

**Pemetrexed:****Alimta<sup>®</sup> ; Axtle<sup>™</sup>; Pemetrexed; Pemfexy<sup>®</sup> ; Pemrydi RTU<sup>®</sup> ;  
(Intravenous)****-E-**

Document Number: OHSU HEALTHSERVICES-0489

**Date Reviewed: 11/2025**

Date of Origin: 08/05/2019

**Dates Approved: 08/2019, 10/2019, 01/2020, 04/2020, 07/2020, 10/2020, 01/2021, 05/2021, 07/2021, 10/2021, 02/2022, 04/2022, 07/2022, 10/2022, 01/2023, 04/2023, 08/2023, 10/2023, 01/2024, 04/2024, 07/2024, 10/2024, 01/06/2025, 04/07/2025, 06/24/2025, 08/05/2025, 10/02/2025, 12/02/2025****I. Length of Authorization** <sup>16,27,29-31,42</sup>

- Initial: Prior authorization validity will be provided initially for 6 months, unless otherwise specified.
  - Thymomas: Prior authorization validity will be provided initially for six (6) cycles.
  - Mesothelioma (including PeM, PM, pericardial mesothelioma and tunica vaginalis testis mesothelioma):
    - In combination with bevacizumab AND platinum chemotherapy: Prior authorization validity will be provided initially for six (6) cycles.
    - In combination with pembrolizumab AND platinum chemotherapy: Prior authorization validity will be provided initially for six (6) doses.
- Renewal: Prior authorization validity may be renewed every 6 months thereafter, unless otherwise specified.
  - Thymomas: Prior authorization validity may NOT be renewed.
  - Mesothelioma (including PeM, PM, pericardial mesothelioma and tunica vaginalis testis mesothelioma) in combination with platinum chemotherapy AND either bevacizumab or pembrolizumab: Prior authorization validity may NOT be renewed.

**II. Dosing Limits****Max Units (per dose and over time) [HCPCS Unit]:**

- Pemfexy (500 mg MDV):

- Primary CNS Lymphoma, Cervical Cancer, Vaginal Cancer, Ovarian Cancer, Fallopian Tube, and Primary Peritoneal Cancer: 225 billable units every 21 days
- Leptomeningeal Metastases from NSCLC: 5 billable units on day 1 and 5 of a 7 day cycle, then 5 billable units every 21 days
- Thymomas, Non-Squamous NSCLC, Mesotheliomas, & Limited or extensive brain metastases: 125 billable units every 21 days
- Pemetrexed (all other manufacturers) (100 mg, 500 mg, 750 mg, 850 mg, and 1000 mg SDV):
  - Primary CNS Lymphoma, Cervical Cancer, Vaginal Cancer, Ovarian Cancer, Fallopian Tube, and Primary Peritoneal Cancer: 230 billable units every 21 days
  - Leptomeningeal Metastases from NSCLC: 10 billable units on day 1 and 5 of a 7 day cycle, then 10 billable units every 21 days
  - Thymomas, Non-Squamous NSCLC, Mesotheliomas, & Limited or extensive brain metastases: 130 billable units every 21 days

### III. Initial Approval Criteria <sup>1-4</sup>

Prior authorization validity is provided in the following conditions:

- Patient must have a contraindication, intolerance, or failure to ALL alternative pemetrexed products prior to consideration of Pemfexy (J9304) and Pemrydi (J9324) and Axtle (J9292); **AND**

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

#### **Central Nervous System (CNS) Cancers ‡ <sup>5,18,29,35,45,46</sup>**

- Patient has Primary Central Nervous System (CNS) Lymphoma (including vitreoretinal lymphoma/PCNSL ocular variant without other CNS involvement); **AND**
  - Used as a single agent; **AND**
    - Used for relapsed or refractory disease; **OR**
- Patient has limited or extensive brain metastases from EGFR-sensitizing mutation positive non-small cell lung cancer (NSCLC) as determined by an FDA-approved or CLIA-compliant test❖; **AND**
  - Used in combination with one of the following:
    - Platinum-based chemotherapy (i.e., cisplatin or carboplatin) and osimertinib; **AND**
      - Used as first-line therapy; **AND**
      - Patient has nonsquamous histology; **AND**
      - Patient has EGFR exon 19 deletions or exon 21 L858R mutations; **OR**
    - Carboplatin and amivantamab (*for exon 19 deletion or L858R*); **AND**
      - Used following disease progression on or after treatment with osimertinib; **AND**
  - Used as treatment for one of the following:

- Initial treatment in patients with small asymptomatic limited brain metastases for newly diagnosed or stable systemic disease or if reasonable systemic treatment options exist; **OR**
- Recurrent limited brain metastases; **OR**
- Primary treatment in patients with small asymptomatic extensive brain metastases; **OR**
- Recurrent extensive brain metastases with stable systemic disease or reasonable systemic treatment options; **OR**
- Patient has leptomeningeal metastases from EGFR mutation-positive NSCLC as determined by an FDA-approved or CLIA-compliant test❖; **AND**
  - Used as a single agent as intra-cerebrospinal fluid (CSF) treatment; **AND**
    - Used as primary treatment in patients with good risk status (i.e., KPS ≥60, no major neurologic deficits, minimal systemic disease, and reasonable systemic treatment options if needed); **OR**
    - Used as maintenance treatment in patients with negative cerebrospinal fluid (CSF) cytology or in clinically stable patients with persistently positive CSF cytology

#### **Cervical Cancer ‡<sup>5,36</sup>**

- Used as subsequent therapy for recurrent or metastatic disease; **AND**
- Patient has squamous cell carcinoma, adenocarcinoma, or adenosquamous carcinoma; **AND**
- Used as a single agent

#### **Peritoneal\* Mesothelioma (PeM) ‡<sup>5,31</sup>**

- Used as adjuvant therapy for medically operable disease following cytoreductive surgery (CRS) + hyperthermic intraperitoneal chemotherapy (HIPEC); **AND**
  - Patient has surgical/pathologic high-risk features\*\*; **AND**
  - Used in combination with cisplatin or carboplatin with or without pembrolizumab as first-line therapy; **OR**
- Used as first-line therapy; **AND**
  - Patient has one or more of the following:
    - Medically inoperable disease
    - Complete cytoreduction is not achievable
    - Presence of any high-risk features\*\*
    - Disease has progressed after prior CRS + HIPEC and no previous adjuvant systemic therapy was given; **AND**
  - Used in combination with one of the following regimens:
    - Cisplatin or carboplatin
    - Bevacizumab AND either cisplatin or carboplatin

- Pembrolizumab AND either cisplatin or carboplatin; **OR**
- Used as subsequent therapy; **AND**
  - Used as a single agent OR in combination with cisplatin or carboplatin, with or without bevacizumab; **AND**
    - Immunotherapy (i.e., nivolumab/ipilimumab) was administered as first-line treatment; **OR**
    - Used as a rechallenge if pemetrexed-based treatment was administered first-line with good response

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

*\*\* High-risk features include Ki-67 >9%, nodal metastasis, thrombocytosis, PS=2, high disease burden/incomplete cytoreduction (Peritoneal Cancer Index [PCI] >17, completeness of cytoreduction (CC) score >1), biphasic/sarcomatoid histology, or bicavitary disease*

**Pleural\* Mesothelioma (PM) † ‡ Φ<sup>1-8,12,28,79e,80e</sup>**

- Used as induction therapy prior to surgical exploration; **AND**
  - Patient has clinical stage I disease and epithelioid histology; **AND**
  - Used in combination with cisplatin or carboplatin; **OR**
- Used as first-line therapy; **AND**
  - Used in combination with cisplatin or carboplatin; **AND**
    - Disease is unresectable or patient is not a candidate for curable surgery; **OR**
  - Used in combination with bevacizumab AND either cisplatin or carboplatin; **AND**
    - Patient has unresectable disease not amendable to curative surgery; **OR**
  - Used in combination with pembrolizumab AND either cisplatin or carboplatin; **AND**
    - Patient has unresectable advanced or metastatic disease; **OR**
- Used as subsequent therapy; **AND**
  - Used as a single agent OR in combination with cisplatin or carboplatin, with or without bevacizumab; **AND**
    - Immunotherapy (i.e., nivolumab/ipilimumab) was administered as first-line treatment; **OR**
    - Used as a rechallenge if pemetrexed-based treatment was administered first-line with good response

