PRIOR AUTHORIZATION POLICY

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

REVIEW DATE: 01/15/2025

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 AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. 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

The National Comprehensive Cancer Network colon (version 5.2024 – August 22, 2024) and rectal (version 4.2024 – August 22, 2024) cancer treatment guidelines 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 the following (A, B, C, and D):
   A) Patient is ≥ 18 years of age; AND
   B) Patient has advanced or metastatic disease; AND
   C) Patient meets ONE of the following (i or ii):
      i. Patient has proficient mismatch repair/microsatellite-stable (pMMR/MSS) disease; OR
      ii. Patient is ineligible for or progressed on checkpoint inhibitor therapy and meets ONE of the following (a or b):
      Note: Examples of checkpoint inhibitors include Keytruda (pembrolizumab intravenous infusion) and Opdivo (nivolumab intravenous infusion).
         a) Patient has deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) disease; OR
         b) Patient is polymerase epsilon/delta (POLE/POLD1) mutation positive; AND
   D) Patient has previously been treated with ALL the following (i, ii, and iii)
      i. Fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy; AND
      Note: Examples of fluoropyrimidine agents include 5-fluorouracil (5-FU) and capecitabine.
      ii. An anti-vascular endothelial growth factor (VEGF) agent; AND
      Note: Examples of anti-VEGF agents include bevacizumab.
      iii. If the tumor is *RAS* wild-type (*KRAS* wild-type and *NRAS* wild-type) [that is, the tumor or metastases are *KRAS* and *NRAS* mutation negative], the patient meets ONE of the following (a or b):
         a) According to the prescriber, anti-epidermal growth factor receptor (EGFR) therapy is NOT medically appropriate; OR
         b) The patient has received an anti-EGFR therapy.
         Note: Examples of anti-EGFR therapy includes Erbitux (cetuximab intravenous infusion) and Vectibix (panitumumab intravenous infusion).

CONDITIONS NOT COVERED

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

is(are) considered experimental, investigational, or unproven for ANY other use(s).

REFERENCES

1. Fruzaqla capsules [prescribing information]. Lexington, MA: Takeda; November 2023.
2. The NCCN Drugs & Biologics Compendium. © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on January 9, 2025. Search term: fruquintinib.

3. The NCCN Colon Cancer Clinical Practice Guidelines in Oncology (version 5.2024 – August 22, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on January 9, 2025.
4. The NCCN Rectal Cancer Clinical Practice Guidelines in Oncology (version 4.2024 – August 22, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on January 9, 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