Bevacizumab Products

Humana

Pharmacy Coverage Policy

Effective Date: March 01, 2023
Revision Date: March 01, 2023
Review Date: February 23, 2023
Line of Business: Medicaid - Ohio
Policy Type: Prior Authorization

Products Affected

Avastin intravenous solution
Mvasi intravenous solution
Zirabev intravenous solution
Vegzelma intravenous solution

Listed Indications

Age Related Macular Degeneration (Applies to Pharmacy claims only)

Does the member meet all of the following criteria?	
Criteria #1	**When a Medical Claim is submitted for Avastin (bevacizumab) used for age related macular degeneration, diabetic macular edema, or macular retinal edema there is no requirement to obtain prior authorization. Medical Claims edits and reviews will still apply to ensure proper diagnosis and dosing for these indications.
Criteria #2	Avastin (bevacizumab) is being used to treat age related macular degeneration
Does the member have any of the following exclusions? If yes, approval may not be appropriate. NOTE: Experimental/Investigational Use – Indications not supported by CMS recognized compendia or acceptable peer reviewed literature.	
Exclusion #1	**The following coverage limitations apply to systemic use of bevacizumab product:** • Lung Cancer – Bevacizumab should not be used in lung cancer members that have small cell or squamous cell disease, recent hemoptysis, history of bleeding, continuing anticoagulation, or as a single agent (unless maintenance as described in Coverage Determinations) • Bevacizumab should not be initiated in members with recent hemoptysis • Bevacizumab should not be used in members who experience a severe arterial thromboembolic event • Bevacizumab should not be used in members with gastrointestinal perforation • Bevacizumab should not be used in members with fistula formation involving internal organs

	• Bevacizumab should not be used in members experiencing a hypertensive crisis or hypertensive encephalopathy • Bevacizumab should not be used for at least 28 days following major surgery or until surgical incision is fully healed • Bevacizumab may not be used in conjunction with Vectibix (panitumumab) • Bevacizumab may not be used in conjunction with Erbitux (cetuximab) • Bevacizumab may not be used in the adjuvant or neoadjuvant setting (except in Epithelial ovarian, fallopian tube, or primary peritoneal cancer adjuvant setting) • Bevacizumab should not be continued or restarted after disease progression, with the exception of metastatic colorectal cancer.
Approval Duration	
Initial	Avastin (bevacizumab), Mvasi (bevacizumab-awwb), Zirabev (bevacizumab-bvzr), and Alymsys (bevacizumab-maly) and Vegzelma (bevacizumab-adcd) will be approved in six month durations. Avastin (bevacizumab) will be approved in plan year durations for ocular indications.

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Diabetic Macular Edema (Applies to Pharmacy claims only)

Does the member meet all of the following criteria?	
Criteria #1	**When a Medical Claim is submitted for Avastin (bevacizumab) used for age related macular degeneration, diabetic macular edema, or macular retinal edema there is no requirement to obtain prior authorization. Medical Claims edits and reviews will still apply to ensure proper diagnosis and dosing for these indications.
Criteria #2	Avastin (bevacizumab) is being used to treat diabetic macular edema
Does the member have any of the following exclusions? If yes, approval may not be appropriate. NOTE: Experimental/Investigational Use – Indications not supported by CMS recognized compendia or acceptable peer reviewed literature.	
Exclusion #1	**The following coverage limitations apply to systemic use of bevacizumab product:** • Lung Cancer – Bevacizumab should not be used in lung cancer members that have small cell or squamous cell disease, recent hemoptysis, history of bleeding, continuing anticoagulation, or as a single agent (unless maintenance as described in Coverage Determinations) • Bevacizumab should not be initiated in members with recent hemoptysis • Bevacizumab should not be used in members who experience a severe arterial thromboembolic event • Bevacizumab should not be used in members with gastrointestinal perforation • Bevacizumab should not be used in members with fistula formation involving internal organs • Bevacizumab should not be used in members experiencing a hypertensive crisis or hypertensive encephalopathy • Bevacizumab should not be used for at least 28 days following major surgery or until surgical incision is fully healed • Bevacizumab may not be used in conjunction with Vectibix (panitumumab) • Bevacizumab may not be used in conjunction with Erbitux (cetuximab) • Bevacizumab may not be used in the adjuvant or neoadjuvant setting (except in Epithelial ovarian, fallopian tube, or primary peritoneal cancer adjuvant setting) • Bevacizumab should not be continued or restarted after disease progression, with the exception of metastatic colorectal cancer.

Approval Duration	
Initial	Avastin (bevacizumab), Mvasi (bevacizumab-awwb), Zirabev (bevacizumab-bvzr), and Alymsys (bevacizumab-maly) and Vegzelma (bevacizumab-adcd) will be approved in six month durations. Avastin (bevacizumab) will be approved in plan year durations for ocular indications.

