Pharmacogenomics and Companion Diagnostics

INDEPENDENT CARE HEALTH PLAN

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Medicare Advantage Medical Coverage Policy

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Disclaimer

The Coverage Summaries are reviewed by the iCare Medicare Utilization Management Committee. Policies in this document may be modified by a member's coverage document. Clinical policy is not intended to preempt the judgment of the reviewing medical director or dictate to health care providers how to practice medicine. Health care providers are expected to exercise their medical judgment in rendering appropriate care. Identification of selected brand names of devices, tests and procedures in a medical coverage policy is for reference only and is not an endorsement of any one device, test, or procedure over another. Clinical technology is constantly evolving, and we reserve the right to review and update this policy periodically. References to CPT® codes or other sources are for definitional purposes only and do not imply any right to reimbursement or guarantee of claims payment. No part of this publication may be reproduced, stored in a retrieval system or transmitted, in any shape or form or by any means, electronic, mechanical, photocopying or otherwise, without permission from iCare.

Related Medicare Advantage Medical/Pharmacy Coverage Policies

Comprehensive Genomic Profiling for Solid Tumors
Genetic Testing
Genetic Testing for Diagnosis and Monitoring of Cancer
Testing for Hereditary Breast Ovarian Pancreatic and Prostate Cancer
Liquid Biopsy
Pharmacogenomics Testing

Related Documents

Please refer to CMS website for the most current applicable National Coverage Determination (NCD)/ Local Coverage Determination (LCD)/Local Coverage Article (LCA)/CMS Online Manual System/Transmittals.

Type	Title	ID Number	Jurisdiction Medicare Administrative Contractors (MACs)	Applicable States/Territories
NCD	Next Generation Sequencing (NGS)	90.2		
LCD	MolDX: Pharmacogenomics Testing	L38435	J5 - Wisconsin Physicians Service Insurance Corporation	IA, KS, MO, NE
LCD	Molecular Pathology Procedures	L35000	J6 - National Government Services, Inc. (Part A/B MAC)	IL, MN, WI
LCD	MolDX: Pharmacogenomics Testing	L38435	J8 - Wisconsin Physicians Service Insurance Corporation	IN, MI
LCD	MolDX: Pharmacogenomics Testing	L38394	J15 - CGS Administrators, LLC (Part A/B MAC)	KY, OH
LCD LCA	MolDX: Pharmacogenomics Testing Billing and Coding: MolDX: Germline testing for use of PARP inhibitors	L38335 A55294	JE - Noridian Healthcare Solutions, LLC	CA, HI, NV, American Samoa, Guam, Northern Mariana Islands
LCD LCA	MolDX: Pharmacogenomics Testing Billing and Coding: MolDX: Germline testing for use of PARP inhibitors	L38335 A55294	JF - Noridian Healthcare Solutions, LLC	AK, AZ, ID, MT, ND, OR, SD, UT, WA, WY
LCD	Pharmacogenomics Testing Biomarkers for Oncology	L39063 L35396	JH - Novitas Solutions, Inc. (Part A/B MAC)	AR, CO, NM, OK, TX, LA, MS
LCD	MolDX: Pharmacogenomics Testing	L38294	JJ - Palmetto GBA (Part A/B MAC)	AL, GA, TN
LCD	Molecular Pathology Procedures	L35000	JK - National Government Services, Inc. (Part A/B MAC	CT, NY, ME, MA, NH, RI, VT
LCD	Pharmacogenomics Testing Biomarkers for Oncology	L39063 L35396	JL - Novitas Solutions, Inc. (Part A/B MAC)	DE, D.C., MD, NJ, PA
LCD	MolDX: Pharmacogenomics Testing	L38294	JM - Palmetto GBA (Part A/B MAC)	NC, SC, VA, WV

LCD	Pharmacogenomics Testing	**L39073**	JN - First Coast Service Options, Inc. (Part A/B MAC)	FL, PR, U.S. VI

Description

Pharmacogenomics and companion diagnostics tests are laboratory studies that use an individual's unique genetic makeup to help determine response to a specific medication. Companion diagnostics differ from pharmacogenomics testing because they are co-developed with a specific drug to help evaluate response or nonresponse to the drug. Companion diagnostics are often approved by the US Food & Drug Administration (FDA) corresponding with a specific pharmacotherapy. Both types of tests are used to guide management for several cancers such as non-small cell lung cancer (NSCLC), breast and colorectal cancer (CRC). Techniques can vary from test to test include, but may not be limited to, fluorescence in situ hybridization (FISH), immunohistochemistry (IHC) and next-generation sequencing (NGS).

Multigene (or expanded) panels analyze a broad set of genes simultaneously (as opposed to single gene testing that searches for variants in one specific gene). Panels often include medically actionable genes but may also include those with unclear medical management.

Coverage Determination

iCare follows the CMS requirement that only allows coverage and payment for services that are reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member except as specifically allowed by Medicare.

Genetic tests must demonstrate clinical utility, analytical and clinical validity and fulfill the CMS "reasonable and necessary" criteria. Analytic validity (test accurately identifies the gene variant), clinical validity (test identifies or predicts the clinically defined disorder) and clinical utility (test measurably improves clinical outcomes) of the genetic test is supported by generally accepted standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, specialty society recommendations, and views of physicians practicing in relevant clinical areas. The test must be ordered by a physician who is treating the beneficiary and the results will be used in the management of a beneficiary's specific medical problem.

For jurisdictions with no Medicare guidance for a particular test, iCare will utilize the MolDX program and Technical Assessments for molecular assays as the standard to evaluate clinical utility, analytical and clinical validity in conjunction with adhering to Medicare's reasonable and necessary requirement.

In interpreting or supplementing the criteria above and in order to determine medical necessity consistently, iCare may consider the following criteria:

Somatic (Acquired) Cancer

Pharmacogenomics and companion diagnostic testing (including single gene, multi-gene panels, and combinatorial tests) in **somatic (acquired) cancer** will be considered medically reasonable and necessary when all the following requirements are met:

- Testing services are performed in a Clinical Laboratory Improvement Amendments (CLIA)-certified laboratory, when ordered by a treating physician; **AND**
- Individual is diagnosed with recurrent, relapsed, refractory, metastatic, or advanced stage III or IV cancer; **AND**
- Individual has not been previously tested with the same test using NGS or other methodology for the same cancer genetic content; **AND**
- Decided to seek further cancer treatment (eg, therapeutic chemotherapy); **AND**
- The diagnostic laboratory test using NGS or other methodology (eg, FISH, IHC) must have:
    - FDA approval or clearance as a companion in vitro diagnostic; **AND**
    - FDA approved or cleared indication for use in that patient's cancer; **AND**
    - Results provided to the treating physician for management of the patient using a report template to specify treatment options

Germline (Inherited) Cancer

Pharmacogenomics and companion diagnostic testing (including single gene, multi-gene panels, and combinatorial tests) in **germline (inherited) cancer (eg, MyChoice CDx [0172U])** when all of the following criteria are met:

- Testing services are performed in a CLIA certified laboratory, when ordered by a treating physician; **AND**
- Individual is diagnosed with ovarian (including fallopian tube, primary peritoneal cancer) or breast cancer; **AND**
- Clinical indication for germline testing for hereditary breast or ovarian cancer (per National Comprehensive Cancer Network [NCCN] guidelines); **AND**
- Risk factor for germline breast or ovarian cancer; **AND**
- Individual has not been previously tested with the same germline test using NGS or other methodology for the same germline genetic content

- The diagnostic laboratory test using NGS or other methodology (eg, FISH, IHC) must have all of the following:

    - FDA approval or clearance; **AND**

    - Results provided to the treating physician for management of the individual using a report template to specify treatment options

The use of the criteria in this Medicare Advantage Medical Coverage Policy provides clinical benefits highly likely to outweigh any clinical harms. Services that do not meet the criteria above are not medically necessary and thus do not provide a clinical benefit. Medically unnecessary services carry risks of adverse outcomes and may interfere with the pursuit of other treatments which have demonstrated efficacy.

