

Pemetrexed:

Alimta®; Pemfexy™

(Intravenous)

Document Number: IC-0007

Last Review Date: 03/01/2022

Date of Origin: 07/20/2010

Dates Reviewed: 09/2010, 12/2010, 03/2011, 06/2011, 09/2011, 12/2011, 03/2012, 06/2012, 09/2012, 12/2012, 03/2013, 06/2013, 09/2013, 12/2013, 03/2014, 06/2014, 09/2014, 12/14, 03/2015, 05/2015, 08/2015, 11/2015, 02/2016, 05/2016, 08/2016, 11/2016, 02/2017, 05/2017, 08/2017, 11/2017, 02/2018, 05/2018, 09/2018, 12/2018, 03/2019, 06/2019, 09/2019, 12/2019, 03/2020, 06/2020, 09/2020, 12/2020, 03/2021, 06/2021, 09/2021, 12/2021, 03/2022

I. Length of Authorization¹⁵

Coverage will be provided for six months and may be renewed unless otherwise specified.

- Thymomas/Thymic Carcinoma: Coverage will be provided for six 21-day cycles and may not be renewed.
- MPeM and MPM: Coverage will be provided for six 21-day cycles and may not be renewed when used in combination with platinum therapy and bevacizumab.
- NSCLC: Coverage will be provided for four 21-day cycles and may not be renewed when used for neoadjuvant or adjuvant therapy.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Alimta 100 mg powder for injection in a single-use vial: 4 vials every 21 days
- Alimta 500 mg powder for injection in a single-use vial: 4 vials every 21 days
- Pemfexy 500 mg solution for injection in a multi-dose vial: 4 vials every 21 days

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

- CNS Lymphoma and Ovarian Cancer: 230 billable units every 21 days
- All other indications: 130 billable units every 21 days

III. Initial Approval Criteria^{1,2}

Coverage is provided in the following conditions:

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

Primary Central Nervous System (CNS) Lymphoma ‡ 3,16,27

- Used as single-agent induction therapy in patients unsuitable for or intolerant to high-dose methotrexate (MTX); **OR**
- Used as single agent therapy for relapsed or refractory disease; **AND**
 - Patient received prior whole brain radiation therapy (RT); **OR**
 - Patient received a prior high-dose MTX-based regimen without prior RT; **OR**
 - Used in combination with whole brain RT or involved field RT in patients who received a prior high-dose MTX-based regimen without prior RT with either no response or short response (<12 month duration) to prior regimen; **OR**
 - Patient received prior high-dose chemotherapy with stem cell rescue

Malignant Peritoneal Mesothelioma* (MPeM) ‡ 3,29

- Used as first-line therapy; **AND**
 - Used in combination with bevacizumab AND cisplatin or carboplatin (if cisplatin ineligible); **AND**
 - Patient has unresectable diffuse disease; **OR**
 - Patient has unresectable recurrent benign multicystic or well-differentiated papillary disease; **OR**
 - Used as a single agent OR in combination with cisplatin or carboplatin (if cisplatin ineligible); **AND**
 - Used as adjuvant treatment of diffuse disease in patients with surgical/pathologic high-risk features** who have not received neoadjuvant therapy; **OR**
 - Patient has unresectable diffuse disease; **OR**
 - Patient has unresectable recurrent benign multicystic or well-differentiated papillary disease; **OR**
- Used as subsequent therapy; **AND**
 - Immunotherapy was administered as first-line treatment; **AND**
 - Used in combination with cisplatin with or without bevacizumab; **OR**
 - Used in combination with carboplatin (if cisplatin ineligible) with or without bevacizumab; **OR**
 - Used as a single agent; **AND**
 - Pemetrexed was not administered first-line; **OR**
 - Used as rechallenge if pemetrexed was administered first-line with a good sustained response at the time initial chemotherapy was interrupted

** Note: May also be used for pericardial mesothelioma and tunica vaginalis testis mesothelioma.*

***High-risk features include Ki-67>9%, nodal metastasis, high tumor burden (Peritoneal Cancer Index [PCI]>17), completeness of cytoreduction (CC) score >1, biphasic disease, or bicavitary disease*

