Stivarga®
(regorafenib) tablets

BAYER

For patients with metastatic colorectal cancer (CRC) who have been previously treated with, or are not considered candidates for, fluoropyrimidine-based chemotherapy, an anti-VEGF therapy, and, if RAS wild type, an anti-EGFR therapy[1]

HARNESS THE POWER OF REGORAFENIB[2,3]

Increase overall survival (OS) potential for patients with metastatic colorectal cancer (mCRC) compare with placebo[2,3]

REFERENCES:

1. Thailand Stivarga product information CCDS10 **2.** Grothey A, Van Cutsem E, Sobrero A, et al; for the CORRECT Study Group. Regorafenib monotherapy for previously treated metastatic colorectal cancer (CORRECT): an international, multicenter, randomized, placebo-controlled, phase 3 trial. Lancet. 2013;381:303-312. **3.** Li J, Qin S, Xu R, et al; on behalf of the CONCUR Investigators. Regorafenib plus best supportive care versus placebo plus best supportive care in Asian patients with previously treated metastatic colorectal cancer (CONCUR): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Oncol. 2015;16(6):619-629.

PRESCRIBING INFORMATION

Stivarga 40 mg film-coated tablets. Each film-coated tablet contains 40 mg of regorafenib. **Indication(s):** 1. Stivarga is indicated for the treatment of patients with metastatic colorectal cancer (CRC) who have been previously treated with, or are not considered candidates for, fluoropyrimidine-based chemotherapy, an anti-VEGF therapy, and, if RAS wild type, an anti-EGFR therapy. 2. Stivarga is indicated for the treatment of patients with gastrointestinal stromal tumors (GIST) who have been previously treated with 2 tyrosine kinase inhibitors. 3.Stivarga is indicated for the treatment of patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib **Dosage regimen:** The recommended dose is 160 mg regorafenib (4 tablets Stivarga each containing 40 mg regorafenib), taken orally once daily for 3 weeks on therapy followed by 1 week off therapy to comprise a cycle of 4 weeks. Stivarga should be taken at the same time each day. The tablets should be swallowed whole with water after a light meal. If a dose of Stivarga is missed, then it should be taken on the same day as soon as the patient remembers. The patient should not take two doses on the same day to make up for a missed dose. **Dose modification:** Dose interruptions and/or dose reductions may be required based on individual safety and tolerability. Dose modifications are to be applied in 40 mg (one tablet) steps. The lowest recommended daily dose is 80 mg. The maximum daily dose is 160 mg. **Special warnings and precautions for use:** Hepatic effects, Infections, Hemorrhage, Gastrointestinal perforation and fistula, Cardiac ischemia and infarction, Reversible Posterior Leukoencephalopathy Syndrome, Arterial hypertension, Wound healing complications, Dermatological toxicity, Biochemical and metabolic laboratory test abnormalities **Interaction with other medicinal products:** Inhibitors/inducers of CYP3A4 , UGT1A1 and UGT1A9 substrates, Breast cancer resistance protein (BCRP) and P-glycoprotein substrates, CYP isoform-selective substrates **Undesirable effects:** The most frequently observed adverse drug reactions (≥30%) in patients receiving Stivarga are pain, hand-foot skin reaction, asthenia/fatigue, diarrhea, decreased appetite and food intake, hypertension and infection. The most serious adverse drug reactions in patients receiving Stivarga are severe liver injury, hemorrhage, gastrointestinal perforation and infection. **Shelf life:** 3 years, do not store above 30°C Keep the bottle tightly closed after first opening. Once the bottle is opened the medicinal product has shown to be stable for 7 weeks even without the desiccant. Thereafter, the medicinal product is to be discarded.

Please refer to approved product information before prescribing. Further information is available on request.

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Regorafenib plus best supportive care versus placebo plus best supportive care in Asian patients with previously treated metastatic colorectal cancer (CONCUR)[3]

A randomized, double-blind, placebo-controlled, phase 3 trial in 25 hospitals in mainland China, Hong Kong, South Korea, Taiwan, and Vietnam, the study recruited Asian patients aged 18 years or older with progressive metastatic colorectal cancer who had received at least two previous treatment lines or were unable to tolerate standard treatments, ECOG 0-1, life expectancy of at least 3 months, and adequate bone marrow, liver, and renal function, without other uncontrolled medical disorders to receive oral regorafenib 160 mg once daily or placebo on days 1–21 of each 28 day cycle; patients in both groups were also to receive best supportive care. 204 patients to receive either regorafenib (136 [67%]) or placebo (68 [33%]). After a median follow-up of 7·4 months (IQR 4·3–12·2), overall survival was significantly better with regorafenib than it was with placebo (hazard ratio 0·55, 95% CI 0·40–0·77, one-sided p=0·00016; median overall survival 8·8 months [95% CI 7·3–9·8] in the regorafenib group vs 6·3 months [4·8–7·6] in the placebo group). Drug-related adverse events occurred in 132 (97%) of 136 regorafenib recipients and 31 (46%) of 68 placebo recipients. The most frequent grade 3 or higher regorafenib-related adverse events were hand–foot skin reaction (22 [16%] of 136 patients in the regorafenib group vs none in the placebo group), hypertension (15 [11%] vs two [3%] of 68 patients in the placebo group), hyperbilirubinaemia (nine [7%] vs one [1%]), hypophosphataemia (nine [7%] vs none), alanine aminotransferase concentration increases (nine [7%] vs none), aspartate aminotransferase concentration increases (eight [6%] vs none), lipase concentration increases (six [4%] vs one [1%]), and maculopapular rash (six [4%] vs none).

Regorafenib monotherapy for previously treated metastatic colorectal cancer (CORRECT)[2]

A randomized, international, multicenter, randomized, placebo-controlled, phase 3 at 114 centers in 16 countries. Patients with documented metastatic colorectal cancer and progression during or within 3 months after the last standard therapy were randomized (in a 2:1 ratio; by computer generated randomization list and interactive voice response system; preallocated block design (block size six); stratified by previous treatment with VEGF-targeting drugs, time from diagnosis of metastatic disease, and geographical region) to receive best supportive care plus oral regorafenib 160 mg or placebo once daily, for the first 3 week s of each 4 week cycle. 760 patients were randomized to receive regorafenib (n=505) or placebo (n=255). The primary endpoint of overall survival was met at a preplanned interim analysis; data cutoff was on July 21, 2011. Median overall survival was 6·4 months in the regorafenib group versus 5·0 months in the placebo group (hazard ratio 0·77; 95% CI 0·64–0·94; one-sided p=0·0052). Treatment-related adverse events occurred in 465 (93%) patients assigned regorafenib and in 154 (61%)

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