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

Laboratory and Genetic Testing for Use of Fluoropyrimidine Chemotherapy (5-FU and Capecitabine) 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

Tests to guide fluoropyrimidine dosing and/or treatment choice in patients with cancer have been proposed. 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 maximize tumor response. Also available is genetic testing for variants affecting 5-FU metabolism in order to determine dosing of 5-FU and capecitabine. Genetic variants may affect activity of enzymes involved in 5-FU metabolism. Currently available genetic 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 (Articles))*	For ***DPYD variant testing offered by laboratories in the health plan's service area:*** ✓ MolDX: Pharmacogenomics Testing (L38337) *(The companion article A57385 can be accessed directly from the LCD. The Article provides actionable drug-gene details.) (Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY) (Also note the "Special Documentation Requirements" section in the LCD.)* ✓ MolDX: Pharmacogenomics Testing (L38335) *(The companion article* A57384 *can be accessed directly from the LCD. The Article provides actionable drug-gene details. (Laboratories in CA and NV) (Also note the "Special Documentation Requirements" section in the LCD.)*
Non-Noridian Healthcare Solutions LCDs and Articles*	For *DPYD* and/or *TYMS* gene testing performed in other jurisdictions: ✓ Billing and Coding: Molecular Pathology Procedures (A56199) *(For performing laboratories in IL, MN, WI, CT, NY, ME, MA, NH, RI, VT) (Look for the gene and/or CPT code in the Group 3 Non-covered Codes section)* **Scroll to the "Public Version(s)" section at the bottom of the LCD for links to prior versions if necessary.
Medical Policy Manual	*Medicare coverage guidance is not available for TYMS gene testing in the health plan's service area. Therefore, the health plan's medical policy is applicable (CPT code 81346).* Laboratory and Genetic Testing for Use of Fluoropyrimidine Chemotherapy (5-FU and Capecitabine) in Patients with Cancer, Lab, Policy No. 64 (see "NOTE" below)

NOTE: If a procedure or device lacks scientific evidence regarding safety and efficacy because it is investigational or experimental, the service is noncovered as not reasonable and necessary to treat illness or injury. (*Medicare IOM Pub. No. 100-04, Ch. 23, §30 A*). According to Title XVIII of the Social Security Act, §1862(a)(1)(A), only medically reasonable and necessary services are covered by Medicare. In the absence of a NCD, LCD, or other coverage guideline, CMS guidelines allow a Medicare Advantage Organization (MAO) to make coverage determinations, applying an ***objective, evidence-based process, based on authoritative evidence***. (*Medicare IOM Pub. No. 100-16, Ch. 4, §90.5*). The Medicare Advantage Medical Policy - Medicine Policy No. M-149 - provides further details regarding the plan's evidence-assessment process (see Cross References).

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.

CROSS REFERENCES

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

REFERENCES

1. HCPCS Public Meeting Agenda Item #19, May 25, 2011, page 38
2. Noridian Medicare Part B Jurisdiction F (J-F) Website: https://med.noridianmedicare.com/web/jfb/policies/moldx
3. Medicare Benefit Policy Manual, Ch. 15, §80.1 - Clinical Laboratory Services
4. 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.*