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Macular Retinal Edema (Applies to Pharmacy claims only)

Does the member meet all of the following criteria?	
Criteria #1	**When a Medical Claim is submitted for Avastin (bevacizumab) used for age related macular degeneration, diabetic macular edema, or macular retinal edema there is no requirement to obtain prior authorization. Medical Claims edits and reviews will still apply to ensure proper diagnosis and dosing for these indications.
Criteria #2	Avastin (bevacizumab) is being used to treat central or branch retinal vein occlusion with macular retinal edema.
Does the member have any of the following exclusions? If yes, approval may not be appropriate. NOTE: Experimental/Investigational Use – Indications not supported by CMS recognized compendia or acceptable peer reviewed literature.	
Exclusion #1	**The following coverage limitations apply to systemic use of bevacizumab product:** • Lung Cancer – Bevacizumab should not be used in lung cancer members that have small cell or squamous cell disease, recent hemoptysis, history of bleeding, continuing anticoagulation, or as a single agent (unless maintenance as described in Coverage Determinations) • Bevacizumab should not be initiated in members with recent hemoptysis • Bevacizumab should not be used in members who experience a severe arterial thromboembolic event • Bevacizumab should not be used in members with gastrointestinal perforation • Bevacizumab should not be used in members with fistula formation involving internal organs • Bevacizumab should not be used in members experiencing a hypertensive crisis or hypertensive encephalopathy • Bevacizumab should not be used for at least 28 days following major surgery or until surgical incision is fully healed • Bevacizumab may not be used in conjunction with Vectibix (panitumumab) • Bevacizumab may not be used in conjunction with Erbitux (cetuximab) • Bevacizumab may not be used in the adjuvant or neoadjuvant setting (except in Epithelial ovarian, fallopian tube, or primary peritoneal cancer adjuvant setting) • Bevacizumab should not be continued or restarted after disease progression, with the exception of metastatic colorectal cancer.
Approval Duration	
Initial	Avastin (bevacizumab), Mvasi (bevacizumab-awwb), Zirabev (bevacizumab-bvzr), and Alymsys (bevacizumab-maly) and Vegzelma (bevacizumab-adcd) will be approved in six month durations. Avastin (bevacizumab) will be approved in plan year durations for ocular indications.

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Cervical Cancer

Does the member meet all of the following criteria?	
Criteria #1	The member has recurrent, or metastatic cervical cancer

Criteria #2	Bevacizumab will be used in combination with paclitaxel and cisplatin or carboplatin and paclitaxel or paclitaxel and topotecan as first line therapy
Does the member have any of the following exclusions? If yes, approval may not be appropriate. NOTE: Experimental/Investigational Use – Indications not supported by CMS recognized compendia or acceptable peer reviewed literature.	
Exclusion #1	**The following coverage limitations apply to systemic use of bevacizumab product:** • Lung Cancer – Bevacizumab should not be used in lung cancer members that have small cell or squamous cell disease, recent hemoptysis, history of bleeding, continuing anticoagulation, or as a single agent (unless maintenance as described in Coverage Determinations) • Bevacizumab should not be initiated in members with recent hemoptysis • Bevacizumab should not be used in members who experience a severe arterial thromboembolic event • Bevacizumab should not be used in members with gastrointestinal perforation • Bevacizumab should not be used in members with fistula formation involving internal organs • Bevacizumab should not be used in members experiencing a hypertensive crisis or hypertensive encephalopathy • Bevacizumab should not be used for at least 28 days following major surgery or until surgical incision is fully healed • Bevacizumab may not be used in conjunction with Vectibix (panitumumab) • Bevacizumab may not be used in conjunction with Erbitux (cetuximab) • Bevacizumab may not be used in the adjuvant or neoadjuvant setting (except in Epithelial ovarian, fallopian tube, or primary peritoneal cancer adjuvant setting) • Bevacizumab should not be continued or restarted after disease progression, with the exception of metastatic colorectal cancer.
Approval Duration	
Initial	Avastin (bevacizumab), Mvasi (bevacizumab-awwb), Zirabev (bevacizumab-bvzr), and Alymsys (bevacizumab-maly) and Vegzelma (bevacizumab-adcd) will be approved in six month durations. Avastin (bevacizumab) will be approved in plan year durations for ocular indications.

