Tecentriq® (atezolizumab)
(Intravenous)

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Document Number: MODA-0388

Last Review Date: 04/06/2021
Date of Origin: 08/05/2019
Dates Reviewed: 08/2019, 10/2019, 01/2020, 04/2020, 07/2020, 09/2020, 01/2021, 04/2021

I. Length of Authorization

Coverage will be provided for six months and may be renewed.

II. Dosing Limits

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

- Tecentriq 1,200 mg single use vial: 1 vial per 21 days
- Tecentriq 840 mg single-use vial: 1 vial per 14 days

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

- 168 billable units every 28 days

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

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

Universal Criteria

- Patient has not received previous therapy with a programmed death (PD-1/PD-L1)-directed therapy (e.g., nivolumab, pembrolizumab, durvalumab, avelumab, cemiplimab, etc.) unless otherwise specified; **AND**

Urothelial Carcinoma (Bladder Cancer) † [4,10,2e,3e]

- Used as a single agent; **AND**
- Patient has one of the following diagnoses:
  - Locally advanced or metastatic urothelial carcinoma; **OR**
  - Muscle invasive bladder cancer with local recurrence or persistent disease in a preserved bladder ‡; **OR**
  - Metastatic or local bladder cancer recurrence post-cystectomy ‡; **OR**
  - Primary carcinoma of the urethra ‡; **AND**

        - Used for recurrent *(excluding recurrence of stage T3-4 disease or palpable inguinal lymph nodes)* or metastatic disease; **OR**
        - Used for stage T3-4, cN1-2 disease or cN1-2 palpable inguinal lymph nodes (first-line therapy only); **OR**
    - Metastatic upper genitourinary (GU) tract tumors ‡; **OR**
    - Metastatic urothelial carcinoma of the prostate ‡; **AND**
- Used as subsequent therapy after previous platinum treatment*; **OR**
- Used as first-line therapy in cisplatin-ineligible patients*; **AND**
    - Patient is carboplatin-ineligible*; **OR**
    - Patient has a PD-L1 expression of ≥ 5% *(PD-L1 stained tumor-infiltrating immune cells [IC] covering ≥ 5% of the tumor area)* as determined by an FDA-approved or CLIA-compliant test❖

* ***Note:*** [7,9]
– *If platinum treatment occurred greater than 12 months ago, the patient should be re-treated with platinum-based therapy if the patient is still platinum eligible (see below for cisplatin- or carboplatin-ineligible comorbidities).*
▪ *Cisplatin-ineligible comorbidities may include the following: GFR < 60 mL/min, PS ≥ 2, hearing loss of ≥ 25 decibels (dB) at two contiguous frequencies, or grades ≥ 2 peripheral neuropathy. Carboplatin may be substituted for cisplatin particularly in those patients with a GFR <60 mL/min or a PS of 2.*
▪ *Carboplatin-ineligible comorbidities may include the following: GFR < 30 mL/min, PS ≥ 3, grade ≥ 3 peripheral neuropathy, or NYHA class ≥ 3, etc.*

Breast Cancer † [1,6,13,20]

- Used in combination with albumin-bound paclitaxel; **AND**
- Used as first-line therapy for unresectable locally advanced, recurrent, or metastatic triple-negative disease (TNBC); **AND**
- Patient has a PD-L1 expression *(PD-L1 stained tumor-infiltrating immune cells [IC] of any intensity covering ≥ 1% of the tumor area)* as determined by an FDA-approved or CLIA-compliant test❖

Non-Small Cell Lung Cancer (NSCLC) † ‡ § [1,5,6,8,11,12,17,9e-11e,14e]

- Patient has recurrent, advanced, or metastatic disease (excluding locoregional recurrence or symptomatic local disease without evidence of disseminated disease) or mediastinal lymph node recurrence with prior radiation therapy; **AND**
    - Used as first-line therapy; **AND**
        - Used for EGFR, ALK, ROS1, BRAF, NTRK1/2/3 gene fusion, MET exon 14 skipping mutation, and RET rearrangement negative* tumors and PD-L1 ≥50% (*PD-L1 stained ≥ 50% of tumor cells [TC ≥ 50%] or PD-L1 stained tumor-infiltrating immune cells [IC] covering ≥ 10% of the tumor area [IC ≥ 10%]*), as determined by an FDA-approved test or CLIA-compliant test❖; **AND**
            - Used as a single agent; **OR**
        - Used for non-squamous disease as one of the following:

- Used in patients with PS 0-1 for EGFR, ALK, ROS1, BRAF, NTRK1/2/3 gene fusion, MET exon 14 skipping mutation, and RET rearrangement negative* tumors and PD-L1 <1% (TC or IC <1%)
- Used in patients with PS 0-2 for EGFR, ALK, ROS1, BRAF, NTRK1/2/3 gene fusion, MET exon 14 skipping mutation, and RET rearrangement negative* tumors and PD-L1 ≥1% (TC or IC ≥1%)
- Used in patients with PS 0-1 for BRAF V600E-mutation, NTRK1/2/3 gene fusion, MET exon-14 skipping mutation, or RET rearrangement positive tumors; **AND**

➢ Used in combination with:

- Carboplatin, paclitaxel, and bevacizumab; **OR**
- Carboplatin and albumin-bound paclitaxel; **OR**

- Used as subsequent therapy; **AND**
  - Used as a single agent; **OR**
  - Used for non-squamous disease as one of the following:
    - Used in patients with PS 0-1 for BRAF V600E-mutation, NTRK1/2/3 gene fusion, MET exon-14 skipping mutation, or RET rearrangement positive tumors
    - Used in patients with PS 0-1 EGFR, ALK, or ROS1 positive tumors and prior targeted therapy§; **AND**

    ➢ Used in combination with:

    - Carboplatin, paclitaxel, and bevacizumab; **OR**
    - Carboplatin and albumin-bound paclitaxel; **OR**
- Used as continuation maintenance therapy in patients who have achieved a tumor response or stable disease following initial therapy; **AND**
  - Used in combination with bevacizumab following a first-line regimen with atezolizumab, carboplatin, paclitaxel, and bevacizumab regimen for non-squamous histology; **OR**
  - Used as a single agent following a first-line regimen with atezolizumab, carboplatin, and albumin-bound paclitaxel regimen for non-squamous histology; **OR**
  - Used as a single agent following a first-line regimen with single agent atezolizumab

** Note: If there is insufficient issue to allow testing for all of EGFR, 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.*

Small Cell Lung Cancer (SCLC) † ‡ Φ [1,6,14,18]

- Patient has extensive stage disease (ES-SCLC) *(excluding patients with poor PS 3-4 not due to SCLC)*; **AND**
  - Used as first-line therapy in combination with etoposide and carboplatin; **OR**

- Used as single-agent maintenance therapy after initial therapy with etoposide and carboplatin

Hepatocellular Carcinoma (HCC) ‡ [1,6,15,16,22]

- Used as first-line therapy in combination with bevacizumab; **AND**
- Patient has Child-Pugh Class A disease; **AND**
- Patient has locally advanced, unresectable, inoperable, or metastatic disease

Cutaneous Melanoma † [1,6,19,21]

- Patient has BRAF V600 mutation positive disease; **AND**
- Patient has unresectable or metastatic disease*; **AND**
- Used as first-line therapy in combination with cobimetinib and vemurafenib

** Metastatic disease includes stage III clinical satellite/in transit metastases or local satellite/in-transit recurrence in patients with limited resectable and unresectable disease, unresectable nodal recurrence, and disseminated (unresectable) distant 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.

❖ *If confirmed using an FDA approved assay - http://www.fda.gov/companiondiagnostics*

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

Genomic Aberration/Mutational Driver Targeted Therapies (Note: *not all inclusive, refer to guidelines for appropriate use*) §
Sensitizing *EGFR* mutation-positive tumors – Afatinib – Erlotinib – Dacomitinib – Gefitinib – Osimertinib
ALK rearrangement-positive tumors – Alectinib – Brigatinib – Ceritinib – Crizotinib – Lorlatinib
ROS1 rearrangement-positive tumors – Ceritinib – Crizotinib – Entrectinib
BRAF V600E-mutation positive tumors – Dabrafenib ± Trametinib – Vemurafenib
NTRK Gene Fusion positive tumors – Larotrectinib

– Entrectinib
PD-1/PD-L1 expression-positive tumors (≥1%) – Pembrolizumab – Atezolizumab – Nivolumab ± ipilimumab
MET Exon-14 skipping mutations – Capmatinib – Crizotinib
RET rearrangement-positive tumors – Selpercatinib – Cabozantinib – Vandetanib

IV. Renewal Criteria [1,4-8,10-16]

Coverage can be renewed based upon the following criteria:

- Patient continues to meet the criteria identified in section III; **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include immune-mediated adverse reactions (e.g., pneumonitis, hepatitis, colitis, endocrinopathies, nephritis/renal dysfunction, rash/dermatitis, etc.), severe infusion-related reactions, etc.

