Medica Coverage Policy

<table>
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<th>Policy Name:</th>
<th>Pharmacogenetic Testing to Predict Toxicity to 5-Fluorouracil (5-FU)/Capecitabine-Based Chemotherapy</th>
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<td>Effective Date:</td>
<td>6/21/2021</td>
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**Important Information – Please Read Before Using This Policy**

These services may or may not be covered by all Medica plans. Please refer to the member’s plan document for specific coverage information. If there is a difference between this general information and the member’s plan document, the member’s plan document will be used to determine coverage. With respect to Medicare and Minnesota Health Care Programs, this policy will apply unless those programs require different coverage. Members may contact Medica Customer Service at the phone number listed on their member identification card to discuss their benefits more specifically. Providers with questions about this Medica coverage policy may call the Medica Provider Service Center toll-free at 1-800-458-5512.

Medica coverage policies are not medical advice. Members should consult with appropriate health care providers to obtain needed medical advice, care and treatment.

**Coverage Policy**
Pharmacogenetic testing to predict toxicity to 5-Fluorouracil (5-FU)/capecitabine-based chemotherapy is investigative and unproven and therefore **NOT COVERED**. There is insufficient reliable evidence in the form of high quality peer-reviewed medical literature to establish the efficacy or effects on health care outcomes.

**Note:** This policy is no longer scheduled for routine review of the scientific literature.

**Description**
Chemotherapeutic agents 5-fluorouracil (5-FU) (Adrucil®; SP Pharmaceuticals) and capecitabine (Xeloda®; Roche Laboratories Inc.) are used in the treatment of a wide variety of malignancies, including colorectal, gastric, pancreatic, head, neck, breast, ovarian, and cervical cancers. In general, 5-FU is relatively well tolerated at standard doses. However, in a small percentage of individuals, severe toxicity has been reported with both agents, resulting in serious side effects and even deaths.

Pharmacogenetic testing to predict toxicity to 5-FU-based chemotherapy is a laboratory test performed on a blood sample to evaluate mutations in the genes associated with two key enzymes, dihydropyrimidine dehydrogenase (DPD) and thymidylate synthetase (TS or TYMS). These enzymes affect how the body metabolizes and responds to 5-FU-based chemotherapy regimens. While researchers theorize that pharmacogenetic testing may be useful in identifying potential toxicity before it occurs, more study is needed to demonstrate its value in the clinical setting.

**FDA Approval**
There are no assay kits approved by the FDA for genetic testing for DPD or TS genotypes. Clinical laboratories that develop and validate tests for in-house use are regulated under the Clinical Laboratory Improvement Amendments (CLIA) of 1988. Examples of commercially available laboratory-developed genetic tests for DPD and/or TS include, but are not limited to, Dihydropyrimidine Dehydrogenase (DPD) Gene Mutation Analysis (Quest Diagnostics, Valencia, CA), Dihydropyrimidine Dehydrogenase (DPD) for Fluorouracil (5-FU) (Genelex, Seattle, WA), Dihydropyrimidine Dehydrogenase (DPYD)/5-FU Sensitivity Test (Molecular Diagnostics Laboratories, Covington, KY), TS Expression (Response Genetics Inc, Los Angeles, CA) and 5FU Panel (ARUP Laboratories, Salt Lake City, UT).
Prior Authorization
Prior authorization is not applicable. Claims for this service are subject to retrospective review and denial of coverage, as investigative services are not eligible for reimbursement.

Coding Considerations
Use the current applicable CPT/HCPCS code(s). The following codes are included below for informational purposes only, and are subject to change without notice. Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement.

CPT Codes:
- 81346 - TYMS (thymidylate synthetase) (eg, 5-fluorouracil/5-FU drug metabolism), gene analysis, common variant(s) (eg, tandem repeat variant)
- 81400 – Molecular pathology procedure, Level 1.
  - Gene description – DPYD (dihydropyrimidine dehydrogenase) (eg, 5-fluorouracil/5-FU and capecitabine drug metabolism), ISV14+1G>A variant
- 81401 – Molecular pathology procedure, Level 2
  - Gene description – TYMS (thymidylate synthetase) (eg, 5-fluorouracil/5-FU drug metabolism), tandem repeat variant

Original Effective Date: 2/1/2012

Re-Review Date(s):
- 12/17/14
- 1/1/2018 – administrative update; codes added
- 3/21/2018
- 2/20/2020 – administrative update; format
- 3/17/2021

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