

Erbitux® (cetuximab) (Intravenous)



Document Number: MODA-0494

Date Approved: 03/04/2025

Date of Origin: 09/03/2019

Dates Reviewed: 09/2019, 01/2020, 04/2020, 07/2020, 10/2020, 01/2021, 04/2021, 06/2021, 10/2021, 02/2022, 04/2022, 07/2022, 10/2022, 01/2023, 04/2023, 07/2023, 10/2023, 01/2024, 04/2024, 06/2024, 09/2024, 11/2024, 01/2025

I. Length of Authorization ^{1,30}

Coverage will be provided for 6 months and may be renewed, (unless otherwise specified).

Head and Neck Cancer

- In combination with radiation therapy: Coverage will be provided starting one week prior and for the duration of radiation therapy (up to 8 total weeks).

II. Dosing Limits

Max Units (per dose and over time) [HCPCS Unit]:

- Colorectal Cancer & Head and Neck Cancer: 280 billable units every 28 days
- NSCLC: 130 billable units every 14 days
- Squamous Cell Skin Cancer & Penile Cancer
 - Loading Dose: 100 billable units for 1 dose
 - Maintenance Dose: 60 billable units every 7 days

III. Initial Approval Criteria ¹

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**

Colorectal Cancer (CRC) † ‡ ^{1,2,12,13,17,19,32,37,2e,5e-8e,10e-12e,15e}

- Will not be used as part of an adjuvant treatment regimen; **AND**
- Patient has not been previously treated with cetuximab or panitumumab; **AND**
- Will not be used in combination with an anti-VEGF agent (e.g., bevacizumab, ramucirumab); **AND**
 - Patient has both KRAS and NRAS mutation negative (wild-type) and BRAF V600E mutation negative (wild-type) disease as determined by an FDA-approved or CLIA-compliant test❖; **AND**

- Used as primary treatment for metastatic or unresectable (or medically inoperable) disease §; **AND**
 - Used in combination with FOLFIRI †; **OR**
 - Used in combination with CapeOX or FOLFOX §; **AND**
 - Patient has proficient mismatch repair/microsatellite-stable (pMMR/MSS) disease; **OR**
 - Patient has deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) disease or polymerase epsilon/delta (POLE/POLD1) mutation; **AND**
 - ❖ Patient is not a candidate for or has progressed on checkpoint inhibitor immunotherapy; **OR**
 - Used in combination with irinotecan; **AND**
 - Patient previously received FOLFOX or CapeOX within the past 12 months; **AND**
 - Patient has proficient mismatch repair/microsatellite-stable (pMMR/MSS) disease; **OR**
- Used as primary treatment for T3, N Any; T1-2, N1-2; T4, N Any rectal cancer; **AND**
 - Used in combination with CapeOX, FOLFOX, or FOLFIRI; **AND**
 - Used if resection is contraindicated following total neoadjuvant therapy; **AND**
 - ❖ Patient has proficient mismatch repair/microsatellite-stable (pMMR/MSS) disease; **OR**
 - ❖ Patient has deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) disease or polymerase epsilon/delta (POLE/POLD1) mutation; **AND**
 - ◆ Patient is not a candidate for or has progressed on checkpoint inhibitor immunotherapy; **OR**
 - Used if resection is contraindicated following neoadjuvant/definitive immunotherapy; **AND**
 - ❖ Patient has deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) disease; **OR**
- Used for progression on non-intensive therapy, except if received previous fluoropyrimidine, with improvement in functional status §; **AND**
 - Used in combination with FOLFOX, CapeOx, or FOLFIRI; **AND**
 - Patient has proficient mismatch repair/microsatellite-stable (pMMR/MSS) disease; **OR**
 - Patient has deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) disease or polymerase epsilon/delta (POLE/POLD1) mutation; **AND**
 - ❖ Patient is not a candidate for or has progressed on checkpoint inhibitor immunotherapy; **OR**
- Used as subsequent therapy for advanced or metastatic disease; **AND**

- Used as a single agent; **AND**
 - Patient has oxaliplatin- and irinotecan-refractory disease †; **OR**
 - Patient has irinotecan-intolerant disease †; **OR**
- Used in combination with irinotecan; **AND**
 - Patient has irinotecan-refractory disease †; **OR**
 - Patient has oxaliplatin-refractory disease or oxaliplatin- and irinotecan-refractory disease; **AND**
 - ❖ Patient has proficient mismatch repair/microsatellite-stable (pMMR/MSS) disease; **OR**
 - ❖ Patient has deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) disease or polymerase epsilon/delta (POLE/POLD1) mutation; **AND**
 - ◆ Patient is not a candidate for or has progressed on checkpoint inhibitor immunotherapy; **OR**
 - Patient has colon cancer that is refractory to therapy without irinotecan or oxaliplatin; **AND**
 - ❖ Patient has proficient mismatch repair/microsatellite-stable (pMMR/MSS) disease; **OR**
 - ❖ Patient has deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) disease or polymerase epsilon/delta (POLE/POLD1) mutation; **AND**
 - ◆ Patient is not a candidate for or has progressed on checkpoint inhibitor immunotherapy; **OR**
- Used in combination with FOLFIRI for oxaliplatin-refractory disease; **AND**
 - Patient has proficient mismatch repair/microsatellite-stable (pMMR/MSS) disease; **OR**
 - Patient has deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) disease or polymerase epsilon/delta (POLE/POLD1) mutation; **AND**
 - ❖ Patient is not a candidate for or has progressed on checkpoint inhibitor immunotherapy; **OR**
- Used in combination with FOLFIRI for colon cancer that is refractory to therapy without irinotecan or oxaliplatin; **AND**
 - Patient has proficient mismatch repair/microsatellite-stable (pMMR/MSS) disease; **OR**
 - Patient has deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) disease or polymerase epsilon/delta (POLE/POLD1) mutation; **AND**
 - ❖ Patient is not a candidate for or has progressed on checkpoint inhibitor immunotherapy; **OR**

