Department:	Pharmacy Management	**Original Approval:**	12/24/2015
Policy No:	PM112	**Last Approval:**	06/12/2026
Policy Title:	Ramucirumab (Cyramza) Clinical Coverage Criteria		
Approved By:	UM Criteria Subcommittee		
Applicable Line(s) of Business:	☒ **Washington Apple Health (Medicaid)** ☐ **Behavioral Health Services Only** ☒ **Apple Health Expansion** ☒ **Medicare Advantage/Special Needs Plan** ☒ **Medicare Advantage Only** ☒ **Cascade Select**		

Required Clinical Documentation for Review

Documentation required to determine medical necessity for Ramucirumab (Cyramza):

- History and/or physical examination notes and relevant specialty consultation notes that address the problem and need for the service
- Diagnosis
- Labs/Diagnostics
- Dosing and duration requested
- Initial/Extended approval
- Medical records from the last 6 months showing the patient's problems, history, prior treatments, response to treatment, imaging and laboratory studies, details of the skilled needs, details of any specific needs related to risk/trauma/cultural etc., assessment and plan
- Prescribed by or in consultation with a specialist, when indicated

Background

Cyramza, a human vascular endothelial growth factor receptor 2 (VEGFR2) antagonist, is approved for the following indications:[1]

1) Gastric or gastroesophageal (GE) junction adenocarcinoma, as a single agent or in combination with paclitaxel injection for the treatment of patients with advanced or metastatic disease with disease progression on or after prior fluoropyrimidine- or platinum-containing chemotherapy.
2) Metastatic non-small cell lung cancer (NSCLC), in combination with docetaxel intravenous injection (Docefrez™, Taxotere®, generics) for the treatment of patients with

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disease progression on or after platinum-based chemotherapy. Patients with epidermal growth factor receptor (*EGFR*) or anaplastic lymphoma kinase (*ALK*) genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Cyramza.

3) Metastatic colorectal cancer (mCRC), in combination with FOLFIRI (irinotecan, leucovorin, and 5-fluorouracil [5-FU]) for the treatment of patients with disease progression on or after prior therapy with Avastin® (bevacizumab intravenous injection), oxaliplatin, and a fluoropyrimidine.
4) Hepatocellular carcinoma (HCC), as a single agent in patients who have an alpha fetoprotein of ≥ 400 ng/mL and have been treated with sorafenib.

Guidelines

The National Comprehensive Cancer Network (NCCN) guidelines on colon cancer and rectal cancer recommend Cyramza as primary therapy and subsequent therapy for patients with unresectable advanced or metastatic disease, and as adjuvant treatment for unresectable metachronous metastases that converted to resectable disease after primary treatment, in combination with either irinotecan or FOLFIRI.[2-4]

The NCCN guidelines on gastric cancer and esophageal and esophagogastric junction cancers recommend Cyramza as palliative treatment for patients who are not surgical candidates or have unresectable locally advanced, recurrent, or metastatic disease.[4-6]

The NCCN guidelines on NSCLC recommend Cyramza as subsequent therapy in combination with docetaxel for metastatic disease for patients who have not previously received docetaxel either following progression on initial cytotoxic therapy or for further progression on a systemic immune checkpoint inhibitor or other systemic therapy.[4,7] Cyramza is also recommended in combination with erlotinib for patients with EGFR mutation positive, recurrent, advanced, or metastatic disease as first-line therapy or as continuation therapy following disease progression on Cyramza and erlotinib.

The NCCN guidelines for hepatocellular carcinoma recommends Cyramza as a single agent for the treatment of patients with progressive disease with an alpha fetoprotein ≥ 400 ng/mL.[4,8]

The NCCN guidelines for malignant pleural mesothelioma recommends Cyramza in combination with gemcitabine after the patient has tried first-line chemotherapy (e.g., cisplatin plus pemetrexed, cisplatin plus gemcitabine, vinorelbine).[9]

The NCCN guidelines for thymomas and thymic carcinomas recommend Cyramza in combination with carboplatin and paclitaxel as first-line therapy for thymic carcinoma.[10] Cyramza plus carboplatin plus paclitaxel will be used on day one, followed by Cyramza as a single agent as maintenance therapy.

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Definitions

None.