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Endometrial Cancer

Does the member meet all of the following criteria?	
Criteria #1	The member has progressive endometrial cancer
Criteria #2	Bevacizumab will be used as a single-agent
Does the member have any of the following exclusions? If yes, approval may not be appropriate. NOTE: Experimental/Investigational Use – Indications not supported by CMS recognized compendia or acceptable peer reviewed literature.	
Exclusion #1	**The following coverage limitations apply to systemic use of bevacizumab product:** • Lung Cancer – Bevacizumab should not be used in lung cancer members that have small cell or squamous cell disease, recent hemoptysis, history of bleeding, continuing anticoagulation, or as a single agent (unless maintenance as described in Coverage Determinations) • Bevacizumab should not be initiated in members with recent hemoptysis • Bevacizumab should not be used in members who experience a severe arterial thromboembolic event • Bevacizumab should not be used in members with gastrointestinal perforation • Bevacizumab should not be used in members with fistula formation involving internal organs

	• Bevacizumab should not be used in members experiencing a hypertensive crisis or hypertensive encephalopathy • Bevacizumab should not be used for at least 28 days following major surgery or until surgical incision is fully healed • Bevacizumab may not be used in conjunction with Vectibix (panitumumab) • Bevacizumab may not be used in conjunction with Erbitux (cetuximab) • Bevacizumab may not be used in the adjuvant or neoadjuvant setting (except in Epithelial ovarian, fallopian tube, or primary peritoneal cancer adjuvant setting) • Bevacizumab should not be continued or restarted after disease progression, with the exception of metastatic colorectal cancer.
Approval Duration	
Initial	Avastin (bevacizumab), Mvasi (bevacizumab-awwb), Zirabev (bevacizumab-bvzr), and Alymsys (bevacizumab-maly) and Vegzelma (bevacizumab-adcd) will be approved in six month durations. Avastin (bevacizumab) will be approved in plan year durations for ocular indications.

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Metastatic colorectal cancer	
Does the member meet all of the following criteria?	
Criteria #1	The member has a diagnosis of metastatic colorectal cancer
Criteria #2	One of the following apply: • Member is using bevacizumab in combination with fluoropyrmidine (e.g.,5- fluorouracil or capecitabine) based chemotherapy for first or second-line therapy • Member is using bevacizumab in combination with fluoropyrimidine-irinotecan or fluoropyrimidine-oxaliplatin-based chemotherapy for second-line therapy in patients who have progressed on first-line bevacizumab-containing regime
Does the member have any of the following exclusions? If yes, approval may not be appropriate. **NOTE: Experimental/Investigational Use – Indications not supported by CMS recognized compendia or acceptable peer reviewed literature.**	
Exclusion #1	**The following coverage limitations apply to systemic use of bevacizumab product:** • Lung Cancer – Bevacizumab should not be used in lung cancer members that have small cell or squamous cell disease, recent hemoptysis, history of bleeding, continuing anticoagulation, or as a single agent (unless maintenance as described in Coverage Determinations) • Bevacizumab should not be initiated in members with recent hemoptysis • Bevacizumab should not be used in members who experience a severe arterial thromboembolic event • Bevacizumab should not be used in members with gastrointestinal perforation • Bevacizumab should not be used in members with fistula formation involving internal organs • Bevacizumab should not be used in members experiencing a hypertensive crisis or hypertensive encephalopathy • Bevacizumab should not be used for at least 28 days following major surgery or until surgical incision is fully healed • Bevacizumab may not be used in conjunction with Vectibix (panitumumab) • Bevacizumab may not be used in conjunction with Erbitux (cetuximab)

	• Bevacizumab may not be used in the adjuvant or neoadjuvant setting (except in Epithelial ovarian, fallopian tube, or primary peritoneal cancer adjuvant setting) • Bevacizumab should not be continued or restarted after disease progression, with the exception of metastatic colorectal cancer.
Approval Duration	
Initial	Avastin (bevacizumab), Mvasi (bevacizumab-awwb), Zirabev (bevacizumab-bvzr), and Alymsys (bevacizumab-maly) and Vegzelma (bevacizumab-adcd) will be approved in six month durations. Avastin (bevacizumab) will be approved in plan year durations for ocular indications.