Continuation Maintenance Therapy for NSCLC or SCLC

- *Refer to Section III for criteria*

V. Dosage/Administration [1,16]

Indication	Dose
NSCLC, Breast Cancer (TNBC), SCLC, HCC, Urothelial Carcinoma (UC)	The recommended dosage is administered intravenously until disease progression or unacceptable toxicity: – 840 mg every 2 weeks or – 1200 mg every 3 weeks or – 1680 mg every 4 weeks
Cutaneous Melanoma	The recommended dosage is administered intravenously until disease progression or unacceptable toxicity: – 840 mg every 2 weeks or – 1200 mg every 3 weeks or – 1680 mg every 4 weeks **Prior to initiating TECENTRIQ, patients should receive a 28 day treatment cycle of cobimetinib 60 mg orally once daily (21 days on and 7 days off) and vemurafenib 960 mg orally twice daily from Days 1-21 and vemurafenib 720 mg orally twice daily from Days 22-28.*

VI. Billing Code/Availability Information

HCPCS Code:

- J9022 – Injection, atezolizumab, 10 mg; 10 mg = 1 billable unit

NDC:

- Tecentriq 1200 mg/20 mL single-dose vial: 50242-0917-xx
- Tecentriq 840 mg/14 mL single-dose vial: 50242-0918-xx

VII. References (STANDARD)

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Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C22.0	Liver cell carcinoma
C22.8	Malignant neoplasm of liver, primary, unspecified as to type
C22.9	Malignant neoplasm of liver, not specified as primary or secondary
C33	Malignant neoplasm of trachea
C34.00	Malignant neoplasm of unspecified main bronchus
C34.01	Malignant neoplasm of right main bronchus
C34.02	Malignant neoplasm of left main bronchus
C34.10	Malignant neoplasm of upper lobe, unspecified bronchus or lung
C34.11	Malignant neoplasm of upper lobe, right bronchus or lung
C34.12	Malignant neoplasm of upper lobe, left bronchus or lung
C34.2	Malignant neoplasm of middle lobe, bronchus or lung
C34.30	Malignant neoplasm of lower lobe, unspecified bronchus or lung
C34.31	Malignant neoplasm of lower lobe, right bronchus or lung
C34.32	Malignant neoplasm of lower lobe, left bronchus or lung
C34.80	Malignant neoplasm of overlapping sites of unspecified bronchus and lung
C34.81	Malignant neoplasm of overlapping sites of right bronchus and lung
C34.82	Malignant neoplasm of overlapping sites of left bronchus and lung

ICD-10	ICD-10 Description
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
C43.0	Malignant melanoma of lip
C43.10	Malignant melanoma of unspecified eyelid, including canthus
C43.11	Malignant melanoma of right eyelid, including canthus
C43.12	Malignant melanoma of left eyelid, including canthus
C43.111	Malignant melanoma of right upper eyelid, including canthus
C43.112	Malignant melanoma of right lower eyelid, including canthus
C43.121	Malignant melanoma of left upper eyelid, including canthus
C43.122	Malignant melanoma of left lower eyelid, including canthus
C43.20	Malignant melanoma of unspecified ear and external auricular canal
C43.21	Malignant melanoma of right ear and external auricular canal
C43.22	Malignant melanoma of left ear and external auricular canal
C43.30	Malignant melanoma of unspecified part of face
C43.31	Malignant melanoma of nose
C43.39	Malignant melanoma of other parts of face
C43.4	Malignant melanoma of scalp and neck
C43.51	Malignant melanoma of anal skin
C43.52	Malignant melanoma of skin of breast
C43.59	Malignant melanoma of other part of trunk
C43.60	Malignant melanoma of unspecified upper limb, including shoulder
C43.61	Malignant melanoma of right upper limb, including shoulder
C43.62	Malignant melanoma of left upper limb, including shoulder
C43.70	Malignant melanoma of unspecified lower limb, including hip
C43.71	Malignant melanoma of right lower limb, including hip
C43.72	Malignant melanoma of left lower limb, including hip
C43.8	Malignant melanoma of overlapping sites of skin
C43.9	Malignant melanoma of skin, unspecified
C50.011	Malignant neoplasm of nipple and areola, right female breast
C50.012	Malignant neoplasm of nipple and areola, left female breast
C50.019	Malignant neoplasm of nipple and areola, unspecified female breast
C50.021	Malignant neoplasm of nipple and areola, right male breast
C50.022	Malignant neoplasm of nipple and areola, left male breast

