BlueCross BlueShield
Federal Employee Program

STIVARGA
(regorafenib)

RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Stivarga (regorafenib) is a small molecule inhibitor of multiple membrane-bound and intracellular kinases involved in normal cellular functions and in pathologic processes such as oncogenesis, tumor angiogenesis, and maintenance of the tumor microenvironment (1).

Regulatory Status

FDA-approved indications: Stivarga is a kinase inhibitor indicated for the treatment of patients with: (1)

1. Metastatic colorectal cancer (CRC) who have been previously treated with fluoropyrimidine-, oxaliplatin- and irinotecan- based chemotherapy, an anti-VEGF therapy, and, if RAS wild type, an anti-EGFR therapy.
2. Locally advanced, unresectable or metastatic gastrointestinal stromal tumor (GIST) in patients who have been previously treated with Gleevec (imatinib) and Sutent (sunitinib).
3. Hepatocellular carcinoma (HCC) who have been previously treated with sorafenib.

Off-Label Uses: (2)

1. Metastatic colorectal cancer (CRC) who have progressed through all available regimens with or without being previously treated with anti-VEGF therapy
2. Cholangiocarcinoma

Stivarga carries a boxed warning for severe and sometimes fatal hepatotoxicity. Liver function tests should be obtained before initiation of Stivarga, and it should be monitored at least every 2 weeks during the first 2 months of treatment. Thereafter, monitor monthly or more frequently as clinically indicated. Monitor liver function tests weekly in patients experiencing elevated liver function tests until improvement to less than 3 times the upper limit normal (ULN) or baseline. Temporarily hold and then reduce or permanently discontinue Stivarga depending on the severity and persistence of hepatotoxicity as manifested by elevated liver function tests or hepatocellular necrosis (1).

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Other adverse events are hemorrhage, dermatological toxicity, hypertension, cardiac ischemia and infarction, wound healing complications, reversible posterior leukoencephalopathy syndrome (RPLS) and gastrointestinal perforation or fistula. Stivarga also carries a pregnancy category D (1).

The safety and effectiveness of Stivarga have not been established in pediatric patients (1).

Summary

Stivarga (regorafenib) is a multi-kinase inhibitor, designed to block enzymes that promote cancer growth. Stivarga is indicated for metastatic colorectal cancer; locally advanced, unresectable or metastatic gastrointestinal stromal tumor (GIST); and hepatocellular carcinoma (HCC). Stivarga is also indicated off-label for use in cholangiocarcinoma (1-2).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Stivarga while maintaining optimal therapeutic outcomes.

References

1. Stivarga [package insert]. Wayne, NJ: Bayer Healthcare Pharmaceuticals Inc.; December 2020.
2. NCCN Drugs & Biologics Compendium® Regorafenib 2024. National Comprehensive Cancer Network, Inc. Accessed on October 3, 2024.