- Used in combination with FOLFOX or CapeOX for irinotecan-refractory disease; **AND**
 - Patient has proficient mismatch repair/microsatellite-stable (pMMR/MSS) disease; **OR**
 - Patient has deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) disease or polymerase epsilon/delta (POLE/POLD1) mutation; **AND**
 - ❖ Patient is not a candidate for or has progressed on checkpoint inhibitor immunotherapy; **OR**
- Patient has BRAF V600E mutation positive disease as determined by an FDA-approved or CLIA-compliant test❖ †; **AND**
 - Used in combination with encorafenib; **AND**
 - Used as initial treatment for unresectable metastatic disease after previous adjuvant FOLFOX or CapeOX within the past 12 months; **AND**
 - Patient has proficient mismatch repair/microsatellite-stable (pMMR/MSS) disease; **OR**
 - Used as subsequent therapy for progression after at least one prior line of treatment in the advanced or metastatic disease setting; **OR**
 - Used in combination with encorafenib AND mFOLFOX6; **AND**
 - Patient has previously untreated metastatic disease; **OR**
- Patient has KRAS G12C mutation positive disease as determined by an FDA-approved or CLIA-compliant test❖ ‡; **AND**
 - Used in combination with adagrasib; **AND**
 - Used as initial treatment for unresectable metastatic disease after previous FOLFOX or CapeOX within the past 12 months; **AND**
 - Patient has proficient mismatch repair/microsatellite-stable (pMMR/MSS) disease; **OR**
 - Used as subsequent therapy for progression of advanced or metastatic disease; **AND**
 - Patient has received prior treatment with fluoropyrimidine-based therapy AND oxaliplatin- or irinotecan-based chemotherapy; **AND**
 - ❖ Patient has proficient mismatch repair/microsatellite-stable (pMMR/MSS) disease; **OR**
 - ❖ Patient has deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) disease or polymerase epsilon/delta (POLE/POLD1) mutation; **AND**
 - ◆ Patient is not a candidate for or has progressed on checkpoint inhibitor immunotherapy

§ *Colon cancer patients must have left-sided tumors only.*

Head and Neck Cancer † ‡ Φ 1,2,14,16,25,29-31,17e-23e,25e-29e

- Patient has squamous cell carcinoma; **AND**
 - Used in combination with radiation as a single agent †; **OR**
 - Used as first-line therapy; **AND**
 - Used in combination with fluorouracil and either cisplatin or carboplatin for unresectable, recurrent/persistent, or metastatic disease (non-nasopharyngeal) †; **OR**
 - Used in combination with cisplatin for very advanced head and neck cancers* (non-nasopharyngeal) AND PS 0-1; **OR**
 - Used in combination with docetaxel and either cisplatin or carboplatin for very advanced head and neck cancers* (non-nasopharyngeal) AND PS 0-1; **OR**
 - Used in combination with paclitaxel with or without platinum-based therapy for very advanced head and neck cancers* (non-nasopharyngeal) AND PS 0-1; **OR**
 - Used in combination with nivolumab for very advanced head and neck cancer* (non-nasopharyngeal) AND PS 0-1; **OR**
 - Used in combination with pembrolizumab for very advanced head and neck cancer* (non-nasopharyngeal) AND PS 0-1; **AND**
 - Patient is platinum-ineligible; **OR**
 - Used as subsequent therapy; **AND**
 - Used as a single agent for unresectable, recurrent/persistent, or metastatic disease after failure on platinum-based therapy †; **OR**
 - Used in combination with nivolumab or pembrolizumab for very advanced head and neck cancer* (non-nasopharyngeal) AND PS 0-1; **AND**
 - Patient has platinum-resistant disease or is platinum-ineligible

* Very Advanced Head and Neck Cancers include: newly diagnosed locally advanced T4b [M0] disease; newly diagnosed unresectable regional nodal disease, typically N3; metastatic disease at initial presentation [M1]; or recurrent or persistent disease.

Squamous Cell Skin Cancer ‡ 2,21,27

- Used as a single agent in combination with radiation therapy Ω; **AND**
 - Patient has locally advanced or unresectable disease; **AND**
 - Used as primary treatment for non-surgical candidates; **OR**
 - Used as additional treatment if positive surgical margins and re-resection not feasible; **OR**
 - Patient has resected high-risk regional disease of the head and neck with pathologic extranodal extension (ENE) or incompletely excised nodal disease; **OR**
 - Patient has regional disease that is unresectable, inoperable, or incompletely resected; **OR**
 - Patient has regional recurrence or distant metastatic disease; **OR**
- Used as a single agent OR in combination with carboplatin and paclitaxel (Ω in combination with carboplatin and paclitaxel only); **AND**

- Patient is not a candidate for or has progressed on immune checkpoint inhibitors AND clinical trials; **AND**
 - Patient has locally advanced or unresectable disease; **AND**
 - Used as primary treatment if curative surgery and curative radiation therapy (RT) are not feasible; **OR**
 - Used as additional treatment if positive surgical margins and curative surgery and curative RT are not feasible; **OR**
 - Patient has regional disease that is unresectable, inoperable, or incompletely resected if curative RT is not feasible; **OR**
 - Patient has regional recurrence or distant metastatic disease

Penile Cancer ‡ Ω^{2,26}

- Used as a single agent; **AND**
- Used as subsequent therapy for metastatic or recurrent disease

Non-Small Cell Lung Cancer (NSCLC) ‡ Ω^{2,24}

- Used in combination with afatinib; **AND**
- Patient has recurrent, advanced, or metastatic disease (excluding locoregional recurrence or symptomatic local disease without evidence of disseminated disease) or mediastinal lymph node recurrence with prior radiation therapy; **AND**
- Used as subsequent therapy; **AND**
- Patient has EGFR exon 19 deletion or exon 21 L858R or EGFR S768I, L861Q, and/or G719X mutation positive tumors as determined by an FDA-approved or CLIA-compliant test ❖; **AND**
- Patient progressed on EGFR tyrosine kinase inhibitor therapy; **AND**
 - Patient has asymptomatic disease, symptomatic brain lesions, or symptomatic systemic limited* progression; **AND**
 - Used following progression on subsequent therapy with erlotinib, afatinib, gefitinib, or dacomitinib therapy; **AND**
 - Patient has T790M negative disease; **OR**
 - Used following subsequent therapy with continuation of osimertinib Ω; **OR**
 - Used following subsequent therapy with continuation of amivantamab-vmjw and lazertinib Ω; **AND**
 - Patient has EGFR exon 19 deletion or exon 21 L858R positive disease; **OR**
 - Patient has multiple symptomatic systemic lesions or symptomatic systemic limited* progression; **AND**
 - Used following initial therapy with erlotinib, afatinib, gefitinib, or dacomitinib therapy; **AND**
 - Patient has T790M negative disease; **OR**

- Used following initial therapy with osimertinib; **OR**
- Used following initial therapy with amivantamab-vmjw and lazertinib; **AND**
 - Patient has EGFR exon 19 deletion or exon 21 L858R positive disease

* Limited progression: Up to 3 to 5 progressing sites.

Preferred therapies and recommendations are determined by review of clinical evidence. NCCN category of recommendation is taken into account as a component of this review. Regimens deemed equally efficacious (i.e., those having the same NCCN categorization) are considered to be therapeutically equivalent.

Ω Please note that the supporting data for this indication has been assessed and deemed to be of insufficient quality based on the review conducted for the Enhanced Oncology Value (EOV) program. However, due to the absence of viable alternative treatment options, this indication will be retained in our policy and evaluated on a case-by-case basis.