Coverage Limitations

US Government Publishing Office. Electronic code of federal regulations: part 411 – 42 CFR § 411.15 - Particular services excluded from coverage

The following services/items will not be considered medically reasonable and necessary:

- Genetic tests that have not demonstrated clinical utility, analytical and clinical validity via the MolDX Program

- Repeat genetic testing utilizing the same tissue sample for the same content

A review of the current medical literature shows that the evidence is insufficient to determine that this service is standard medical treatment for these indications. There remains an absence of randomized blinded clinical studies examining benefit and long-term clinical outcomes establishing the value of this service in clinical management for these indications.

Screening services such as presymptomatic genetic tests and services used to detect and undiagnosed diseased or disease predisposition are not a Medicare benefit and are not covered.

The following test types are examples of testing services that may not be considered a benefit (statutory excluded) and denied as Medicare Excluded tests[123]:

- Tests considered screening in the absence of clinical signs and symptoms of disease that are not specifically identified by the law; **OR**

- Tests that confirm a diagnosis or known information; **OR**

- Tests to determine risk for developing a disease or condition; **OR**

- Tests performed to measure the quality of a process; **OR**

- Tests without diagnosis specific indications; **OR**
- Tests identified as investigational by available literature and/or the literature supplied by the developer and are not a part of a clinical trial

Coding Information

Any codes listed on this policy are for informational purposes only. Do not rely on the accuracy and inclusion of specific codes. Inclusion of a code does not guarantee coverage and/or reimbursement for a service or procedure.

CPT® Code(s)	Description	Comments
81191	NTRK1 (neurotrophic receptor tyrosine kinase 1) (eg, solid tumors) translocation analysis	
81192	NTRK2 (neurotrophic receptor tyrosine kinase 2) (eg, solid tumors) translocation analysis	
81193	NTRK3 (neurotrophic receptor tyrosine kinase 3) (eg, solid tumors) translocation analysis	
81194	NTRK (neurotrophic-tropomyosin receptor tyrosine kinase 1, 2, and 3) (eg, solid tumors) translocation analysis	
81232	DPYD (dihydropyrimidine dehydrogenase) (eg, 5-fluorouracil/5-FU and capecitabine drug metabolism), gene analysis, common variant(s) (eg, *2A, *4, *5, *6)	
81233	BTK (Bruton's tyrosine kinase) (eg, chronic lymphocytic leukemia) gene analysis, common variants (eg, C481S, C481R, C481F)	
81236	EZH2 (enhancer of zeste 2 polycomb repressive complex 2 subunit) (eg, myelodysplastic syndrome, myeloproliferative neoplasms) gene analysis, full gene sequence	
81237	EZH2 (enhancer of zeste 2 polycomb repressive complex 2 subunit) (eg, diffuse large B-cell lymphoma) gene analysis, common variant(s) (eg, codon 646)	
81275	KRAS (Kirsten rat sarcoma viral oncogene homolog) (eg, carcinoma) gene analysis; variants in exon 2 (eg, codons 12 and 13)	
81276	KRAS (Kirsten rat sarcoma viral oncogene homolog) (eg, carcinoma) gene analysis; additional variant(s) (eg, codon 61, codon 146)	

81301	Microsatellite instability analysis (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) of markers for mismatch repair deficiency (eg, BAT25, BAT26), includes comparison of neoplastic and normal tissue, if performed	
81309	PIK3CA (phosphatidylinositol-4, 5-biphosphate 3-kinase, catalytic subunit alpha) (eg, colorectal and breast cancer) gene analysis, targeted sequence analysis (eg, exons 7, 9, 20)	
81320	PLCG2 (phospholipase C gamma 2) (eg, chronic lymphocytic leukemia) gene analysis, common variants (eg, R665W, S707F, L845F)	
81346	TYMS (thymidylate synthetase) (eg, 5-fluorouracil/5-FU drug metabolism), gene analysis, common variant(s) (eg, tandem repeat variant)	
81350	UGT1A1 (UDP glucuronosyltransferase 1 family, polypeptide A1) (eg, drug metabolism, hereditary unconjugated hyperbilirubinemia [Gilbert syndrome]) gene analysis, common variants (eg, *28, *36, *37)	
81381	HLA Class I typing, high resolution (ie, alleles or allele groups); one allele or allele group (eg, B*57:01P), each	
81400	MOLECULAR PATHOLOGY PROCEDURE LEVEL 1	
81401	MOLECULAR PATHOLOGY PROCEDURE LEVEL 2	
81403	MOLECULAR PATHOLOGY PROCEDURE LEVEL 4	
81404	MOLECULAR PATHOLOGY PROCEDURE LEVEL 5	
81445	Targeted genomic sequence analysis panel, solid organ neoplasm, DNA analysis, and RNA analysis when performed, 5-50 genes (eg, ALK, BRAF, CDKN2A, EGFR, ERBB2, KIT, KRAS, NRAS, MET, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed	
81455	Targeted genomic sequence analysis panel, solid organ or hematolymphoid neoplasm, DNA analysis, and RNA analysis when performed, 51 or greater genes (eg, ALK, BRAF, CDKN2A, CEBPA, DNMT3A, EGFR, ERBB2, EZH2, FLT3, IDH1, IDH2, JAK2, KIT, KRAS, MLL, NPM1, NRAS, MET, NOTCH1, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed	
81479	Unlisted molecular pathology procedure	
84999	Unlisted chemistry procedure	
88341	Immunohistochemistry or immunocytochemistry, per specimen; each additional single antibody stain procedure (List separately in addition to code for primary procedure)	

88342	Immunohistochemistry or immunocytochemistry, per specimen; initial single antibody stain procedure	
88360	Morphometric analysis, tumor immunohistochemistry (eg, Her-2/neu, estrogen receptor/progesterone receptor), quantitative or semiquantitative, per specimen, each single antibody stain procedure; manual	
0037U	Targeted genomic sequence analysis, solid organ neoplasm, DNA analysis of 324 genes, interrogation for sequence variants, gene copy number amplifications, gene rearrangements, microsatellite instability and tumor mutational burden	
0111U	Oncology (colon cancer), targeted KRAS (codons 12, 13, and 61) and NRAS (codons 12, 13, and 61) gene analysis utilizing formalin-fixed paraffin-embedded tissue	
0154U	Oncology (urothelial cancer), RNA, analysis by real-time RT-PCR of the FGFR3 (fibroblast growth factor receptor 3) gene analysis (ie, p.R248C [c.742C>T], p.S249C [c.746C>G], p.G370C [c.1108G>T], p.Y373C [c.1118A>G], FGFR3-TACC3v1, and FGFR3-TACC3v3) utilizing formalin-fixed paraffin-embedded urothelial cancer tumor tissue, reported as FGFR gene alteration status	
0155U	Oncology (breast cancer), DNA, PIK3CA (phosphatidylinositol-4,5-bisphosphate 3-kinase, catalytic subunit alpha) (eg, breast cancer) gene analysis (ie, p.C420R, p.E542K, p.E545A, p.E545D [g.1635G>T only], p.E545G, p.E545K, p.Q546E, p.Q546R, p.H1047L, p.H1047R, p.H1047Y), utilizing formalin-fixed paraffin-embedded breast tumor tissue, reported as PIK3CA gene mutation status	
0172U	Oncology (solid tumor as indicated by the label), somatic mutation analysis of BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) and analysis of homologous recombination deficiency pathways, DNA, formalin-fixed paraffin-embedded tissue, algorithm quantifying tumor genomic instability score	
0177U	Oncology (breast cancer), DNA, PIK3CA (phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha) gene analysis of 11 gene variants utilizing plasma, reported as PIK3CA gene mutation status	
0249U	Oncology (breast), semiquantitative analysis of 32 phosphoproteins and protein analytes, includes laser capture microdissection, with algorithmic analysis and interpretative report	

