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 indication: Stivarga is a kinase inhibitor indicated for the treatment of patients with:

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.

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 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).

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 has been approved to treat colorectal cancer that has spread despite prior treatment and for locally advanced gastrointestinal cancer. Stivarga is indicated for metastatic colorectal cancer in patients who have been previously treated with fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy and an anti-VEGF therapy. If the patient has the KRAS wild type, they must have previously been treated with an anti-EGFR therapy. Stivarga is also indicated for locally advanced, unresectable or metastatic gastrointestinal stromal tumor (GIST) who have been previously treated with Gleevec (imatinib) and Sutent (sunitinib). Additionally, Stivarga is indicated for the treatment of hepatocellular carcinoma (HCC) who have been previously treated with sorafenib (1).

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

References