ICD-10	ICD-10 Description
C50.029	Malignant neoplasm of nipple and areola, unspecified male breast
C50.111	Malignant neoplasm of central portion of right female breast
C50.112	Malignant neoplasm of central portion of left female breast
C50.119	Malignant neoplasm of central portion of unspecified female breast
C50.121	Malignant neoplasm of central portion of right male breast
C50.122	Malignant neoplasm of central portion of left male breast
C50.129	Malignant neoplasm of central portion of unspecified male breast
C50.211	Malignant neoplasm of upper-inner quadrant of right female breast
C50.212	Malignant neoplasm of upper-inner quadrant of left female breast
C50.219	Malignant neoplasm of upper-inner quadrant of unspecified female breast
C50.221	Malignant neoplasm of upper-inner quadrant of right male breast
C50.222	Malignant neoplasm of upper-inner quadrant of left male breast
C50.229	Malignant neoplasm of upper-inner quadrant of unspecified male breast
C50.311	Malignant neoplasm of lower-inner quadrant of right female breast
C50.312	Malignant neoplasm of lower-inner quadrant of left female breast
C50.319	Malignant neoplasm of lower-inner quadrant of unspecified female breast
C50.321	Malignant neoplasm of lower-inner quadrant of right male breast
C50.322	Malignant neoplasm of lower-inner quadrant of left male breast
C50.329	Malignant neoplasm of lower-inner quadrant of unspecified male breast
C50.411	Malignant neoplasm of upper-outer quadrant of right female breast
C50.412	Malignant neoplasm of upper-outer quadrant of left female breast
C50.419	Malignant neoplasm of upper-outer quadrant of unspecified female breast
C50.421	Malignant neoplasm of upper-outer quadrant of right male breast
C50.422	Malignant neoplasm of upper-outer quadrant of left male breast
C50.429	Malignant neoplasm of upper-outer quadrant of unspecified male breast
C50.511	Malignant neoplasm of lower-outer quadrant of right female breast
C50.512	Malignant neoplasm of lower-outer quadrant of left female breast
C50.519	Malignant neoplasm of lower-outer quadrant of unspecified female breast
C50.521	Malignant neoplasm of lower-outer quadrant of right male breast
C50.522	Malignant neoplasm of lower-outer quadrant of left male breast
C50.529	Malignant neoplasm of lower-outer quadrant of unspecified male breast
C50.611	Malignant neoplasm of axillary tail of right female breast
C50.612	Malignant neoplasm of axillary tail of left female breast
C50.619	Malignant neoplasm of axillary tail of unspecified female breast

ICD-10	ICD-10 Description
C50.621	Malignant neoplasm of axillary tail of right male breast
C50.622	Malignant neoplasm of axillary tail of left male breast
C50.629	Malignant neoplasm of axillary tail of unspecified male breast
C50.811	Malignant neoplasm of overlapping sites of right female breast
C50.812	Malignant neoplasm of overlapping sites of left female breast
C50.819	Malignant neoplasm of overlapping sites of unspecified female breast
C50.821	Malignant neoplasm of overlapping sites of right male breast
C50.822	Malignant neoplasm of overlapping sites of left male breast
C50.829	Malignant neoplasm of overlapping sites of unspecified male breast
C50.911	Malignant neoplasm of unspecified site of right female breast
C50.912	Malignant neoplasm of unspecified site of left female breast
C50.919	Malignant neoplasm of unspecified site of unspecified female breast
C50.921	Malignant neoplasm of unspecified site of right male breast
C50.922	Malignant neoplasm of unspecified site of left male breast
C50.929	Malignant neoplasm of unspecified site of unspecified male breast
C61	Malignant neoplasm of prostate
C65.1	Malignant neoplasm of right renal pelvis
C65.2	Malignant neoplasm of left renal pelvis
C65.9	Malignant neoplasm of unspecified renal pelvis
C66.1	Malignant neoplasm of right ureter
C66.2	Malignant neoplasm of left ureter
C66.9	Malignant neoplasm of unspecified ureter
C67.0	Malignant neoplasm of trigone of bladder
C67.1	Malignant neoplasm of dome of bladder
C67.2	Malignant neoplasm of lateral wall of bladder
C67.3	Malignant neoplasm of anterior wall of bladder
C67.4	Malignant neoplasm of posterior wall of bladder
C67.5	Malignant neoplasm of bladder neck
C67.6	Malignant neoplasm of ureteric orifice
C67.7	Malignant neoplasm of urachus
C67.8	Malignant neoplasm of overlapping sites of bladder
C67.9	Malignant neoplasm of bladder, unspecified
C68.0	Malignant neoplasm of urethra
C7A.1	Malignant poorly differentiated neuroendocrine tumors