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

**Non-Squamous Non-Small Cell Lung Cancer (NS-NSCLC) † ‡<sup>1-5,9-11,13,14,30,32,45,50e,51e,54e,56e-58e,81e-83e,91e-95e,99e</sup>**

- Used only in combination with carboplatin or cisplatin; **OR**

- Used in combination with bevacizumab, pembrolizumab, cemiplimab, or durvalumab for continuation maintenance therapy if previously used first-line and patient achieved a tumor response or stable disease following initial therapy; **OR**
- Used in combination with either nivolumab, pembrolizumab, or durvalumab AND platinum-chemotherapy as neoadjuvant therapy for resectable disease (tumors  $\geq$  4 cm or node positive); **OR**
- 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 in combination with bevacizumab and either cisplatin or carboplatin; **OR**
  - Used in combination with cemiplimab and either cisplatin or carboplatin; **OR**
  - Used in combination with osimertinib and either cisplatin or carboplatin as first-line therapy for EGFR exon 19 deletion or exon 21 L858R mutation positive disease; **OR**
  - Used in combination with amivantamab and carboplatin as first-line therapy for EGFR exon 20 insertion mutation positive disease; **OR**
  - Used in combination with amivantamab and carboplatin following disease progression on or after osimertinib for EGFR exon 19 deletion or exon 21 L858R mutation positive disease; **OR**
  - Used in combination with pembrolizumab and either cisplatin or carboplatin; **AND**

- Use of pemetrexed will be restricted to patients with a contraindication or intolerance to cemiplimab/pemetrexed/(carboplatin or cisplatin); **OR**
  - Used in combination with tremelimumab, durvalumab, and either cisplatin or carboplatin; **AND**

- Use of pemetrexed will be restricted to patients with a contraindication or intolerance to cemiplimab/(paclitaxel or pemetrexed)/(carboplatin or cisplatin); **OR**
  - Used in combination with nivolumab, ipilimumab, and either cisplatin or carboplatin; **AND**

- Use of pemetrexed will be restricted to patients with a contraindication or intolerance to cemiplimab/(paclitaxel or pemetrexed)/(carboplatin or cisplatin); **OR**
  - Used as a single agent; **AND**
    - Used as first-line therapy for tumors that are negative for actionable molecular biomarkers<sup>†‡</sup>; **OR**
    - Used as first-line therapy for EGFR exon 20 insertion mutation, BRAF V600E-mutation, NTRK1/2/3 gene fusion, MET exon 14 skipping mutation, NRG1 gene fusion, or ERBB2 (HER2) mutation positive tumors; **OR**
    - Used as subsequent therapy; **OR**

- Used as continuation or switch maintenance therapy in patients who have achieved a tumor response or stable disease following initial platinum-based therapy

♦ *Note: Actionable molecular genomic biomarkers include EGFR, KRAS, ALK, ROS1, BRAF, NTRK1/2/3, MET, RET, NRG1, and ERBB2 (HER2). Complete genotyping for EGFR, KRAS, ALK, ROS1, BRAF, NTRK1/2/3, MET, RET, NRG1, and ERBB2 (HER2), via biopsy and/or plasma testing. If a clinically actionable marker is found, it is reasonable to start therapy based on the identified marker. Treatment is guided by available results and, if unknown, these patients are treated as though they do not have driver oncogenes.*

¥ *May also be used for patients with KRAS G12C mutation positive tumors.*

**Thymomas ‡<sup>5,16,17,27,68e</sup>**

- Used as a single agent; **AND**
- Used as second-line therapy; **AND**
- Patient has unresectable or metastatic disease

**Ovarian, Fallopian Tube, and Primary Peritoneal Cancer ‡<sup>5,15,26,74e,75e</sup>**

- Used as a single agent; **AND**
- Patient has platinum-resistant disease; **AND**
  - Patient has recurrent or persistent Grade 1 Endometrioid Carcinoma, Carcinosarcoma (Malignant Mixed Müllerian Tumors), Mucinous Neoplasms of the Ovary, Epithelial Ovarian/Fallopian Tube/Primary Peritoneal Cancer, or Clear Cell Carcinoma of the Ovary; **AND**
    - Patient is not experiencing an immediate biochemical relapse (i.e., rising CA-125 without radiographic evidence of disease); **OR**
  - Patient has recurrent Low-Grade Serous Carcinoma

**Vaginal Cancer ‡<sup>5,37</sup>**

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

**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.**

**Enhanced Oncology Value (EOV) Program – Redacted indications**

Uses not listed above have inadequate data to support efficacy and are excluded from coverage.

Other treatment options including, but are not limited to, the following may be appropriate: radiation therapy, surgery, traditional chemotherapy (e.g., platinum, taxane), compassionate use/expanded access programs, clinical trials, supportive care, integrative and complementary therapies.

▼ If confirmed using an immunotherapy assay – <http://www.fda.gov/companiondiagnostics>

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

**IV. Renewal Criteria <sup>1-4</sup>**

Prior authorization validity 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**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: myelosuppression (e.g., neutropenia, febrile neutropenia, thrombocytopenia, anemia), renal toxicity (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

**V. Dosage/Administration <sup>1-4,12,15,17,18,28,30-35,38-46</sup>**

Indication	Dose
Non-Squamous NSCLC	Administer up to 500 mg/m <sup>2</sup> intravenously every 21 days
Mesotheliomas (peritoneal, pleural, pericardial and tunica vaginalis testis)	Administer 500 mg/m <sup>2</sup> intravenously every 21 days <ul style="list-style-type: none"> <li>– For 6 cycles only when used in combination with bevacizumab AND platinum chemotherapy</li> <li>– For 6 doses only when used in combination with pembrolizumab AND platinum chemotherapy</li> <li>– All others until disease progression or unacceptable toxicity</li> </ul>
Ovarian, Fallopian Tube, and Primary Peritoneal Cancer,	Administer up to 900 mg/m <sup>2</sup> intravenously every 21 days, until disease progression or unacceptable toxicity

Cervical Cancer, Vaginal Cancer	
Thymomas	Administer 500 mg/m <sup>2</sup> intravenously every 21 days for a maximum of 6 cycles or until disease progression or unacceptable toxicity
CNS Cancers	<p><u>Primary CNS Lymphoma</u> Administer 900 mg/m<sup>2</sup> intravenously every 21 days, until disease progression or unacceptable toxicity</p> <p><u>Limited or extensive brain metastases from EGFR-sensitizing mutation positive NSCLC</u> Administer 500 mg/m<sup>2</sup> intravenously every 21 days, until disease progression or unacceptable toxicity</p> <p><u>Leptomeningeal metastases from EGFR mutation-positive NSCLC</u></p> <ul style="list-style-type: none"> <li>– Primary Treatment: Administer 50 mg intrathecally on Days 1 and 5 of a 7-day cycle, followed by 50 mg intrathecally every 21 days until disease progression or unacceptable toxicity</li> <li>– Maintenance Treatment: Administer 50 mg intrathecally every 28 days, until disease progression or unacceptable toxicity</li> </ul>
<ul style="list-style-type: none"> <li>• Supplement with oral folic acid and intramuscular vitamin B12.</li> <li>• Avoid administration of ibuprofen for 2 days before, the day of, and 2 days following administration in patients with CrCl &lt;80 mL/min.</li> <li>• Do not administer in patients with CrCl &lt;45 mL/min.</li> </ul>	

