Drug Therapy Guidelines

Applicable

<table>
<thead>
<tr>
<th>Medical Benefit</th>
<th>Effective: 11/1/18</th>
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<tbody>
<tr>
<td>Pharmacy- Formulary 1</td>
<td>x Next Review: 9/19</td>
</tr>
<tr>
<td>Pharmacy- Formulary 2</td>
<td>x Date of Origin: 12/2012</td>
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<tr>
<td>Pharmacy- Formulary 3/Exclusive</td>
<td>x Review Dates: 12/12, 12/13, 12/14, 9/15, 9/16, 9/17, 9/18</td>
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<td>Pharmacy- Formulary 4/AON</td>
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I. Medication Description

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. In *in vitro* biochemical or cellular assays, regorafenib or its major human active metabolites M-2 and M-5 inhibited the activity of RET, VEGFR1, VEGFR2, VEGFR3, KIT, PDGFR-alpha, PDGFR-beta, FGFR1, FGFR2, TIE2, DDR2, Trk2A, Eph2A, RAF-1, BRAF, BRAFV600E, SAPK2, PTK5, and Abl at concentrations of regorafenib that have been achieved clinically. In *in vivo* models, regorafenib demonstrated anti-angiogenic activity in a rat tumor model, and inhibition of tumor growth as well as anti-metastatic activity in several mouse xenograft models including some for human colorectal carcinoma.

II. Position Statement

Coverage is determined through a prior authorization process with supporting clinical documentation for every request.

III. Policy

Coverage of Stivarga is available when the following criteria have been met:

- Member is at least 18 years of age AND
- The medication is prescribed by a hematologist/oncologist AND
- The requested use is supported by the National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines (NCCN Guidelines®) and/or NCCN Drugs & Biologics Compendium (NCCN Compendium®) with a recommendation of category level 1 or 2A.

IV. Quantity Limitations

84 tablets per month are covered to allow for FDA-approved dosing.

V. Coverage Duration

Coverage is granted for 6 months and may be renewed.

VI. Coverage Renewal Criteria

Coverage can be renewed based upon the following criteria:

- Stabilization of disease or in absence of disease progression AND
Drug Therapy Guidelines

Stivarga® (regorafenib)

Last Review Date: 9/2018

- Absence of unacceptable toxicity from the drug

VII. Billing/Coding Information

Available as 40mg tablets

VIII. Summary of Policy Changes

- 3/15/13: new policy
- 3/15/14: no policy changes
- 3/15/15: no policy changes
- 7/1/15: formulary distinctions made
- 12/15/15: no policy changes
- 9/15/16: policy updated to correspond with current NCCN treatment guidelines
- 10/16/17: coverage criteria updated to allow use as supported by current NCCN guidelines
- 11/1/18: no policy changes

IX. References


The Plan fully expects that only appropriate and medically necessary services will be rendered. The Plan reserves the right to conduct pre-payment and post-payment reviews to assess the medical appropriateness of the above-referenced therapies.

The preceding policy applies only to members for whom the above named pharmacy benefit medications are included on their covered formulary. Members with closed formulary benefits are subject to trying all appropriate formulary alternatives before a coverage exception for a non-formulary medication will be considered.

The preceding policy is a guideline to allow for coverage of the pertinent medication/product, and is not meant to serve as a clinical practice guideline.