancer ○ Initial dose of 4 mg/kg IV, then 2 mg/kg weekly for 12 weeks (with paclitaxel or docetaxel) or 18 weeks (with docetaxel/carboplatin). One week after the last weekly dose, give 6 mg/kg every three weeks to complete a total of 52 weeks of therapy, or ○ Initial dose of 8 mg/kg IV, then 6 mg/kg every three weeks for 52 weeks • Metastatic HER2-overexpressing breast cancer ○ Initial dose of 4 mg/kg IV, followed by subsequent weekly doses of 2 mg/kg	Q5113	9999

		• Metastatic HER2-overexpressing gastric cancer ○ Initial dose of 8 mg/kg IV, followed by 6 mg/kg every 3 weeks • Do not substitute for or with ado-trastuzumab emtansine		

Ogivri™ (trastuzumab-dkst)
 	
intravenous (IV) infusion
	• HER2-overexpressing breast cancer
	
	• HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma
		• Adjuvant treatment of HER2-overexpressing breast cancer
		  ○ Initial dose of 4 mg/kg IV, then 2 mg/kg weekly for 12 weeks (with paclitaxel or docetaxel) or 18 weeks (with docetaxel/carboplatin). One week after the last weekly dose, give 6 mg/kg every three weeks to complete a total of 52 weeks of therapy, or
		  ○ Initial dose of 8 mg/kg IV, then 6 mg/kg every three weeks for 52 weeks
		• Metastatic HER2-overexpressing breast cancer
		  ○ Initial dose of 4 mg/kg IV, followed by subsequent weekly doses of 2 mg/kg
		• Metastatic HER2-overexpressing gastric cancer
			Q5114	9999

		○ Initial dose of 8 mg/kg IV, followed by 6 mg/kg every 3 weeks • Do not substitute for or with ado-trastuzumab emtansine		
Ontruzant™ (trastuzumab-dttb) intravenous (IV) infusion	• HER2-overexpressing breast cancer • HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma	• Adjuvant treatment of HER2-overexpressing breast cancer ○ Initial dose of 4 mg/kg IV, then 2 mg/kg weekly for 12 weeks (with paclitaxel or docetaxel) or 18 weeks (with docetaxel/carboplatin). One week after the last weekly dose, give 6 mg/kg every three weeks to complete a total of 52 weeks of therapy, or ○ Initial dose of 8 mg/kg IV, then 6 mg/kg every three weeks for 52 weeks • Metastatic HER2-overexpressing breast cancer ○ Initial dose of 4 mg/kg IV, followed by subsequent weekly doses of 2 mg/kg • Metastatic HER2-overexpressing gastric cancer ○ Initial dose of 8 mg/kg IV, followed by 6 mg/kg every 3 weeks	Q5112	9999

		• Do not substitute for or with ado-trastuzumab emtansine		
Riabni® (rituximab-arrx) intravenous (IV) infusion	• Relapsed or refractory, low grade or follicular, CD20-positive Bcell NHL as a single agent • Previously untreated follicular, CD20-positive, B-cell NHL in combination with first line chemotherapy and, in patients achieving a complete or partial response to a rituximab product in combination with chemotherapy, as single-agent maintenance therapy • Non-progressing (including stable disease), low-grade, CD20-positive, B-cell NHL as a single agent after first-line cyclophosphamide, vincristine, and prednisone (CVP) chemotherapy • Previously untreated diffuse large B-cell, CD20-positive NHL in combination with	NHL: 375 mg/m^2 IV CLL: 375 mg/m^2 IV in the first cycle and 500 mg/m^2 in cycles 2-6, in combination with FC, administered every 28 days	Q5123	9999