Malignant Pleural* Mesothelioma (MPM) † ⊕ 1-6,10,26

- Used as induction therapy; **AND**
 - Used in combination with cisplatin or carboplatin (if cisplatin ineligible); **AND**
 - Patient has stage I-IIIa disease with epithelioid histology; **OR**
- Used as first-line therapy; **AND**
 - Used in combination with bevacizumab **AND** cisplatin or carboplatin (if cisplatin ineligible); **AND**
 - Patient has unresectable stage I-IIIa disease with epithelioid histology and has not previously been treated with induction chemotherapy; **OR**
 - Patient has stage IIIB or IV disease, sarcomatoid or biphasic histology, or medically inoperable tumors; **OR**
 - Used as a single agent **OR** in combination with cisplatin or carboplatin (if cisplatin ineligible); **AND**
 - Patient has unresectable stage I-IIIa disease with epithelioid histology and has not previously been treated with induction chemotherapy; **OR**
 - Patient has resected stage I-IIIa disease with epithelioid histology and has not previously been treated with induction chemotherapy; **OR**
 - Patient has stage IIIB or IV disease, sarcomatoid or biphasic histology, or medically inoperable tumors; **OR**
- Used as subsequent therapy; **AND**
 - Immunotherapy was administered as first-line treatment; **AND**
 - Used in combination with cisplatin with or without bevacizumab; **OR**
 - Used in combination with carboplatin (if cisplatin ineligible) with or without bevacizumab; **OR**
 - Used as a single agent; **AND**
 - Pemetrexed was not administered first-line; **OR**
 - Used as rechallenge if pemetrexed was administered first-line with a good sustained response at the time initial chemotherapy was interrupted

** Note: May also be used for pericardial mesothelioma and tunica vaginalis testis mesothelioma.*

Non-Squamous Non-Small Cell Lung Cancer (NS-NSCLC) † 1-3,7-9,11,12,28

- Used in combination with carboplatin or cisplatin; **AND**
 - Used as induction, neoadjuvant, or adjuvant therapy; **OR**
 - Used as concurrent chemoradiation for locoregional recurrence or symptomatic local disease in the mediastinal lymph nodes or for superior vena cava obstruction; **OR**
 - Used as initial therapy as definitive concurrent chemoradiation for unresectable, advanced, or metastatic disease; **OR**
- Used for 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 first-line therapy; **AND**
 - Used for PD-L1 $\geq 1\%$ tumors that have negative actionable molecular markers *; **AND**
 - Used in combination with bevacizumab and either cisplatin or carboplatin in patients with PS 0-1; **OR**
 - Used in combination with pembrolizumab and either carboplatin or cisplatin in patients with PS 0-2; **OR**
 - Used in combination with nivolumab, ipilimumab, and either carboplatin or cisplatin in patients with PS 0-2; **OR**
 - Used in combination with cisplatin in patients with PS 0-1; **OR**
 - Used in combination with carboplatin in patients with PS 0-2; **OR**
 - Used as a single agent in patients with PS 2; **OR**
 - Used for one of the following:
 - PD-L1 $< 1\%$ and tumors that have negative actionable molecular markers *; **OR**
 - BRAF V600E-mutation, NTRK1/2/3 gene fusion, MET exon-14 skipping mutation, EGFR exon 20 mutation, KRAS G12C mutation, or RET rearrangement positive tumors; **AND**
 - Used as a single agent in patients with PS 2; **OR**
 - Used in combination with pembrolizumab and either carboplatin or cisplatin in patients with PS 0-1; **OR**
 - Used in combination with cisplatin in patients with PS 0-1; **OR**
 - Used in combination with carboplatin in patients with PS 0-2; **OR**
 - Used in combination with nivolumab, ipilimumab, and either carboplatin or cisplatin in patients with PS 0-1; **OR**
 - Used in combination with bevacizumab and either cisplatin or carboplatin in patients with PS 0-1; **OR**
- Used as subsequent therapy; **AND**
 - Used as a single-agent (if not previously given) in patients with a PS 0-2; **AND**
 - Used for first progression after initial systemic therapy; **OR**
 - Used for one of the following:
 - EGFR exon 19 deletion or L858R; EGFR S768I, L861Q, and/or G719X; ALK rearrangement; or ROS1 rearrangement positive tumors and prior targeted therapy§ for those aberrations; **OR**
 - BRAF V600E-mutation, NTRK1/2/3 gene fusion, MET exon-14 skipping mutation, or RET rearrangement positive tumors; **OR**
 - PD-L1 $\geq 1\%$ tumors that have negative actionable molecular markers* with prior PD-1/PD-L1 inhibitor therapy but no prior platinum doublet chemotherapy; **AND**
 - Used in combination with pembrolizumab and either carboplatin or cisplatin in patients with PS 0-1; **OR**
 - Used in combination with cisplatin in patients with PS 0-1; **OR**