ICD-10	ICD-10 Description
C78.00	Secondary malignant neoplasm of unspecified lung
C78.01	Secondary malignant neoplasm of right lung
C78.02	Secondary malignant neoplasm of left lung
C79.31	Secondary malignant neoplasm of brain
C79.51	Secondary malignant neoplasm of bone
C79.52	Secondary malignant neoplasm of bone marrow
D09.0	Carcinoma in situ of bladder
Z85.118	Personal history of other malignant neoplasm of bronchus and lung
Z85.51	Personal history of malignant neoplasm of bladder
Z85.59	Personal history of malignant neoplasm of other urinary tract organ

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: http://www.cms.gov/medicare-coverage-database/search/advanced-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, 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, 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

Appendix 3 – CLINICAL LITERATURE REVIEW

OS = overall survival; PFS = progression-free survival; ORR = objective response rate; CR = complete response; PR = partial response; DoR = duration of response; TTP = time to progression; FFS = failure-free survival; EFS = event-free survival; PFR = progression free rate

Bladder Cancer/Urothelial Carcinoma

First-line in cisplatin-ineligible patients							
Regimen	**NCCN Category**	**FDA Approved**	**Trial Design**	**Comparator**	**Primary End-Point**	**Line of Therapy**	**Conclusion**
Atezolizumab	2A preferred	Yes	Phase 2 (IMvigor210 – Cohort 1), single-arm, multi-center	N/A	ORR	First-line	• Atezolizumab was associated with an ORR of 23% and with a median OS of 15.9 months.
Atezolizumab or Atezolizumab + gemcitabine + carboplatin (or cisplatin)	2A preferred	Yes	Phase 3 (IMvigor130), multi-center, randomized, placebo-controlled *Ongoing*	Placebo + gemcitabine + carboplatin (or cisplatin)	PFS OS	First-line in cisplatin-eligible and cisplatin-ineligible	• PD-L1 < 5% treated with atezolizumab monotherapy had decreased survival compared to patients receiving platinum-based chemotherapy • It was recommended to close the monotherapy arm to further accrual of patients with low PD-L1
Pembrolizumab	2A preferred	Yes	Phase 2 (KEYNOTE-052), open-label	N/A	ORR	First-line	• Results from the KEYNOTE-052 study showed pembrolizumab elicits an ORR of 27% and durable responses with a 6-month OS rate of 67% in cisplatin-ineligible patients with urothelial carcinoma.

Avelumab + best supportive care	1 preferred as first-line maintenance therapy	Yes as maintenance treatment	Phase 3 (JAVELIN Bladder 100), randomized, multi-center, open-label	Best supportive care (BSC)	OS	Patients without progression on platinum-based induction chemotherapy (4-6 cycles of gemcitabine + cisplatin or carboplatin)	• First-line maintenance therapy with avelumab in patients with advanced urothelial cancer whose disease has not progressed with platinum-based induction chemotherapy demonstrated a significantly longer OS compared to best supportive care in both overall and PD-L1-positive populations.
Gemcitabine + carboplatin	2A preferred	No	Phase 2/3 (EORTC Study 30986), randomized	Methotrexate + carboplatin + vinblastine (M-CAVI)	OS	Chemo-naïve Cisplatin-ineligible (GFR between 30-60mL/min and/or ECOG ≥2)	• There were no significant differences in efficacy between the two treatment groups. The incidence of severe acute toxicities was higher for those receiving M-CAVI.
Subsequent therapy after previous platinum treatment							
Regimen	**NCCN Category**	**FDA Approved**	**Trial Design**	**Comparator**	**Primary End-Point**	**Line of Therapy**	**Conclusion**
Atezolizumab	2A alternative preferred (post-platinum)	Yes	Phase 2 (IMvigor210 – Cohort 2), single-arm, multicenter	N/A	ORR	Subsequent therapy after platinum-based therapy	• Atezolizumab showed durable activity with an ORR of 15% and good tolerability. Increased levels of PD-L1 expression on immune cells were associated with increased response.
Atezolizumab	2A alternative preferred (post-platinum)	Yes	Phase 3 (IMvigor211), randomized, controlled	Chemotherapy (vinflunine, paclitaxel, or docetaxel)	OS in patients with PD-L1 ≥5%	After platinum-therapy	• Atezolizumab was not associated with significantly longer overall survival than chemotherapy in patients with platinum-refractory metastatic urothelial carcinoma overexpressing PD-L1 (IC2/3).