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Non-small cell lung cancer (non-squamous cell histology)	
Does the member meet all of the following criteria?	
Criteria #1	Member has NSCLC with non-squamous cell histology
Criteria #2	• Member is using bevacizumab in combination with cisplatin or carboplatin based regimens for unresectable, locally advanced, recurrent, or metastatic NSCLC and one of the following applies: • The member will be using for first line therapy OR The member will be using subsequent therapy immediately after one of the following situations: ◦ EGFR mutation-positive tumors after prior therapy (if cytotoxic therapy not previously not given*) ◦ ALK-positive tumors after prior therapy (if cytotoxic therapy not previously not given*) ◦ ROS-1 positive disease after prior therapy (if cytotoxic therapy not previously not given*) ◦ Pembrolizumab (with PD-L1 expression of greater than or equal to 1%) administered as first line therapy and EGFR, ALK, V600E, and ROS1 negative tumors (if cytotoxic therapy not previously not given*) ◦ The member has BRAF V600E positive disease (if cytotoxic therapy not previously not given*) • Member is using bevacizumab as single-agent continuation maintenance therapy if bevacizumab was used as first line treatment for recurrence or metastasis **OR** • Member has disease with no EGFR or ALK genomic tumor aberrations **AND** ◦ Bevacizumab will be given in combination with carboplatin and paclitaxel and Tecentriq (atezolizumab) as first line therapy followed by maintenance therapy with combination Tecentriq (atezolizumab) plus bevacizumab
Does the member have any of the following exclusions? If yes, approval may not be appropriate. **NOTE: Experimental/Investigational Use – Indications not supported by CMS recognized compendia or acceptable peer reviewed literature.**	
Exclusion #1	**The following coverage limitations apply to systemic use of bevacizumab product:** • Lung Cancer – Bevacizumab should not be used in lung cancer members that have small cell or squamous cell disease, recent hemoptysis, history of bleeding, continuing anticoagulation, or as a single agent (unless maintenance as described in Coverage Determinations) • Bevacizumab should not be initiated in members with recent hemoptysis • Bevacizumab should not be used in members who experience a severe arterial thromboembolic event • Bevacizumab should not be used in members with gastrointestinal perforation • Bevacizumab should not be used in members with fistula formation involving internal organs • Bevacizumab should not be used in members experiencing a hypertensive crisis or hypertensive encephalopathy

	• Bevacizumab should not be used for at least 28 days following major surgery or until surgical incision is fully healed • Bevacizumab may not be used in conjunction with Vectibix (panitumumab) • Bevacizumab may not be used in conjunction with Erbitux (cetuximab) • Bevacizumab may not be used in the adjuvant or neoadjuvant setting (except in Epithelial ovarian, fallopian tube, or primary peritoneal cancer adjuvant setting) • Bevacizumab should not be continued or restarted after disease progression, with the exception of metastatic colorectal cancer.
Approval Duration	
Initial	Avastin (bevacizumab), Mvasi (bevacizumab-awwb), Zirabev (bevacizumab-bvzr), and Alymsys (bevacizumab-maly) and Vegzelma (bevacizumab-adcd) will be approved in six month durations. Avastin (bevacizumab) will be approved in plan year durations for ocular indications.

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Metastatic breast cancer (Effectiveness based on improvement in progression-free survival. No data available demonstrating improvement in disease-related symptoms or survival with bevacizumab)	
Does the member meet all of the following criteria?	
Criteria #1	Member has metastatic HER-2 negative breast cancer
Criteria #2	Member is using bevacizumab in combination with paclitaxel
Does the member have any of the following exclusions? If yes, approval may not be appropriate. NOTE: Experimental/Investigational Use – Indications not supported by CMS recognized compendia or acceptable peer reviewed literature.	
Exclusion #1	**The following coverage limitations apply to systemic use of bevacizumab product:** • Lung Cancer – Bevacizumab should not be used in lung cancer members that have small cell or squamous cell disease, recent hemoptysis, history of bleeding, continuing anticoagulation, or as a single agent (unless maintenance as described in Coverage Determinations) • Bevacizumab should not be initiated in members with recent hemoptysis • Bevacizumab should not be used in members who experience a severe arterial thromboembolic event • Bevacizumab should not be used in members with gastrointestinal perforation • Bevacizumab should not be used in members with fistula formation involving internal organs • Bevacizumab should not be used in members experiencing a hypertensive crisis or hypertensive encephalopathy • Bevacizumab should not be used for at least 28 days following major surgery or until surgical incision is fully healed • Bevacizumab may not be used in conjunction with Vectibix (panitumumab) • Bevacizumab may not be used in conjunction with Erbitux (cetuximab) • Bevacizumab may not be used in the adjuvant or neoadjuvant setting (except in Epithelial ovarian, fallopian tube, or primary peritoneal cancer adjuvant setting) • Bevacizumab should not be continued or restarted after disease progression, with the exception of metastatic colorectal cancer.
Approval Duration	

Initial	Avastin (bevacizumab), Mvasi (bevacizumab-awwb), Zirabev (bevacizumab-bvzr), and Alymsys (bevacizumab-maly) and Vegzelma (bevacizumab-adcd) will be approved in six month durations. Avastin (bevacizumab) will be approved in plan year durations for ocular indications.