- Used in combination with carboplatin in patients with PS 0-2; **OR**
- Used in combination with nivolumab, ipilimumab, and either carboplatin or cisplatin in patients with PS 0-1; **OR**
- Used in combination with bevacizumab and either cisplatin or carboplatin in patients with PS 0-1; **OR**
- Used as maintenance therapy in patients who have achieved tumor response or stable disease following initial therapy; **AND**
 - Used as a single agent for continuation maintenance therapy; **OR**
 - Used as a single agent for switch maintenance therapy; **OR**
 - Used for continuation maintenance therapy in combination with bevacizumab following a first-line bevacizumab/pemetrexed/platinum chemotherapy regimen; **OR**
 - Used for continuation maintenance therapy in combination with pembrolizumab following a first-line pembrolizumab/pemetrexed and either carboplatin or cisplatin regimen

** Note: Actionable molecular genomic biomarkers include EGFR, KRAS, ALK, ROS1, BRAF, NTRK1/2/3, MET exon 14 skipping mutation, and RET rearrangement. If there is insufficient tissue to allow testing for all of the EGFR, KRAS, ALK, ROS1, BRAF, NTRK1/2/3, MET, and RET, repeat biopsy and/or plasma testing should be done. If these are not feasible, treatment is guided by available results and, if unknown, these patients are treated as though they do not have driver oncogenes.*

‡ Note: Contraindications for treatment with PD-1/PD-L1 inhibitors may include active or previously documented auto-immune disease and/or current use of immunosuppressive agents, or presence of an oncogene (e.g., EGFR [exon 19 deletions, p.L858R point mutation in exon 21], ALK rearrangements), which would predict lack of benefit.

Thymomas/Thymic Carcinoma ‡^{3,14,15,25}

- Used as a single agent; **AND**
 - Used as first line therapy or postoperative treatment in patients who are unable to tolerate first-line combination regimens; **OR**
 - Used as second-line therapy for unresectable or metastatic disease

Ovarian Cancer (epithelial ovarian/fallopian tube/primary peritoneal cancer) ‡^{3,13,24}

- Patient has recurrent or persistent disease; **AND**
- Patient is not experiencing an immediate biochemical relapse (i.e., rising CA-125 without radiographic evidence of disease); **AND**
- Used as a single agent; **AND**
 - Patient has platinum-resistant disease; **AND**
 - Used for progression on primary, maintenance, or recurrence therapy; **OR**
 - Used for stable or persistent disease if not currently on maintenance therapy; **OR**
 - Used for relapsed disease <6 months following complete remission from prior chemotherapy; **OR**
 - Patient has platinum-sensitive disease; **AND**

- Used for radiographic and/or clinical relapse ≥ 6 months after complete remission from prior chemotherapy

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

Genomic Aberration/Mutational Driver Targeted Therapies (Note: not all inclusive, refer to guidelines for appropriate use) §				
Sensitizing <i>EGFR</i> mutation-positive tumors	<i>ALK</i> rearrangement-positive tumors	<i>ROS1</i> rearrangement-positive tumors	<i>BRAF</i> V600E-mutation positive tumors	<i>NTRK</i> gene fusion positive tumors
<ul style="list-style-type: none"> – Afatinib – Erlotinib – Dacomitinib – Gefitinib – Osimertinib – Amivantamab (<i>exon-20 insertion</i>) – Mobocertinib (<i>exon-20 insertion</i>) 	<ul style="list-style-type: none"> – Alectinib – Brigatinib – Ceritinib – Crizotinib – Lorlatinib 	<ul style="list-style-type: none"> – Ceritinib – Crizotinib – Entrectinib – Lorlatinib 	<ul style="list-style-type: none"> – Dabrafenib – \pm trametinib – Vemurafenib 	<ul style="list-style-type: none"> – Larotrectinib – Entrectinib
PD-L1 tumor expression $\geq 1\%$	PD-L1 tumor expression $\geq 50\%$	<i>MET</i> exon-14 skipping mutations	<i>RET</i> rearrangement-positive tumors	<i>KRAS</i> G12C mutation positive tumors
<ul style="list-style-type: none"> – Pembrolizumab – Atezolizumab – Nivolumab + ipilimumab 	<ul style="list-style-type: none"> – Pembrolizumab – Atezolizumab – Nivolumab + ipilimumab – Cemiplimab 	<ul style="list-style-type: none"> – Capmatinib – Crizotinib – Tepotinib 	<ul style="list-style-type: none"> – Selpercatinib – Cabozantinib – Pralsetinib 	<ul style="list-style-type: none"> – Sotorasib

IV. Renewal Criteria ^{1,2}

Coverage can be renewed based upon the following criteria:

- Patient continues to meet indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: bone marrow suppression (e.g., neutropenia, febrile neutropenia, thrombocytopenia, anemia), renal impairment (CrCl < 45 mL/min), bullous and exfoliative skin toxicity (e.g., Stevens-Johnson Syndrome/Toxic epidermal necrolysis), interstitial pneumonitis, radiation recall, etc.; **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**

Continuation of Maintenance Therapy for Non-Squamous Non-Small Cell Lung Cancer (NSCLC)

- Refer to Section III for criteria

Non-Squamous Non-Small Cell Lung Cancer (NSCLC) (neoadjuvant or adjuvant therapy)

- May not be renewed

MPeM and MPM

- May not be renewed when used in combination with platinum therapy and bevacizumab

Thymomas/Thymic Carcinoma

- May not be renewed

V. Dosage/Administration ^{1,2,13,15,16,26,29}

Indication	Dose
Non-Squamous NSCLC	Administer 500 mg/m ² intravenously every 21 days, until disease progression or unacceptable toxicity* <i>(*Note: When used for neoadjuvant or adjuvant therapy, treatment is given up to 4 cycles)</i>
MPM, MPeM	Administer 500 mg/m ² intravenously every 21 days – For 6 cycles only when used in combination with platinum therapy and bevacizumab – All others until disease progression or unacceptable toxicity
Primary CNS Lymphoma, Ovarian Cancer	Administer 900 mg/m ² intravenously every 21 days, until disease progression or unacceptable toxicity
Thymomas/Thymic Carcinoma	Administer 500 mg/m ² intravenously every 21 days for a maximum of 6 cycles in absence of disease progression or unacceptable toxicity
<ul style="list-style-type: none"> • Supplement with oral folic acid and intramuscular vitamin B₁₂ • Avoid administration of ibuprofen for 2 days before, the day of, and 2 days following administration in patients with CrCl <80 mL/min. • Do not dose in patients with CrCl <45 mL/min 	

VI. Billing Code/Availability Information

HCPCS Code:

- J9305 – Injection, pemetrexed, not otherwise specified, 10 mg; 1 billable unit = 10mg
- J9304 – Injection, pemetrexed (pemfexy), 10 mg; 1 billable unit = 10mg

NDC:

- Alimta 100 mg powder for injection; single-use vial: 00002-7640-xx
- Alimta 500 mg powder for injection; single-use vial: 00002-7623-xx
- Pemfexy 500 mg/20 mL solution for injection, multi-dose vial: 42367-0531-xx

VII. References

1. Alimta [package insert]. Indianapolis, IN; Eli Lilly; February 2021. Accessed February 2022.
2. Pemfexy [package insert]. Woodcliff Lake, NJ; Eagle Pharmaceuticals, Inc; June 2020. Accessed February 2022.
3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium[®]) for pemetrexed. National Comprehensive Cancer Network, 2022. 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 February 2022.

4. Castagneto B, Botta M, Aitini E, et al, “Phase II Study of Pemetrexed in Combination With Carboplatin in Patients With Malignant Pleural Mesothelioma (MPM),” *Ann Oncol*, 2008, 19(2):370-3.
5. Ceresoli GL, Zucali PA, Favaretto AG, et al, “Phase II Study of Pemetrexed plus Carboplatin in Malignant Pleural Mesothelioma,” *J Clin Oncol*, 2006, 24(9):1443-8.
6. Taylor P, Castagneto B, Dark G, et al, “Single-Agent Pemetrexed for Chemonaïve and Pretreated Patients With Malignant Pleural Mesothelioma: Results of an International Expanded Access Program,” *J Thorac Oncol*, 2008, 3(7):764-71
7. Ciuleanu T, Brodowicz T, Zielinski C, et al, “Maintenance Pemetrexed Plus Best Supportive Care versus Placebo Plus Best Supportive Care for Non-Small-Cell Lung Cancer: A Randomised, Double-Blind, Phase 3 Study,” *Lancet*, 2009, 374(9699):1432-40.
8. Grønberg BH, Bremnes RM, Fløtten O, et al, “Phase III Study by the Norwegian Lung Cancer Study Group: Pemetrexed Plus Carboplatin Compared With Gemcitabine Plus Carboplatin as First-Line Chemotherapy in Advanced Non-Small-Cell Lung Cancer,” *J Clin Oncol*, 2009, 27(19):3217-24.
9. Hanna N, Shepherd FA, Fossella FV, et al, “Randomized Phase III Trial of Pemetrexed versus Docetaxel in Patients With Non-Small-Cell Lung Cancer Previously Treated With Chemotherapy,” *J Clin Oncol*, 2004, 22(9):1589-97.
10. Jassem J, Ramlau R, Santoro A, et al, “Phase III Trial of Pemetrexed Plus Best Supportive Care Compared With Best Supportive Care in Previously Treated Patients With Advanced Malignant Pleural Mesothelioma,” *J Clin Oncol*, 2008, 26(10):1698-704.
11. Scagliotti GV, Parikh P, von Pawel J, et al, “Phase III Study Comparing Cisplatin Plus Gemcitabine With Cisplatin Plus Pemetrexed in Chemotherapy-Naïve Patients With Advanced-Stage Non-Small-Cell Lung Cancer,” *J Clin Oncol*, 2008, 26(21):3543-51.
12. Langer CJ, Gadgeel SM, Borghaei H, et al. Carboplatin and pemetrexed with or without pembrolizumab for advanced, non-squamous non-small-cell lung cancer: a randomised, phase 2 cohort of the open-label KEYNOTE-021 study. *Lancet Oncol*. 2016;17(11):1497-1508.
13. Miller DS, Blessing JA, Krasner CN, et al. Phase II Evaluation of Pemetrexed in the Treatment of Recurrent or Persistent Platinum-Resistant Ovarian or Primary Peritoneal Carcinoma: A Study of the Gynecologic Oncology Group. *J Clin Oncol*, 2009, 27(16):2686-91.
14. Liang Y, Padda SK, Riess JW, et al. Pemetrexed in patients with thymic malignancies previously treated with chemotherapy. *Lung Cancer*. 2015 Jan;87(1):34-8.
15. Gbolahan OB, Porter RF, Salter JT, et al. A Phase II Study of Pemetrexed in Patients with Recurrent Thymoma and Thymic Carcinoma. *J Thorac Oncol*. 2018 Dec;13(12):1940-1948.

16. Raizer JJ, Rademaker A, Evens AM, et al. Pemetrexed in the treatment of relapsed/refractory primary central nervous system lymphoma. *Cancer*. 2012 Aug 1;118(15):3743-8.
17. 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.
18. Hematology/Oncology Pharmacy Association (2019). Intravenous Cancer Drug Waste Issue Brief. Retrieved from http://www.hoparx.org/images/hopa/advocacy/Issue-Briefs/Drug_Waste_2019.pdf
19. Bach PB, Conti RM, Muller RJ, et al. Overspending driven by oversized single dose vials of cancer drugs. *BMJ*. 2016 Feb 29;352:i788.
20. Gandhi L, Rodríguez-Abreu D, Gadgeel S, et al. Pembrolizumab plus Chemotherapy in Metastatic Non-Small-Cell Lung Cancer. *N Engl J Med*. 2018;378(22):2078-2092. doi:10.1056/NEJMoa1801005.
21. Wu YL, Lu S, Cheng Y, et al. Efficacy and safety of pemetrexed/cisplatin versus gemcitabine/cisplatin as first-line treatment in Chinese patients with advanced nonsquamous non-small cell lung cancer. *Lung Cancer*. 2014;85(3):401-407. doi:10.1016/j.lungcan.2014.07.007.
22. Paz-Ares L, de Marinis F, Dediu M, et al. Maintenance therapy with pemetrexed plus best supportive care versus placebo plus best supportive care after induction therapy with pemetrexed plus cisplatin for advanced non-squamous non-small-cell lung cancer (PARAMOUNT): a double-blind, phase 3, randomised controlled trial. *Lancet Oncol*. 2012;13(3):247-255. doi:10.1016/S1470-2045(12)70063-3.
23. Vogelzang NJ, Rusthoven JJ, Symanowski J, et al. Phase III study of pemetrexed in combination with cisplatin versus cisplatin alone in patients with malignant pleural mesothelioma. *J Clin Oncol*. 2003;21(14):2636-2644. doi:10.1200/JCO.2003.11.136.
24. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Ovarian Cancer Including Fallopian Tube Cancer and Primary Peritoneal Cancer Version 1.2022. National Comprehensive Cancer Network, 2022. 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 February 2022.
25. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Thymomas and Thymic Carcinomas Version 1.2022. National Comprehensive Cancer Network, 2022. 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 February 2022.

26. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Malignant Pleural Mesothelioma Version 1.2022. National Comprehensive Cancer Network, 2022. 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 February 2022.
27. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Central Nervous System Cancers Version 2.2021. National Comprehensive Cancer Network, 2022. 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 February 2022.
28. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer Version 1.2022. National Comprehensive Cancer Network, 2022. 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 February 2022.
29. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Malignant Peritoneal Mesothelioma Version 1.2022. National Comprehensive Cancer Network, 2022. 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 February 2022.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
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 or lung

ICD-10	ICD-10 Description
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
C37	Malignant neoplasm of thymus
C45.0	Mesothelioma of pleura
C45.1	Mesothelioma of peritoneum
C45.2	Mesothelioma of pericardium
C45.7	Mesothelioma of other sites
C45.9	Mesothelioma, unspecified
C48.1	Malignant neoplasm of specified parts of peritoneum
C48.2	Malignant neoplasm of peritoneum, unspecified
C48.8	Malignant neoplasm of overlapping sites of retroperitoneum and peritoneum
C56.1	Malignant neoplasm of right ovary
C56.2	Malignant neoplasm of left ovary
C56.3	Malignant neoplasm of bilateral ovaries
C56.9	Malignant neoplasm of unspecified ovary
C57.00	Malignant neoplasm of unspecified fallopian tube
C57.01	Malignant neoplasm of right fallopian tube
C57.02	Malignant neoplasm of left fallopian tube
C57.10	Malignant neoplasm of unspecified broad ligament
C57.11	Malignant neoplasm of right broad ligament
C57.12	Malignant neoplasm of left broad ligament
C57.20	Malignant neoplasm of unspecified round ligament
C57.21	Malignant neoplasm of right round ligament
C57.22	Malignant neoplasm of left round ligament
C57.3	Malignant neoplasm of parametrium
C57.4	Malignant neoplasm of uterine adnexa, unspecified
C57.7	Malignant neoplasm of other specified female genital organs
C57.8	Malignant neoplasm of overlapping sites of female genital organs
C57.9	Malignant neoplasm of female genital organ, unspecified
C83.30	Diffuse large B-cell lymphoma unspecified site
C83.39	Diffuse large B-cell lymphoma extranodal and solid organ sites
C83.80	Other non-follicular lymphoma, unspecified site

ICD-10	ICD-10 Description
C83.89	Other non-follicular lymphoma, extranodal and solid organ sites
C85.89	Other specified types of non-Hodgkin lymphoma, extranodal and solid organ sites
C85.99	Non-Hodgkin's lymphoma extranodal and solid organ sites
D15.0	Benign neoplasm of thymus
Z85.118	Personal history of other malignant neoplasm of bronchus and lung
Z85.43	Personal history of malignant neoplasm of ovary

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

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 Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: <https://www.cms.gov/medicare-coverage-database/search.aspx>. Additional indications may be covered 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,	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp
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
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
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