Indications/Criteria

Medicaid Members	***Continue to criteria for approval below.***
Individual & Family (Cascade Select)	***Continue to criteria for approval below.***
Medicare Members	***Continue to criteria for approval below.***

Coverage of Cyramza is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. **Colon or Rectal Cancer**. Approve for 1 year if the patient meets the following criteria (A, B, C and D):

A) Cyramza is prescribed by or in consultation with an oncologist; AND
B) Patient has metastatic disease; AND
C) The patient has tried first-line therapy (e.g. FOLFOX, CAPEOX, FOLFIRI, FOLFIRINOX, etc.); AND
D) Cyramza will be used in combination with irinotecan or with FOLFIRI (irinotecan, folinic acid [leucovorin], and 5-fluorouracil [5-FU]).

Dosing: Approve the following dosing regimen: Up to 8 mg/kg as an intravenous infusion administered no more frequently than once every 2 weeks.

The recommended dose is 8 mg/kg every 2 weeks given as an intravenous infusion over 60 minutes prior to FOLFIRI administration.[1] Cyramza is continued until disease progression or unacceptable toxicity. Dose modifications are recommended in the prescribing information for infusion-related reactions, hypertension, proteinuria, arterial thromboembolic events, gastrointestinal perforation, or Grade 3 or 4 bleeding. Therapy with Cyramza is interrupted before scheduled surgery until the wound is fully healed. Management of AEs may require that Cyramza be withheld or permanently discontinued as determined by the prescribing physician.

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2. **Gastric, Esophagogastric Junction, or Esophageal Cancer**. Approve for 1 year if the patient meets the following criteria (A, B, and C):

A) Cyramza is prescribed by or in consultation with an oncologist; AND

B) The patient meets one of the following criteria (i, ii, iii or iv):
- **i.** Cyramza will be used alone; OR
- **ii.** Cyramza will be used in combination with paclitaxel; OR
- **iii.** Cyramza will be used in combination with fluorouracil and irinotecan; OR
- **iv.** Cyramza will be used in combination with irinotecan; AND

C) The patient has received chemotherapy with at least ONE of the following (i or ii):
- **i.** 5-Fluorouracil (5-FU) or capecitabine; OR
- **ii.** Cisplatin, carboplatin, or oxaliplatin.

Dosing: *Approve the following dosing regimen: Up to 8 mg/kg as an intravenous infusion administered no more frequently than once every 2 weeks.*

The recommended dose, either as a single agent or in combination with weekly paclitaxel, is 8 mg/kg every 2 weeks given as an intravenous infusion over 60 minutes.[1] Cyramza is continued until disease progression or unacceptable toxicity. When used in combination, Cyramza is given before administering paclitaxel. Dose modifications are recommended in the prescribing information for infusion-related reactions, hypertension, proteinuria, arterial thromboembolic events, gastrointestinal perforation, or Grade 3 or 4 bleeding. Therapy with Cyramza is interrupted before scheduled surgery until the wound is fully healed. Management of AEs may require that Cyramza be withheld or permanently discontinued as determined by the prescribing physician.

3. **Non-Small Cell Lung Cancer (NSCLC).** Approve for 1 year if the patient meets the following criteria (A, B and C):

A) Cyramza is prescribed by or in consultation with an oncologist; AND

B) Patient has advanced or metastatic disease; AND

C) The patient meets one of the following criteria (i or ii):
- **i.** If Cyramza will be used as first-line therapy, the patient meets all of the following (a and b):
  - **a.** The patient has epidermal growth factor receptor (EGFR) positive disease exon 19 deletions or exon 21 (L858R) substitution mutations; AND
  - **b.** Cyramza will be used in combination with erlotinib (Tarceva®, generics); OR
- **ii.** If Cyramza will be used as subsequent therapy, the patient meets all of the following (a and b):
  - **a.** Cyramza will be used in combination with docetaxel intravenous injection (Docefrez™, Taxotere®, generics); AND

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b. The patient has received targeted drug therapy if the patient's tumor is positive for a targetable mutation (i.e., sensitizing epidermal growth factor receptor mutation, anaplastic lymphoma kinase fusions).

Dosing: *Approve the following dosing regimen: Up to 10 mg/kg as an intravenous infusion no more frequently than once every 3 weeks.*

The approved dosing of Cyramza in NSCLC is 10 mg/kg given intravenously over about 60 minutes on Day 1 of a 21-day cycle prior to infusion of docetaxel.[1] Cyramza is continued until disease progression or unacceptable toxicity. Dose modifications are recommended in the prescribing information for infusion-related reactions, hypertension, proteinuria, arterial thromboembolic events, gastrointestinal perforation, or Grade 3 or 4 bleeding. Therapy with Cyramza is interrupted before scheduled surgery until the wound is fully healed. Management of AEs may require that Cyramza be withheld or permanently discontinued as determined by the prescribing physician.