	(cyclophosphamide, doxorubicin, vincristine, and prednisone) (CHOP) or other anthracycline-based chemotherapy regimens • Previously untreated and previously treated CD20-positive chronic lymphocytic leukemia (CLL) in adults, in combination with fludarabine and cyclophosphamide (FC)			
Rituxan® (rituximab) intravenous (IV) infusion	• Relapsed or refractory, low grade or follicular, CD20-positive Bcell NHL as a single agent • Previously untreated follicular, CD20-positive, B-cell NHL in combination with first line chemotherapy and, in patients achieving a complete or partial response to a rituximab product in combination with chemotherapy, as single-agent maintenance therapy • Non-progressing (including stable disease), low-grade, CD20-positive, B-cell NHL as a single agent after first-line	NHL: 375 mg/m^2 IV CLL: 375 mg/m^2 IV in the first cycle and 500 mg/m^2 in cycles 2-6, in combination with FC, administered every 28 days	J9312	9999

	cyclophosphamide, vincristine, and prednisone (CVP) chemotherapy • Previously untreated diffuse large B-cell, CD20-positive NHL in combination with (cyclophosphamide, doxorubicin, vincristine, and prednisone) (CHOP) or other anthracycline-based chemotherapy regimens • Previously untreated and previously treated CD20-positive chronic lymphocytic leukemia (CLL) in adults, in combination with fludarabine and cyclophosphamide (FC) • Mature B-cell NHL and mature B-cell acute leukemia (B-AL): Previously untreated, advanced stage, CD20-positive, diffuse large B-cell lymphoma (DLBCL), Burkitt lymphoma (BL), Burkitt-like lymphoma (BLL) or mature B-cell acute leukemia (B-AL) in combination with chemotherapy			

Rituxan Hycela® (rituximab and hyaluronidase) subcutaneous (SC) injection	• Relapsed or refractory, FL as a single agent • Previously untreated FL in combination with first-line chemotherapy and, in patients achieving a complete or partial response to rituximab in combination with chemotherapy, as single-agent maintenance therapy • Non-progressing (including stable disease), FL as a single agent after first-line cyclophosphamide, vincristine, and prednisone (CVP) chemotherapy • Previously untreated diffuse large B-cell lymphoma in combination with cyclophosphamide, doxorubicin, vincristine, prednisone (CHOP) or other anthracycline-based chemotherapy regimens • Previously untreated and previously treated CLL in combination with fludarabine and cyclophosphamide (FC)	All patients must receive at least one full dose of a rituximab product by IV infusion before receiving Rituxan Hycela by SC injection. FL/DLBCL: Administer 1,400 mg/23,400 Units (1,400 mg rituximab and 23,400 Units hyaluronidase human) SC CLL: Administer 1,600 mg/26,800 Units (1,600 mg rituximab and 26,800 Units hyaluronidase human) SC	J9311	9999

Vegzelma® (bevacizumab-adcd)
 	
intravenous (IV) infusion
	• Metastatic colorectal cancer
	  ○ in combination with IV fluorouracil-based chemotherapy for first- or second-line treatment
	  ○ in combination with fluoropyrimidine-irinotecan- or fluoropyrimidine-oxaliplatin-based chemotherapy for second-line treatment after progression on a first-line bevacizumab product-containing regimen
	
	• Unresectable, locally advanced, recurrent or metastatic non-squamous non-small cell lung cancer, in combination with carboplatin and paclitaxel, as first-line
	
	• Recurrent glioblastoma in adults
	
	• Metastatic renal cell carcinoma in combination with interferon alfa
	
	• Persistent, recurrent, or metastatic cervical cancer in combination with paclitaxel and cisplatin, or paclitaxel and topotecan
		• Metastatic colorectal cancer:
		  ○ 5 mg/kg every 2 weeks with bolus-IFL
		  ○ 10 mg/kg every 2 weeks with FOLFOX4
		  ○ 5 mg/ kg every 2 weeks or 7.5 mg/kg every 3 weeks with fluoropyrimidine-irinotecan- or fluoropyrimidine-oxaliplatin-based chemotherapy after progression on a first-line bevacizumab product containing regimen
		