0332U	Oncology (pan-tumor), genetic profiling of 8 DNA-regulatory (epigenetic) markers by quantitative polymerase chain reaction (qPCR), whole blood, reported as a high or low probability of responding to immune checkpoint–inhibitor therapy	
CPT® Category III Code(s)	**Description**	**Comments**
No code(s) identified		
HCPCS Code(s)	**Description**	**Comments**
No code(s) identified		

References

1. American Society of Clinical Oncology (ASCO). Biomarkers for adjuvant endocrine and chemotherapy in early-stage breast cancer: ASCO guideline update. https://www.asco.org. Published April 19, 2022. Accessed May 5, 2022.

2. American Society of Clinical Oncology (ASCO). Biomarkers for systemic therapy in metastatic breast cancer: ASCO guideline update. https://www.asco.org. Published June 2022. Accessed January 27, 2023.

3. American Society of Clinical Oncology (ASCO). Endocrine treatment and targeted therapy for hormone receptor–positive, human epidermal growth factor receptor 2–negative metastatic breast cancer: ASCO guideline update. https://www.asco.org. Published July 2021. Accessed August 3, 2022.

4. American Society of Clinical Oncology (ASCO). Molecular testing guideline for the selection of patients with lung cancer for treatment with targeted tyrosine kinase inhibitors: American Society of Clinical Oncology endorsement of the College of American Pathologists/International Association for the study of lung cancer/association for molecular pathology clinical practice guideline update. https://www.asco.org. Published February 2018. Updated March 20, 2018. Accessed May 2, 2023.

5. American Society of Clinical Oncology (ASCO). Poly(ADP-ribose) polymerase inhibitors in the management of ovarian cancer: ASCO guideline rapid recommendation update. https://www.asco.org. Published August 13, 2020. Updated September 23, 2022. Accessed February 1, 2023.

6. American Society of Clinical Oncology (ASCO). Somatic genomic testing in patients with metastatic or advanced cancer. https://www.asco.org. Published February 17, 2022. Accessed February 8, 2023.

7. American Society of Clinical Oncology (ASCO). Treatment of metastatic colorectal cancer: ASCO guideline. https://www.asco.org. Published October 17, 2022. Accessed May 2, 2023.

8. Association for Molecular Pathology (AMP). Standards and guidelines for the interpretation and reporting of sequence variants in cancer: A joint consensus recommendation of the Association for Molecular Pathology, American Society of Clinical Oncology, and College of American Pathologists. https://www.amp.org. Published January 1, 2017. Accessed October 12, 2022.

9. Association for Molecular Pathology (AMP). Updated molecular testing guideline for the selection of lung cancer patients for treatment with targeted tyrosine kinase inhibitors: guideline from the College of American Pathologists, the International Association for the Study of Lung Cancer, and the Association for Molecular Pathology. https://www.amp.org. Published January 23, 2018. Accessed May 2, 2023.

10. Centers for Medicare & Medicaid Services (CMS). Local Coverage Article (LCA). Billing and Coding: MolDX: Germline testing for use of PARP inhibitors (A55294). https://www.cms.gov. Published October 15, 2017. Updated July 28, 2022. Accessed September 18, 2023.

11. Centers for Medicare & Medicaid Services (CMS). Local Coverage Article (LCA). Billing and Coding: MolDX: Germline testing for use of PARP inhibitors (A55295). https://www.cms.gov. Published October 15, 2017. Updated July 28, 2022. Accessed September 18, 2023.

12. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). Biomarkers for Oncology (L35396). https://www.cms.gov. Published October 1, 2015. Updated December 12, 2020. Accessed September 13, 2023.

13. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). MolDX: Pharmacogenomics Testing (L38294). https://www.cms.gov. Published July 26, 2020. Updated August 24, 2023. Accessed September 13, 2023.

14. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). MolDX: Pharmacogenomics Testing (L38335). https://www.cms.gov. Published August 17, 2020. Updated August 24, 2023. Accessed September 12, 2023.

15. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). MolDX: Pharmacogenomics Testing (L38337). https://www.cms.gov. Published August 17, 2020. Updated August 24, 2023. Accessed September 12, 2023.

16. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). MolDX: Pharmacogenomics Testing (L38394). https://www.cms.gov. Published August 3, 2020. Updated August 24, 2023. Accessed September 12, 2023.

17. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). MolDX: Pharmacogenomics Testing (L38435). https://www.cms.gov. Published July 26, 2020. Updated August 24, 2023. Accessed September 13, 2023.

18. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). Molecular Pathology Procedures (L35000). https://www.cms.gov. Published October 1, 2015. Updated August 6, 2023. Accessed September 14, 2023.

19. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). Pharmacogenomics Testing (L39063). https://www.cms.gov. Published December 12, 2021. Accessed September 13, 2023.

20. Centers for Medicare & Medicaid Services (CMS). Local Coverage Determination (LCD). Pharmacogenomics Testing (L39073). https://www.cms.gov. Published December 12, 2021. Accessed September 13, 2022.

21. Centers for Medicare & Medicaid Services (CMS). National Coverage Determination (NCD). Next Generation Sequencing (NGS) 90.2. https://www.cms.gov. Published January 27, 2020. Accessed September 13, 2023.

22. Clinical Pharmacogenetics Implementation Consortium (CPIC). CPIC gene-drugs for ERCC1. https://www.cpic.com. Published April 3, 2023. Accessed May 15, 2023.

23. Clinical Pharmacogenetics Implementation Consortium (CPIC). CPIC gene-drugs for UGT1A1. https://www.cpic.com. Updated June 1, 2022. Accessed October 11, 2022.

24. ClinicalKey. Clinical Overview. Bladder cancer. https://www.clinicalkey.com. Updated May 2, 2022. Accessed February 3, 2023.

25. ClinicalKey. Clinical Overview. Breast cancer in females. https://www.clinicalkey.com. Updated May 12, 2022. Accessed January 31, 2023.

26. ClinicalKey. Clinical Overview. Breast cancer in males. https://www.clinicalkey.com. Updated April 4, 2022. Accessed May 11, 2022.

27. ClinicalKey. Clinical Overview. Cervical cancer. https://www.clinicalkey.com. Updated April 21, 2022. Accessed August 17, 2022.

28. ClinicalKey. Clinical Overview. Cholangiocarcinoma. https://www.clinicalkey.com. Updated July 26, 2022. Accessed February 3, 2023.

29. ClinicalKey. Clinical Overview. Chronic lymphocytic leukemia. https://www.clinicalkey.com. Updated January 1, 2023. Accessed January 31, 2023.

30. ClinicalKey. Clinical Overview. Colorectal cancer. https://www.clinicalkey.com. Updated April 26, 2022. Accessed April 25, 2023.