## VI. Billing Code/Availability Information

Product Formulation	Drug	Manufacturer	Type	HCPCS Code	NDC
Pemetrexed Disodium Hemipentahydrate Solution for injection	Pemrydi RTU 100 mg/10 mL SDV $\Psi$	Amneal	Brand	J9324	70121-2453-xx
	Pemrydi RTU 500 mg/50 mL SDV $\Psi$				70121-2461-xx
	Pemrydi RTU 1000 mg/100 mL SDV $\Psi$				70121-2462-xx
Pemetrexed Disodium Lyophilisate for injection	Alimta 100 mg powder for inj. SDV $\S$	Lilly	Brand	J9305	00002-7640-xx
	Alimta 500 mg powder for inj. SDV $\S$				00002-7623-xx
	Pemetrexed 750 mg powder for inj. SDV $\S$	Multiple	Generic	J9305	Multiple
	Pemetrexed 1000 mg powder for inj. SDV $\S$				
	Pemetrexed 100 mg powder for inj. SDV $\Psi$	BluePoint	Brand	J9322	68001-0543-xx
	Pemetrexed 500 mg powder for inj. SDV $\Psi$				68001-0544-xx
	Pemetrexed 750 mg powder for inj. SDV $\Psi$				68001-0545-xx
	Pemetrexed 1000 mg powder for inj. SDV $\Psi$				68001-0546-xx
Pemetrexed Disodium Solution for injection	Pemetrexed 100 mg/4 mL inj. SDV $\Psi$	Sandoz	Brand	J9297	00781-3518-xx
		Accord	Brand	J9296	16729-0522-xx
		Hospira	Brand	J9294	00409-1045-xx
	Pemetrexed 500 mg/20 mL inj. SDV $\Psi$	Sandoz	Brand	J9297	00781-3519-xx
		Accord	Brand	J9296	16729-0522-xx
		Hospira	Brand	J9294	00409-2188-xx
	Pemetrexed 850 mg/34mL inj. SDV $\Psi$	Accord	Brand	J9296	16729-0522-xx
	Pemetrexed 1000 mg/40 mL inj. SDV $\Psi$	Accord	Brand	J9296	16729-0522-xx

		Hospira	Brand	J9294	00409-3532-xx
Pemetrexed Solution for injection	Pemfexy 500 mg/20 mL inj. MDV	Eagle	Brand	J9304	42367-0531-xx
	Pemetrexed 100 mg/4mL inj. SDV Ψ	Teva	Brand	J9314	00480-4516-xx
	Pemetrexed 500 mg/20 mL inj. SDV Ψ	Teva	Brand	J9314	00480-4514-xx
	Pemetrexed 1000 mg/40 mL inj. SDV Ψ	Teva	Brand	J9314	00480-4515-xx
Pemetrexed Ditromethamine Lyophilisate for injection	Pemetrexed 100 mg powder for inj. SDV Ψ	Hospira	Brand	J9323	00409-1060-xx
	Pemetrexed 500 mg powder for inj. SDV Ψ				00409-1061-xx
Pemetrexed Dipotassium Lyophilisate for injection	Axtle 100 mg powder for inj. SDV Ψ	Avyxa	Brand	J9292	83831-0131-xx
	Axtle 500 mg powder for inj. SDV Ψ				83831-0132-xx

**§ Multiple manufacturers produce ANDA generics**

Ψ Designated products approved by the FDA as a 505(b)(2) NDA of the innovator product. These products may be available from several different manufacturers. For a complete list of all available products and NDCs please reference the FDA website at [National Drug Code Directory](#) for Pemetrexed. These products are not rated as therapeutically equivalent to their reference listed drug in the Food and Drug Administration’s (FDA) Orange Book and are therefore considered single source products based on the statutory definition of “single source drug” in section 1847A(c)(6) of the Act. For a complete list of all approved 505(b)(2) NDA products please reference the latest edition of the Orange Book: [Approved Drug Products with Therapeutic Equivalence Evaluations | Orange Book | FDA](#)

- J9292 – Injection, pemetrexed dipotassium, 10 mg
- J9294 – Injection, pemetrexed (hospira), not therapeutically equivalent to J9305, 10 mg
- J9296 – Injection, pemetrexed (accord), not therapeutically equivalent to J9305, 10 mg
- J9297 – Injection, pemetrexed (sandoz), not therapeutically equivalent to J9305, 10 mg
- J9304 – Injection, pemetrexed (pemfexy), 10 mg
- J9305 – Injection, pemetrexed, not otherwise specified, 10 mg
- J9314 – Injection, pemetrexed (teva), not therapeutically equivalent to J9305, 10 mg
- J9322 – Injection, pemetrexed (bluepoint), not therapeutically equivalent to J9305, 10 mg
- J9323 – Injection, pemetrexed ditromethamine, 10 mg
- J9324 – Injection, pemetrexed (pemrydi rtu), 10 mg
- J9999 – Injection, pemetrexed various, 10 mg

## VII. References (STANDARD)

1. Alimta [package insert]. Indianapolis, IN; Eli Lilly and Company; May 2023. Accessed November 2025.
2. Pemfexy [package insert]. Woodcliff Lake, NJ; Eagle Pharmaceuticals, Inc; December 2022. Accessed November 2025.
3. Pemrydi RTU [package insert]. Bridgewater, NJ; Amneal Pharmaceuticals LLC; November 2024. Accessed November 2025.
4. Axtle [package insert]. Parsippany, NJ; Avyxa Pharma, LLC; December 2024. Accessed November 2025.
5. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for pemetrexed. 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 November 2025.

6. 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.
7. 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.
8. 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.
9. 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.
10. 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.
11. 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.
12. 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. [PubMed 18375898]
13. 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.
14. 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.
15. 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.
16. 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.
17. 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.
18. 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.

19. 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.
20. 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](http://www.hoparx.org/images/hopa/advocacy/Issue-Briefs/Drug_Waste_2019.pdf)
21. Bach PB, Conti RM, Muller RJ, et al. Overspending driven by oversized single dose vials of cancer drugs. *BMJ*. 2016 Feb 29;352:i788.
22. 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.
23. 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.
24. 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.
25. 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.
26. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Ovarian Cancer Including Fallopian Tube Cancer and Primary Peritoneal 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 September 2025.
27. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Thymomas and Thymic Carcinomas. 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 September 2025.

28. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Mesothelioma: Pleural 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 September 2025.
29. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Central Nervous System Cancers 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 September 2025.
30. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Non-Small Cell Lung Cancer Version 8.2025. 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 September 2025.
31. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Mesothelioma: Peritoneal Version 2.2026. 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 November 2025.
32. Forde P, Spicer J, Provencio M, et al. Abstract CT003: Nivolumab (NIVO) + platinum-doublet chemotherapy (chemo) vs chemo as neoadjuvant treatment (tx) for resectable (IB-IIIa) non-small cell lung cancer (NSCLC) in the phase 3 CheckMate 816 trial. *Cancer Res* (2021) 81 (13\_Supplement): CT003. <https://doi.org/10.1158/1538-7445.AM2021-CT003>
33. Miller DS, Blessing JA, Bodurka DC, et al. Evaluation of pemetrexed (Alimta, LY231514) as second line chemotherapy in persistent or recurrent carcinoma of the cervix: a phase II study of the Gynecologic Oncology Group. *Gynecol Oncol*. 2008 Jul;110(1):65-70. doi: 10.1016/j.ygyno.2008.03.009.
34. Zalcman G, Mazieres J, Margery J, et al. Bevacizumab for newly diagnosed pleural mesothelioma in the Mesothelioma Avastin Cisplatin Pemetrexed Study (MAPS): a randomised, controlled, open-label, phase 3 trial. *Lancet*. 2016 Apr 2;387(10026):1405-1414. doi: 10.1016/S0140-6736(15)01238-6.

35. Fan C, Zhao Q, Li L, et al. Efficacy and Safety of Intrathecal Pemetrexed Combined With Dexamethasone for Treating Tyrosine Kinase Inhibitor-Failed Leptomeningeal Metastases From EGFR-Mutant NSCLC-a Prospective, Open-Label, Single-Arm Phase 1/2 Clinical Trial (Unique Identifier: ChiCTR1800016615). *J Thorac Oncol*. 2021 Aug;16(8):1359-1368. doi: 10.1016/j.jtho.2021.04.018.
36. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines<sup>®</sup>) for Cervical Cancer Version 4.2025. National Comprehensive Cancer Network, 2025. NATIONAL COMPREHENSIVE CANCER NETWORK<sup>®</sup>, NCCN<sup>®</sup>, and NCCN GUIDELINES<sup>®</sup> 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 September 2025.
37. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines<sup>®</sup>) for Vaginal Cancer Version 5.2025. National Comprehensive Cancer Network, 2025. NATIONAL COMPREHENSIVE CANCER NETWORK<sup>®</sup>, NCCN<sup>®</sup>, and NCCN GUIDELINES<sup>®</sup> 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 September 2025.
38. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines<sup>®</sup>) for Intrathecal PEMEtrexed: Central Nervous System Cancers Chemotherapy Order Template, CNS110. National Comprehensive Cancer Network, 2025. NATIONAL COMPREHENSIVE CANCER NETWORK<sup>®</sup>, NCCN<sup>®</sup>, and NCCN GUIDELINES<sup>®</sup> 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 July 2025.
39. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines<sup>®</sup>) for PEMEtrexed: Vaginal Cancer Chemotherapy Order Template, VAG28. National Comprehensive Cancer Network, 2025. NATIONAL COMPREHENSIVE CANCER NETWORK<sup>®</sup>, NCCN<sup>®</sup>, and NCCN GUIDELINES<sup>®</sup> 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 July 2025.
40. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines<sup>®</sup>) for PEMEtrexed: Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer Chemotherapy Order Template, OVA47. National Comprehensive Cancer Network, 2025. NATIONAL COMPREHENSIVE CANCER NETWORK<sup>®</sup>, NCCN<sup>®</sup>, and NCCN GUIDELINES<sup>®</sup> 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 November 2025.
41. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines<sup>®</sup>) for PEMEtrexed: Cervical Cancer Chemotherapy Order Template, CRV19. National Comprehensive Cancer Network, 2025. NATIONAL COMPREHENSIVE CANCER NETWORK<sup>®</sup>,

NCCN<sup>®</sup>, and NCCN GUIDELINES<sup>®</sup> 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 July2025.

