PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Fruzaqla Prior Authorization Policy
- Fruzaqla™ (fruquintinib capsules – Takeda)

REVIEW DATE: 01/07/2026

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT WHERE APPROPRIATE AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. WHERE COVERAGE FOR CARE OR SERVICES DOES NOT DEPEND ON SPECIFIC CIRCUMSTANCES, REIMBURSEMENT WILL ONLY BE PROVIDED IF A REQUESTED SERVICE(S) IS SUBMITTED IN ACCORDANCE WITH THE RELEVANT CRITERIA OUTLINED IN THE APPLICABLE COVERAGE POLICY, INCLUDING COVERED DIAGNOSIS AND/OR PROCEDURE CODE(S). REIMBURSEMENT IS NOT ALLOWED FOR SERVICES WHEN BILLED FOR CONDITIONS OR DIAGNOSES THAT ARE NOT COVERED UNDER THIS COVERAGE POLICY (SEE "CODING INFORMATION" BELOW). WHEN BILLING, PROVIDERS MUST USE THE MOST APPROPRIATE CODES AS OF THE EFFECTIVE DATE OF THE SUBMISSION. CLAIMS SUBMITTED FOR SERVICES THAT ARE NOT ACCOMPANIED BY COVERED CODE(S) UNDER THE APPLICABLE COVERAGE POLICY WILL BE DENIED AS NOT COVERED. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Fruzaqla, a kinase inhibitor of vascular endothelial growth factor receptors (VEGFR)-1, -2, and -3, is indicated for the treatment of **metastatic colorectal cancer** in adults who have been previously treated with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy, an anti-vascular endothelial growth factor (VEGF) therapy, and if *RAS* wild-type and medically appropriate an anti-epidermal growth factor receptor (EGFR) therapy.[1]

Guidelines

Fruzaqla is discussed in guidelines from National Comprehensive Cancer Network (NCCN):

- **Appendiceal Neoplasms and Cancers:** NCCN guidelines (version 1.2026 – October 30, 2025) recommends Fruzaqla as subsequent therapy as a single agent or in combination with bevacizumab for advanced or metastatic disease (category 2A).[5] This recommendation is for patients who have

progressed through all available regimens, besides Fruzaqla™ (fruquintinib capsules), Stivarga® (regorafenib tablets), or Lonsurf® (trifluridine/tipiracil) with or without bevacizumab.

- **Colon and Rectal Cancer**: NCCN colon cancer guidelines (version 5.2025 – October 30, 2025) and rectal cancer guidelines (version .2025 – October 31, 2025) recommend Fruzaqla for the subsequent treatment of advanced or metastatic colon, rectal, or appendiceal cancer as a single agent (category 2A).[2-4] Patients should have proficient mismatch repair/microsatellite-stable disease, or be ineligible for or progressed on checkpoint inhibitor therapy for deficient mismatch repair/microsatellite instability-high or polymerase epsilon/delta mutation positive disease. Patients should have progressed through all available regimens except Fruzaqla, Lonsurf® (trifluridine, tipiracil tablet), and Stivarga® (regorafenib tablet).

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Fruzaqla. All approvals are provided for the duration noted below.

- **Fruzaqla™ (fruquintinib capsules - Takeda)**

is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indication

1. **Colon, Rectal, or Appendiceal Cancer.** Approve for 1 year if the patient meets ALL of the following (A, B, and C):
   A) Patient is ≥ 18 years of age; AND
   B) Patient has advanced or metastatic disease; AND
   C) Patient has previously been treated with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy.
   Note: Examples of fluoropyrimidine agents include 5-fluorouracil (5-FU) and capecitabine.

CONDITIONS NOT COVERED

- **Fruzaqla™ (fruquintinib capsules - Takeda)**

is(are) considered not medically necessary for ANY other use(s); criteria will be updated as new published data are available.

REFERENCES

1. Fruzaqla capsules [prescribing information]. Lexington, MA: Takeda; February 2025.
2. The NCCN Drugs & Biologics Compendium. © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on December 31 , 2025. Search term: fruquintinib.

3. The NCCN Colon Cancer Clinical Practice Guidelines in Oncology (version 5.2025 – October 30 , 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on December 31, 2025.
4. The NCCN Rectal Cancer Clinical Practice Guidelines in Oncology (version 4.2025 – October 31, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on December 31, 2025.
5. The NCCN Appendiceal Neoplasms and Cancers Clinical Practice Guidelines in Oncology (version 1.2026 – October 30, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on December 31, 2025.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	11/15/2023
Selected Revision	**Colon, Rectal, or Appendiceal Cancer:** Added Appendiceal to the condition of approval. Added "advanced" to the requirement that the patient has advanced or metastatic disease.	12/13/2023
Annual Revision	**Colon, Rectal, or Appendiceal Cancer:** Added requirement that the patient is proficient mismatch repair/microsatellite-stable, or is ineligible or progressed on checkpoint inhibitor therapy and is either deficient mismatch repair/microsatellite instability-high or polymerase epsilon/delta mutation positive.	01/15/2025
Annual Revision	**Colon, Rectal, or Appendiceal Cancer:** The requirements that the patient has proficient mismatch repair/microsatellite stable (pMMR/MSS) disease, patient is ineligible for or progressed on checkpoint inhibitor therapy, patient has deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) disease, patient is polymerase epsilon/delta (POLE/POLD1) mutation positive, patient has previously been treated with an anti-vascular endothelial growth factor agent, and all the associated notes were removed. The option for approval where the tumor is wild-type *RAS* (*KRAS* wild-type and *NRAS* wild-type) [that is, the tumors or metastases are *KRAS* and *NRAS* mutation negative], and its associated requirements and notes were all removed.	01/07/2026