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Medicare Advantage Policy Manual **Policy ID:** M-LAB64

Laboratory and Genetic Testing for Use of 5-Fluorouracil (5-FU) in Patients with Cancer

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IMPORTANT REMINDER

The Medicare Advantage Medical Policy manual is not intended to override the member Evidence of Coverage (EOC), which defines the insured's benefits, nor is it intended to dictate how providers are to practice medicine. Physicians and other health care providers are expected to exercise their medical judgment in providing the most appropriate care for the individual member.

The Medicare Advantage Medical Policies are designed to provide guidance regarding the decision-making process for the coverage or non-coverage of services or procedures in accordance with the member EOC and the Centers of Medicare and Medicaid Services (CMS) policies, when available. In the event of a conflict, applicable CMS policy or EOC language will take precedence over the Medicare Advantage Medical Policy. In the absence of CMS guidance for a requested service or procedure, the health plan may apply their Medical Policy Manual or MCG™ criteria, both of which are developed with an objective, evidence-based process using scientific evidence, current generally accepted standards of medical practice, and authoritative clinical practice guidelines.

Medicare and EOCs exclude from coverage, among other things, services or procedures considered to be investigational, cosmetic, or not medically necessary, and in some cases, providers may bill members for these non-covered services or procedures. Providers are encouraged to inform members in advance when they may be financially responsible for the cost of non-covered or excluded services.

DESCRIPTION

Dosing of 5-fluorouracil (5-FU) in cancer patients to a predetermined area under the curve (AUC) target has been proposed as a method to reduce variability in systemic exposure to 5-FU, reduce toxicity, and improve tumor response. Also available is genetic testing for variants affecting 5-FU metabolism. Genetic variants may affect activity of enzymes involved in 5-FU metabolism. Currently-available polymerase chain reaction (PCR) tests assess specific variants in genes encoding dihydropyrimidine reductase (DPYD) and thymidylate synthase (TYMS), enzymes in the catabolic and anabolic pathways of 5-FU metabolism, respectively.

MEDICARE ADVANTAGE POLICY CRITERIA

CMS Coverage Manuals* None

National Coverage Determinations (NCDs)*	None
Noridian Healthcare Solutions (Noridian) Local Coverage Determinations (LCDs) and Articles (LCAs)*	For ***DPYD variant testing***: ✓ Excluded Test List – as of 08/01/2016 *(For laboratories in the health plan's service area – search by gene name)* ✓ Excluded Test List – as of 08/01/2016 *(For testing performed in California – search by gene name)* **Note:** Through the MolDX review process, DPYD gene testing was determined to be an excluded test and will be denied as not medically reasonable or necessary. For ***TYMS variant testing offered by laboratories in the health plan's service area:*** ✓ Noridian web page for MolDX Approved Gene Testing (M00041) – search by gene name) ✓ *TYMS testing is listed as an approved test. Therefore, according to Medicare medical necessity rules for diagnostic laboratory services, when documentation clearly indicates how the test results are expected to be promptly used by the treating physician to treat and manage a specific medical problem, this testing may be considered medically necessary.*
Non-Noridian Healthcare Solutions LCDs and LCAs*	For the ***MY5-FU™ 5-fluorouracil exposure optimization test (Saladax Biomedical Laboratories, Bethlehem, PA)***: ✓ The Novitas LCD L35679 was retired effective October 4, 2018, based on annual review findings for the test in question, Therefore, this test is considered medically necessary on and after this date. **Note:** This test is offered by Saladex Biomedical laboratory (Pennsylvania). The health care plan is required to use coverage determinations published by the contractor assigned jurisdiction over the service area in which the tests are performed in accordance with Medicare compliance guidelines.[4] **Scroll to the "Public Version(s)" section at the bottom of the LCD for links to prior versions if necessary.

POLICY GUIDELINES

REQUIRED DOCUMENTATION

The information below **must** be submitted for review to determine whether policy criteria are met. If any of these items are not submitted, it could impact our review and decision outcome:

- The specific name of the genetic or diagnostic laboratory test;
- Name of the performing laboratory;
- The exact gene(s) being tested;
- Applicable CPT and/or HCPCS code(s);
- Brief explanation and medical records documenting how the results of this testing is expected to guide treatment decisions relevant to the member's personal medical history.

REGULATORY STATUS

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratories offering such tests as a clinical service must meet the general regulatory standards of the Clinical Laboratory Improvement Act (CLIA) and must be licensed by CLIA for high-complexity testing. (ARUP Laboratories, Myriad Genetics, and Saladax Biomedical are CLIA-licensed laboratories.)

- My5-FU™ was originally marketed in the U.S. by Myriad Genetics as OnDose® under patents licensed from Saladex Biomedical. In June 2013, rights to the assay reverted back to Saladex Biomedical.(2) The My5-FU™ is designed to measure patients' exposure to 5-FU to help oncologists adjust and optimize 5-FU dosing.
- Myriad Genetics, ARUP Laboratories, and other laboratories may offer DPYD and TYMS variant testing. For example, TheraGuide® 5-FU is offered by Myriad Genetics as a laboratory-developed test

CROSS REFERENCES

Genetic and Molecular Diagnostics – Single Gene or Variant Testing, Genetic Testing, Policy No. M-20

Chemoresistance and Chemosensitivity Assays (CSRAs), Laboratory, Policy No. M-06

REFERENCES

1. HCPCS Public Meeting Agenda Item #19, May 25, 2011, page 38
2. PRNewswire. Saladax Biomedical Laboratories to Offer the Full Portfolio of MyCare™ Therapeutic Dose Management Assays in the United States. February 11, 2013. [cited 11/26/2014]; Available from: http://www.prnewswire.com/news-releases/saladax-biomedical-laboratories-to-offer-the-full-portfolio-of-mycare-therapeutic-dose-management-assays-in-the-united-states-190681031.html

3. Noridian Medicare Part B Jurisdiction F (J-F) Website: https://med.noridianmedicare.com/web/jfb/policies/moldx
4. Medicare Managed Care Manual, Pub. #100-16, Chapter 4 - Benefits and Beneficiary Protections, §90.4.1 – MACS with Exclusive Jurisdiction over a Medicare Item or Service
5. Medicare Benefit Policy Manual, Ch. 15, §80.1 - Clinical Laboratory Services
6. Social Security Act §1862(a)(1)(A) http://www.ssa.gov/OP_Home/ssact/title18/1862.htm

CODING

NOTE: HCPCS code S3722 is a Medicare Status "I" code, and therefore, is not valid for Medicare or Medicare Advantage use.

Codes	Number	Description
CPT	81232	DPYD (dihydropyrimidine dehydrogenase) (eg, 5-fluorouracil/5-FU and capecitabine drug metabolism), gene analysis, common variant(s) (eg, *2A, *4, *5, *6)
	81346	TYMS (thymidylate synthetase) (eg, 5-fluorouracil/5-FU drug metabolism), gene analysis, common variant(s) (eg, tandem repeat variant)
	84999	Unlisted chemistry procedure
HCPCS	S3722	Dose optimization by area-under-the-curve (AUC) analysis for infusional 5-fluorouracil (5-FU) *(Not valid for Medicare purposes)*

***IMPORTANT NOTE:** Medicare Advantage medical policies use the most current Medicare references available at the time the policy was developed. Links to Medicare references will take viewers to external websites outside of the health plan's web control as these sites are not maintained by the health plan.*