❖ If confirmed using an FDA approved assay – <http://www.fda.gov/companiondiagnostics>

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria ^{1,30}

Coverage may be renewed based upon the following criteria:

- Patient continues to meet the indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Duration of authorization has not been exceeded (*refer to Section I*); **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: severe infusion reactions/anaphylactic reactions, cardiopulmonary arrest, pulmonary toxicity/interstitial lung disease, dermatologic toxicity, hypomagnesemia/electrolyte abnormalities, etc.

V. Dosage/Administration ^{1,12,13,20-23,29-36}

Indication	Dose
Colorectal Cancer	400 mg/m ² loading dose intravenously, then 250 mg/m ² intravenously every 7 days until disease progression or unacceptable toxicity OR 500 mg/m ² intravenously every 14 days until disease progression or unacceptable toxicity
NSCLC	500 mg/m ² intravenously every 14 days until disease progression or unacceptable toxicity

Head and Neck Cancer	<p><u>In combination with radiation therapy:</u> 400 mg/m² loading dose intravenously 1 week prior to radiation therapy, then 250 mg/m² intravenously every 7 days for the duration of radiation therapy (up to 8 total weeks of therapy)</p> <p><u>Monotherapy, in combination with paclitaxel, or in combination with platinum-based therapy:</u> 400 mg/m² loading dose intravenously, then 250 mg/m² intravenously every 7 days until disease progression or unacceptable toxicity</p> <p>OR</p> <p>500 mg/m² intravenously every 14 days until disease progression or unacceptable toxicity</p> <p><u>In combination with nivolumab:</u> 500 mg/m² intravenously every 14 days until disease progression or unacceptable toxicity</p> <p><u>In combination with pembrolizumab:</u> 400 mg/m² loading dose intravenously, then 250 mg/m² intravenously every 7 days until disease progression or unacceptable toxicity</p>
Squamous Cell Skin Cancer & Penile Cancer	400 mg/m ² loading dose intravenously, then 250 mg/m ² intravenously every 7 days until disease progression or unacceptable toxicity

VI. Billing Code/Availability Information

HCPCS Code:

- J9055 – Injection, cetuximab, 10 mg; 1 billable unit = 10 mg

NDC(s):

- Erbitux 100 mg/50 mL single-dose vial, solution for injection: 66733-0948-xx
- Erbitux 200 mg/100 mL single-dose vial, solution for injection: 66733-0958-xx

VII. References (STANDARD)

1. Erbitux [package insert]. Branchburg, NJ; ImClone LLC; September 2021; Accessed January 2025.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) cetuximab. National Comprehensive Cancer Network, 2025. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed January 2025.
3. Bouchahda M, Macarulla G, Lledo F, et al. Efficacy and safety of cetuximab (C) given with a simplified, every other week (q2w), schedule in patients (pts) with advanced colorectal cancer (aCRC): a multicenter, retrospective study. J Clin Oncol. 2008; 26(15S): Abstract 15118.

Presented at: The 44th American Society of Clinical Oncology Annual Meeting (ASCO). May 30–June 3, 2008. Chicago, Illinois.

4. Mrabti H, La Fouchardiere C, Desseigne F, Dussart S, Negrier S, Errihani H. Irinotecan associated with cetuximab given every 2 weeks versus cetuximab weekly in metastatic colorectal cancer. *J Can Res Ther*. 2009; 5:272-6.
5. Shitara K, Yuki S, Yoshida M, et al. Phase II study of combination chemotherapy with biweekly cetuximab and irinotecan for wild-type KRAS metastatic colorectal cancer refractory to irinotecan, oxaliplatin, and fluoropyrimidines *World J Gastroenterol*, 2011, April 14; 17(14): 1879-1888
6. Pfeiffer P, Bjerregarrd JK, Qvortrup C, et al, “Simplification of Cetuximab (Cet) Administration: Double Dose Every Second Week as a 60 Minute Infusion,” *J Clin Oncol*, 2007, 25(18S):4133 [abstract 4133 from 2007 ASCO Annual Meeting Proceedings, Part I].
7. Pfeiffer P, Nielsen D, Bjerregaard J, et al, “Biweekly Cetuximab and Irinotecan as Third-Line Therapy in Patients with Advanced Colorectal Cancer after Failure to Irinotecan, Oxaliplatin and 5-Fluorouracil,” *Ann Oncol*, 2008, 19(6):1141-5.
8. Carneiro BA, Ramanathan RK, Fakih MG, et al. Phase II study of irinotecan and cetuximab given every 2 weeks as second-line therapy for advanced colorectal cancer. *Clin Colorectal Cancer*. 2012 Mar; 11(1):53-9.
9. Fahrenbruch R, Kintzel P, Bott AM, et al. Dose Rounding of Biologic and Cytotoxic Anticancer Agents: A Position Statement of the Hematology/Oncology Pharmacy Association. *J Oncol Pract*. 2018 Mar;14(3):e130-e136.
10. Hematology/Oncology Pharmacy Association (2019). Intravenous Cancer Drug Waste Issue Brief. Retrieved from <https://www.hoparx.org/about-us/advocacy-awareness/issue-briefs/>
11. Bach PB, Conti RM, Muller RJ, et al. Overspending driven by oversized single dose vials of cancer drugs. *BMJ*. 2016 Feb 29;352:i788
12. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Colon Cancer, Version 6.2024. National Comprehensive Cancer Network, 2025. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed January 2025.
13. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Rectal Cancer, Version 5.2024. National Comprehensive Cancer Network, 2025. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed January 2025.
14. Bonner JA, Harari PM, Giralt J, et al. Radiotherapy plus cetuximab for squamous-cell carcinoma of the head and neck. *N Engl J Med*. 2006 Feb 9;354(6):567-78.