4. **Hepatocellular Carcinoma.** Approve for 1 year if the patient meets the following criteria (A, B, C, and D):
   A) Cyramza is prescribed by or in consultation with an oncologist; AND
   B) The patient has been treated with Nexavar® (sorafenib tablet); AND
   C) Cyramza will be used as a single agent; AND
   D) The patient has an alpha fetoprotein of ≥ 400 ng/mL.

Dosing. Approve the following dosing regimen: Up to 8 mg/kg as an intravenous infusion administered no more frequently than once every 14 days.

The approved dosing of Cyramza in hepatocellular carcinoma is 8 mg/kg given intravenously over about 60 minutes on Day 1 of a 14-day cycle.[1] Cyramza is continued until disease progression or unacceptable toxicity. Dose modifications are recommended in the prescribing information for infusion-related reactions, hypertension, proteinuria, arterial thromboembolic events, gastrointestinal perforation, or Grade 3 or 4 bleeding. Therapy with Cyramza is interrupted before scheduled surgery until the wound is fully healed. Management of AEs may require that Cyramza be withheld or permanently discontinued as determined by the prescribing physician.

Other Uses with Supportive Evidence

5. **Malignant Pleural Mesothelioma.** Approve for 1 year if the patient meets the following criteria (A, B, and C):

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A) The patient has tried first-line chemotherapy (e.g., cisplatin plus pemetrexed, cisplatin plus gemcitabine, vinorelbine); AND
B) The medication will be used in combination with gemcitabine; AND
C) The medication is prescribed by or in consultation with an oncologist

Dosing. Approve the following dosing regimen: Up to 10 mg/kg as an intravenous infusion administered no more frequently than once every 21 days.

6. **Thymic Carcinoma.** Approve for 1 year if the patient meets the following criteria (A and B):
   A) The medication will be used in combination with carboplatin and paclitaxel; AND
   B) The medication is prescribed by or in consultation with an oncologist

Dosing. Approve the following dosing regimen: Up to 10 mg/kg as an intravenous infusion administered no more frequently than once every 21 days.

Waste Management for All Indications.

Dosing for Cyramza is based on body weight (mg/kg). The dose should be calculated, and the number of vials needed assessed.

Conditions Not Recommended for Approval

Cyramza has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

Special Considerations

None.

Limitations/Exclusions

Please see link to member coverage documents below:

Line of Business	Link to Member Coverage Documents
Medicare Advantage Plans (Including D-SNP)	https://medicare.chpw.org/ Select the appropriate plan from the "Plans" drop down on the top navigation bar.

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Apple Health	https://www.chpw.org/for-members/benefits-and-coverage-imc/
Individual & Family (Cascade Select)	https://chnwhealthinsurance.chpw.org/member-center/plan-benefits/

List of Appendices

None.

Citations & References

CFR	42 CFR § 438.210	
WAC	WAC 284-43-2050	
RCW		
LOB & Contract Citation	☒ **WAHIMC** ☐ **BHSO** ☐ **Wraparound** ☐ **SMAC** ☐ **HH**	IMC Section 11.3: Medical Necessity Determination
	☒ **AHE**	AHE Section 11.3: Medical Necessity Determination
	☒ **MA/DSNP**	P&P supports all LOB requirements
	☒ **CS**	P&P supports all LOB requirements
Other Requirements		
NCQA Elements		
References	1. Cyramza® injection for intravenous use [prescribing information]. Indianapolis, IN: Eli Lilly and Company; April 2025. 2. The NCCN Colon Cancer Clinical Practice Guidelines in Oncology (Version 4.2025 – June 27, 2025). © 2025 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on August 21, 2025. 3. The NCCN Rectal Cancer Clinical Practice Guidelines in Oncology (Version 2.2025 – March 31, 2025). © 2025 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on August 21, 2025. 4. The NCCN Drugs & Biologics Compendium. © 2025 National Comprehensive Cancer Network, Inc. Available at:	