							However, the safety profile for atezolizumab was favorable compared with chemotherapy.
Pembrolizumab	1 preferred (post-platinum)	Yes	Phase 3 (KEYNOTE-045), open-label, international	Investigator's choice (IC) of chemotherapy with paclitaxel, docetaxel, or vinflunine	OS PFS	After platinum-therapy	• Pembrolizumab was associated with significantly longer overall survival (by approximately 3 months) and with a lower rate of treatment-related adverse events than chemotherapy as second-line therapy for platinum-refractory advanced urothelial carcinoma
Nivolumab	2A alternative preferred (post-platinum)	Yes	Phase 2 (CheckMate 275), multicenter, single-arm	N/A	ORR	Subsequent therapy after platinum-based therapy	• Nivolumab monotherapy provided meaningful clinical benefit, with an ORR of 19.6% irrespective of PD-L1 expression, and was associated with an acceptable safety profile in previously treated patients with metastatic or surgically unresectable urothelial carcinoma
Avelumab	2A alternative preferred (post-platinum)	Yes	Pooled results from two expansion cohorts of an open-label, phase 1 trial (JAVELIN Solid Tumor)	N/A	ORR	Subsequent therapy after platinum-based therapy	• Avelumab showed anti-tumor activity with an ORR of 17% in the treatment of patients with platinum-refractory metastatic urothelial carcinoma; a manageable safety profile was reported in all avelumab-treated patients
Erdafitinib	2A alternative preferred (post-platinum,	Yes (for FGFR3 or FGFR2	Phase 2 (BLC2001), open-label	N/A	ORR	After ≥ 1 line of prior chemo or ≤ 12 mon of [neo]adjuvant	• Treatment with erdafitinib yielded an ORR of 42% and was tolerable in patients with chemorefractory metastatic

	FGFR3 or FGFR2 genetic alterations)	genetic alterations)				chemo, or were cisplatin ineligible, chemo naïve	urothelial carcinoma and FGFR generic alterations.

Breast Cancer

Triple-negative disease - Unresectable locally advanced, recurrent, or metastatic disease							
Regimen	**NCCN Category**	**FDA Approved**	**Trial Design**	**Comparator**	**Primary End-Point**	**Line of Therapy**	**Conclusion**
Atezolizumab + nab-paclitaxel	1 preferred (first-line) 1 (subsequent)	Yes (for PD-L1-positive triple negative breast cancer)	Phase 3 (IMpassion130), randomized	Nab-paclitaxel + placebo	PFS OS	Treatment naïve metastatic disease	• Atezolizumab plus nab-paclitaxel prolonged progression-free survival among patients with metastatic triple-negative breast cancer in both the intention-to-treat population and the PD-L1–positive subgroup.
Pembrolizumab + chemotherapy (taxane or platinum-based therapy)	1 preferred	Yes for PD-L1 (CPS ≥10)	Phase 3 (KEYNOTE-355), randomized, double-blind	Placebo + chemotherapy	PFS	First-line; ≥6 months disease free interval	• Pembrolizumab combined with several chemotherapy partners showed a statistically significant and clinically meaningful improvement in PFS vs chemo alone in patients with previously untreated locally recurrent inoperable or metastatic TNBC whose tumors expressed PD-L1 (CPS ≥10). Pembrolizumab + chemotherapy was generally well tolerated, with no new safety concerns.

Non-Small Cell Lung Cancer (NSCLC)

Squamous recurrent, advanced, or metastatic disease – First-line therapy							
Regimen	**NCCN Category**	**FDA Approved**	**Trial Design**	**Comparator**	**Primary End-Point**	**Line of Therapy**	**Conclusion**
Atezolizumab	1 preferred for PD-L1 ≥50%	Yes for TC ≥50% or IC ≥10%	Phase 3 (IMpower110), randomized, open-label	Carboplatin or cisplatin + pemetrexed (non-squamous) or gemcitabine (squamous)	OS	First-line	• IMpower110 met the primary OS endpoint with statistically significant and clinically meaningful improvement as first-line therapy in patients with TC ≥50% or IC ≥10%.
Cemiplimab-rwlc	1 preferred for PD-L1 ≥50%	Yes for TPS ≥50%	Phase 3 (EMPOWER-Lung 1), randomized, multi-center, open-label, controlled	Platinum-doublet chemotherapy	OS PFS	First-line	• Cemiplimab monotherapy significantly improved overall survival and progression-free survival compared with chemotherapy in patients with advanced non-small-cell lung cancer with PD-L1 of at least 50%.
Nonsquamous recurrent, advanced, or metastatic disease – First-line therapy							
Regimen	**NCCN Category**	**FDA Approved**	**Trial Design**	**Comparator**	**Primary End-Point**	**Line of Therapy**	**Conclusion**
Atezolizumab	1 preferred for PD-L1 ≥50%	Yes for TC ≥50% or IC ≥10%	Phase 3 (IMpower110), randomized, open-label	Carboplatin or cisplatin + pemetrexed (non-squamous) or gemcitabine (squamous)	OS	First-line	• IMpower110 met the primary OS endpoint with statistically significant and clinically meaningful improvement as first-line therapy in patients with TC ≥50% or IC ≥10%.
Atezolizumab + carboplatin +	1 other (for adeno-	Yes	Phase 3 (IMpower150),	Atezolizumab + carboplatin +	PFS	First-line	• The addition of atezolizumab to bevacizumab plus chemotherapy