31. ClinicalKey. Clinical Overview. Endometrial carcinoma. https://www.clinicalkey.com. Updated April 22, 2022. Accessed May 15, 2023.

32. ClinicalKey. Clinical Overview. Esophageal cancer. https://www.clinicalkey.com. Updated June 21, 2022. Accessed August 17, 2022.

33. ClinicalKey. Clinical Overview. Follicular lymphoma. https://www.clinicalkey.com. Updated March 9, 2022. Accessed October 7, 2022.

34. ClinicalKey. Clinical Overview. Lung cancer (non-small cell). https://www.clinicalkey.com. Updated October 6, 2022. Accessed April 25, 2023.

35. ClinicalKey. Clinical Overview. Lung cancer (small cell). https://www.clinicalkey.com. Updated February 23, 2022. Accessed October 18, 2022.

36. ClinicalKey. Clinical Overview. Ovarian cancer. https://www.clinicalkey.com. Updated August 8, 2022. Accessed January 31, 2023.

37. ClinicalKey. Clinical Overview. Thyroid cancer. https://www.clinicalkey.com. Updated January 25, 2022. Accessed January 28, 2022.

38. College of American Pathologists (CAP). Mismatch repair and microsatellite instability testing for immune checkpoint inhibitor therapy statements and strengths of recommendations. https://www.cap.org. Published August 2022. Accessed May 9, 2023.

39. College of American Pathologists (CAP). Molecular biomarkers for the evaluation of colorectal cancer: guideline from the American Society for Clinical Pathology, College of American Pathologists, Association for Molecular Pathology, and the American Society of Clinical Oncology. https://www.cap.org. Published May 2017. Accessed May 2, 2023.

40. Drilon A, Laetsch T, Kummar S et al. Efficacy of larotrectinib in TRK fusion positive cancers in adults and children. *N Engl J Med*. 2018;378:731-739. https://www.ncbi.nlm.nih.gov. Accessed February 6, 2023.

41. Dugay F, Llamas-Gutierrez, Gournay, Marjory, et al. Clinicopathological characteristics of ROS1- and RET-rearranged NSCLC in caucasian patients: data from a cohort of 713 non-squamous NSCLC lacking KRAS/EGFR/HER2/BRAF/ PIK3CA/ALK alterations. *Oncotarget*. 2017;8(32):53336-53351. https://www.ncbi.nlm.nih.gov. Accessed May 15, 2023.

42. ECRI Institute. ECRIgene Genetic Test Assessment. cobas EZH2 mutation test (Roche Molecular Diagnostics) to determine eligibility for Tazemetostat (tazverik) therapy for follicular lymphoma. https://www.ecri.org. Published August 2020. Accessed October 7, 2022.

43. ECRI Institute. ECRIgene Genetic Test Assessment. MyChoice CDx (Myriad Genetics, Inc.) for determining eligibility for targeted treatment for ovarian cancer. https://www.ecri.org. Published October 5, 2020. Accessed August 2, 2022.

44. ECRI Institute. ECRIgene Genetic Test Assessment. Paradigm cancer diagnostic PCDx test (Paradigm Diagnostics, Inc.) for guiding targeted therapy for solid tumors. https://www.ecri.org. Published March 9, 2021. Accessed October 18, 2022.

45. ECRI Institute. ECRIgene Genetic Test Assessment. Praxis extended RAS panel (Illumina, Inc) to determine eligibility for panitumumab (Vectibix) to treat colorectal cancer. https://www.ecri.org. Published October 2020. Accessed April 25, 2023.

46. ECRI Institute. ECRIgene Genetic Test Assessment. Ventana PD-L1 (SP142) Assay (Ventana Medical Systems Inc. A Roche Group Co) to determine eligibility for Tecentriq (Atezolizumab) to treat NSCLC. https://www.ecri.org. Published October 27, 2020. Accessed August 17, 2022.

47. ECRI Institute. ECRIgene Genetic Test Product Brief. cobas KRAS (Roche Molecular Systems, Inc.) for determining eligibility for Erbitux (Cetuximab) or Vectibix (Panitumumab) treatment for colorectal cancer. https://www.ecri.org. Published July 2017. Accessed April 25, 2023.

48. ECRI Institute. ECRIgene Genetic Test Product Brief. FoundationOne CDx (Foundation Medicine, Inc.) genomic profiling test for guiding targeted therapy for cancer. https://www.ecri.org. Published August 29, 2018. Updated September 2019. Accessed January 24, 2023.

49. ECRI Institute. ECRIgene Genetic Test Product Brief. Therascreen FGFR RGQ RT-PCR kit (Qiagen GmbH) for determining eligibility for erdafitinib (balversa) treatment for urothelial cancer. https://www.ecri.org. Published May 20, 2019. Accessed January 24, 2023.

50. ECRI Institute. ECRIgene Genetic Test Product Brief. Therascreen KRAS RGQ PCR kit (Qiagen N.V.) for determining eligibility for vectibix or erbitux treatment for colorectal cancer. https://www.ecri.org. Published July1, 2016. Updated March 27, 2019. Accessed April 25, 2023.

51. ECRI Institute. ECRIgene Genetic Test Product Brief. Therascreen PIK3CA RGQ PCR kit (Qiagen GmbH) for determining eligibility for alpelisib (Piqray) treatment for breast cancer. https://www.ecri.org. Updated June 13, 2019. Accessed August 3, 2022.

52. ECRI Institute. ECRIgene Genetic Test Product Brief. Ventana ALK (D5F3) CDx Assay (Ventana Medical Systems) for determining eligibility for alecensa, xalkori, or zykadia for treating non-small cell lung cancer. https://www.ecri.org. Published August 1, 2018. Accessed May 4, 2023.

53. Farago A, Taylor M, Doebele R, et al. Clinicopathologic features of non-small-cell lung cancer harboring an *NTRK* gene fusion. *JCO Precis Oncol*. 2018;10.120. https://www.ncbi.nlm.nih.gov. Accessed February 6, 2023.

54. Febbo P, Ladanyi M, Aldape K, et al. NCCN Task Force report: evaluating the clinical utility of tumor markers in oncology. *J Natl Compr Canc Netw.* 2011;9:S-1-S-33. https://www.nccn.org. Accessed May 15, 2023.

55. Garon E, Rizvi N, Hui R, et al. Pembrolizumab for the treatment of non-small-cell lung cancer. *N Engl J Med*. 2015;372:2018-2028. https://www.nejm.org. Accessed May 13, 2020.

56. Hayes, Inc. Emerging Technology Report (ARCHIVED). Balversa (erdafitinib) for urothelial carcinoma. https://evidence.hayesinc.com. Published August 19, 2019. Updated September 21, 2020. Accessed January 24, 2023.

57. Hayes, Inc. Emerging Technology Report (ARCHIVED). Pemazyre (pemigatinib). https://evidence.hayesinc.com. Published April 21, 2020. Accessed January 24, 2023.

58. Hayes, Inc. Emerging Technology Report (ARCHIVED). Rozlytrek (entrectinib). https://evidence.hayesinc.com. Published August 19, 2019. Updated September 11, 2020. Accessed February 6, 2023.

59. Hayes, Inc. Emerging Technology Report (ARCHIVED). Vitrakvi (larotrectinib). https://evidence.hayesinc.com. Published November 27, 2018. Updated May 8, 2020. Accessed February 6, 2023.

60. Hayes, Inc. Emerging Technology Report (ARCHIVED). Zejula (niraparib). https://evidence.hayesinc.com. Published March 29, 2017. Updated May 31, 2018. Accessed November 21, 2022.