42. Chu Q, Perrone F, Greillier L, et al. Pembrolizumab plus chemotherapy versus chemotherapy in untreated advanced pleural mesothelioma in Canada, Italy, and France: a phase 3, open-label, randomised controlled trial. *Lancet* 2023; 16;402:2295-2306.
43. Lee KK, Morris JC 3rd, Kumar A, et al. Pemetrexed-carboplatin salvage therapy in advanced thyroid cancers. *Head Neck*. 2025 Mar;47(3):813-821. doi: 10.1002/hed.27940. Epub 2024 Oct 27. PMID: 39462887.
44. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines<sup>®</sup>) for CARBOplatin/PEMEtrexed: Papillary Carcinoma Chemotherapy Order Template, PAP19. National Comprehensive Cancer Network, 2025. NATIONAL COMPREHENSIVE CANCER NETWORK<sup>®</sup>, NCCN<sup>®</sup>, and NCCN GUIDELINES<sup>®</sup> 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 July2025.
45. Passaro A, Wang J, Wang Y, et al. Amivantamab plus chemotherapy with and without lazertinib in EGFR-mutant advanced NSCLC after disease progression on osimertinib: primary results from the phase III MARIPOSA-2 study. *Ann Oncol* 2024;35:77-90.
46. Planchard D, Jänne PA, Cheng Y, et al. Osimertinib with or without chemotherapy in EGFR-mutated advanced NSCLC. *N Engl J Med* 2023;389:1935-1948.

## VIII. References (ENHANCED)

- 1e. Sweeney CJ, Roth BJ, Kabbinavar FF, et al. Phase II study of pemetrexed for second-line treatment of transitional cell cancer of the urothelium. *J Clin Oncol*. 2006 Jul 20;24(21):3451-7.
- 2e. Bellmunt J, de Wit R, Vaughn DJ, et al. Pembrolizumab as Second-Line Therapy for Advanced Urothelial Carcinoma. *N Engl J Med*. 2017;376(11):1015–1026.
- 3e. Rosenberg JE, Hoffman-Censits J, Powles T, et al. Atezolizumab in patients with locally advanced and metastatic urothelial carcinoma who have progressed following treatment with platinum-based chemotherapy: a single-arm, multicentre, phase 2 trial. *Lancet*. 2016;387(10031):1909–1920.
- 4e. Powles T, Durán I, van der Heijden MS, et al. Atezolizumab versus chemotherapy in patients with platinum-treated locally advanced or metastatic urothelial carcinoma (IMvigor211): a multicentre, open-label, phase 3 randomised controlled trial. *Lancet*. 2018 Feb 24;391(10122):748-757.
- 5e. Sharma P, Retz M, Siefker-Radtke A, et al. Nivolumab in metastatic urothelial carcinoma after platinum therapy (CheckMate 275): a multicentre, single-arm, phase 2 trial. *Lancet Oncol*. 2017 Mar;18(3):312-322.

- 6e. Massard C, Gordon MS, Sharma S, et al. Safety and Efficacy of Durvalumab (MEDI4736), an Anti-Programmed Cell Death Ligand-1 Immune Checkpoint Inhibitor, in Patients With Advanced Urothelial Bladder Cancer. *J Clin Oncol*. 2016;34(26):3119–3125.
- 7e. Patel MR, Ellerton J, Infante J, et al. Avelumab in metastatic urothelial carcinoma after platinum failure (JAVELIN Solid Tumor): pooled results from two expansion cohorts of an open-label, phase 1 trial. *Lancet Oncol*. 2018 Jan;19(1):51-64.
- 8e. Ko YJ, et al. Nanoparticle albumin-bound paclitaxel for second-line treatment of metastatic urothelial carcinoma: a single group, multicentre, phase 2 study. *Lancet Oncol*. 2013 Jul;14(8):769-76.
- 9e. Lorusso V, et al. A phase II study of gemcitabine in patients with transitional cell carcinoma of the urinary tract previously treated with platinum. Italian Co-operative Group on Bladder Cancer. *Eur J Cancer*. 1998 Jul;34(8):1208-12.
- 10e. Meluch AA, et al. Paclitaxel and gemcitabine chemotherapy for advanced transitional-cell carcinoma of the urothelial tract: a phase II trial of the Minnie pearl cancer research network.. *J Clin Oncol*. 2001 Jun 15;19(12):3018-24.
- 11e. von der Maase H, et al. Gemcitabine and Cisplatin Versus Methotrexate, Vinblastine, Doxorubicin, and Cisplatin in Advanced or Metastatic Bladder Cancer: Results of a Large, Randomized, Multinational, Multicenter, Phase III Study. *Journal of Clinical Oncology* 2000 18:17, 3068-3077.
- 12e. De Santis M, Bellmunt J, Mead G, et al. Randomized phase II/III trial assessing gemcitabine/ carboplatin and methotrexate/carboplatin/vinblastine in patients with advanced urothelial cancer "unfit" for cisplatin-based chemotherapy: phase II--results of EORTC study 30986. *J Clin Oncol*. 2009;27(33):5634–5639.
- 13e. McCaffrey JA, et al. Phase II trial of docetaxel in patients with advanced or metastatic transitional-cell carcinoma. *J Clin Oncol*. 1997 May;15(5):1853-7.
- 14e. Vaughn DJ, et al. Phase II trial of weekly paclitaxel in patients with previously treated advanced urothelial cancer. *J Clin Oncol*. 2002 Feb 15;20(4):937-40.
- 15e. Petrylak DP, et al. Ramucirumab plus docetaxel versus placebo plus docetaxel in patients with locally advanced or metastatic urothelial carcinoma after platinum-based therapy (RANGE): a randomised, double-blind, phase 3 trial. *Lancet*. 2017 Nov 18;390(10109):2266-2277.
- 16e. Witte RS, et al. Eastern Cooperative Oncology Group phase II trial of ifosfamide in the treatment of previously treated advanced urothelial carcinoma. *J Clin Oncol*. 1997 Feb;15(2):589-93.
- 17e. Siefker-Radtke AO, Dinney CP, Shen Y, et al. A phase 2 clinical trial of sequential neoadjuvant chemotherapy with ifosfamide, doxorubicin, and gemcitabine followed by cisplatin, gemcitabine, and ifosfamide in locally advanced urothelial cancer: final results. *Cancer*. 2012;119(3):540-7.