paclitaxel + bevacizumab (ABCP), followed by atezolizumab, bevacizumab, or both	carcinoma only; PS 0-1)		open-label, randomized (1:1:1)	paclitaxel (ACP), followed by atezolizumab vs. bevacizumab + carboplatin + paclitaxel (BCP), followed by bevacizumab			significantly improved progression-free survival and overall survival among patients with metastatic nonsquamous NSCLC, regardless of PD-L1 expression and EGFR or ALK genetic alteration status
Atezolizumab + carboplatin + nab-paclitaxel, followed by atezolizumab maintenance	2A other	Yes	Phase 3 (IMpower130), randomized, multi-center, open-label	Carboplatin + paclitaxel	PFS OS	First-line for stage IV disease	• IMpower130 showed a significant and clinically meaningful improvement in overall survival and a significant improvement in progression-free survival with atezolizumab plus chemotherapy versus chemotherapy as first-line treatment of patients with stage IV non-squamous non-small-cell lung cancer and no ALK or EGFR mutations.
Pembrolizumab	1 preferred (for PD-L1 ≥ 50%)	Yes	Phase 3 (KEYNOTE-024), open-label, randomized	Platinum-based chemotherapy	PFS	First-line	• In patients with advanced NSCLC and PD-L1 expression on at least 50% of tumor cells, pembrolizumab was associated with significantly longer progression-free and overall survival and with fewer adverse events than was platinum-based chemotherapy
Cemiplimab-rwlc	1 preferred for PD-L1 ≥50%	Yes for TPS ≥50%	Phase 3 (EMPOWER-Lung 1), randomized, multi-center, open-label, controlled	Platinum-doublet chemotherapy	OS PFS	First-line	• Cemiplimab monotherapy significantly improved overall survival and progression-free survival compared with chemotherapy in patients with advanced non-small-cell lung cancer with PD-L1 of at least 50%.

Pembrolizumab + carboplatin (or cisplatin) + pemetrexed, followed by pembrolizumab + pemetrexed (for up to 35 cycles)	1 preferred	Yes	Phase 3 (KEYNOTE-189), double-blind, randomized (2:1)	Carboplatin (or cisplatin) + pemetrexed + placebo, followed by placebo + pemetrexed (for up to 35 cycles)	OS PFS	First-line	• In patients with previously untreated metastatic nonsquamous NSCLC without EGFR or ALK mutations, the addition of pembrolizumab to standard chemotherapy of pemetrexed and a platinum-based drug resulted in significantly longer overall survival and progression-free survival than chemotherapy alone regardless of PD-L1 expression levels.
Nivolumab + ipilimumab	2A (certain circumstances)	Yes for PD-L1 ≥1%	Phase 3 (CheckMate-227), randomized, open-label	Platinum-doublet chemotherapy	OS PFS	First-line	• First-line treatment with nivolumab plus ipilimumab resulted in a longer duration of overall survival than did chemotherapy in patients with NSCLC, independent of the PD-L1 expression level.
Nivolumab + ipilimumab + 2 cycles platinum doublet chemotherapy	2A other	Yes	Phase 3 (CheckMate-9LA), randomized	Chemotherapy	OS	First-line	• CheckMate 9LA met its primary endpoint. A statistically significant improvement in OS was observed with nivolumab + ipilimumab + chemotherapy versus chemotherapy alone in first-line advanced NSCLC.
Recurrent, advanced, or metastatic disease – Subsequent therapy							
Regimen	**NCCN Category**	**FDA Approved**	**Trial Design**	**Comparator**	**Primary End-Point**	**Line of Therapy**	**Conclusion**
Atezolizumab	1 (for first progression) 2A (for subsequent progression)	Yes (after platinum therapy)	Phase 3 (OAK), open-label, multicenter randomized (1:1)	Docetaxel	OS	Second- or third-line	• Atezolizumab treatment results in a statistically significant and clinically relevant improvement in OS versus docetaxel in second- and third-line NSCLC, regardless of PD-L1 expression and histology