15. Vermorken JB, Mesia R, Rivera F, et al. Platinum-based chemotherapy plus cetuximab in head and neck cancer. *N Engl J Med*. 2008 Sep 11;359(11):1116-27. doi: 10.1056/NEJMoa0802656.
16. Vermorken JB, Trigo J, Hitt R, et al. Open-label, uncontrolled, multicenter phase II study to evaluate the efficacy and toxicity of cetuximab as a single agent in patients with recurrent and/or metastatic squamous cell carcinoma of the head and neck who failed to respond to platinum-based therapy. *J Clin Oncol*. 2007 Jun 1;25(16):2171-7.
17. Van Cutsem E, Köhne CH, et al. Cetuximab and chemotherapy as initial treatment for metastatic colorectal cancer. *N Engl J Med*. 2009 Apr 2;360(14):1408-17. doi: 10.1056/NEJMoa0805019.
18. Jonker DJ, O'Callaghan CJ, Karapetis CS, et al. Cetuximab for the treatment of colorectal cancer. *N Engl J Med*. 2007 Nov 15;357(20):2040-8.
19. Cunningham D, Humblet Y, Siena S, et al. Cetuximab monotherapy and cetuximab plus irinotecan in irinotecan-refractory metastatic colorectal cancer. *N Engl J Med*. 2004 Jul 22;351(4):337-45.
20. Samstein RM, Ho AL, Lee NY, et al. Locally advanced and unresectable cutaneous squamous cell carcinoma: outcomes of concurrent cetuximab and radiotherapy. *J Skin Cancer*. 2014;2014:284582. doi: 10.1155/2014/284582. Epub 2014 Jul 21.
21. Maubec E, Petrow P, Scheer-Senyarich I, et al. Phase II study of cetuximab as first-line single-drug therapy in patients with unresectable squamous cell carcinoma of the skin. *J Clin Oncol*. 2011 Sep 1;29(25):3419-26. doi: 10.1200/JCO.2010.34.1735. Epub 2011 Aug 1.
22. Carthon BC, Ng CS, Pettaway CA, et al. Epidermal growth factor receptor-targeted therapy in locally advanced or metastatic squamous cell carcinoma of the penis. *BJU Int*. 2014 Jun;113(6):871-7. doi: 10.1111/bju.12450.
23. Janjigian YY, Smit EF, Groen HJ, et al. Dual inhibition of EGFR with afatinib and cetuximab in kinase inhibitor-resistant EGFR-mutant lung cancer with and without T790M mutations. *Cancer Discov*. 2014 Sep;4(9):1036-45. doi: 10.1158/2159-8290.CD-14-0326. Epub 2014 Jul 29.
24. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Non-Small Cell Lung Cancer, Version 3.2025. National Comprehensive Cancer Network, 2025. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed January 2025.
25. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Head and Neck Cancers, Version 2.2025. National Comprehensive Cancer Network, 2025. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed January 2025.

26. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Penile Cancer. Version 2.2025. National Comprehensive Cancer Network, 2025. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed January 2025.
27. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Squamous Cell Skin Cancer. Version 1.2025. National Comprehensive Cancer Network, 2025. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed January 2025.
28. Kopetz S, Grothey A, Yaeger R, et al. Encorafenib, Binimetinib, and Cetuximab in BRAF V600E-Mutated Colorectal Cancer. *N Engl J Med*. 2019 Oct 24;381(17):1632-1643. doi: 10.1056/NEJMoa1908075. Epub 2019 Sep 30.
29. Chung C, Li J, Steuer C, et al. Phase II Multi-institutional Clinical Trial Result of Concurrent Cetuximab and Nivolumab in Recurrent and/or Metastatic Head and Neck Squamous Cell Carcinoma. *Clin Cancer Res*. 2022 Jun 1;28(11):2329-2338. doi: 10.1158/1078-0432.CCR-21-3849.
30. Mesía R, Vázquez S, Grau JJ, et al; Spanish Head and Neck Cancer Cooperative Group (TTCC). A Phase 2 Open Label, Single-Arm Trial to Evaluate the Combination of Cetuximab Plus Taxotere, Cisplatin, and 5-Fluorouracil as an Induction Regimen in Patients With Unresectable Squamous Cell Carcinoma of the Head and Neck. *Int J Radiat Oncol Biol Phys*. 2016 Feb 1;94(2):289-96.
31. Sacco AG, Chen R, Worden FP, et al. Pembrolizumab plus cetuximab in patients with recurrent or metastatic head and neck squamous cell carcinoma: an open-label, multi-arm, non-randomised, multicentre, phase 2 trial. *Lancet Oncol* 2021;22:883-892.
32. Yaeger R, Weiss J, Pelster M, et al. Adagrasib with or without Cetuximab in Colorectal Cancer with Mutated KRAS G12C. *N Engl J Med* 2023;388:44- 54.
33. Carinato H, Burgy M, Ferry R, et al. Weekly Paclitaxel, Carboplatin, and Cetuximab as First-Line Treatment of Recurrent and/or Metastatic Head and Neck Squamous Cell Carcinoma for Patients Ineligible to Cisplatin-Based Chemotherapy: A Retrospective Monocentric Study in 60 Patients. *Front Oncol*. 2021 Oct 27;11:714551. doi: 10.3389/fonc.2021.714551.
34. Tahara M, Kiyota N, Yokota T, et al. Phase II trial of combination treatment with paclitaxel, carboplatin and cetuximab (PCE) as first-line treatment in patients with recurrent and/or metastatic squamous cell carcinoma of the head and neck (CSPOR-HN02). *Ann Oncol*. 2018 Apr 1;29(4):1004-1009. doi: 10.1093/annonc/mdy040.

35. Geraghty L, Schultz TE, Hoffman SE, et al. Weekly vs. 3-weekly paclitaxel, carboplatin, and cetuximab (PCC) in recurrent/metastatic head and neck cancer. *Mol Clin Oncol*. 2021 Nov;15(5):240. doi: 10.3892/mco.2021.2403.
36. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Cetuximab: Head and Neck Cancers, HDN134. National Comprehensive Cancer Network, 2025. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed January 2025.
37. Kopetz S, Yoshino T, Kim TW, et al. BREAKWATER: An open-label, multicenter, randomized, phase 3 study, with a safety lead-in (SLI), of first-line (1L) encorafenib (E) + cetuximab (C) ± chemotherapy (CT) vs standard-of-care (SOC) CT for BRAF V600E-mutant metastatic colorectal cancer (mCRC). *Journal of Clinical Oncology* [Volume 41, Number 16 suppl. https://doi.org/10.1200/JCO.2023.41.16_suppl.TPS3627](https://doi.org/10.1200/JCO.2023.41.16_suppl.TPS3627)