- 18e. Sternberg CN, et al. Randomized phase III trial of high-dose-intensity methotrexate, vinblastine, doxorubicin, and cisplatin (MVAC) chemotherapy and recombinant human granulocyte colony-stimulating factor versus classic MVAC in advanced urothelial tract tumors: European Organization for Research and Treatment of Cancer Protocol no. 30924. *J Clin Oncol*. 2001 May 15;19(10):2638-46.
- 19e. Plotkin SR, Betensky RA, Hochberg FH, et al. Treatment of relapsed central nervous system lymphoma with high-dose methotrexate. *Clin Cancer Res*. 2004 Sep 1;10(17):5643-6.
- 20e. Nayak L, Abrey LE, Drappatz J, et al. Multicenter phase II study of rituximab and temozolomide in recurrent primary central nervous system lymphoma. *Leuk Lymphoma*. 2013;54(1):58–61.
- 21e. Krug LM, Pass HI, Rusch VW, et al. Multicenter phase II trial of neoadjuvant pemetrexed plus cisplatin followed by extrapleural pneumonectomy and radiation for malignant pleural mesothelioma. *J Clin Oncol*. 2009;27(18):3007–3013.
- 22e. Santoro A, O'Brien ME, Stahel RA, et al. Pemetrexed plus cisplatin or pemetrexed plus carboplatin for chemo-naïve patients with malignant pleural mesothelioma: results of the International Expanded Access Program. *J Thorac Oncol*. 2008 Jul;3(7):756-63.
- 23e. Zalcman G, Mazieres J, Margery J, et al. Bevacizumab for newly diagnosed pleural mesothelioma in the Mesothelioma Avastin Cisplatin Pemetrexed Study (MAPS): a randomised, controlled, open-label, phase 3 trial. *Lancet*. 2016 Apr 2;387(10026):1405-1414.
- 24e. Ceresoli GL, Zucali PA, Mencoboni M, et al. Phase II study of pemetrexed and carboplatin plus bevacizumab as first-line therapy in malignant pleural mesothelioma. *Br J Cancer*. 2013;109(3):552–558.
- 25e. Muers MF, Stephens RJ, Fisher P, et al. Active symptom control with or without chemotherapy in the treatment of patients with malignant pleural mesothelioma (MS01): a multicentre randomised trial. *Lancet*. 2008;371(9625):1685–1694.
- 26e. Zucali PA, Simonelli M, Michetti G, et al. Second-line chemotherapy in malignant pleural mesothelioma: results of a retrospective multicenter survey. *Lung Cancer*. 2012 Mar;75(3):360-7.
- 27e. Scherpereel A, Mazieres J, Greillier L, et al. Nivolumab or nivolumab plus ipilimumab in patients with relapsed malignant pleural mesothelioma (IFCT-1501 MAPS2): a multicentre, open-label, randomised, non-comparative, phase 2 trial. *Lancet Oncol*. 2019 Feb;20(2):239-253.
- 28e. Scherpereel A, Mazieres J, Greillier L, et al. Second or 3rd line nivolumab (Nivo) versus nivo plus ipilimumab (Ipi) in malignant pleural mesothelioma (MPM) patients: Updated results of the IFCT-1501 MAPS2 randomized phase 2 trial. *Ann Oncol*. 2017 Sept;28(5):mdx440.074.
- 29e. Disselhorst MJ, Quispel-Janssen J, Lalezari F, et al. Ipilimumab and nivolumab in the treatment of recurrent malignant pleural mesothelioma (INITIATE): results of a prospective, single-arm, phase 2 trial. *Lancet Respir Med*. 2019 Mar;7(3):260-270.

- 30e. Quispel-Janssen J, van der Noort V, de Vries JF, et al. Programmed Death 1 Blockade With Nivolumab in Patients With Recurrent Malignant Pleural Mesothelioma. *J Thorac Oncol*. 2018 Oct;13(10):1569-1576.
- 31e. Alley EW, Lopez J, Santoro A, et al. Clinical safety and activity of pembrolizumab in patients with malignant pleural mesothelioma (KEYNOTE-028): preliminary results from a non-randomised, open-label, phase 1b trial. *Lancet Oncol*. 2017 May;18(5):623-630.
- 32e. Alley EW, Lopez J, Santoro A, et al. Long-Term Overall Survival for Patients with Malignant Pleural Mesothelioma on Pembrolizumab Enrolled in KEYNOTE-028. *J Thorac Oncol*. 2017 Jan;12(1):S294.
- 33e. Metaxas Y, Rivalland G, Mauti LA, et al. Pembrolizumab as Palliative Immunotherapy in Malignant Pleural Mesothelioma. *J Thorac Oncol*. 2018 Nov;13(11):1784-1791.
- 34e. Stebbing J, Powles T, McPherson K, et al. The efficacy and safety of weekly vinorelbine in relapsed malignant pleural mesothelioma. *Lung Cancer*. 2009 Jan;63(1):94-7.
- 35e. Zauderer MG, Kass SL, Woo K, Sima CS, Ginsberg MS, Krug LM. Vinorelbine and gemcitabine as second- or third-line therapy for malignant pleural mesothelioma. *Lung Cancer*. 2014;84(3):271-274.
- 36e. Kim JS, Lim SY, Hwang J, Kang EJ, Choi YJ. A Case Report of Primary Pericardial Malignant Mesothelioma Treated with Pemetrexed and Cisplatin. *J Korean Med Sci*. 2017;32(11):1879-1884.
- 37e. Carteni G, Manegold C, Garcia GM, et al. Malignant peritoneal mesothelioma-Results from the International Expanded Access Program using pemetrexed alone or in combination with a platinum agent. *Lung Cancer*. 2009 May;64(2):211-8.
- 38e. Zhang L, Ou W, Liu Q, Li N, Liu L, Wang S. Pemetrexed plus carboplatin as adjuvant chemotherapy in patients with curative resected non-squamous non-small cell lung cancer. *Thorac Cancer*. 2014;5(1):50-56.
- 39e. Kreuter M, Vansteenkiste J, Fischer JR, et al. Randomized phase 2 trial on refinement of early-stage NSCLC adjuvant chemotherapy with cisplatin and pemetrexed versus cisplatin and vinorelbine: the TREAT study. *Ann Oncol*. 2013 Apr;24(4):986-92.
- 40e. Kenmotsu H, Yamamoto N, Yamanaka T, et al. Randomized phase III study of pemetrexed/cisplatin (Pem/Cis) versus vinorelbine /cisplatin (Vnr/Cis) for completely resected stage II-IIIa non-squamous non-small-cell lung cancer (Ns-NSCLC): The JIPANG study. *J Clin Oncol*, 2019; 37(15\_suppl):8501.
- 41e. Arriagada R, Bergman B, Dunant A, et al. Cisplatin-based adjuvant chemotherapy in patients with completely resected non-small-cell lung cancer. *N Engl J Med*. 2004 Jan 22;350(4):351-60.
- 42e. Scagliotti GV, Pastorino U, Vansteenkiste JF, et al. Randomized phase III study of surgery alone or surgery plus preoperative cisplatin and gemcitabine in stages IB to IIIa non-small-cell lung cancer. *J Clin Oncol*. 2012 Jan 10;30(2):172-8.

- 43e. Strauss GM, Herndon JE 2nd, Maddaus MA, et al. Adjuvant paclitaxel plus carboplatin compared with observation in stage IB non-small-cell lung cancer: CALGB 9633 with the Cancer and Leukemia Group B, Radiation Therapy Oncology Group, and North Central Cancer Treatment Group Study Groups. *J Clin Oncol*. 2008;26(31):5043–5051.
- 44e. Usami N, Yokoi K, Hasegawa Y, et al. Phase II study of carboplatin and gemcitabine as adjuvant chemotherapy in patients with completely resected non-small cell lung cancer: a report from the Central Japan Lung Study Group, CJLSG 0503 trial. *Int J Clin Oncol*. 2010 Dec;15(6):583-7.
- 45e. Senan S, Brade A, Wang LH, et al. PROCLAIM: Randomized Phase III Trial of Pemetrexed-Cisplatin or Etoposide-Cisplatin Plus Thoracic Radiation Therapy Followed by Consolidation Chemotherapy in Locally Advanced Nonsquamous Non-Small-Cell Lung Cancer. *J Clin Oncol*. 2016 Mar 20;34(9):953-62.
- 46e. Curran WJ Jr, Paulus R, Langer CJ, et al. Sequential vs. concurrent chemoradiation for stage III non-small cell lung cancer: randomized phase III trial RTOG 9410 [published correction appears in *J Natl Cancer Inst*. 2012 Jan 4;104(1):79]. *J Natl Cancer Inst*. 2011;103(19):1452–1460.
- 47e. Belani CP, Choy H, Bonomi P, et al. Combined chemoradiotherapy regimens of paclitaxel and carboplatin for locally advanced non-small-cell lung cancer: a randomized phase II locally advanced multi-modality protocol. *J Clin Oncol*. 2005 Sep 1;23(25):5883-91.
- 48e. Yang JC, Hirsh V, Schuler M, et al. Symptom control and quality of life in LUX-Lung 3: a phase III study of afatinib or cisplatin/pemetrexed in patients with advanced lung adenocarcinoma with EGFR mutations. *J Clin Oncol*. 2013 Sep 20;31(27):3342-50.
- 49e. Zukin M, Barrios CH, Pereira JR, et al. Randomized phase III trial of single-agent pemetrexed versus carboplatin and pemetrexed in patients with advanced non-small-cell lung cancer and Eastern Cooperative Oncology Group performance status of 2. *J Clin Oncol*. 2013 Aug 10;31(23):2849-53.
- 50e. Gridelli C, Kaukel E, Gregorc V, et al. Single-agent pemetrexed or sequential pemetrexed/gemcitabine as front-line treatment of advanced non-small cell lung cancer in elderly patients or patients ineligible for platinum-based chemotherapy: a multicenter, randomized, phase II trial. *J Thorac Oncol*. 2007 Mar;2(3):221-9.
- 51e. Rusthoven JJ, Eisenhauer E, Butts C, et al. Multitargeted antifolate LY231514 as first-line chemotherapy for patients with advanced non-small-cell lung cancer: A phase II study. National Cancer Institute of Canada Clinical Trials Group. *J Clin Oncol*. 1999 Apr;17(4):1194.
- 52e. Patel JD, Socinski MA, Garon EB, et al. PointBreak: a randomized phase III study of pemetrexed plus carboplatin and bevacizumab followed by maintenance pemetrexed and bevacizumab versus paclitaxel plus carboplatin and bevacizumab followed by maintenance bevacizumab in patients with stage IIIB or IV nonsquamous non-small-cell lung cancer. *J Clin Oncol*. 2013;31(34):4349–4357.
- 53e. Barlesi F, Scherpereel A, Rittmeyer A, et al. Randomized phase III trial of maintenance bevacizumab with or without pemetrexed after first-line induction with bevacizumab, cisplatin,

