

Reimbursement Policy

Therapeutic Drug Monitoring for 5-Fluorouracil

[POLICY DESCRIPTION](#) | [INDICATIONS AND/OR LIMITATIONS OF COVERAGE](#) | [APPLICABLE STATE AND FEDERAL REGULATIONS](#) | [APPLICABLE CPT/HCPCS PROCEDURE CODES](#) | [EVIDENCE-BASED SCIENTIFIC REFERENCES](#) | [REVISION HISTORY](#)

I. Policy Description

Chemotherapeutic agents are incredibly potent drugs, often carrying cytotoxic side effects. Most chemotherapeutic drugs have a steep dose-response relationship and a narrow therapeutic index (a range where an agent provides therapeutic effect without major side effects). Identification of the optimal dose of a chemotherapeutic agent, such as 5-fluorouracil, has been proposed as a potential improvement for the management of cancer patients.¹

This policy does not address pharmacogenetic testing to aid or direct chemotherapies. For pharmacogenetic testing, please refer to AHS-M2021.

II. Indications and/or Limitations of Coverage

Application of coverage criteria is dependent upon an individual's benefit coverage at the time of the request. Specifications pertaining to Medicare and Medicaid can be found in the "Applicable State and Federal Regulations" section of this policy document.

- 1) For individuals who are undergoing 5-fluorouracil chemotherapy, therapeutic drug monitoring (TDM) to aid in managing dose adjustment **MEETS COVERAGE CRITERIA**.

The following does not meet coverage criteria due to a lack of available published scientific literature confirming that the test(s) is/are required and beneficial for the diagnosis and treatment of an individual's illness.

- 2) To aid in managing dose adjustment for individuals undergoing 5-fluorouracil chemotherapy, the following tests **DO NOT MEET COVERAGE CRITERIA**:
 - a) Uracil breath tests.
 - b) Dihydrouracil/uracil ratio testing of plasma, serum, or urine samples.

III. Applicable State and Federal Regulations

DISCLAIMER: If there is a conflict between this Policy and any relevant, applicable government policy for a particular member [e.g., Local Coverage Determinations (LCDs) or National Coverage Determinations (NCDs) for Medicare and/or state coverage for Medicaid], then the government policy will be used to make the determination. For the most up-to-date Medicare policies and coverage, please

Reimbursement Policy

visit the Medicare search website: <https://www.cms.gov/medicare-coverage-database/search.aspx>. For the most up-to-date Medicaid policies and coverage, visit the applicable state Medicaid website.

Food and Drug Administration (FDA)

Many labs have developed specific tests that they must validate and perform in house. These laboratory-developed tests (LDTs) are regulated by the Centers for Medicare and Medicaid (CMS) as high-complexity tests under the Clinical Laboratory Improvement Amendments of 1988 (CLIA '88). LDTs are not approved or cleared by the U. S. Food and Drug Administration; however, FDA clearance or approval is not currently required for clinical use.

The FDA's "Prescribing Information" documents for fluorouracil, paclitaxel, imatinib, and docetaxel do not include AUC as a method to adjust dosage.⁴⁰⁻⁴³

IV. Applicable CPT/HCPCS Procedure Codes

CPT	Code Description
S3722	Dose optimization by area under the curve (AUC) analysis, for infusional 5-fluorouracil
80299	Quantitation of therapeutic drug, not elsewhere specified
82542	Column chromatography, includes mass spectrometry, if performed (eg, HPLC, LC, LC/MS, LC/MS-MS, GC, GC/MS-MS, GC/MS, HPLC/MS), non-drug analyte(s) not elsewhere specified, qualitative or quantitative, each specimen
83789	Mass spectrometry and tandem mass spectrometry (eg, MS, MS/MS, MALDI, MS-TOF, QTOF), non-drug analyte(s) not elsewhere specified, qualitative or quantitative, each specimen

Current Procedural Terminology© American Medical Association. All Rights reserved.

Procedure codes appearing in Medical Policy documents are included only as a general reference tool for each policy. They may not be all-inclusive.