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http://www.nccn.org. Accessed on August 21, 2025. Search term: ramucirumab.
5. The NCCN Gastric Cancer Clinical Practice Guidelines in Oncology (Version 2.2025 – April 4, 2025). © 2025 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on August 21, 2025.
6. The NCCN Esophageal and Esophagogastric Junction Cancer Clinical Practice Guidelines in Oncology (Version 3.2025 – April 22, 2025). © 2025 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on August 21, 2025.
7. The NCCN Non-Small Cell Lung Cancer Clinical Practice Guidelines in Oncology (Version 8.2025 – August 15, 2025). © 2025 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on August 21, 2025.
8. The NCCN Hepatocellular Carcinoma Clinical Practice Guidelines in Oncology (Version 1.2025 – March 20, 2025). © 2025 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on August 21, 2025.
9. The NCCN Mesothelioma: Pleural Clinical Practice Guidelines in Oncology (Version 2.2025 – January 14, 2025). © 2025 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on August 21, 2025.
10. The NCCN Thymomas and Thymic Carcinomas Clinical Practice Guidelines in Oncology (Version 2.2025 – May 19, 2025). © 2025 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on August 21, 2025.

Revision History

Revision Date	Revision Description	Revision Made By
12/23/2015	New	Kelly Force; Yusuf Rashid, RPh
12/24/2015	Approval	MMLT
01/11/2017	No revisions	Fran McGaugh
01/12/2017	Approval	MMLT
07/24/2017	Criteria completely updated and revised	Michael Sporck, Pharmacy Intern; Sophia Yun, PharmD

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07/25/2017	Approved	MMLT
03/09/2018	Reassigned from UM to PM	Cindy Bush
04/25/2018	Transferred to new template	Cindy Bush
05/23/2018	No revisions	Jennifer Farley, PharmD
06/14/2018	Approval	UM Committee
08/09/2018	Annual revision: For NSCLC, section divided into non-squamous and squamous. Non-squamous requires testing for mutations for EGFR and ALK for approval	Jennifer Farley, PharmD
09/19/2018	Approval	UM Committee
08/15/2019	Annual revision: new indication for hepatocellular carcinoma. Change from colorectal cancer to colon or rectal cancer. For gastric, esophageal, and nsclc, removed requirement that it must be advanced or metastatic. Changed duration of approval to 1 yr.	Jennifer Farley, PharmD
09/12/2019	Approval	UM Pharmacy Subcommittee
08/04/2020	Annual revision: For Gastric, Esophagogastric Junction, or Esophageal Cancer: Added criteria for use of Cyramza in combination with fluorouracil and irinotecan. For Non-Small Cell Lung Cancer: Added criteria for the use of Cyramza in combination with erlotinib as first-line therapy for patients with EGFR positive disease. Removed criteria for histologic subtypes of NSCLC.	Jennifer Farley, PharmD
08/20/2020	Approval	UM Pharmacy Subcommittee
6/18/2021	No revisions	Catherine Vu, PharmD
07/01/2021	Approval	UM Pharmacy Subcommittee
05/04/2022	Annual revision: Gastric cancer: Cyramza may be used in combination with irinotecan for gastric cancer. For non-small cell lung cancer, specified type of epidermal growth factor receptor (EGFR) disease for first line-therapy (i.e., exon 19 deletions or exon 21 (L858R) substitution mutations). Added that disease is metastatic or advanced.	Alan Gabot, PharmD

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05/05/2022	Approval	UM Pharmacy Subcommittee
03/01/2023	Annual revision: Updated criteria for colorectal cancer to also require patients to have previously received bevacizumab. Added criteria for malignant pleural mesothelioma.	Alan Gabot, PharmD
03/02/2023	Approval	UM Pharmacy Subcommittee
01/04/2024	Annual revision: Clarified the Cyramza can be used in patients that have epidermal growth factor receptor exon 21 (L858R) substitution mutations.	Alan Gabot, PharmD
01/10/2024	Approval	UM Criteria Subcommittee
11/12/2024	Annual revision. Added criteria for thymic carcinomas.	Alan Gabot, PharmD
11/13/2024	Approval	UM Criteria Subcommittee
8/21/2025	Annual Review. For “Colon and Rectal Cancer”, bevacizumab was removed as a requirement for first-line therapy and changed to FOLFOX, CAPEOX, FOLFIRI, and FOLFIRINOX.	Michael Tom, PharmD
09/10/2025	Approval	UM Criteria Subcommittee
06/11/2026	Annual Review. For Thymic Carcinoma, removed the phrase “on day 1” in the criteria.	Alan Gabot, PharmD
06/12/2026	Approval	UM Criteria Subcommittee

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