- and pemetrexed in advanced nonsquamous non-small-cell lung cancer: AVAPERL (MO22089). *J Clin Oncol*. 2013 Aug 20;31(24):3004-11.
- 54e. Reck M, Rodríguez-Abreu D, Robinson AG, et al. Pembrolizumab versus Chemotherapy for PD-L1–Positive Non–Small-Cell Lung Cancer. *N Engl J Med* 2016; 375:1823-1833.
- 55e. Socinski MA, Jotte RM, Capuzzo F, et al. Atezolizumab for First-Line Treatment of Metastatic Nonsquamous NSCLC. *N Engl J Med* 2018; 378:2288-2301.
- 56e. Cardenal F, López-Cabrerizo MP, Antón A, et al. Randomized phase III study of gemcitabine-cisplatin versus etoposide-cisplatin in the treatment of locally advanced or metastatic non-small-cell lung cancer. *J Clin Oncol*. 1999 Jan;17(1):12-8.
- 57e. Fossella F, Pereira JR, von Pawel J, et al. Randomized, multinational, phase III study of docetaxel plus platinum combinations versus vinorelbine plus cisplatin for advanced non-small-cell lung cancer: the TAX 326 study group. *J Clin Oncol*. 2003 Aug 15;21(16):3016-24.
- 58e. Zatloukal P, Kanitz E, Magyar P, et al. Gemcitabine in locally advanced and metastatic non-small cell lung cancer: the Central European phase II study. *Lung Cancer*. 1998 Dec;22(3):243-50.
- 59e. Pujol JL, Breton JL, Gervais R, et al. Gemcitabine-docetaxel versus cisplatin-vinorelbine in advanced or metastatic non-small-cell lung cancer: a phase III study addressing the case for cisplatin. *Ann Oncol*. 2005 Apr;16(4):602-10.
- 60e. Tan EH, Szczesna A, Krzakowski M, et al. Randomized study of vinorelbine--gemcitabine versus vinorelbine--carboplatin in patients with advanced non-small cell lung cancer. *Lung Cancer*. 2005 Aug;49(2):233-40.
- 61e. Paz-Ares L, de Marinis F, Dediu M, et al. PARAMOUNT: Final Overall Survival Results of the Phase III Study of Maintenance Pemetrexed Versus Placebo Immediately After Induction Treatment With Pemetrexed Plus Cisplatin for Advanced Nonsquamous Non–Small-Cell Lung Cancer. *J Clin Oncol*. 2013 Aug 10;31(23):2895-902.
- 62e. Anderson H, Hopwood P, Stephens RJ, et al. Gemcitabine plus best supportive care (BSC) vs BSC in inoperable non-small cell lung cancer--a randomized trial with quality of life as the primary outcome. UK NSCLC Gemcitabine Group. *Non-Small Cell Lung Cancer*. *Br J Cancer*. 2000;83(4):447–453.
- 63e. Borghaei H, Paz-Ares L, Horn L, et al. Nivolumab versus Docetaxel in Advanced Nonsquamous Non-Small-Cell Lung Cancer. *N Engl J Med*. 2015;373(17):1627–1639.
- 64e. Herbst RS, Baas P, Kim DW, et al. Pembrolizumab versus docetaxel for previously treated, PD-L1-positive, advanced non-small-cell lung cancer (KEYNOTE-010): a randomised controlled trial. *Lancet*. 2016 Apr 9;387(10027):1540-50.
- 65e. Barlesi F, Park K, Ciardiello F, et al. Primary analysis from OAK, a randomized phase III study comparing atezolizumab with docetaxel in 2L/3L NSCLC. *Ann Oncol*. 2016 Oct;27(6):LBA44\_PR.
- 66e. Garon EB, Ciuleanu TE, Arrieta O, et al. Ramucirumab plus docetaxel versus placebo plus docetaxel for second-line treatment of stage IV non-small-cell lung cancer after disease

- progression on platinum-based therapy (REVEL): a multicentre, double-blind, randomised phase 3 trial. *Lancet*. 2014 Aug 23;384(9944):665-73.
- 67e. Ceresoli GL, Gregorc V, Cordio S, et al. Phase II study of weekly paclitaxel as second-line therapy in patients with advanced non-small cell lung cancer. *Lung Cancer*. 2004 May;44(2):231-9.
- 68e. Palmieri G, Buonerba C, Ottaviano M, et al. Capecitabine plus gemcitabine in thymic epithelial tumors: final analysis of a Phase II trial. *Future Oncol*. 2014 Nov;10(14):2141-7.
- 69e. Thomas A, Rajan A, Berman A, et al. Sunitinib in patients with chemotherapy-refractory thymoma and thymic carcinoma: an open-label phase 2 trial [published correction appears in *Lancet Oncol*. 2015 Mar;16(3):e105]. *Lancet Oncol*. 2015;16(2):177–186.
- 70e. Zucali PA, De Pas T, Palmieri G, et al. Phase II Study of Everolimus in Patients With Thymoma and Thymic Carcinoma Previously Treated With Cisplatin-Based Chemotherapy. *J Clin Oncol*. 2018 Feb 1;36(4):342-349.
- 71e. Loehrer PJ Sr, Wang W, Johnson DH, et al. Octreotide alone or with prednisone in patients with advanced thymoma and thymic carcinoma: an Eastern Cooperative Oncology Group Phase II Trial. *J Clin Oncol*. 2004 Jan 15;22(2):293-9.
- 72e. Umemura S, Segawa Y, Fujiwara K, et al. A case of recurrent metastatic thymoma showing a marked response to paclitaxel monotherapy. *Jpn J Clin Oncol*. 2002 Jul;32(7):262-5.
- 73e. Bluthgen MV, Boutros C, Fayard F, et al. Activity and safety of oral etoposide in pretreated patients with metastatic or recurrent thymic epithelial tumors (TET): A single-institution experience. *Lung Cancer*. 2016 Sep;99:111-6.
- 74e. Rose PG, Blessing JA, Ball HG, et al. A phase II study of docetaxel in paclitaxel-resistant ovarian and peritoneal carcinoma: a Gynecologic Oncology Group study. *Gynecol Oncol*. 2003 Feb;88(2):130-5.
- 75e. Rose PG, Blessing JA, Mayer AR, Homesley HD. Prolonged oral etoposide as second-line therapy for platinum-resistant and platinum-sensitive ovarian carcinoma: a Gynecologic Oncology Group study. *J Clin Oncol*. 1998 Feb;16(2):405-10.
- 76e. Gordon AN, Tonda M, Sun S, et al. Long-term survival advantage for women treated with pegylated liposomal doxorubicin compared with topotecan in a phase 3 randomized study of recurrent and refractory epithelial ovarian cancer. *Gynecol Oncol*. 2004 Oct;95(1):1-8.
- 77e. Sehoul J, Stengel D, Harter P, et al. Topotecan Weekly Versus Conventional 5-Day Schedule in Patients With Platinum-Resistant Ovarian Cancer: a randomized multicenter phase II trial of the North-Eastern German Society of Gynecological Oncology Ovarian Cancer Study Group. *J Clin Oncol*. 2011 Jan 10;29(2):242-8.
- 78e. Kindler HL, Ismaila N, Armato III, SG, et al. Treatment of Malignant Pleural Mesothelioma: American Society of Clinical Oncology Clinical Practice Guideline. *J Clin Oncol*. 2018 Jan;36(13):1343-1373.