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Recurrent Ovarian Cancer

Does the member meet all of the following criteria?	
Criteria #1	Bevacizumab is being used to treat recurrent or persistent ovarian cancer for one of the following situations: • in combination with liposomal doxorubicin or weekly paclitaxel or topotecan for platinum resistant disease • in combination with carboplatin and gemcitabine for platinum sensitive disease • as monotherapy
Does the member have any of the following exclusions? If yes, approval may not be appropriate. NOTE: Experimental/Investigational Use – Indications not supported by CMS recognized compendia or acceptable peer reviewed literature.	
Exclusion #1	**The following coverage limitations apply to systemic use of bevacizumab product:** • Lung Cancer – Bevacizumab should not be used in lung cancer members that have small cell or squamous cell disease, recent hemoptysis, history of bleeding, continuing anticoagulation, or as a single agent (unless maintenance as described in Coverage Determinations) • Bevacizumab should not be initiated in members with recent hemoptysis • Bevacizumab should not be used in members who experience a severe arterial thromboembolic event • Bevacizumab should not be used in members with gastrointestinal perforation • Bevacizumab should not be used in members with fistula formation involving internal organs • Bevacizumab should not be used in members experiencing a hypertensive crisis or hypertensive encephalopathy • Bevacizumab should not be used for at least 28 days following major surgery or until surgical incision is fully healed • Bevacizumab may not be used in conjunction with Vectibix (panitumumab) • Bevacizumab may not be used in conjunction with Erbitux (cetuximab) • Bevacizumab may not be used in the adjuvant or neoadjuvant setting (except in Epithelial ovarian, fallopian tube, or primary peritoneal cancer adjuvant setting) • Bevacizumab should not be continued or restarted after disease progression, with the exception of metastatic colorectal cancer.
Approval Duration	
Initial	Avastin (bevacizumab), Mvasi (bevacizumab-awwb), Zirabev (bevacizumab-bvzr), and Alymsys (bevacizumab-maly) and Vegzelma (bevacizumab-adcd) will be approved in six month durations. Avastin (bevacizumab) will be approved in plan year durations for ocular indications.

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Stage IV/Metastatic (Unresectable) Renal Cell Carcinoma

Does the member meet all of the following criteria?	
Criteria #1	Member has renal cell cancer

Criteria #2	Member is using bevacizumab to treat stage IV unresectable kidney cancer in combination with interferon alpha **OR** Member is using bevacizumab as systemic therapy for non-clear cell histology
Does the member have any of the following exclusions? If yes, approval may not be appropriate. NOTE: Experimental/Investigational Use – Indications not supported by CMS recognized compendia or acceptable peer reviewed literature.	
Exclusion #1	**The following coverage limitations apply to systemic use of bevacizumab product:** • Lung Cancer – Bevacizumab should not be used in lung cancer members that have small cell or squamous cell disease, recent hemoptysis, history of bleeding, continuing anticoagulation, or as a single agent (unless maintenance as described in Coverage Determinations) • Bevacizumab should not be initiated in members with recent hemoptysis • Bevacizumab should not be used in members who experience a severe arterial thromboembolic event • Bevacizumab should not be used in members with gastrointestinal perforation • Bevacizumab should not be used in members with fistula formation involving internal organs • Bevacizumab should not be used in members experiencing a hypertensive crisis or hypertensive encephalopathy • Bevacizumab should not be used for at least 28 days following major surgery or until surgical incision is fully healed • Bevacizumab may not be used in conjunction with Vectibix (panitumumab) • Bevacizumab may not be used in conjunction with Erbitux (cetuximab) • Bevacizumab may not be used in the adjuvant or neoadjuvant setting (except in Epithelial ovarian, fallopian tube, or primary peritoneal cancer adjuvant setting) • Bevacizumab should not be continued or restarted after disease progression, with the exception of metastatic colorectal cancer.
Approval Duration	
Initial	Avastin (bevacizumab), Mvasi (bevacizumab-awwb), Zirabev (bevacizumab-bvzr), and Alymsys (bevacizumab-maly) and Vegzelma (bevacizumab-adcd) will be approved in six month durations. Avastin (bevacizumab) will be approved in plan year durations for ocular indications.

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Recurrent Primary CNS Tumor (including Glioblastoma multiforme)

Does the member meet all of the following criteria?	
Criteria #1	The member has a diagnosis of progressive or recurrent glioblastoma or anaplastic glioma
Criteria #2	Bevacizumab is being used as a single agent or in combination with irinotecan, carmustine, lomustine, or temozolomide.
Criteria #3	The member does not have a CNS hemorrhage
Does the member have any of the following exclusions? If yes, approval may not be appropriate. NOTE: Experimental/Investigational Use – Indications not supported by CMS recognized compendia or acceptable peer reviewed literature.	
Exclusion #1	**The following coverage limitations apply to systemic use of bevacizumab product:** • Lung Cancer – Bevacizumab should not be used in lung cancer members that have small cell or squamous cell disease, recent hemoptysis, history of bleeding, continuing anticoagulation, or as a single agent (unless maintenance as described in Coverage Determinations) • Bevacizumab should not be initiated in members with recent hemoptysis

	• Bevacizumab should not be used in members who experience a severe arterial thromboembolic event • Bevacizumab should not be used in members with gastrointestinal perforation • Bevacizumab should not be used in members with fistula formation involving internal organs • Bevacizumab should not be used in members experiencing a hypertensive crisis or hypertensive encephalopathy • Bevacizumab should not be used for at least 28 days following major surgery or until surgical incision is fully healed • Bevacizumab may not be used in conjunction with Vectibix (panitumumab) • Bevacizumab may not be used in conjunction with Erbitux (cetuximab) • Bevacizumab may not be used in the adjuvant or neoadjuvant setting (except in Epithelial ovarian, fallopian tube, or primary peritoneal cancer adjuvant setting) • Bevacizumab should not be continued or restarted after disease progression, with the exception of metastatic colorectal cancer.
Approval Duration	
Initial	Avastin (bevacizumab), Mvasi (bevacizumab-awwb), Zirabev (bevacizumab-bvzr), and Alymsys (bevacizumab-maly) and Vegzelma (bevacizumab-adcd) will be approved in six month durations. Avastin (bevacizumab) will be approved in plan year durations for ocular indications.

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Soft Tissue Sarcoma

Does the member meet all of the following criteria?	
Criteria #1	The member has a diagnosis of angiosarcoma and bevacizumab is being used as a single agent **OR** The member has a diagnosis of solitary fibrous tumor and hemangiopericytoma and bevacizumab is being used in combination with temozolomide
Does the member have any of the following exclusions? If yes, approval may not be appropriate. **NOTE: Experimental/Investigational Use – Indications not supported by CMS recognized compendia or acceptable peer reviewed literature.**	
Exclusion #1	**The following coverage limitations apply to systemic use of bevacizumab product:** • Lung Cancer – Bevacizumab should not be used in lung cancer members that have small cell or squamous cell disease, recent hemoptysis, history of bleeding, continuing anticoagulation, or as a single agent (unless maintenance as described in Coverage Determinations) • Bevacizumab should not be initiated in members with recent hemoptysis • Bevacizumab should not be used in members who experience a severe arterial thromboembolic event • Bevacizumab should not be used in members with gastrointestinal perforation • Bevacizumab should not be used in members with fistula formation involving internal organs • Bevacizumab should not be used in members experiencing a hypertensive crisis or hypertensive encephalopathy • Bevacizumab should not be used for at least 28 days following major surgery or until surgical incision is fully healed • Bevacizumab may not be used in conjunction with Vectibix (panitumumab) • Bevacizumab may not be used in conjunction with Erbitux (cetuximab) • Bevacizumab may not be used in the adjuvant or neoadjuvant setting (except in Epithelial ovarian, fallopian tube, or primary peritoneal cancer adjuvant setting) • Bevacizumab should not be continued or restarted after disease progression, with the exception of

	metastatic colorectal cancer.
Approval Duration	
Initial	Avastin (bevacizumab), Mvasi (bevacizumab-awwb), Zirabev (bevacizumab-bvzr), and Alymsys (bevacizumab-maly) and Vegzelma (bevacizumab-adcd) will be approved in six month durations. Avastin (bevacizumab) will be approved in plan year durations for ocular indications.

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Malignant Pleural Mesothelioma

Does the member meet all of the following criteria?	
Criteria #1	The member has a diagnosis of unresectable malignant pleural mesothelioma
Criteria #2	Bevacizumab will be used in combination with cisplatin and pemetrexed followed by bevacizumab as monotherapy for maintenance therapy (for responders)
Does the member have any of the following exclusions? If yes, approval may not be appropriate. NOTE: Experimental/Investigational Use – Indications not supported by CMS recognized compendia or acceptable peer reviewed literature.	
Exclusion #1	**The following coverage limitations apply to systemic use of bevacizumab product:** • Lung Cancer – Bevacizumab should not be used in lung cancer members that have small cell or squamous cell disease, recent hemoptysis, history of bleeding, continuing anticoagulation, or as a single agent (unless maintenance as described in Coverage Determinations) • Bevacizumab should not be initiated in members with recent hemoptysis • Bevacizumab should not be used in members who experience a severe arterial thromboembolic event • Bevacizumab should not be used in members with gastrointestinal perforation • Bevacizumab should not be used in members with fistula formation involving internal organs • Bevacizumab should not be used in members experiencing a hypertensive crisis or hypertensive encephalopathy • Bevacizumab should not be used for at least 28 days following major surgery or until surgical incision is fully healed • Bevacizumab may not be used in conjunction with Vectibix (panitumumab) • Bevacizumab may not be used in conjunction with Erbitux (cetuximab) • Bevacizumab may not be used in the adjuvant or neoadjuvant setting (except in Epithelial ovarian, fallopian tube, or primary peritoneal cancer adjuvant setting) • Bevacizumab should not be continued or restarted after disease progression, with the exception of metastatic colorectal cancer.
Approval Duration	
Initial	Avastin (bevacizumab), Mvasi (bevacizumab-awwb), Zirabev (bevacizumab-bvzr), and Alymsys (bevacizumab-maly) and Vegzelma (bevacizumab-adcd) will be approved in six month durations. Avastin (bevacizumab) will be approved in plan year durations for ocular indications.

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Epithelial ovarian, fallopian tube, or primary peritoneal cancer

Does the member meet all of the following criteria?	
Criteria #1	• The member has a diagnosis of epithelial ovarian, fallopian tube, or primary peritoneal cancer **AND**

	○ The member has Stage III or IV disease **AND** ○ Bevacizumab is initially being given in combination with carboplatin and paclitaxel after initial surgical resection followed by bevacizumab as monotherapy **OR** • Member has a diagnosis of advanced epithelial ovarian, fallopian tube or primary peritoneal cancer **AND** ○ Member's disease is associated with homologous recombination deficiency (HRD) positive status defined by either: ▪ a deleterious or suspected deleterious BRCA mutation OR genomic instability as defined by FDA approved test **AND** ○ Member is in complete response or partial response to first line treatment with platinum based chemotherapy **AND** ○ Bevacizumab is given in combination with Lynparza (olaparib)
Does the member have any of the following exclusions? If yes, approval may not be appropriate. **NOTE: Experimental/Investigational Use – Indications not supported by CMS recognized compendia or acceptable peer reviewed literature.**	
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Approval Duration	
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Hepatocellular carcinoma	
Does the member meet all of the following criteria?	
Criteria #1	The member has a diagnosis of unresectable or metastatic hepatocellular carcinoma
Criteria #2	Bevacizumab will be used will be used as first line therapy in combination with Tecentriq (atezolizumab)
Does the member have any of the following exclusions? If yes, approval may not be appropriate.	

NOTE: Experimental/Investigational Use – Indications not supported by CMS recognized compendia or acceptable peer reviewed literature.	
Exclusion #1	**The following coverage limitations apply to systemic use of bevacizumab product:** • Lung Cancer – Bevacizumab should not be used in lung cancer members that have small cell or squamous cell disease, recent hemoptysis, history of bleeding, continuing anticoagulation, or as a single agent (unless maintenance as described in Coverage Determinations) • Bevacizumab should not be initiated in members with recent hemoptysis • Bevacizumab should not be used in members who experience a severe arterial thromboembolic event • Bevacizumab should not be used in members with gastrointestinal perforation • Bevacizumab should not be used in members with fistula formation involving internal organs • Bevacizumab should not be used in members experiencing a hypertensive crisis or hypertensive encephalopathy • Bevacizumab should not be used for at least 28 days following major surgery or until surgical incision is fully healed • Bevacizumab may not be used in conjunction with Vectibix (panitumumab) • Bevacizumab may not be used in conjunction with Erbitux (cetuximab) • Bevacizumab may not be used in the adjuvant or neoadjuvant setting (except in Epithelial ovarian, fallopian tube, or primary peritoneal cancer adjuvant setting) • Bevacizumab should not be continued or restarted after disease progression, with the exception of metastatic colorectal cancer.
Approval Duration	
Initial	Avastin (bevacizumab), Mvasi (bevacizumab-awwb), Zirabev (bevacizumab-bvzr), and Alymsys (bevacizumab-maly) and Vegzelma (bevacizumab-adcd) will be approved in six month durations. Avastin (bevacizumab) will be approved in plan year durations for ocular indications.

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Background

This is a prior authorization policy about Avastin (bevacizumab) or Mvasi (bevacizumab-awwb) or Zirabev (bevacizumab-bvzr) or Alymsys (bevacizumab-maly) or Vegzelma (bevacizumab-adcd).
Please refer to current full prescribing infomation for further details on Black Box Warnings, Warnings/Precautions, Dosing and Dose Reductions, etc.

Black Box Warnings:

- **Gastrointestinal perforations**

  Bevacizumab administration can result in the development of gastrointestinal perforation. Occurs in 3.2% of bevacizumab- treated patients. If gastrointestinal perforation is present, discontinue bevacizumab treatment.
- **Wound Healing Complications**

  Bevacizumab administration can result in the development of wound dehiscence and is recommended to be discontinued. Bevacizumab should be discontinued at least 28 days prior to elective surgery. Re-initiation of bevacizumab therapy may not be started again for at least 28 days after surgery and until the surgical wound is fully healed.

- **Hemorrhage**

  Fatal or severe hemorrhage, can occur in patients .