VIII. References (ENHANCED)

- 1e. Van Cutsem E, Köhne CH, Láng I, et al. Cetuximab plus irinotecan, fluorouracil, and leucovorin as first-line treatment for metastatic colorectal cancer: updated analysis of overall survival according to tumor KRAS and BRAF mutation status. *J Clin Oncol*. 2011 May 20;29(15):2011-9.
- 2e. Qin S, Li J, Wang L, et al. Efficacy and Tolerability of First-Line Cetuximab Plus Leucovorin, Fluorouracil, and Oxaliplatin (FOLFOX-4) Versus FOLFOX-4 in Patients With RAS Wild-Type Metastatic Colorectal Cancer: The Open-Label, Randomized, Phase III TAILOR Trial. *J Clin Oncol*. 2018;36(30):3031–3039. doi:10.1200/JCO.2018.78.3183
- 3e. Douillard JY, Oliner KS, Siena S, et al. Panitumumab-FOLFOX4 treatment and RAS mutations in colorectal cancer. *N Engl J Med*. 2013 Sep 12;369(11):1023-34.
- 4e. Douillard JY, Siena S, Cassidy J, et al. Final results from PRIME: randomized phase III study of panitumumab with FOLFOX4 for first-line treatment of metastatic colorectal cancer. *Ann Oncol*. 2014 Jul;25(7):1346-55.
- 5e. Heinemann V, von Weikersthal LF, Decker T, et al. FOLFIRI plus cetuximab versus FOLFIRI plus bevacizumab as first-line treatment for patients with metastatic colorectal cancer (FIRE-3): a randomised, open-label, phase 3 trial. *Lancet Oncol*. 2014 Sep;15(10):1065-75.
- 6e. Heinemann V, Modest DP, von Weikersthal LF, et al. Gender and tumor location as predictors for efficacy: Influence on endpoints in first-line treatment with FOLFIRI in combination with cetuximab or bevacizumab in the AIO KRK 0306 (FIRE3) trial. *J Clin Oncol*. 2014;32:(15_suppl):3600.
- 7e. Venook AP, Niedzwiecki D, Innocenti F, et al. Impact of primary (1^o) tumor location on overall survival (OS) and progression-free survival (PFS) in patients (pts) with metastatic colorectal cancer (mCRC): Analysis of CALGB/SWOG 80405 (Alliance). *ASCO Meeting Abstracts* 2016; 34:3504.
- 8e. Schwartzberg LS, Rivera F, Karthaus M, et al. PEAK: a randomized, multicenter phase II study of panitumumab plus modified fluorouracil, leucovorin, and oxaliplatin (mFOLFOX6) or

- bevacizumab plus mFOLFOX6 in patients with previously untreated, unresectable, wild-type KRAS exon 2 metastatic colorectal cancer. *J Clin Oncol*. 2014 Jul 20;32(21):2240-7.
- 9e. Rivera F, Karthaus M, Hecht JR, et al. Final analysis of the randomised PEAK trial: overall survival and tumour responses during first-line treatment with mFOLFOX6 plus either panitumumab or bevacizumab in patients with metastatic colorectal carcinoma. *Int J Colorectal Dis*. 2017;32(8):1179–1190. doi:10.1007/s00384-017-2800-1.
- 10e. Sobrero AF, Maurel J, Fehrenbacher L, et al. EPIC: phase III trial of cetuximab plus irinotecan after fluoropyrimidine and oxaliplatin failure in patients with metastatic colorectal cancer. *J Clin Oncol*. 2008 May 10;26(14):2311-9.
- 11e. Price TJ, Peeters M, Kim TW, et al. Panitumumab versus cetuximab in patients with chemotherapy-refractory wild-type KRAS exon 2 metastatic colorectal cancer (ASPECCT): a randomised, multicentre, open-label, non-inferiority phase 3 study. *Lancet Oncol*. 2014 May;15(6):569-79.
- 12e. Karapetis CS, Khambata-Ford S, Jonker DJ, et al. K-ras mutations and benefit from cetuximab in advanced colorectal cancer. *N Engl J Med*. 2008 Oct 23;359(17):1757-65.
- 13e. Kopetz S, McDonogh SL, Lenz HJ, et al. Randomized trial of irinotecan and cetuximab with or without vemurafenib in BRAF-mutant metastatic colorectal cancer (SWOG S1406). *J Clin Oncol* 2017;35 (suppl):3505.
- 14e. Corcoran RB, André T, Atreya CE, et al. Combined BRAF, EGFR, and MEK Inhibition in Patients with BRAFV600E-Mutant Colorectal Cancer. *Cancer Discov*. 2018;8(4):428–443. doi:10.1158/2159-8290.CD-17-1226
- 15e. Kopetz S, Grothey A, Van Cutsem E, et al. Encorafenib plus cetuximab with or without binimetinib for BRAF V600E-mutant metastatic colorectal cancer: Quality-of-life results from a randomized, three-arm, phase III study versus the choice of either irinotecan or FOLFIRI plus cetuximab (BEACON CRC) [abstract]. *J Clin Oncol* 2020;38,(suppl 4;abstr 8).
- 16e. Adelstein DJ, Li Y, Adams GL, Wagner H Jr, et al. An intergroup phase III comparison of standard radiation therapy and two schedules of concurrent chemoradiotherapy in patients with unresectable squamous cell head and neck cancer. *J Clin Oncol*. 2003 Jan 1;21(1):92-8.
- 17e. Magrini SM, Buglione M, Corvò R, et al. Cetuximab and Radiotherapy Versus Cisplatin and Radiotherapy for Locally Advanced Head and Neck Cancer: A Randomized Phase II Trial. *J Clin Oncol*. 2016 Feb 10;34(5):427-35.
- 18e. Gillison ML, Trotti AM, Harris J, et al. Radiotherapy plus cetuximab or cisplatin in human papillomavirus-positive oropharyngeal cancer (NRG Oncology RTOG 1016): a randomised, multicentre, non-inferiority trial. *Lancet*. 2019 Jan 5;393(10166):40-50.
- 19e. Ang KK, Zhang Q, Rosenthal DI, et al. Randomized phase III trial of concurrent accelerated radiation plus cisplatin with or without cetuximab for stage III to IV head and neck carcinoma: RTOG 0522. *J Clin Oncol*. 2014;32(27):2940–2950. doi:10.1200/JCO.2013.53.5633.
- 20e. Mehanna H, Robinson M, Hartley A, et al. Radiotherapy plus cisplatin or cetuximab in low-risk human papillomavirus-positive oropharyngeal cancer (De-ESCALaTE HPV): an open-label randomised controlled phase 3 trial. *Lancet*. 2019;393(10166):51–60. doi:10.1016/S0140-6736(18)32752-1.