- 79e. Nowak AK, Byrne MJ, Williamson R, et al. A multicentre phase II study of cisplatin and gemcitabine for malignant mesothelioma. *Br J Cancer*. 2002;87(5):491-496.
- 80e. van Haarst JM, Baas P, Manegold Ch, et al. Multicentre phase II study of gemcitabine and cisplatin in malignant pleural mesothelioma. *Br J Cancer*. 2002;86(3):342-345.
- 81e. Spigel D et al. IMpower110: Interim OS Analysis of a Phase III Study of Atezolizumab (atezo) vs Platinum-Based Chemotherapy (chemo) as 1L Treatment (tx) in PD-L1–selected NSCLC [ESMO 2019 Abstract LBA78].
- 82e. Reck M, Ciuleanu T-E, Dols MC, et al. Nivolumab (NIVO) + ipilimumab (IPI) + 2 cycles of platinum-doublet chemotherapy (chemo) vs 4 cycles chemo as first-line (1L) treatment (tx) for stage IV/recurrent non-small cell lung cancer (NSCLC): CheckMate 9LA [abstract]. *J Clin Oncol* 2020;38:Abstract 9501-9501.
- 83e. West H, McCleod M, Hussein M, et al. Atezolizumab in combination with carboplatin plus nab-paclitaxel chemotherapy compared with chemotherapy alone as first-line treatment for metastatic non-squamous non-small-cell lung cancer (IMpower130): a multicentre, randomised, open-label, phase 3 trial. *Lancet Oncol*. 2019;20(7):924-937.
- 84e. Zalcman G, Peters S, Mansfield AS, et al. Checkmate 743: A phase 3, randomized, open-label trial of nivolumab (nivo) plus ipilimumab (ipi) vs pemetrexed plus cisplatin or carboplatin as first-line therapy in unresectable pleural mesothelioma. *Journal of Clinical Oncology* 2017 35:15\_suppl, TPS8581-TPS8581.
- 85e. Sezer A, Kilickap S, Gümüş M, et al. Cemiplimab monotherapy for first-line treatment of advanced non-small-cell lung cancer with PD-L1 of at least 50%: a multicentre, open-label, global, phase 3, randomised, controlled trial. *Lancet*. 2021 Feb 13;397(10274):592-604.
- 86e. Scagliotti GV, Shin DM, Kindler HL, et al. Phase II study of pemetrexed with and without folic acid and vitamin B12 as front-line therapy in malignant pleural mesothelioma. *J Clin Oncol*. 2003 Apr 15;21(8):1556-61.
- 87e. Jänne PA, Wozniak AJ, Belani CP, et al. Open-label study of pemetrexed alone or in combination with cisplatin for the treatment of patients with peritoneal mesothelioma: outcomes of an expanded access program. *Clin Lung Cancer*. 2005 Jul;7(1):40-6.
- 88e. Gogishvili M, Melkadze T, Makharadze T, et al. LBA51 EMPOWER-Lung 3: Cemiplimab in combination with platinum doublet chemotherapy for first-line (1L) treatment of advanced non-small cell lung cancer (NSCLC). *Annals of Oncology*, ISSN: 0923-7534, Vol: 32, SUPPLEMENT 5, S1328, SEPTEMBER 01, 2021. DOI10.1016/j.annonc.2021.08.2130.
- 89e. Johnson ML, Cho BC, Luft A, et al. Durvalumab With or Without Tremelimumab in Combination With Chemotherapy as First-Line Therapy for Metastatic Non-Small-Cell Lung Cancer: The Phase III POSEIDON Study. *J Clin Oncol*. 2023 Feb 20;41(6):1213-1227.
- 90e. Bijelic L, Stuart OA, Sugarbaker P. Adjuvant bidirectional chemotherapy with intraperitoneal pemetrexed combined with intravenous Cisplatin for diffuse malignant peritoneal mesothelioma. *Gastroenterol Res Pract*. 2012;2012:890450.

- 91e. Wakelee H, Liberman M, Kato T, et al. Perioperative Pembrolizumab for Early-Stage Non-Small-Cell Lung Cancer. *N Engl J Med*. 2023 Aug 10;389(6):491-503. doi: 10.1056/NEJMoa2302983. Epub 2023 Jun 3. PMID: 37272513.
- 92e. Novello S, Mazières J, Oh JJ, et al. Alectinib versus chemotherapy in crizotinib-pretreated anaplastic lymphoma kinase (ALK)-positive non-small-cell lung cancer: results from the phase III ALUR study. *Ann Oncol*. 2018;29(6):1409-1416. doi:10.1093/annonc/mdy121.
- 93e. Kim DW, Tiseo M, Ahn MJ, et al. Brigatinib in Patients With Crizotinib-Refractory Anaplastic Lymphoma Kinase-Positive Non-Small-Cell Lung Cancer: A Randomized, Multicenter Phase II Trial. *J Clin Oncol*. 2017 Aug 1;35(22):2490-2498. doi: 10.1200/JCO.2016.71.5904.
- 94e. Shaw AT, Kim DW, Nakagawa K, et al. Crizotinib versus chemotherapy in advanced ALK-positive lung cancer. *N Engl J Med*. 2013 Jun 20;368(25):2385-94. doi: 10.1056/NEJMoa1214886.
- 95e. Solomon BJ, Besse B, Bauer TM, et al. Lorlatinib in patients with ALK-positive non-small-cell lung cancer: results from a global phase 2 study [published correction appears in *Lancet Oncol*. 2019 Jan;20(1):e10]. *Lancet Oncol*. 2018;19(12):1654–1667. doi:10.1016/S1470-2045(18)30649-1.
- 96e. Zhou C, Tang KJ, Cho BC, et al; PAPILLON Investigators. Amivantamab plus Chemotherapy in NSCLC with EGFR Exon 20 Insertions. *N Engl J Med*. 2023 Nov 30;389(22):2039-2051. doi: 10.1056/NEJMoa2306441. Epub 2023 Oct 21.
- 97e. Hainsworth JD, Waterhouse DM, Shih KC, et al. Phase II trial of preoperative pemetrexed plus carboplatin in patients with stage IB-III nonsquamous non-small cell lung cancer (NSCLC). *Lung Cancer*. 2018;118:6-12. doi:10.1016/j.lungcan.2018.01.009.
- 98e. Soussain C, Choquet S, Blonski M, et al. Ibrutinib monotherapy for relapse or refractory primary CNS lymphoma and primary vitreoretinal lymphoma: Final analysis of the phase II 'proof-of-concept' iLOC study by the Lymphoma study association (LYSA) and the French oculo-cerebral lymphoma (LOC) network. *Eur J Cancer*. 2019;117:121-130. doi:10.1016/j.ejca.2019.05.024.
- 99e. Heymach JV, Harpole D, Mitsudomi T, et al; AEGEAN Investigators. Perioperative Durvalumab for Resectable Non-Small-Cell Lung Cancer. *N Engl J Med*. 2023 Nov 2;389(18):1672-1684. doi: 10.1056/NEJMoa2304875. Epub 2023 Oct 23. PMID: 37870974.
- 100e. Yang JCH, Kim SW, Kim DW, et al. Osimertinib in Patients With Epidermal Growth Factor Receptor Mutation-Positive Non-Small-Cell Lung Cancer and Leptomeningeal Metastases: The BLOOM Study. *J Clin Oncol*. 2020;38(6):538-547. doi:10.1200/JCO.19.00457.
- 101e. Nanjo S, Hata A, Okuda C, Kaji R, Okada H, Tamura D, Irie K, Okada H, Fukushima S, Katakami N. Standard-dose osimertinib for refractory leptomeningeal metastases in T790M-positive EGFR-mutant non-small cell lung cancer. *Br J Cancer*. 2018 Jan;118(1):32-37.
- 102e. Homesley HD, Meltzer NP, Nieves L, Vaccarello L, Lowendowski GS, Elbendary AA. A phase II trial of weekly 1-hour paclitaxel as second-line therapy for endometrial and cervical cancer. *Int J Clin Oncol*. 2008;13(1):62-65. doi:10.1007/s10147-007-0731-5.