V. Evidence-based Scientific References

1. Eaton K, Lyman, Gary. Dosing of anticancer agents in adults. Updated October 22, 2025. <https://www.uptodate.com/contents/dosing-of-anticancer-agents-in-adults>
2. Mindt S, Aida S, Merx K, et al. Therapeutic drug monitoring (TDM) of 5-fluorouracil (5-FU): new preanalytic aspects. *Clin Chem Lab Med*. Jun 26 2019;57(7):1012-1016. doi:10.1515/cclm-2018-1177
3. Cancer Research UK. Fluorouracil (5FU). Updated July 26, 2024. <https://www.cancerresearchuk.org/about-cancer/cancer-in-general/treatment/cancer-drugs/drugs/fluorouracil>
4. Kang JS, Lee MH. Overview of therapeutic drug monitoring. *Korean J Intern Med*. Mar 2009;24(1):1-10. doi:10.3904/kjim.2009.24.1.1
5. Hashimoto Y, Yoshida Y, Yamada T, et al. Current Status of Therapeutic Drug Monitoring of 5-Fluorouracil Prodrugs. *Anticancer Res*. Aug 2020;40(8):4655-4661. doi:10.21873/anticancer.14464
6. MyCare. Clinical Studies. <https://mycaretests.com/oncology/clinicians/#process>
7. MyCare. You're not getting chemo the right way. <https://mycaretests.com/oncology/>

Reimbursement Policy

8. NICE. Fluorouracil chemotherapy: The My5-FU assay for guiding dose adjustment. Updated December 10, 2014. <https://www.nice.org.uk/guidance/dg16/resources/fluorouracil-chemotherapy-the-my5fu-assay-for-guiding-dose-adjustment-pdf-1053633149125>
9. Cunha-Junior GF, De Marco L, Bastos-Rodrigues L, et al. (13)C-uracil breath test to predict 5-fluorouracil toxicity in gastrointestinal cancer patients. *Cancer Chemother Pharmacol*. Dec 2013;72(6):1273-82. doi:10.1007/s00280-013-2309-4
10. Ezzeldin HH, Acosta EP, Mattison LK, Fourie J, Modak A, Diasio RB. (13)C-5-FU breath test current status and future directions: a comprehensive review. *J Breath Res*. Dec 2009;3(4):047002. doi:10.1088/1752-7155/3/4/047002
11. Buchel B, Sistonen J, Joerger M, Aebi Y, Schurch S, Largiader CR. Comparative evaluation of the My5-FU immunoassay and LC-MS/MS in monitoring the 5-fluorouracil plasma levels in cancer patients. *Clin Chem Lab Med*. Aug 2013;51(8):1681-8. doi:10.1515/cclm-2012-0641
12. Yang R, Zhang Y, Zhou H, et al. Individual 5-Fluorouracil Dose Adjustment via Pharmacokinetic Monitoring Versus Conventional Body-Area-Surface Method: A Meta-Analysis. *Therapeutic drug monitoring*. Feb 2016;38(1):79-86. doi:10.1097/ftd.0000000000000238
13. Fang L, Xin W, Ding H, et al. Pharmacokinetically guided algorithm of 5-fluorouracil dosing, a reliable strategy of precision chemotherapy for solid tumors: a meta-analysis. *Scientific reports*. May 27 2016;6:25913. doi:10.1038/srep25913
14. Morawska K, Goirand F, Marceau L, et al. 5-FU therapeutic drug monitoring as a valuable option to reduce toxicity in patients with gastrointestinal cancer. *Oncotarget*. Feb 20 2018;9(14):11559-11571. doi:10.18632/oncotarget.24338
15. Macaire P, Morawska K, Vincent J, et al. Therapeutic drug monitoring as a tool to optimize 5-FU-based chemotherapy in gastrointestinal cancer patients older than 75 years. *Eur J Cancer*. Apr 2019;111:116-125. doi:10.1016/j.ejca.2019.01.102
16. Wilhelm M, Mueller L, Miller MC, et al. Prospective, Multicenter Study of 5-Fluorouracil Therapeutic Drug Monitoring in Metastatic Colorectal Cancer Treated in Routine Clinical Practice. *Clinical Colorectal Cancer*. 2016;15(4):381-388. doi:10.1016/j.clcc.2016.04.001
17. Gamelin E, Delva R, Jacob J, et al. Individual fluorouracil dose adjustment based on pharmacokinetic follow-up compared with conventional dosage: results of a multicenter randomized trial of patients with metastatic colorectal cancer. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. May 01 2008;26(13):2099-105. doi:10.1200/jco.2007.13.3934
18. Engels FK, Loos WJ, van der Bol JM, et al. Therapeutic Drug Monitoring for the Individualization of Docetaxel Dosing: A Randomized Pharmacokinetic Study. *Clinical Cancer Research*. 2011;17(2):353. doi:10.1158/1078-0432.CCR-10-1636
19. Joerger M, Huitema ADR, Richel DJ, et al. Population Pharmacokinetics and Pharmacodynamics of Paclitaxel and Carboplatin in Ovarian Cancer Patients: A Study by the European Organization for Research and Treatment of Cancer-Pharmacology and Molecular Mechanisms Group and New Drug Development Group. *Clinical Cancer Research*. 2007;13(21):6410. doi:10.1158/1078-0432.CCR-07-0064
20. Moeung S, Chevreau C, Broutin S, et al. Therapeutic Drug Monitoring of Carboplatin in High-Dose Protocol (TI-CE) for Advanced Germ Cell Tumors: Pharmacokinetic Results of a Phase II Multicenter Study. *Clin Cancer Res*. Dec 1 2017;23(23):7171-7179. doi:10.1158/1078-0432.Ccr-17-1344