Bevacizumab for Ocular Indications:
Bevacizumab , given by intravitreal injection, is considered "medically reasonable and necessary for patients diagnosed with neovascular (wet) AMD." The American Academy of Ophthalmology (AAO) and the American Society of Retinal Specialists (ASRS) support the use of bevacizumab .
The NIH-sponsored Ranibizumab and Bevacizumab for Neovascular Age-Related Macular Degeneration CATT study suggests that at two years, Avastin (bevacizumab) and Lucentis (ranibizumab) have equivalent effects on visual acuity when administered according to the same schedule for the treatment of age-related macular degeneration (AMD).
Doses utilized in ophthalmic conditions generally range from 6.2 mcg to 2.5 mg. Therefore, bevacizumab in vials is often divided into single-dose, prefilled syringes for intravitreal use by compounding pharmacies. Compounding pharmacies must comply with United States Pharmacopeia (USP) Chapter 797, which sets standards for the compounding, transportation, and storage of compounded sterile products (CSP).
The American Society of Retinal Specialists (ASRS) is committed to ensuring that retina specialists have access to compounded drugs (e.g., bevacizumab) that are prepared with high-quality material following good quality controls and sound engineering design by appropriately trained personnel. Please refer to their information page at https://www.asrs.org/advocacy-practice/access-to-safe-compounded-agents for resources pertaining to access of safe compounded agents.

Bevacizumab is a recombinant humanized monoclonal IgG1 antibody. Bevacizumab binds to vascular endothelial growth factor (VEGF) and inhibits the interaction of VEGF to Flt1 and KDR receptors on the surface of endothelial cells. In the process, it prevents the proliferation of endothelial cells and formation of new blood vessels .Vascular endothelial growth factor (VEGF) is an important signaling protein involved in angiogenesis (the growth of blood vessels from pre-existing vasculature). As its name implies, VEGF activity has been mostly studied on cells of the vascular endothelium, although it does have effects on a number of other cell types (e.g. stimulation monocyte/macrophage migration, neurons, cancer cells, kidney epithelial cells).

Avastin (bevacizumab) is indicated for:

- Metastatic colorectal cancer
    - In combination with 5-fluorouracil-based chemotherapy as first-line or second-line therapy

  In combination with fluoropyrimidine-irinotecan- or fluoropyrimidine-oxaliplatin-based chemotherapy as second-line therapy in patients who have progressed on a first-line bevacizumab-containing regimen
- Non-squamous non-small cell lung cancer, with carboplatin and paclitaxel for first line treatment of unresectable, locally advanced, recurrent or metastatic disease.
  Glioblastoma, as a single agent for patients with progressive disease following prior therapy:
    - Effectiveness based on improvement in objective response rate. No data available demonstrating improvement in disease-related symptoms or survival with bevacizumab
- Metastatic renal cell carcinoma, in combination with interferon alfa.
- Cervical cancer, in combination with paclitaxel and cisplatin or paclitaxel and topotecan in persistent, recurrent, or metastatic disease

- Platinum-resistant recurrent epithelial ovarian cancer, fallopian tube or primary peritoneal cancer, in combination with paclitaxel, pegylated liposomal doxorubicin or topotecan
- Epithelial ovarian, fallopian tube, or primary peritoneal cancer (Stage III or IV) and Avastin is initially being given in combination with carboplatin and paclitaxel after initial surgical resection followed by Avastin as monotherapy
- unresectable or metastatic hepatocellular carcinoma in combination with Tecentriq

Bevacizumab is available as Avastin in an Intravenous Solution: 25 MG/ML (100mg and 400mg vials).

Bevacizumab-awwb is available as Mvasi as injection: 25mg/mL (100mg and 400mg vials)

Bevacizumab-bvzris available as Zirabev as injection: 25mg/mL (100mg and 400mg vials)

Bevacizumab-maly available as Alymsys as injection: 25 mg/mL (100 mg or 400 mg) in a single-dose vial

Bevacizumab-adcd available as Vegzelma as injection: 100 mg/4 mL (25 mg/mL) or 400 mg/16 mL (25 mg/mL) in a single-dose vial

Provider Claim Codes

For medically billed requests, please visit www.humana.com/PAL. Select applicable Preauthorization and Notification List(s) for medical and procedural coding information.

Medical Terms

Avastin; bevacizumab; colorectal cancer, lung cancer, breast cancer, glioblastoma multiforme; cervical cancer; renal cancer; endometrial cancer; ovarian cancer; IV infusion; VEGF inhibitor; Mvasi; bevacizumab-awwb; Zirabev; bevacizumab-bvzr; hepatocellular carcinoma; Alymsys; bevacizumab-maly; Vegzelma; bevacizumab-adcd

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