- 103e. Garcia AA, Blessing JA, Vaccarello L, Roman LD; Gynecologic Oncology Group Study. Phase II clinical trial of docetaxel in refractory squamous cell carcinoma of the cervix: a Gynecologic Oncology Group Study. *Am J Clin Oncol*. 2007;30(4):428-431. doi:10.1097/COC.0b013e31803377c8.
- 104e. Look KY, Blessing JA, Gallup DG, Lentz SS. A phase II trial of 5-fluorouracil and high-dose leucovorin in patients with recurrent squamous cell carcinoma of the cervix: a Gynecologic Oncology Group study. *Am J Clin Oncol*. 1996;19(5):439-441. doi:10.1097/00000421-199610000-00002.
- 105e. Schilder RJ, Blessing J, Cohn DE. Evaluation of gemcitabine in previously treated patients with non-squamous cell carcinoma of the cervix: a phase II study of the Gynecologic Oncology Group. *Gynecol Oncol*. 2005;96(1):103-107. doi:10.1016/j.ygyno.2004.09.027.
- 106e. Bookman MA, Blessing JA, Hanjani P, Herzog TJ, Andersen WA. Topotecan in squamous cell carcinoma of the cervix: A Phase II study of the Gynecologic Oncology Group. *Gynecol Oncol*. 2000;77(3):446-449. doi:10.1006/gyno.2000.5807.
- 107e. Muggia FM, Blessing JA, Method M, et al. Evaluation of vinorelbine in persistent or recurrent squamous cell carcinoma of the cervix: a Gynecologic Oncology Group study. *Gynecol Oncol*. 2004;92(2):639-643. doi:10.1016/j.ygyno.2003.10.045.
- 108e. Verschraegen CF, Levy T, Kudelka AP, et al. Phase II study of irinotecan in prior chemotherapy-treated squamous cell carcinoma of the cervix. *J Clin Oncol*. 1997;15(2):625-631. doi:10.1200/JCO.1997.15.2.625
- 109e. Giaccone G, Kim C, Thompson J, et al. Pembrolizumab in patients with thymic carcinoma: a single-arm, single-centre, phase 2 study. *Lancet Oncol*. 2018;19(3):347-355. doi:10.1016/S1470-2045(18)30062-7.
- 110e. Cho J, Kim HS, Ku BM, et al. Pembrolizumab for Patients With Refractory or Relapsed Thymic Epithelial Tumor: An Open-Label Phase II Trial. *J Clin Oncol*. 2018 Jun 15;JCO2017773184. Doi: 10.1200/JCO.2017.77.3184. [Epub ahead of print].
- 111e. Sato J, Satouchi M, Itoh S, et al. Lenvatinib in patients with advanced or metastatic thymic carcinoma (REMORA): a multicentre, phase 2 trial. *Lancet Oncol*. 2020;21(6):843-850. doi:10.1016/S1470-2045(20)30162-5.
- 112e. Thieke C, Nicolay N, Sterzing F, et al. Long-term results in malignant pleural mesothelioma treated with neoadjuvant chemotherapy, extrapleural pneumonectomy and intensity-modulated radiotherapy. *Radiat Oncol*. 2015 Dec 30;10:267.
- 113e. Chu Q, Perrone F, Greillier L, et al. Pembrolizumab plus chemotherapy versus chemotherapy in untreated advanced pleural mesothelioma in Canada, Italy, and France: a phase 3, open-label, randomised controlled trial. *Lancet*. 2023 Dec 16;402(10419):2295-2306.
- 114e. Baas P, Scherpereel A, Nowak AK, et al. First-line nivolumab plus ipilimumab in unresectable malignant pleural mesothelioma (CheckMate 743): a multicentre, randomised, open-label,

phase 3 trial [published correction appears in *Lancet*. 2021 Feb 20;397(10275):670. doi: 10.1016/S0140-6736(21)00369-X]. *Lancet*. 2021;397(10272):375-386.

- 115e. Zalcman G, Mazieres J, Margery J, et al.; French Cooperative Thoracic Intergroup (IFCT). Bevacizumab for newly diagnosed pleural mesothelioma in the Mesothelioma Avastin Cisplatin Pemetrexed Study (MAPS): a randomised, controlled, open-label, phase 3 trial. *Lancet*. 2016 Apr 2;387(10026):1405-1414.
- 116e. Raghav KPS, Overman MJ, Liu S, et al. A phase II trial of atezolizumab and bevacizumab in patients with relapsed/refractory and unresectable malignant peritoneal mesothelioma. *J Clin Oncol* 2020;38:9013-9013.
- 117e. Kepenekian V, Elias D, Passot G, et al.; French Network for Rare Peritoneal Malignancies (RENAPE). Diffuse malignant peritoneal mesothelioma: Evaluation of systemic chemotherapy with comprehensive treatment through the RENAPE Database: Multi-Institutional Retrospective Study. *Eur J Cancer*. 2016 Sep;65:69-79.
- 118e. Makino K, Nakamura H, Hide T, Kuratsu J. Salvage treatment with temozolomide in refractory or relapsed primary central nervous system lymphoma and assessment of the MGMT status. *J Neurooncol*. 2012 Jan;106(1):155-60.
- 119e. Ceresoli GL, Zucali PA, De Vincenzo F, et al. Retreatment with pemetrexed-based chemotherapy in patients with malignant pleural mesothelioma. *Lung Cancer*. 2011 Apr;72(1):73-7.
- 120e. Lee KK, Morris JC, 3rd, Kumar A, et al. Pemetrexed-carboplatin salvage therapy in advanced thyroid cancers. *Head Neck* 2024;47:813-821.
- 121e. Prime Therapeutics Management. Pemetrexed Clinical Literature Review Analysis. Last updated November 2025. Accessed November 2025.

### Appendix A – Non-Quantitative Treatment Limitations (NQTL) Factor Checklist

Non-quantitative treatment limitations (NQTLs) refer to the methods, guidelines, standards of evidence, or other conditions that can restrict how long or to what extent benefits are provided under a health plan. These may include things like utilization review or prior authorization. The utilization management NQTL applies comparably, and not more stringently, to mental health/substance use disorder (MH/SUD) Medical Benefit Prescription Drugs and medical/surgical (M/S) Medical Benefit Prescription Drugs. The table below lists the factors that were considered in designing and applying prior authorization to this drug/drug group, and a summary of the conclusions that Prime’s assessment led to for each.

Factor	Conclusion
Indication	Yes: Consider for PA
Safety and efficacy	No: PA not a priority
Potential for misuse/abuse	No: PA not a priority
Cost of drug	Yes: Consider for PA

## 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
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
C52	Malignant neoplasm of vagina
C53.0	Malignant neoplasm of endocervix
C53.1	Malignant neoplasm of exocervix
C53.8	Malignant neoplasm of overlapping sites of cervix uteri
C53.9	Malignant neoplasm of cervix uteri, unspecified

ICD-10	ICD-10 Description
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
C79.31	Secondary malignant neoplasm of brain
C79.32	Secondary malignant neoplasm of cerebral meninges
C83.30	Diffuse large B-cell lymphoma unspecified site
C83.390	Primary central nervous system lymphoma
C83.398	Diffuse large B-cell lymphoma of other extranodal and solid organ sites
C83.59	Lymphoblastic (diffuse) lymphoma, extranodal and solid organ sites
C83.79	Burkitt lymphoma, extranodal and solid organ sites
C83.80	Other non-follicular lymphoma, unspecified site
C83.89	Other non-follicular lymphoma, extranodal and solid organ sites
C84.49	Peripheral T-cell lymphoma, not elsewhere classified, 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
D38.4	Neoplasm of uncertain behavior of thymus

ICD-10	ICD-10 Description
Z85.118	Personal history of other malignant neoplasm of bronchus and lung
Z85.238	Personal history of other malignant neoplasm of thymus
Z85.43	Personal history of malignant neoplasm of ovary

## 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