- 21e. Tao Y, Auperin A, Sire C, et al. Improved Outcome by Adding Concurrent Chemotherapy to Cetuximab and Radiotherapy for Locally Advanced Head and Neck Carcinomas: Results of the GORTEC 2007-01 Phase III Randomized Trial. *J Clin Oncol*. 2018 Jun 7;JCO2017762518.
- 22e. Burtneß B, Goldwasser MA, Flood W, et al. Phase III randomized trial of cisplatin plus placebo compared with cisplatin plus cetuximab in metastatic/recurrent head and neck cancer: an Eastern Cooperative Oncology Group study. *J Clin Oncol*. 2005 Dec 1;23(34):8646-54.
- 23e. Bossi P, Miceli R, Locati LD, et al. A randomized, phase 2 study of cetuximab plus cisplatin with or without paclitaxel for the first-line treatment of patients with recurrent and/or metastatic squamous cell carcinoma of the head and neck. *Ann Oncol*. 2017 Nov 1;28(11):2820-2826.
- 24e. Gibson MK, Li Y, Murphy B, et al. Randomized phase III evaluation of cisplatin plus fluorouracil versus cisplatin plus paclitaxel in advanced head and neck cancer (E1395): an intergroup trial of the Eastern Cooperative Oncology Group. *J Clin Oncol*. 2005 May 20;23(15):3562-7.
- 25e. Rischin D, Harrington KJ, Greil R, et al. Protocol-specified final analysis of the phase 3 KEYNOTE-048 trial of pembrolizumab (pembro) as first-line therapy for recurrent/metastatic head and neck squamous cell carcinoma (R/M HNSCC). ASCO 2019.
- 26e. Zhang L, Huang Y, Hong S, et al. Gemcitabine plus cisplatin versus fluorouracil plus cisplatin in recurrent or metastatic nasopharyngeal carcinoma: a multicentre, randomised, open-label, phase 3 trial. *Lancet*. 2016 Oct 15;388(10054):1883-1892.
- 27e. Ferris RL, Blumenschein G Jr, Fayette J, et al. Nivolumab for Recurrent Squamous-Cell Carcinoma of the Head and Neck. *N Engl J Med*. 2016;375(19):1856–1867. doi:10.1056/NEJMoa1602252.
- 28e. Cohen EEW, Soulières D, Le Tourneau C, et al. Pembrolizumab versus methotrexate, docetaxel, or cetuximab for recurrent or metastatic head-and-neck squamous cell carcinoma (KEYNOTE-040): a randomised, open-label, phase 3 study. *Lancet*. 2019 Jan 12;393(10167):156-167.
- 29e. Martinez-Trufero J, Isla D, Adansa JC, et al. Phase II study of capecitabine as palliative treatment for patients with recurrent and metastatic squamous head and neck cancer after previous platinum-based treatment. *Br J Cancer*. 2010;102(12):1687–1691. doi:10.1038/sj.bjc.6605697.
- 30e. Grau JJ, Caballero M, Verger E, Monzó M, Blanch JL. Weekly paclitaxel for platin-resistant stage IV head and neck cancer patients. *Acta Otolaryngol*. 2009 Nov;129(11):1294-9.
- 31e. Chan AT, Hsu MM, Goh BC, et al. Multicenter, phase II study of cetuximab in combination with carboplatin in patients with recurrent or metastatic nasopharyngeal carcinoma. *J Clin Oncol*. 2005 May 20;23(15):3568-76.
- 32e. Reigneau M, Robert C, Routier E, et al. Efficacy of neoadjuvant cetuximab alone or with platinum salt for the treatment of unresectable advanced nonmetastatic cutaneous squamous cell carcinomas. *Br J Dermatol*. 2015 Aug;173(2):527-34.
- 33e. Sadek H, Azli N, Wendling JL, et al. Treatment of advanced squamous cell carcinoma of the skin with cisplatin, 5-fluorouracil, and bleomycin. *Cancer*. 1990 Oct 15;66(8):1692-6.

- 34e. Jarkowski A 3rd, Hare R, Loud P, et al. Systemic Therapy in Advanced Cutaneous Squamous Cell Carcinoma (CSCC): The Roswell Park Experience and a Review of the Literature. *Am J Clin Oncol*. 2016 Dec;39(6):545-548.
- 35e. Trodello C1, Pepper JP, Wong M, Wysong A. Cisplatin and Cetuximab Treatment for Metastatic Cutaneous Squamous Cell Carcinoma: A Systematic Review. *Dermatol Surg*. 2017 Jan;43(1):40-49.
- 36e. Le DT, Durham JN, Smith KN, et al. Mismatch repair deficiency predicts response of solid tumors to PD-1 blockade. *Science*. 2017;357(6349):409–413. doi:10.1126/science.aan6733.
- 37e. Di Lorenzo G, Federico P, Buonerba C, et al. Paclitaxel in pretreated metastatic penile cancer: final results of a phase 2 study. *Eur Urol*. 2011 Dec;60(6):1280-4.
- 38e. Hecht JR, Cohn A, Dakhil S, et al. SPIRITT: A Randomized, Multicenter, Phase II Study of Panitumumab with FOLFIRI and Bevacizumab with FOLFIRI as Second-Line Treatment in Patients with Unresectable Wild Type KRAS Metastatic Colorectal Cancer. *Clin Colorectal Cancer*. 2015 Jun;14(2):72-80.
- 39e. Herbst RS, Arquette M, Shin DM, et al. Phase II multicenter study of the epidermal growth factor receptor antibody cetuximab and cisplatin for recurrent and refractory squamous cell carcinoma of the head and neck. *J Clin Oncol*. 2005;23(24):5578-5587. doi:10.1200/JCO.2005.07.120.
- 40e. Burtneess B, Harrington KJ, Greil R, et al. Pembrolizumab alone or with chemotherapy versus cetuximab with chemotherapy for recurrent or metastatic squamous cell carcinoma of the head and neck (KEYNOTE-048): a randomised, open-label, phase 3 study [published correction appears in *Lancet*. 2020 Jan 25;395(10220):272] [published correction appears in *Lancet*. 2020 Feb 22;395(10224):564]. *Lancet*. 2019;394(10212):1915-1928. doi:10.1016/S0140-6736(19)32591-7.
- 41e. Migden MR, Rischin D, Schmults CD, et al. PD-1 Blockade with Cemiplimab in Advanced Cutaneous Squamous-Cell Carcinoma. *N Engl J Med*. 2018 Jul 26;379(4):341-351. doi: 10.1056/NEJMoa1805131.
- 42e. Grob JJ, Gonzalez R, Basset-Seguín N, et al. Pembrolizumab Monotherapy for Recurrent or Metastatic Cutaneous Squamous Cell Carcinoma: A Single-Arm Phase II Trial (KEYNOTE-629). *J Clin Oncol*. 2020 Sep 1;38(25):2916-2925. doi: 10.1200/JCO.19.03054.
- 43e. Hiret S, Borg C, Bertaut A, et al. Bevacizumab or cetuximab plus chemotherapy after progression with bevacizumab plus chemotherapy in patients with wtKRAS metastatic colorectal cancer: A randomized phase II study (Prodige 18 –UNICANCER GI). *Journal of Clinical Oncology* 2016 34:15_suppl, 3514-3514.
- 44e. Iwamoto S, Maeda H, Hazama S, et al. Efficacy of CapeOX plus Cetuximab Treatment as a First-Line Therapy for Patients with Extended RAS/BRAF/PIK3CA Wild-Type Advanced or Metastatic Colorectal Cancer. *J Cancer*. 2018 Oct 18;9(22):4092-4098. doi: 10.7150/jca.26840.
- 45e. Moretto R, Cremolini C, Rossini D, et al. Location of Primary Tumor and Benefit From Anti-Epidermal Growth Factor Receptor Monoclonal Antibodies in Patients With RAS and BRAF Wild-Type Metastatic Colorectal Cancer. *Oncologist*. 2016 Aug;21(8):988-94. doi: 10.1634/theoncologist.2016-0084. Epub 2016 Jul 5.