		• First-line non-squamous non-small cell lung cancer: 15 mg/kg every 3 weeks with carboplatin and paclitaxel
		
		• Recurrent glioblastoma: 10 mg/kg every 2 weeks
		
		• Metastatic renal cell carcinoma: 10 mg/kg every 2 weeks with interferon alfa
		
		• Persistent, recurrent, or metastatic cervical cancer: 15 mg/kg every 3 weeks with paclitaxel and cisplatin, or paclitaxel and topotecan
			Q5129	9999

	• Epithelial ovarian, fallopian tube, or primary peritoneal cancer: ○ Stage III or IV disease following initial surgical resection	• Stage III or IV epithelial ovarian, fallopian tube, or primary peritoneal cancer following initial surgical resection: 15 mg/kg every 3 weeks with carboplatin and paclitaxel for up to 6 cycles, followed by 15 mg/kg every 3 weeks as a single agent, for a total of up to 22 cycles		

	○ Platinum-resistant recurrent disease in patients who received no more than 2 prior chemotherapy regimens	• Platinum-resistant recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer:
		  ○ 10 mg/kg every 2 weeks with paclitaxel, pegylated liposomal doxorubicin, or topotecan given every week
		  ○ 15 mg/kg every 3 weeks with topotecan given every 3 weeks		

	○ Platinum-sensitive recurrent disease	• Platinum-sensitive recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer:
		  ○ 15 mg/kg every 3 weeks with carboplatin and paclitaxel for 6-8 cycles, followed by 15 mg/kg every 3 weeks as a single agent
		  ○ 15 mg/kg every 3 weeks with carboplatin and gemcitabine for 6-10 cycles, followed by 15 mg/kg every 3 weeks as a single agent		

****Non-specific assigned HCPCS codes, must submit requested product NDC**

References: all information referenced is from FDA package insert unless otherwise noted below.

Policy Implementation/Update Information: Criteria and treatment protocols are reviewed annually by the Blue Cross NC P&T Committee, regardless of change. This policy is reviewed in Q3 annually.

April 2024: Criteria change: Changed requirement for trial and failure of preferred trastuzumab biosimilar products to include Kanjinti and Trazimera; adjusted non-preferred trastuzumab biosimilar products to include Herzuma, Ogivri, and Ontruzant. Added Ogivri (Q5114) to restricted products; removed Trazimera (Q5116) from restricted products (unrestricted). **Policy notification given 1/8/2024 for effective date 4/1/2024**.
January 2024: Criteria update: Added new to market biosimilar product Avzivi (bevacizumab-tnjn) to policy as non-preferred with same criteria as Avastin.
April 2023: Coding update: Added HCPCS code Q5129 for Vegzelma to dosing reference table effective 4/1/2023; deleted C9399, J3490, J3590, and J9999 for Vegzelma termed 3/31/2023.
January 2023: Coding update: Added HCPCS code Q5126 for Alymsys to dosing reference table effective 1/1/2023, deleted C9142, J3490, J3590, and J9999 for Alymsys termed 12/31/2022.
November 2022: Criteria update: Added new to market product Vegzelma (bevacizumab-adcd) to policy as non-preferred with same criteria as Avastin.
October 2022: Coding update: Added HCPCS code C9142 for Alymsys to dosing reference table effective 10/1/2022, deleted C9399 for Alymsys termed 9/30/2022.
October 2022: Criteria update: Added Herceptin Hylecta to policy as a non-preferred product with same criteria as Herceptin. Added Rituxan Hycela to policy as a non-preferred product with same criteria as Rituxan. **Policy notification given 8/4/2022 for effective date 10/1/2022**.
June 2022: Criteria update: Added new to market Alymsys (bevacizumab-maly) to policy as non-preferred with same criteria as Avastin. Adjusted policy formatting for clarity with no change to policy intent.
June 2022: Original medical policy criteria issued. Criteria from these restricted products remains the same from previous medical policy (Injectable and Healthcare Administered Oncology Drugs).