61. Hayes, Inc. Genetic Test Evaluation (GTE) Report (ARCHIVED). Anaplastic lymphoma kinase (ALK) gene rearrangement testing in non-small cell lung cancer (NSCLC). https://evidence.hayesinc.com. Published July 26, 2012. Updated July 9, 2014. Accessed May 4, 2023.

62. Hayes, Inc. Genetic Test Evaluation (GTE) Report (ARCHIVED). ERCC1 expression analysis non-small cell lung cancer (NSCLC). https://evidence.hayesinc.com. Published January 17, 2014. Updated January 8, 2015. Accessed May 8, 2023.

63. Hayes, Inc. Genetic Test Evaluation (GTE) Report (ARCHIVED). KRAS sequence variant analysis for predicting response to colorectal cancer drug therapy. https://evidence.hayesinc.com. Published December 2011. Updated May 27, 2015. Accessed April 25, 2023.

64. Hayes, Inc. Genetic Test Evaluation (GTE) Report (ARCHIVED). KRAS sequence variant analysis for predicting response to epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKIs) in the treatment of non-small cell lung cancer (NSCLC). https://evidence.hayesinc.com. Published April 26, 2012. Updated April 13, 2015. Accessed April 25, 2023.

65. Hayes, Inc. Genetic Test Evaluation (GTE) Report (ARCHIVED). Neuroblastoma RAS viral oncogene (NRAS) testing to predict treatment response in colorectal cancer. https://evidence.hayesinc.com. Published February 5, 2012. Updated January 19, 2019. Accessed April 25, 2023.

66. Hayes, Inc. Genetic Test Evaluation (GTE) Report (ARCHIVED). TheraGuide 5-FU (Myriad Genetic Laboratories Inc.) for predicting toxicity to 5-fluorouracil (5-FU)/capecitabine-based chemotherapy. https://evidence.hayesinc.com. Published May 5, 2009. Updated May 14, 2013. Accessed October 7, 2022.

67. Hayes, Inc. Genetic Test Evaluation (GTE) Report (ARCHIVED). UGT1A1 sequence variant testing for predicting response to Irinotecan therapy in colorectal cancer. https://evidence.hayesinc.com. Updated January 2014. Accessed October 7, 2022.

68. Hayes, Inc. Genetic Testing Evaluation (GTE) Synopsis (ARCHIVED). ROS1 gene rearrangements in NSCLC. https://evidence.hayesinc.com. Published February 2015. Updated September 12, 2018. Accessed May 4, 2023.

69. Hayes, Inc. Molecular Test Assessment. FoundationOne CDx (Foundation Medicine Inc.) for the intended use as a broad molecular profiling tool. https://evidence.hayesinc.com. Published August 29, 2018. Updated April 26, 2022. Accessed January 26, 2023.

70. Hayes, Inc. Precision Medicine Insights. Comprehensive molecular profiling test(s) for solid tumors intended to be used as broad molecular profiling tool to assigned matched therapy. https://evidence.hayesinc.com. Published January 11, 2022. Updated April 26, 2022. Accessed August 2, 2022.

71. Kummar S, Lassen U. TRK inhibition: a new tumor-agnostic treatment strategy. *U.N. Targ Oncol*. 2018;13:545-556. https://www.ncbi.nlm.nih.gov. Accessed January 30, 2019.

72. Liu B, Song Y, Liu, Delong. Recent development in clinical applications of PD-1 and PD-L1 antibodies for cancer immunotherapy. *J Hematol Oncol.* 2017:10:174. https://www.ncbi.nlm.nih.gov/pmc. Accessed August 17, 2022.

73. Maio M, Ascierto PA, Manzyuk L, et al. Pembrolizumab in microsatellite instability high or mismatch repair deficient cancers: updated analysis from the phase II KEYNOTE-158 study. Ann Oncol. 2022;33(9):929-938. https://www.ncbi.nlm.nih.gov. Accessed November 21, 2022.

74. MCG Health. 5-fluorouracil pharmacogenetics – DPYD, MTHFR, and TYMS genes. 26th edition. https://www.mcg.com. Accessed October 7, 2022.

75. MCG Health. Colorectal cancer – KRAS and NRAS genes. 26th edition. https://www.mcg.com. Accessed April 25, 2023.

76. MCG Health. Emerging Guidelines Preview. Oncology companion diagnostic testing – FoundationOne CDx. https://www.mcg.com. Accessed May 4, 2023.

77. MCG Health. Irinotecan pharmacogenetics UGT1A1 gene. 26th edition. https://www.mcg.com. Accessed October 7, 2022.

78. MCG Health. Non-small cell lung cancer – gene testing (somatic or therapeutic). 26th edition. https://www.mcg.com. Accessed April 25, 2023.

79. Merck Manual: Professional Version. Bladder cancer. https://www.merckmanuals.com. Updated January 2022. Accessed July 26, 2022.

80. Merck Manual: Professional Version. Chronic lymphocytic leukemia. https://www.merckmanuals.com. Updated September 2022. Accessed January 31, 2023.

81. Merck Manual: Professional Version. Lung carcinoma. https://www.merckmanuals.com. Updated September 2022. Accessed April 25, 2023.

82. National Cancer Institute (NCI). Bile duct cancer (cholangiocarcinoma) treatment (PDQ) – health professional version. https://www.cancer.gov. Updated June 2, 2022. Accessed February 3, 2023.

83. National Cancer Institute (NCI). Bladder cancer treatment (PDQ) – health professional version. https://www.cancer.gov. Updated February 4, 2022. Accessed July 28, 2022.

84. National Cancer Institute (NCI). Breast cancer treatment (PDQ) – health professional version. https://www.cancer.gov. Updated May 27, 2022. Accessed August 15, 2022.

85. National Cancer Institute (NCI). Cervical cancer treatment (PDQ) – health professional version. https://www.cancer.gov. Updated April 28, 2022. Accessed August 17, 2022.

86. National Cancer Institute (NCI). Colorectal cancer treatment (PDQ) – health professional version. https://www.cancer.gov. Updated January 20, 2023. Accessed May 2, 2023.

87. National Cancer Institute (NCI). Esophageal cancer treatment (PDQ) – health professional version. https://www.cancer.gov. Updated July 15, 2022. Accessed August 17, 2022.

88. National Cancer Institute (NCI). Head and neck cancer treatment (PDQ) – health professional version. https://www.cancer.gov. Updated March 2, 2022. Accessed August 17, 2022.

89. National Cancer Institute (NCI). Non-small cell lung cancer treatment (PDQ) – health professional version. https://www.cancer.gov. Updated February 17, 2023. Accessed May 2, 2023.

90. National Cancer Institute (NCI). Ovarian epithelial, fallopian tube, and primary peritoneal cancer treatment (PDQ) – health professional version. https://www.cancer.gov. Updated June 17, 2022. Accessed August 3, 2022.

91. National Cancer Institute (NCI). Thyroid cancer treatment (PDQ) – health professional version. https://www.cancer.gov. Updated February 18, 2022. Accessed February 8, 2023.

92. National Center for Biotechnology Information (NCBI). Genetic Testing Registry. ALK receptor tyrosine kinase. https://www.ncbi.nlm.nih.gov. Updated April 24, 2022. Accessed May 5, 2023.

93. National Center for Biotechnology Information (NCBI). Genetic Testing Registry. Dihydropyrimidine dehydrogenase. https://www.ncbi.nlm.nih.gov. Updated July 13, 2021. Accessed October 11, 2022.

94. National Center for Biotechnology Information (NCBI). Genetic Testing Registry. ERCC excision repair 1, endonuclease non-catalytic subunit. https://www.ncbi.nlm.nih.gov. Updated May 1, 2023. Accessed May 9, 2023.

95. National Center for Biotechnology Information (NCBI). Genetic Testing Registry. FLT3 fms related receptor tyrosine kinase 3. https://www.ncbi.nlm.nih.gov. Updated October 2, 2022. Accessed October 12, 2022.

96. National Center for Biotechnology Information (NCBI). Genetic Testing Registry. KRAS proto-oncogene, GTPase. https://www.ncbi.nlm.nih.gov. Updated May 8, 2022. Accessed May 2, 2023.

97. National Center for Biotechnology Information (NCBI). Genetic Testing Registry. MET proto-oncogene, receptor tyrosine kinase. https://www.ncbi.nlm.nih.gov. Updated April 24, 2022. Accessed May 5, 2023.

98. National Center for Biotechnology Information (NCBI). Genetic Testing Registry. NTRK neurotrophic receptor tyrosine kinase. https://www.ncbi.nlm.nih.gov. Updated February 5, 2023. Accessed February 8, 2023.

99. National Center for Biotechnology Information (NCBI). Genetic Testing Registry. PD-L1 22C3 IHC with combined positive score (CPS) interpretation, pembrolizumab. https://www.ncbi.nlm.nih.gov. Updated July 29, 2022. Accessed August 17, 2022.

100. National Center for Biotechnology Information (NCBI). Genetic Testing Registry. RET proto-oncogene. https://www.ncbi.nlm.nih.gov. Updated April 24, 2022. Accessed May 5, 2023.

101. National Center for Biotechnology Information (NCBI). Genetic Testing Registry. ROS proto-oncogene 1, receptor tyrosine kinase. https://www.ncbi.nlm.nih.gov. Updated April 24, 2022. Accessed May 5, 2023.

102. National Center for Biotechnology Information (NCBI). Genetic Testing Registry. UGT1A1. https://www.ncbi.nlm.nih.gov. Updated October 12, 2021. Accessed October 11, 2022.

103. National Comprehensive Cancer Network (NCCN). NCCN Biomarkers Compendium: ALK, BRCA1, BRCA2, BTK, EZH2 FGFR, FLT3, KRAS, PD-L1, PIK3CA, PLCG2, MET, NTRK, RET, ROS1, TMB. https://www.nccn.org. Published 2023. Accessed May 2, 2023.

104. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. B-cell lymphoma. https://www.nccn.org. Updated July 12, 2022. Accessed October 7, 2022.

105. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Bladder cancer. https://www.nccn.org. Updated December 21, 2022. Accessed February 3, 2023.

106. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Breast cancer. https://www.nccn.org. Updated June 2022. Accessed January 26, 2023.

107. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Central nervous system cancers. https://www.nccn.org. Updated October 18, 2019. Accessed November 21, 2022.

108. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Cervical cancer. https://www.nccn.org. Updated October 26, 2021. Accessed August 19, 2022.

109. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Chronic lymphocytic leukemia/small lymphocytic lymphoma. https://www.nccn.org. Updated January 25, 2023. Accessed February 1, 2023.

110. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Colon cancer. https://www.nccn.org. Updated April 25, 2023. Accessed May 2, 2023.

111. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Esophageal and esophagogastric junction cancers. https://www.nccn.org. Updated July 19, 2022. Accessed August 19, 2022.

112. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Gastric cancer. https://www.nccn.org. Updated January 11, 2022. Accessed October 20, 2022.

113. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Head and neck cancers. https://www.nccn.org. Updated April 26, 2022. Accessed August 19, 2022.

114. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Hepatobiliary cancer. https://www.nccn.org. Updated January 13, 2023. Accessed February 10, 2023.

115. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Melanoma: uveal. https://www.nccn.org. Updated May 4, 2023. Accessed May 8, 2023.

116. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Non-small cell lung cancer. https://www.nccn.org. Updated April 13, 2023. Accessed May 2, 2023.

117. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Ovarian cancer. https://www.nccn.org. Updated December 22, 2022. Accessed January 26, 2023.

118. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Pancreatic cancer. https://www.nccn.org. Updated December 6, 2022. Accessed January 27, 2023.

119. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Prostate cancer. https://www.nccn.org. Updated January 10, 2022. Accessed February 9, 2022.

120. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Rectal cancer. https://www.nccn.org. Updated September 10, 2021. Accessed February 10, 2022.

121. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Thyroid carcinoma. https://www.nccn.org. Updated May 5, 2022. Accessed October 20, 2022.

122. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Uterine neoplasms. https://www.nccn.org. Updated April 28, 2023. Accessed May 8, 2023.

123. Palmetto GBA. Molecular diagnostic program (MolDX®): coverage, coding, and pricing standards and requirements (M00106). https://www.palmettogba.com/MolDx. Published December 2019. Accessed September 27, 2023.

124. Ray-Coquard I, Pautier P, Pignata S, et al. Olaparib plus bevacizumab as first-line maintenance in ovarian cancer. *N Engl J Med*. 2019;381:2416-2428. https://www.nejm.org. Accessed September 15, 2020.

125. Rebuzzi SE, Zullo L, Rossi G, et al. Novel emerging molecular targets in non-small cell lung cancer. *Int J Mol Sci*. 2021;22(5):2625. https://www.ncbi.nlm.nih.gov. Accessed April 21, 2022.

126. Rossi G, Jocollé G, Conti A, et al. Detection of ROS1 rearrangement in non-small cell lung cancer: current and future perspectives. *Dove Press Journal.* 2017;8:45-55. https://www.ncbi.nlm.nih.gov/pubmed. Accessed April 26, 2022.

127. Sha D, Jin Z, Budczies J, et al. Tumor mutational burden as a predictive biomarker in solid tumors. *Cancer Discov*. 2020;10(12):1808-1825. doi:10.1158/2159-8290.CD-20-0522. https://www.ncbi.nlm.nih.gov/pubmed. Accessed November 18, 2021.

128. Testing.com: for health professionals. ALK mutation (gene rearrangement). https://www.testing.com. Updated June 28, 2021. Accessed May 5, 2023.

129. Testing.com: for health professionals. KRAS mutation. https://www.testing.com. Updated November 15, 2019. Accessed May 5, 2023.

130. UpToDate, Inc. Anaplastic lymphoma kinase (ALK) fusion oncogene positive non-small cell lung cancer. https://www.uptodate.com. Updated April 2023. Accessed May 4, 2023.

131. UpToDate, Inc. Chemotherapy associated diarrhea, constipation and intestinal perforation: pathogenesis, risk factors, and clinical presentation. https://www.uptodate.com. Updated September 2022. Accessed October 10, 2022.

132. UpToDate, Inc. Diagnosis of amyotrophic lateral sclerosis and other forms of motor neuron disease. https://www.uptodate.com. Updated July 2023. Accessed August 29, 2023.

133. UpToDate, Inc. Dosing of anticancer agents in adults. https://www.uptodate.com. Updated September 2022. Accessed October 10, 2022.

134. UpToDate, Inc. ER/PR negative, HER2-negative (triple-negative) breast cancer. https://www.uptodate.com. Updated August 2022. Accessed August 17, 2022.

135. UpToDate, Inc. First-line chemotherapy for advanced (stage III or IV) epithelial ovarian, fallopian tubal, and peritoneal cancer. https://www.uptodate.com. Updated October 2022. Accessed November 21, 2022.