Nivolumab	1 (for first progression) 2A (for subsequent progression)	Yes	Phase 3 (CheckMate 057), randomized, open-label	Docetaxel	OS	Subsequent	• Among patients with advanced nonsquamous NSCLC that had progressed during or after platinum-based chemotherapy, overall survival was longer with nivolumab than with docetaxel
Pembrolizumab (2mg/kg or 10mg/kg)	1 preferred (for PS 0-2; PD-L1 ≥ 1%)	Yes (after platinum therapy)	Phase 2/3 (KEYNOTE-010), randomized (1:1:1), open-label	Docetaxel	OS PFS	Previously treated	• Pembrolizumab prolongs overall survival compared to docetaxel and has a favorable benefit-to-risk profile in patients with previously treated, PD-L1-positive, advanced non-small-cell lung cancer.
Recurrent, advanced, or metastatic disease – Continuation maintenance therapy							
Regimen	**NCCN Category**	**FDA Approved**	**Trial Design**	**Comparator**	**Primary End-Point**	**Line of Therapy**	**Conclusion**
Atezolizumab + carboplatin + paclitaxel + bevacizumab (ABCP), followed by atezolizumab, bevacizumab, or both	1 (for adeno-carcinoma only)	Yes	Phase 3 (IMpower150), open-label, randomized (1:1:1)	Atezolizumab + carboplatin + paclitaxel (ACP), followed by atezolizumab vs. bevacizumab + carboplatin + paclitaxel (BCP), followed by bevacizumab	PFS	First-line, continuation maintenance	• The addition of atezolizumab to bevacizumab plus chemotherapy significantly improved progression-free survival and overall survival among patients with metastatic nonsquamous NSCLC, regardless of PD-L1 expression and EGFR or ALK genetic alteration status

Small Cell Lung Cancer (SCLC)

Initial treatment for extensive stage disease							
Regimen	**NCCN Category**	**FDA Approved**	**Trial Design**	**Comparator**	**Primary End-Point**	**Line of Therapy**	**Conclusion**
Atezolizumab + carboplatin + etoposide, followed by maintenance atezolizumab	1 preferred	Yes	Phase 3 (IMpower133), double-blind, placebo-controlled, randomized	Placebo + carboplatin + etoposide, followed by maintenance placebo	PFS OS	Treatment naïve	• The addition of atezolizumab to chemotherapy in the first-line treatment of extensive-stage small-cell lung cancer resulted in significantly longer overall survival and progression-free survival than chemotherapy alone.
Durvalumab + platinum + etoposide, followed by maintenance durvalumab	1 preferred	Yes	Phase 3 (CASPIAN), randomized, controlled, open-label	Platinum + etoposide	OS	First-line in ES-SCLC	• First-line durvalumab plus platinum-etoposide significantly improved overall survival in patients with ES-SCLC versus a clinically relevant control group.

Hepatocellular Carcinoma (HCC)

First-line therapy							
Regimen	**NCCN Category**	**FDA Approved**	**Trial Design**	**Comparator**	**Primary End-Point**	**Line of Therapy**	**Conclusion**
Bevacizumab + atezolizumab	1 preferred for Child-Pugh Class A only	Yes	Phase 3 (IMbrave150), multicenter, open-label, randomized	Sorafenib	PFS PS	First-line	• In patients with unresectable hepatocellular carcinoma, atezolizumab combined with bevacizumab resulted in better overall and progression-free survival outcomes than sorafenib.

Cutaneous Melanoma

First-line therapy							
Regimen	**NCCN Category**	**FDA Approved**	**Trial Design**	**Comparator**	**Primary End-Point**	**Line of Therapy**	**Conclusion**
Atezolizumab + vemurafenib + cobimetinib	2A other	Yes	Phase 3 (IMspire150), randomized, double-blind, placebo controlled	Placebo + vemurafenib + cobimetinib (control group)	PFS	First-line	• The addition of atezolizumab to targeted therapy with vemurafenib and cobimetinib was safe and tolerable and significantly increased progression-free survival in patients with BRAFV600 mutation-positive advanced melanoma.