- 46e. Guigay J, Fayette J, Dillies AF, et al. Cetuximab, docetaxel, and cisplatin as first-line treatment in patients with recurrent or metastatic head and neck squamous cell carcinoma: a multicenter, phase II GORTEC study. *Ann Oncol*. 2015 Sep;26(9):1941-1947. doi: 10.1093/annonc/mdv268.
- 47e. Kuboki Y, Yaeger R, Fakih MG, et al. Sotorasib in combination with panitumumab in refractory KRAS G12C-mutated colorectal cancer: Safety and efficacy for phase Ib full expansion cohort. *Ann Oncol* 2022;33:S136-S196.
- 48e. Chevalier T, Daste A, Saada-Bouzid E, et al. Cetuximab combined with paclitaxel or paclitaxel alone for patients with recurrent or metastatic head and neck squamous cell carcinoma progressing after EXTREME. *Cancer Med*. 2021 Jun;10(12):3952-3963.
- 49e. Hitt R, Irigoyen A, Cortes-Funes H, et al. Phase II study of the combination of cetuximab and weekly paclitaxel in the first-line treatment of patients with recurrent and/or metastatic squamous cell carcinoma of head and neck. *Ann Oncol*. 2012 Apr;23(4):1016-22.
- 50e. Sacco AG, Chen R, Worden FP, et al. Pembrolizumab plus cetuximab in patients with recurrent or metastatic head and neck squamous cell carcinoma: an open-label, multi-arm, non-randomised, multicentre, phase 2 trial. *Lancet Oncol*. 2021 Jun;22(6):883-892.
- 51e. Fakih MG, Salvatore L, Esaki T, et al. Sotorasib plus Panitumumab in Refractory Colorectal Cancer with Mutated KRAS G12C. *N Engl J Med*. 2023 Oct 22;389(23):2125-2139. doi: 10.1056/NEJMoa2308795. Epub 2023 Oct 22.
- 52e. Fakih M, Salvatore L, Esaki T, et al. Overall survival (OS) of phase 3 CodeBreakK 300 study of sotorasib plus panitumumab (soto+pani) versus investigator's choice of therapy for KRAS G12C-mutated metastatic colorectal cancer (mCRC). *J Clin Oncol*. 2024 42:17_suppl, LBA3510-LBA3510.
- 53e. Lu SM, Lien W. Concurrent Radiotherapy With Cetuximab or Platinum-based Chemotherapy for Locally Advanced Cutaneous Squamous Cell Carcinoma of the Head and Neck. *Am J Clin Oncol*. 2018 Jan;41(1):95-99
- 54e. Samstein RM, Ho AL, Lee NY, et al. Locally advanced and unresectable cutaneous squamous cell carcinoma: outcomes of concurrent cetuximab and radiotherapy. *J Skin Cancer*. 2014:2014:284582
- 55e. Guthrie TH, Porubsky ES, Luxenberg MN, et al. Cisplatin-based chemotherapy in advanced basal and squamous cell carcinomas of the skin: results in 28 patients including 13 patients receiving multimodality therapy. *J Clin Oncol*. 1990 Feb;8(2):342-6. doi: 10.1200/JCO.1990.8.2.342.
- 56e. Prime Therapeutics Management. Erbitux Clinical Literature Review Analysis. Last updated January 2025. Accessed January 2025.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C00.0	Malignant neoplasm of external upper lip
C00.1	Malignant neoplasm of external lower lip
C00.2	Malignant neoplasm of external lip, unspecified

ICD-10	ICD-10 Description
C00.3	Malignant neoplasm of upper lip, inner aspect
C00.4	Malignant neoplasm of lower lip, inner aspect
C00.5	Malignant neoplasm of lip, unspecified, inner aspect
C00.6	Malignant neoplasm of commissure of lip, unspecified
C00.8	Malignant neoplasm of overlapping sites of lip
C00.9	Malignant neoplasm of lip, unspecified
C01	Malignant neoplasm of base of tongue
C02.0	Malignant neoplasm of dorsal surface of tongue
C02.1	Malignant neoplasm of border of tongue
C02.2	Malignant neoplasm of ventral surface of tongue
C02.3	Malignant neoplasm of anterior two-thirds of tongue, part unspecified
C02.4	Malignant neoplasm of lingual tonsil
C02.8	Malignant neoplasm of overlapping sites of tongue
C02.9	Malignant neoplasm of tongue, unspecified
C03.0	Malignant neoplasm of upper gum
C03.1	Malignant neoplasm of lower gum
C03.9	Malignant neoplasm of gum, unspecified
C04.0	Malignant neoplasm of anterior floor of mouth
C04.1	Malignant neoplasm of lateral floor of mouth
C04.8	Malignant neoplasm of overlapping sites of floor of mouth
C04.9	Malignant neoplasm of floor of mouth, unspecified
C05.0	Malignant neoplasm of hard palate
C05.1	Malignant neoplasm of soft palate
C05.8	Malignant neoplasm of overlapping sites of palate
C05.9	Malignant neoplasm of palate, unspecified
C06.0	Malignant neoplasm of cheek mucosa
C06.2	Malignant neoplasm of retromolar area
C06.80	Malignant neoplasm of overlapping sites of unspecified parts of mouth
C06.89	Malignant neoplasm of overlapping sites of other parts of mouth
C06.9	Malignant neoplasm of mouth, unspecified
C09.0	Malignant neoplasm of tonsillar fossa
C09.1	Malignant neoplasm of tonsillar pillar (anterior) (posterior)
C09.8	Malignant neoplasm of overlapping sites of tonsil
C09.9	Malignant neoplasm of tonsil, unspecified
C10.0	Malignant neoplasm of vallecula
C10.1	Malignant neoplasm of anterior surface of epiglottis
C10.2	Malignant neoplasm of lateral wall of oropharynx