136. UpToDate, Inc. Malignant salivary gland tumors: treatment of recurrent and metastatic disease. https://www.uptodate.com. Updated January 2023. Accessed February 6, 2023.

137. UpToDate, Inc. Management of acute chemotherapy-related diarrhea. https://www.uptodate.com. Updated October 2022. Accessed November 21, 2022.

138. UpToDate, Inc. Management of advanced non-small cell lung cancer lacking a driver mutation: immunotherapy. https://www.uptodate.com. Updated July 2022. Accessed August 17, 2022.

139. UpToDate, Inc. Management of recurrent high-grade gliomas. https://www.uptodate.com. Updated January 2023. Accessed February 6, 2023.

140. UpToDate, Inc. Management of recurrent or metastatic cervical cancer. https://www.uptodate.com. Updated July 2022. Accessed August 17, 2022.

141. UpToDate, Inc. Medical treatment for relapsed epithelial ovarian, fallopian tubal, or peritoneal cancer: platinum-resistant disease. https://www.uptodate.com. Updated January 2022. Accessed February 7, 2022.

142. UpToDate, Inc. Metastatic uveal melanoma. https://www.uptodate.com. Updated April 2023. Accessed May 8, 2023.

143. UpToDate, Inc. Methods to overcome radiation resistance in head and neck cancer. https://www.uptodate.com. Updated April 2023. Accessed May 8, 2023.

144. UpToDate, Inc. Molecular genetics of colorectal cancer. https://www.uptodate.com. Updated March 2023. Accessed April 25, 2023.

145. UpToDate, Inc. Overview of pharmacogenomics. https://www.uptodate.com. Updated October 2022. Accessed November 21, 2022.

146. UpToDate, Inc. Overview of the initial treatment of advanced non-small cell lung cancer. https://www.uptodate.com. Updated April 2023. Accessed May 4, 2023.

147. UpToDate, Inc. Pathology and prognostic determinants of colorectal cancer. https://www.uptodate.com. Updated March 2023. Accessed April 25, 2023.

148. UpToDate, Inc. Personalized genotype-directed therapy for advanced non-small cell lung cancer. https://www.uptodate.com. Updated March 2023. Accessed April 25, 2023.

149. UpToDate, Inc. Selection and administration of adjuvant chemotherapy for HER2-negative breast cancer. https://www.uptodate.com. Updated December 2022. Accessed January 26, 2023.

150. UpToDate, Inc. Systemic therapy for advanced cholangiocarcinoma. https://www.uptodate.com. Updated January 2023. Accessed January 24, 2023.

151. UpToDate, Inc. Systemic therapy for nonoperable metastatic colorectal cancer: Selecting the initial therapeutic approach. https://www.uptodate.com. Updated September 2022. Accessed October 10, 2022.

152. UpToDate, Inc. Systemic treatment of metastatic soft tissue sarcoma. https://www.uptodate.com. Updated January 2023. Accessed February 6, 2023.

153. UpToDate, Inc. Tissue-agnostic cancer therapy: DNA mismatch repair deficiency, tumor mutational burden, and response to immune checkpoint blockade in solid tumors. https://www.uptodate.com. Updated September 2022. Accessed October 18, 2022.

154. UpToDate, Inc. Toxicities associated with checkpoint inhibitor immunotherapy. https://www.uptodate.com. Updated July 2022. Accessed August 19, 2022.

155. UpToDate, Inc. Treatment approach to metastatic hormone receptor-positive, HER2-negative breast cancer: Endocrine therapy and targeted agents. https://www.uptodate.com. Updated July 2022. Accessed August 3, 2022.

156. UpToDate, Inc. Treatment of metastatic and recurrent head and neck cancer. https://www.uptodate.com. Updated July 2022. Accessed August 17, 2022.

157. UpToDate, Inc.Treatment of metastatic endometrial cancer. https://www.uptodate.com. Updated April 2023. Accessed May 8, 2023.

158. UpToDate, Inc. Treatment of metastatic urothelial cancer of the bladder and urinary tract. https://www.uptodate.com. Updated December 2022. Accessed January 24, 2023.

159. UpToDate, Inc. Treatment of relapsed or refractory chronic lymphocytic leukemia. https://www.uptodate.com. Updated December 2022. Accessed January 31, 2023.

160. UpToDate, Inc. Treatment of relapsed or refractory follicular lymphoma. https://www.uptodate.com. Updated September 2022. Accessed October 7, 2022.

161. UpToDate, Inc. TRK fusion-positive cancers and TRK inhibitor therapy. https://www.uptodate.com. Updated January 2023. Accessed February 6, 2023.

162. US Food & Drug Administration (FDA). 510(k) substantial equivalence determination decision summary: Invader assay UGT1A1. https://www.fda.gov. Published 2008. Accessed January 7, 2018.

163. US Food & Drug Administration (FDA). De novo summary: SeCore CDx HLA sequencing system. https://www.fda.gov. Published November 28, 2022. Accessed May 8, 2023.

164. US Food & Drug Administration (FDA). Full prescribing information: Alecensa (alectinib). https://www.fda.gov. Published January 2021. Updated September 2021. Accessed May 3, 2023.

165. US Food & Drug Administration (FDA). Full prescribing information: Alunbrig (brigatinib). https://www.fda.gov. Published April 28, 2017. Updated February 2022. Accessed May 3, 2023.

166. US Food & Drug Administration (FDA). Full prescribing information: Avastin (bevacizumab). https://www.fda.gov. Published December 2020. Accessed July 29, 2022.

167. US Food & Drug Administration (FDA). Full prescribing information: Balversa (erdafitinib). https://www.fda.gov. Published April 2019. Updated January 11, 2023. Accessed February 3, 2023.

168. US Food & Drug Administration (FDA). Full prescribing information: Camptosar (Irinotecan). https://www.fda.gov. Published December 19, 2014. Updated January 2022. Accessed October 10, 2022.

169. US Food & Drug Administration (FDA). Full prescribing information: Elahere (mirvetuximab soravtansine-gynx). https://www.fda.gov. Published November 2022. Accessed February 1, 2023.

170. US Food & Drug Administration (FDA). Full prescribing information: Eloxatin (oxaliplatin). https://www.fda.gov. Updated March 2020. Accessed May 13, 2021.

171. US Food & Drug Administration (FDA). Full prescribing information: Erbitux (cetuximab). https://www.fda.gov. Updated September 2021. Accessed April 24, 2023.

172. US Food & Drug Administration (FDA). Full prescribing information: Faslodex (fulvestrant). https://www.fda.gov. Updated April 2020. Accessed September 10, 2020.

173. US Food & Drug Administration (FDA). Full prescribing information: Fluorouracil. https://www.fda.gov. Published July 2016. Accessed October 7, 2022.

174. US Food & Drug Administration (FDA). Full prescribing information: Gavreto (pralsetinib). https://www.fda.gov. Updated September 2022. Accessed May 3, 2023.

175. US Food & Drug Administration (FDA). Full prescribing information: Jemperli (dostarlimab-gxly)). https://www.fda.gov. Updated April 2022. Accessed October 18, 2022.

176. US Food & Drug Administration (FDA). Full prescribing information: Keytruda (pembrolizumab). https://www.fda.gov. Updated April 2023. Accessed May 8, 2023.

177. US Food & Drug Administration (FDA). Full prescribing information: Kimmtrak (tebentafusp-tebn). https://www.fda.gov. Published November 2022. Accessed May 8, 2023.

178. US Food & Drug Administration (FDA). Full prescribing information: Krazati (adagrasib). https://www.fda.gov. Published December 2022. Accessed April 24, 2023.

179. US Food & Drug Administration (FDA). Full prescribing information: Libtayo (cemiplimab-rwlc). https://www.fda.gov. Updated February 2021. Accessed August 16, 2022.

180. US Food & Drug Administration (FDA). Full prescribing information: Lorbrena (lorlatinib). https://www.fda.gov. Updated March 2021. Accessed May 3, 2023.

181. US Food & Drug Administration (FDA). Full prescribing information: Lumakras (sotorasib). https://www.fda.gov. Updated January 2023. Accessed April 24, 2023.

182. US Food & Drug Administration (FDA). Full prescribing information: Lynparza (olaparib). https://www.fda.gov. Updated October 2022. Accessed January 25, 2023.

183. US Food & Drug Administration (FDA). Full prescribing information: Lytgobi (futibatinib). https://www.fda.gov. Updated September 2022. Accessed January 24, 2023.

184. US Food & Drug Administration (FDA). Full prescribing information: Ogivri (trastuzumab-dkst). https://www.fda.gov. Updated April 17, 2019. Accessed May 10, 2019.

185. US Food & Drug Administration (FDA). Full prescribing information: Opdivo (nivolumab). https://www.fda.gov. Published March 2015. Updated July 2022. Accessed August 16, 2022.

186. US Food & Drug Administration (FDA). Full prescribing information: Paraplatin (carboplatin). https://www.fda.gov. Updated 2010. Accessed May 13, 2021.

187. US Food & Drug Administration (FDA). Full prescribing information: Pemazyre (pemigatinib). https://www.fda.gov. Updated August 2022. Accessed February 3, 2023.

188. US Food & Drug Administration (FDA). Full prescribing information: Piqray (alpelisib). https://www.fda.gov. Updated May 2022. Accessed August 3, 2022.

189. US Food & Drug Administration (FDA). Full prescribing information: Platinol (cisplatin). https://www.fda.gov. Published February 2019. Accessed May 13, 2021.

190. US Food & Drug Administration (FDA). Full prescribing information: Retevmo (selpercatinib). https://www.fda.gov. Updated September 2022. Accessed May 3, 2023.

191. US Food & Drug Administration (FDA). Full prescribing information: Rozlytrek (entrectinib). https://www.fda.gov. Updated July 2022. Accessed May 10, 2023.

192. US Food & Drug Administration (FDA). Full prescribing information: Tabrecta (capmatinib). https://www.fda.gov. Updated March 2023. Accessed May 3, 2023.

193. US Food & Drug Administration (FDA). Full prescribing information: Tazverik (tazemetostat). https://www.fda.gov. Updated June 18, 2020. Accessed October 7, 2022.

194. US Food & Drug Administration (FDA). Full prescribing information: Tecentriq (atezolizumab). https://www.fda.gov. Updated January 2022. Accessed August 16, 2022.

195. US Food & Drug Administration (FDA). Full prescribing information: Tepmetko (tepotinib). https://www.fda.gov. Updated March 2023. Accessed May 3, 2023.

196. US Food & Drug Administration (FDA). Full prescribing information: Truseltiq (infigratinib). https://www.fda.gov. Updated May 2021. Accessed February 3, 2023.

197. US Food & Drug Administration (FDA). Full prescribing information: Vectibix (panitumumab). https://www.fda.gov. Updated August 2021. Accessed April 24, 2023.

198. US Food & Drug Administration (FDA). Full prescribing information: Vitrakvi (larotrectinib). https://www.fda.gov. Updated November 2022. Accessed February 6, 2023.

199. US Food & Drug Administration (FDA). Full prescribing information: Xalkori (crizotinib). https://www.fda.gov. Updated July 2022. Accessed May 3, 2023.

200. US Food & Drug Administration (FDA). Full prescribing information: Yervoy (ipilimumab). https://www.fda.gov. Updated May 2022. Accessed August 17, 2022.

201. US Food & Drug Administration (FDA). Full prescribing information: Zejula (niraparib). https://www.fda.gov. Updated July 2021. Accessed July 29, 2022.

202. US Food & Drug Administration (FDA). Full prescribing information: Zykadia (ceritinib). https://www.fda.gov. Updated October 2021. Accessed May 3, 2023.

203. US Food & Drug Administration (FDA). Premarket approval. Cobas EZH2 mutation test. https://www.fda.gov. Published June 18, 2020. Accessed October 7, 2022.

204. US Food & Drug Administration (FDA). Premarket approval. Cobas KRAS mutation test. https://www.fda.gov. Published May 7, 2015. Updated September 2016. Accessed May 6, 2022.

205. US Food & Drug Administration (FDA). Premarket approval. FoundationOne CDx. https://www.fda.gov. Published June 2, 2017. Updated March 16, 2022. Accessed May 3, 2023.

206. US Food & Drug Administration (FDA). Premarket approval. LeukoStrat CDx FLT3 Mutation Assay. https://www.fda.gov. Updated 2018. Accessed October 12, 2022.

207. US Food & Drug Administration (FDA). Premarket approval. MyChoice HRD CDx. https://www.fda.gov. Updated 2020. Accessed July 29, 2022.

208. US Food & Drug Administration (FDA). Premarket approval. Praxis Extended RAS Panel. https://www.fda.gov. Updated 2017. Accessed May 16, 2022.

209. US Food & Drug Administration (FDA). Premarket approval. PD-L1 IHC 22C3 PharmDx. https://www.fda.gov. Updated February 2021. Accessed August 16, 2022.

210. US Food & Drug Administration (FDA). Premarket approval. PD-L1 IHC 28-8 PharmDx. https://www.fda.gov. Updated May 2020. Accessed August 16, 2022.

211. US Food & Drug Administration (FDA). Premarket approval. Therascreen FGFR RGQ PCR Kit. https://www.fda.gov. Updated 2019. Accessed July 26, 2022.

212. US Food & Drug Administration (FDA). Premarket approval. Therascreen KRAS RGQ PCR Kit. https://www.fda.gov. Updated 2022. Accessed April 24, 2023.

213. US Food & Drug Administration (FDA). Premarket approval. Therascreen PIK3CA RGQ PCR Kit. https://www.fda.gov. Updated 2019. Accessed August 3, 2022.

214. US Food & Drug Administration (FDA). Premarket approval. Ventana ALK (D5F3) CDx assay – P140025. https://www.fda.gov. Updated March 3, 2021. Accessed May 3, 2023.

215. US Food & Drug Administration (FDA). Premarket approval. Ventana FOLR1 (FOLR-2.1) RxDx Assay – P220006. https://www.fda.gov. Updated November 18, 2022. Accessed February 1, 2023.

216. US Food & Drug Administration (FDA). Premarket approval. Ventana MMR RxDx Panel – P200019. https://www.fda.gov. Updated June 16, 2022. Accessed May 8, 2023.

217. US Food & Drug Administration (FDA). Premarket approval. Ventana PD-L1 (SP263) Assay – P160046. https://www.fda.gov. Updated October 15, 2021. Accessed August 16, 2022.

218. US Food & Drug Administration (FDA). Premarket approval. Vysis ALK Break Apart Fish Probe Kit. https://www.fda.gov. Updated May 5, 2020. Accessed May 3, 2023.

219. Zhang C, Liu H, Ma B, et al. The impact of the expression level of intratumoral dihydropyrimidine dehydrogenase on chemotherapy sensitivity and survival of patients in gastric cancer: a meta-analysis. *Dis Markers*. 2017;2017:9202676. https://www.ncbi.nlm.nih.gov. Accessed August 12, 2019.

Change Summary

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