Reimbursement Policy

21. Morrow A, Garland C, Yang F, De Luna M, Herrington JD. Analysis of carboplatin dosing in patients with a glomerular filtration rate greater than 125 mL/min: To cap or not to cap? A retrospective analysis and review. *J Oncol Pharm Pract.* Oct 2019;25(7):1651-1657. doi:10.1177/1078155218805136
22. Guilhot F, Hughes TP, Cortes J, et al. Plasma exposure of imatinib and its correlation with clinical response in the Tyrosine Kinase Inhibitor Optimization and Selectivity Trial. *Haematologica.* 2012;97(5):731. doi:10.3324/haematol.2011.045666
23. Freeman K, Connock M, Cummins E, et al. Fluorouracil plasma monitoring: systematic review and economic evaluation of the My5-FU assay for guiding dose adjustment in patients receiving fluorouracil chemotherapy by continuous infusion. *Health technology assessment (Winchester, England).* Nov 2015;19(91):1-321, v-vi. doi:10.3310/hta19910
24. Lee JJ, Beumer JH, Chu E. Therapeutic drug monitoring of 5-fluorouracil. September 1 2016;78:447-464. doi:10.1007/s00280-016-3054-2
25. Deng R, Shi L, Zhu W, et al. Pharmacokinetics-based Dose Management of 5-Fluorouracil Clinical Research in Advanced Colorectal Cancer Treatment. *Mini Rev Med Chem.* 2020;20(2):161-167. doi:10.2174/1389557519666191011154923
26. Dolat M, Macaire P, Goirand F, et al. Association of 5-FU Therapeutic Drug Monitoring to DPD Phenotype Assessment May Reduce 5-FU Under-Exposure. *Pharmaceuticals (Basel).* Nov 23 2020;13(11)doi:10.3390/ph13110416
27. Vithanachchi DT, Maujean A, Downes MJ, Scuffham P. A comprehensive review of economic evaluations of therapeutic drug monitoring interventions for cancer treatments. *Br J Clin Pharmacol.* Feb 2021;87(2):271-283. doi:10.1111/bcp.14494
28. Lares N, Konecki C, Brugel M, et al. Impact of Guidelines Regarding Dihydropyrimidine Dehydrogenase (DPD) Deficiency Screening Using Uracil-Based Phenotyping on the Reduction of Severe Side Effect of 5-Fluorouracil-Based Chemotherapy: A Propension Score Analysis. *Pharmaceutics.* 2022;14(10):2119. doi:10.3390/pharmaceutics14102119
29. Tejedor-Tejada E, Calvo DR, Andreo AG. Determination of plasma uracil as a screening for dihydropyrimidine dehydrogenase deficiency: clinical application in oncological treatments. *European Journal of Hospital Pharmacy.* 2022:ejhpharm-2021-003210. doi:10.1136/ejhpharm-2021-003210
30. Glewis S, Michael M, Gurney H, et al. Feasibility and population exposure of 5-fluorouracil using therapeutic drug monitoring (PREDICT-5FU): A multicentre clinical trial. *Br J Clin Pharmacol.* Jul 2025;91(7):1965-1974. doi:10.1002/bcp.70006
31. Beumer JH, Chu E, Allegra C, et al. Therapeutic Drug Monitoring in Oncology: International Association of Therapeutic Drug Monitoring and Clinical Toxicology Recommendations for 5-Fluorouracil Therapy. *Clinical pharmacology and therapeutics.* Mar 2019;105(3):598-613. doi:10.1002/cpt.1124
32. NCCN. NCCN Clinical Practice Guidelines in Oncology - Antiemesis Version 2.2025. Updated May 12, 2025. https://www.nccn.org/professionals/physician_gls/pdf/antiemesis.pdf
33. NCCN. NCCN Clinical Practice Guidelines in Oncology - Head and Neck Cancers Version 5.2025. Updated August 12, 2025. https://www.nccn.org/professionals/physician_gls/pdf/head-and-neck.pdf
34. NCCN. NCCN Clinical Practice Guidelines in Oncology - Colon Cancer Version 4.2025. Updated June 27, 2025. https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf

Reimbursement Policy

35. NICE. Review of DG16: Fluorouracil chemotherapy: The My5-FU assay for guiding dose adjustment. <https://www.nice.org.uk/guidance/dg16/evidence/review-decision-february-2018-pdf-4777017085>
36. Amstutz U, Henricks LM, Offer SM, et al. Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for Dihydropyrimidine Dehydrogenase Genotype and Fluoropyrimidine Dosing: 2017 Update. *Clinical pharmacology and therapeutics*. Feb 2018;103(2):210-216. doi:10.1002/cpt.911
37. Lemaitre F, Goirand F, Launay M, et al. [5-fluorouracil therapeutic drug monitoring: Update and recommendations of the STP-PT group of the SFPT and the GPCO-Unicancer]. *Bull Cancer*. Sep 2018;105(9):790-803. Suivi thérapeutique pharmacologique du 5-fluorouracile : mise au point et recommandations du groupe STP-PT de la SFPT et du GPCO-Unicancer. doi:10.1016/j.bulcan.2018.06.008
38. Etienne-Grimaldi M-C, Pallet N, Boige V, et al. Current diagnostic and clinical issues of screening for dihydropyrimidine dehydrogenase deficiency. *European Journal of Cancer*. 2023;181:3-17. doi:10.1016/j.ejca.2022.11.028
39. EMA. *Fluorouracil and fluorouracil related substances (capecitabine, tegafur and flucytosine) containing medicinal products*. 2020. March 27. https://www.ema.europa.eu/en/documents/referral/fluorouracil-and-fluorouracil-related-substances-article-31-referral-assessment-report_en.pdf
40. FDA. Label for NDA 012209 FLUOROURACIL. https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/012209s040lbl.pdf
41. FDA. ABRAXANE for Injectable Suspension (paclitaxel protein-bound particles for injectable suspension) (albumin-bound) https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/021660s045lbl.pdf
42. FDA. GLEEVEC (imatinib mesylate) tablets for oral use https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/021588s047lbl.pdf
43. FDA. Docetaxel Injection, Solution for Intravenous Infusion. https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/205934s003lbl.pdf

VI. Revision History

Revision Date	Summary of Changes
12/03/2025	Reviewed and Updated: Updated background, guidelines, and evidence-based scientific references. Literature review did not necessitate any modification to the coverage criteria.