ICD-10	ICD-10 Description
C10.3	Malignant neoplasm of posterior wall of oropharynx
C10.4	Malignant neoplasm of branchial cleft
C10.8	Malignant neoplasm of overlapping sites of oropharynx
C10.9	Malignant neoplasm of oropharynx, unspecified
C11.0	Malignant neoplasm of superior wall of nasopharynx
C11.1	Malignant neoplasm of posterior wall of nasopharynx
C11.2	Malignant neoplasm of lateral wall of nasopharynx
C11.3	Malignant neoplasm of anterior wall of nasopharynx
C11.8	Malignant neoplasm of overlapping sites of nasopharynx
C11.9	Malignant neoplasm of nasopharynx, unspecified
C12	Malignant neoplasm of pyriform sinus
C13.0	Malignant neoplasm of postcricoid region
C13.1	Malignant neoplasm of aryepiglottic fold, hypopharyngeal aspect
C13.2	Malignant neoplasm of posterior wall of hypopharynx
C13.8	Malignant neoplasm of overlapping sites of hypopharynx
C13.9	Malignant neoplasm of hypopharynx, unspecified
C14.0	Malignant neoplasm of pharynx, unspecified
C14.2	Malignant neoplasm of Waldeyer's ring
C14.8	Malignant neoplasm of overlapping sites of lip, oral cavity and pharynx
C18.0	Malignant neoplasm of cecum
C18.1	Malignant neoplasm of appendix
C18.2	Malignant neoplasm of ascending colon
C18.3	Malignant neoplasm of hepatic flexure
C18.4	Malignant neoplasm of transverse colon
C18.5	Malignant neoplasm of splenic flexure
C18.6	Malignant neoplasm of descending colon
C18.7	Malignant neoplasm of sigmoid colon
C18.8	Malignant neoplasm of overlapping sites of large intestines
C18.9	Malignant neoplasm of colon, unspecified
C19	Malignant neoplasm of rectosigmoid junction
C20	Malignant neoplasm of rectum
C21.8	Malignant neoplasm of overlapping sites of rectum, anus and anal canal
C30.0	Malignant neoplasm of nasal cavity
C31.0	Malignant neoplasm of maxillary sinus
C31.1	Malignant neoplasm of ethmoidal sinus
C32.0	Malignant neoplasm of glottis
C32.1	Malignant neoplasm of supraglottis

ICD-10	ICD-10 Description
C32.2	Malignant neoplasm of subglottis
C32.3	Malignant neoplasm of laryngeal cartilage
C32.8	Malignant neoplasm of overlapping sites of larynx
C32.9	Malignant neoplasm of larynx, unspecified
C33	Malignant neoplasm of trachea
C34.00	Malignant neoplasm of unspecified main bronchus
C34.01	Malignant neoplasm of right main bronchus
C34.02	Malignant neoplasm of left main bronchus
C34.10	Malignant neoplasm of upper lobe, unspecified bronchus or lung
C34.11	Malignant neoplasm of upper lobe, right bronchus or lung
C34.12	Malignant neoplasm of upper lobe, left bronchus or lung
C34.2	Malignant neoplasm of middle lobe, bronchus or lung
C34.30	Malignant neoplasm of lower lobe, unspecified bronchus or lung
C34.31	Malignant neoplasm of lower lobe, right bronchus or lung
C34.32	Malignant neoplasm of lower lobe, left bronchus or lung
C34.80	Malignant neoplasm of overlapping sites of unspecified bronchus and lung
C34.81	Malignant neoplasm of overlapping sites of right bronchus and lung
C34.82	Malignant neoplasm of overlapping sites of left bronchus and lung
C34.90	Malignant neoplasm of unspecified part of unspecified bronchus or lung
C34.91	Malignant neoplasm of unspecified part of right bronchus or lung
C34.92	Malignant neoplasm of unspecified part of left bronchus or lung
C44.00	Unspecified malignant neoplasm of skin of lip
C44.02	Squamous cell carcinoma of skin of lip
C44.09	Other specified malignant neoplasm of skin of lip
C44.121	Squamous cell carcinoma of skin of unspecified eyelid, including canthus
C44.1221	Squamous cell carcinoma of skin of right upper eyelid, including canthus
C44.1222	Squamous cell carcinoma of skin of right lower eyelid, including canthus
C44.1291	Squamous cell carcinoma of skin of left upper eyelid, including canthus
C44.1292	Squamous cell carcinoma of skin of left lower eyelid, including canthus
C44.221	Squamous cell carcinoma of skin of unspecified ear and external auricular canal
C44.222	Squamous cell carcinoma of skin of right ear and external auricular canal
C44.229	Squamous cell carcinoma of skin of left ear and external auricular canal
C44.320	Squamous cell carcinoma of skin of unspecified parts of face
C44.321	Squamous cell carcinoma of skin of nose
C44.329	Squamous cell carcinoma of skin of other parts of face
C44.42	Squamous cell carcinoma of skin of scalp and neck
C44.520	Squamous cell carcinoma of anal skin

ICD-10	ICD-10 Description
C44.521	Squamous cell carcinoma of skin of breast
C44.529	Squamous cell carcinoma of skin of other part of trunk
C44.621	Squamous cell carcinoma of skin of unspecified upper limb, including shoulder
C44.622	Squamous cell carcinoma of skin of right upper limb, including shoulder
C44.629	Squamous cell carcinoma of skin of left upper limb, including shoulder
C44.721	Squamous cell carcinoma of skin of unspecified lower limb, including hip
C44.722	Squamous cell carcinoma of skin of right lower limb, including hip
C44.729	Squamous cell carcinoma of skin of left lower limb, including hip
C44.82	Squamous cell carcinoma of overlapping sites of skin
C44.92	Squamous cell carcinoma of skin, unspecified
C60.0	Malignant neoplasm of prepuce
C60.1	Malignant neoplasm of glans penis
C60.2	Malignant neoplasm of body of penis
C60.8	Malignant neoplasm of overlapping sites of penis
C60.9	Malignant neoplasm of penis, unspecified
C63.7	Malignant neoplasm of other specified male genital organs
C63.8	Malignant neoplasm of overlapping sites of male genital organs
C76.0	Malignant neoplasm of head, face and neck
C77.0	Secondary and unspecified malignant neoplasm of lymph nodes of head, face and neck
C78.00	Secondary malignant neoplasm of unspecified lung
C78.01	Secondary malignant neoplasm of right lung
C78.02	Secondary malignant neoplasm of left lung
C78.6	Secondary malignant neoplasm of retroperitoneum and peritoneum
C78.7	Secondary malignant neoplasm of liver and intrahepatic bile duct
C79.89	Secondary malignant neoplasm of other specified sites
D37.01	Neoplasm of uncertain behavior of lip
D37.02	Neoplasm of uncertain behavior of tongue
D37.05	Neoplasm of uncertain behavior of pharynx
D37.09	Neoplasm of uncertain behavior of other specified sites of the oral cavity
D38.0	Neoplasm of uncertain behavior of larynx
D38.5	Neoplasm of uncertain behavior of other respiratory organs
D38.6	Neoplasm of uncertain behavior of respiratory organ, unspecified
Z85.038	Personal history of other malignant neoplasm of large intestine

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15,

§50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: <https://www.cms.gov/medicare-coverage-database/search.aspx>. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	Applicable State/US Territory	Contractor
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC