

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use TECENTRIQ safely and effectively. See full prescribing information for TECENTRIQ.

TECENTRIQ® (atezolizumab) injection, for intravenous use
Initial U.S. Approval: 2016

RECENT MAJOR CHANGES

| | |
|--|---------|
| Indications and Usage, Urothelial Carcinoma (1.1) | 7/2018 |
| Indications and Usage, Non-Small Cell Lung Cancer (1.2) | 12/2018 |
| Indications and Usage, Triple-Negative Breast Cancer (1.3) | 3/2019 |
| Indications and Usage, Small Cell Lung Cancer (1.4) | 3/2019 |
| Dosage and Administration (2.1, 2.3, 2.4, 2.5, 2.7) | 3/2019 |
| Warnings and Precautions (5.1, 5.2, 5.3, 5.4) | 3/2019 |
| Warnings and Precautions (5.6, 5.7) | 12/2018 |

INDICATIONS AND USAGE

TECENTRIQ is a programmed death-ligand 1 (PD-L1) blocking antibody indicated:

Urothelial Carcinoma

- for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma who:
 - are not eligible for cisplatin-containing chemotherapy and whose tumors express PD-L1 (PD-L1 stained tumor-infiltrating immune cells [IC] covering $\geq 5\%$ of the tumor area), as determined by an FDA-approved test, or
 - are not eligible for any platinum-containing chemotherapy regardless of PD-L1 status, or
 - have disease progression during or following any platinum-containing chemotherapy, or within 12 months of neoadjuvant or adjuvant chemotherapy. (1.1)

This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s). (1.1)

Non-Small Cell Lung Cancer (NSCLC)

- in combination with bevacizumab, paclitaxel, and carboplatin, for the first-line treatment of adult patients with metastatic non-squamous NSCLC with no EGFR or ALK genomic tumor aberrations. (1.2)
- for the treatment of adult patients with metastatic NSCLC who have disease progression during or following platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for NSCLC harboring these aberrations prior to receiving TECENTRIQ. (1.2)

Triple-Negative Breast Cancer (TNBC)

- in combination with paclitaxel protein-bound for the treatment of adult patients with unresectable locally advanced or metastatic TNBC whose tumors express PD-L1 (PD-L1 stained tumor-infiltrating immune cells [IC] of any intensity covering $\geq 1\%$ of the tumor area), as determined by an FDA approved test. This indication is approved under accelerated approval based on progression free survival. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s). (1.3)

Small Cell Lung Cancer (SCLC)

- in combination with carboplatin and etoposide, for the first-line treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC). (1.4)

DOSAGE AND ADMINISTRATION

Urothelial Carcinoma

- TECENTRIQ 1200 mg intravenously over 60 minutes every 3 weeks.

NSCLC

- TECENTRIQ 1200 mg intravenously over 60 minutes every 3 weeks. If administering in combination, administer TECENTRIQ prior to

chemotherapy or other antineoplastic drugs when administered on the same day.

Metastatic Treatment of TNBC

- TECENTRIQ 840 mg IV over 60 minutes, followed by 100 mg/m² paclitaxel protein-bound. For each 28 day cycle, TECENTRIQ is administered on days 1 and 15, and paclitaxel protein-bound is administered on days 1, 8, and 15.

Small Cell Lung Cancer

- TECENTRIQ 1200 mg intravenously over 60 minutes every 3 weeks. When administering in combination, administer TECENTRIQ prior to chemotherapy when administered on the same day.

If the first infusion is tolerated, all subsequent infusions may be delivered over 30 minutes. (2.2, 2.3, 2.4, 2.5)

DOSAGE FORMS AND STRENGTHS

Injection: 840 mg/14 mL (60 mg/mL) and 1200 mg/20 mL (60 mg/mL) solution in a single-dose vial (3)

CONTRAINDICATIONS

None. (4)

WARNINGS AND PRECAUTIONS

- Immune-Mediated Pneumonitis: Withhold or permanently discontinue based on severity of pneumonitis. (2.6, 5.1)
- Immune-Mediated Hepatitis: Monitor for changes in liver function. Withhold or permanently discontinue based on severity of transaminase or total bilirubin elevation. (2.6, 5.2)
- Immune-Mediated Colitis: Withhold or permanently discontinue based on severity of colitis. (2.6, 5.3)
- Immune-Mediated Endocrinopathies (2.6, 5.4):
 - Hypophysitis: Withhold based on severity of hypophysitis.
 - Thyroid Disorders: Monitor for changes in thyroid function. Withhold based on severity of hyperthyroidism.
 - Adrenal Insufficiency: Withhold based on severity of adrenal insufficiency.
 - Type 1 Diabetes Mellitus: Withhold based on severity of hyperglycemia.
- Infections: Withhold for severe or life-threatening infection. (2.6, 5.6)
- Infusion-Related Reactions: Interrupt, slow the rate of infusion, or permanently discontinue based on severity of infusion reactions. (2.6, 5.7)
- Embryo-Fetal Toxicity: Can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and use of effective contraception. (5.8, 8.1, 8.3)

ADVERSE REACTIONS

- Most common adverse reactions (reported in $\geq 20\%$ of patients) with TECENTRIQ as a single-agent were fatigue/asthenia, nausea, cough, dyspnea, and decreased appetite. (6.1)
- Most common adverse reactions (reported in $\geq 20\%$ of patients) with TECENTRIQ in combination with other antineoplastic drugs in patients with NSCLC and SCLC were fatigue/asthenia, nausea, alopecia, constipation, diarrhea, and decreased appetite (6.1)
- The most common adverse reactions (reported in $\geq 20\%$ of patients) with TECENTRIQ in combination with paclitaxel protein-bound in patients with TNBC were alopecia, peripheral neuropathies, fatigue, nausea, diarrhea, anemia, constipation, cough, headache, neutropenia, vomiting, and decreased appetite. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Genentech at 1-888-835-2555 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

USE IN SPECIFIC POPULATIONS

Lactation: Advise not to breastfeed. (8.2)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 3/2019

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1 FULL PRESCRIBING INFORMATION

2 1 INDICATIONS AND USAGE

3 1.1 Urothelial Carcinoma

4 TECENTRIQ is indicated for the treatment of adult patients with locally advanced or metastatic
5 urothelial carcinoma who:

- 6 • are not eligible for cisplatin-containing chemotherapy and whose tumors express PD-L1 (PD-
7 L1 stained tumor-infiltrating immune cells [IC] covering $\geq 5\%$ of the tumor area), as
8 determined by an FDA-approved test [see *Dosage and Administration (2.1)*], or
- 9 • are not eligible for any platinum-containing chemotherapy regardless of PD-L1 status, or
- 10 • have disease progression during or following any platinum-containing chemotherapy, or
11 within 12 months of neoadjuvant or adjuvant chemotherapy

12 This indication is approved under accelerated approval based on tumor response rate and
13 durability of response [see *Clinical Studies (14.1)*]. Continued approval for this indication may
14 be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

15 1.2 Non-Small Cell Lung Cancer

- 16 • TECENTRIQ, in combination with bevacizumab, paclitaxel, and carboplatin, is indicated for
17 the first-line treatment of adult patients with metastatic non-squamous non-small cell lung
18 cancer (NSq NSCLC) with no EGFR or ALK genomic tumor aberrations.
- 19 • TECENTRIQ, as a single-agent, is indicated for the treatment of adult patients with
20 metastatic NSCLC who have disease progression during or following platinum-containing
21 chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease
22 progression on FDA-approved therapy for NSCLC harboring these aberrations prior to
23 receiving TECENTRIQ.

24 1.3 Locally Advanced or Metastatic Triple-Negative Breast Cancer

25 TECENTRIQ, in combination with paclitaxel protein-bound, is indicated for the treatment of
26 adult patients with unresectable locally advanced or metastatic triple-negative breast cancer
27 (TNBC) whose tumors express PD-L1 (PD-L1 stained tumor-infiltrating immune cells [IC] of
28 any intensity covering $\geq 1\%$ of the tumor area), as determined by an FDA-approved test [see
29 *Dosage and Administration (2.1)*].

30 This indication is approved under accelerated approval based on progression free survival [see
31 *Clinical Studies (14.3)*]. Continued approval for this indication may be contingent upon
32 verification and description of clinical benefit in a confirmatory trial(s).

33 1.4 Small Cell Lung Cancer

34 TECENTRIQ, in combination with carboplatin and etoposide, is indicated for the first-line
35 treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC).

36 2 DOSAGE AND ADMINISTRATION

37 2.1 Patient Selection for Treatment of Urothelial Carcinoma and Triple-Negative Breast 38 Cancer

39 Select cisplatin-ineligible patients with previously untreated locally advanced or metastatic
40 urothelial carcinoma for treatment with TECENTRIQ based on the PD-L1 expression on tumor-
41 infiltrating immune cells [see *Clinical Studies (14.1)*].

42 Select patients with locally advanced or metastatic triple-negative breast cancer for treatment
43 with TECENTRIQ in combination with paclitaxel protein-bound based on the PD-L1 expression
44 on tumor infiltrating immune cells [see *Clinical Studies (14.3)*].

45 Information on FDA-approved tests for the determination of PD-L1 expression in locally
46 advanced or metastatic urothelial carcinoma or triple-negative breast cancer are available at:
47 <http://www.fda.gov/CompanionDiagnostics>

48 **2.2 Recommended Dosage for Urothelial Carcinoma**

49 The recommended dosage of TECENTRIQ is 1200 mg intravenously over 60 minutes every
50 3 weeks until disease progression or unacceptable toxicity. If the first infusion is tolerated, all
51 subsequent infusions may be delivered over 30 minutes.

52 **2.3 Recommended Dosage for NSCLC**

53 The recommended dosage of TECENTRIQ is 1200 mg intravenously over 60 minutes every 3
54 weeks until disease progression or unacceptable toxicity. If the first infusion of TECENTRIQ is
55 tolerated, all subsequent infusions may be delivered over 30 minutes.

56 When administering TECENTRIQ in combination with chemotherapy or other antineoplastic
57 drugs, administer TECENTRIQ prior to chemotherapy or other antineoplastic drugs when given
58 on the same day.

59 Refer to the Prescribing Information for the chemotherapy agents or other antineoplastic drugs
60 administered in combination with TECENTRIQ for recommended dosing information.

61 **2.4 Recommended Dosage for Locally Advanced or Metastatic TNBC**

62 The recommended dosage of TECENTRIQ is 840 mg administered as an intravenous infusion
63 over 60 minutes, followed by 100 mg/m² paclitaxel protein-bound.

64 For each 28 day cycle, TECENTRIQ is administered on days 1 and 15, and paclitaxel protein-
65 bound is administered on days 1, 8, and 15 until disease progression or unacceptable toxicity.

66 TECENTRIQ and paclitaxel protein-bound may be discontinued for toxicity independently of
67 each other.

68 If the first infusion is tolerated, all subsequent infusions of TECENTRIQ may be delivered over
69 30 minutes. See also the prescribing information for paclitaxel protein-bound prior to initiation.

70 **2.5 Recommended Dosage for SCLC**

71 The recommended dosage of TECENTRIQ is 1200 mg intravenously over 60 minutes every 3
72 weeks until disease progression or unacceptable toxicity. If the first infusion of TECENTRIQ is
73 tolerated, all subsequent infusions may be delivered over 30 minutes.

74 When administering TECENTRIQ in combination with chemotherapy, administer TECENTRIQ
75 prior to chemotherapy when given on the same day.

76 Refer to the Prescribing Information for the chemotherapy agents administered in combination
77 with TECENTRIQ for recommended dosing information.

78 **2.6 Dosage Modifications for Adverse Reactions**

79 No dose reductions of TECENTRIQ are recommended. Recommendations for dosage
80 modifications are provided in Table 1.

81

Table 1: Recommended Dosage Modifications for Adverse Reactions

| Adverse Reaction | Severity of Adverse Reaction¹ | Dosage Modifications |
|---|---|---|
| Pneumonitis [see Warnings and Precautions (5.1)] | Grade 2 | Withhold dose until Grade 1 or resolved and corticosteroid dose is less than or equal to prednisone 10 mg per day (or equivalent) |
| | Grade 3 or 4 | Permanently discontinue |
| Hepatitis [see Warnings and Precautions (5.2)] | AST or ALT more than 3 and up to 8 times the upper limit of normal or total bilirubin more than 1.5 and up to 3 times the upper limit of normal | Withhold dose until Grade 1 or resolved and corticosteroid dose is less than or equal to prednisone 10 mg per day (or equivalent) |
| | AST or ALT more than 8 times the upper limit of normal or total bilirubin more than 3 times the upper limit of normal | Permanently discontinue |
| Colitis or diarrhea [see Warnings and Precautions (5.3)] | Grade 2 or 3 | Withhold dose until Grade 1 or resolved and corticosteroid dose is less than or equal to prednisone 10 mg per day (or equivalent) |
| | Grade 4 | Permanently discontinue |
| Endocrinopathies (including but not limited to hypophysitis, adrenal insufficiency, hyperthyroidism, and type 1 diabetes mellitus) [see Warnings and Precautions (5.4)] | Grade 2, 3, or 4 | Withhold dose until Grade 1 or resolved and clinically stable on hormone replacement therapy. |
| Other immune-mediated adverse reactions involving a major organ [see Warnings and Precautions (5.5)] | Grade 3 | Withhold dose until Grade 1 or resolved and corticosteroid dose is less than or equal to prednisone 10 mg per day (or equivalent) |
| | Grade 4 | Permanently discontinue |
| Infections [see Warnings and Precautions (5.6)] | Grade 3 or 4 | Withhold dose until Grade 1 or resolved |
| Infusion-Related Reactions [see Warnings and Precautions (5.7)] | Grade 1 or 2 | Interrupt or slow the rate of infusion |
| | Grade 3 or 4 | Permanently discontinue |
| Persistent Grade 2 or 3 adverse reaction (excluding endocrinopathies) | Grade 2 or 3 adverse reaction that does not recover to Grade 0 or 1 within 12 weeks after last TECENTRIQ dose | Permanently discontinue |

| Adverse Reaction | Severity of Adverse Reaction ¹ | Dosage Modifications |
|---|---|-------------------------|
| Inability to taper corticosteroid | Inability to reduce to less than or equal to prednisone 10 mg per day (or equivalent) within 12 weeks after last TECENTRIQ dose | Permanently discontinue |
| Recurrent Grade 3 or 4 adverse reaction | Recurrent Grade 3 or 4 (severe or life-threatening) adverse reaction | Permanently discontinue |

83 ¹ National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) version 4.0

84 **2.7 Preparation and Administration**

85 Preparation

86 Visually inspect drug product for particulate matter and discoloration prior to administration,
87 whenever solution and container permit. Discard the vial if the solution is cloudy, discolored, or
88 visible particles are observed. Do not shake the vial.

89 Prepare the solution for infusion as follows:

- 90 • Select the appropriate vial(s) based on the prescribed dose.
- 91 • Withdraw the required volume of TECENTRIQ from the vial(s).
- 92 • Dilute into a 250 mL polyvinyl chloride (PVC), polyethylene (PE), or polyolefin (PO)
93 infusion bag containing 0.9% Sodium Chloride Injection, USP.
- 94 • Dilute with only 0.9% Sodium Chloride Injection, USP.
- 95 • Mix diluted solution by gentle inversion. Do not shake.
- 96 • Discard used or empty vials of TECENTRIQ.

97 Storage of Infusion Solution

98 This product does not contain a preservative.

99 Administer immediately once prepared. If diluted TECENTRIQ infusion solution is not used
100 immediately, store solution either:

- 101 • At room temperature for no more than 6 hours from the time of preparation. This includes
102 room temperature storage of the infusion in the infusion bag and time for administration of
103 the infusion, or
- 104 • Under refrigeration at 2°C to 8°C (36°F to 46°F) for no more than 24 hours from time of
105 preparation.

106 Do not freeze.

107 Do not shake.

108 Administration

109 Administer the initial infusion over 60 minutes through an intravenous line with or without a
110 sterile, non-pyrogenic, low-protein binding in-line filter (pore size of 0.2–0.22 micron). If the
111 first infusion is tolerated, all subsequent infusions may be delivered over 30 minutes.

112 Do not coadminister other drugs through the same intravenous line.

113 Do not administer as an intravenous push or bolus.

114 **3 DOSAGE FORMS AND STRENGTHS**

115 Injection: 840 mg/14 mL (60 mg/mL) and 1200 mg/20 mL (60 mg/mL) colorless to slightly
116 yellow solution in a single-dose vial.

117 **4 CONTRAINDICATIONS**

118 None.

119 **5 WARNINGS AND PRECAUTIONS**

120 **5.1 Immune-Mediated Pneumonitis**

121 TECENTRIQ can cause immune-mediated pneumonitis or interstitial lung disease, defined as
122 requiring use of systemic corticosteroids, including fatal cases. Monitor patients for signs and
123 symptoms of pneumonitis. Evaluate patients with suspected pneumonitis with radiographic
124 imaging. Administer corticosteroids, prednisone 1–2 mg/kg/day or equivalents, followed by a
125 taper for Grade 2 or higher pneumonitis. Withhold or permanently discontinue TECENTRIQ
126 based on the severity [*see Dosage and Administration (2.6)*].

127 In clinical studies enrolling 2616 patients with various cancers who received TECENTRIQ as a
128 single-agent [*see Adverse Reactions (6.1)*], pneumonitis occurred in 2.5% of patients, including
129 Grade 3 (0.6%), Grade 4 (0.1%), and Grade 5 (< 0.1%) immune-mediated pneumonitis. The
130 median time to onset of pneumonitis was 3.6 months (3 days to 20.5 months) and median
131 duration of pneumonitis was 1.4 months (1 day to 15.1 months). Pneumonitis resolved in 67% of
132 patients. Pneumonitis led to discontinuation of TECENTRIQ in 0.4% of the 2616 patients.
133 Systemic corticosteroids were required in 1.5% of patients, including 0.8% who received high-
134 dose corticosteroids (prednisone \geq 40 mg per day or equivalent) for a median duration of 4 days
135 (1 day to 45 days) followed by a corticosteroid taper.

136 In clinical studies enrolling 2421 patients with NSCLC and SCLC who received TECENTRIQ in
137 combination with platinum-based chemotherapy [*see Adverse Reactions (6.1)*], immune-
138 mediated pneumonitis occurred in 5.5% of patients, including Grades 3-4 in 1.4% of patients.
139 Systemic corticosteroids were required in 4.2% of patients, including 3.1% who received high-
140 dose corticosteroids (prednisone \geq 40 mg per day or equivalent) for a median duration of 5 days
141 (1 day to 98 days) followed by a corticosteroid taper.

142 **5.2 Immune-Mediated Hepatitis**

143 TECENTRIQ can cause liver test abnormalities and immune-mediated hepatitis, defined as
144 requiring use of systemic corticosteroids. Fatal cases have been reported. Monitor patients for
145 signs and symptoms of hepatitis, during and after discontinuation of TECENTRIQ, including
146 clinical chemistry monitoring. Administer corticosteroids, prednisone 1–2 mg/kg/day or
147 equivalents, followed by a taper for Grade 2 or higher elevations of ALT, AST and/or total
148 bilirubin. Interrupt or permanently discontinue TECENTRIQ based on the severity [*see Dosage
149 and Administration (2.6)*].

150 In clinical studies enrolling 2616 patients with various cancers who received TECENTRIQ as a
151 single-agent [*see Adverse Reactions (6.1)*], hepatitis occurred in 9% of patients, including Grade
152 3 (2.3%), Grade 4 (0.6%), and Grade 5 (< 0.1%). The median time to onset of hepatitis was 1.4
153 months (1 day to 25.8 months) and median duration was 24 days (1 day to 13 months). Hepatitis
154 resolved in 71% of patients. Hepatitis led to discontinuation of TECENTRIQ in 0.4% of 2616
155 patients. Systemic corticosteroids were required in 2% of the patients, with 1.3% requiring high-
156 dose corticosteroids (prednisone \geq 40 mg per day or equivalent) for a median duration of 3 days
157 (1 day to 35 days) followed by a corticosteroid taper.

158 In clinical studies enrolling 2421 patients with NSCLC and SCLC who received TECENTRIQ in
159 combination with platinum-based chemotherapy [see *Adverse Reactions (6.1)*], immune-
160 mediated hepatitis occurred in 14% of patients, including Grades 3-4 in 4.1% of patients.
161 Systemic corticosteroids were required in 4.8% of patients, including 3.4% who received high-
162 dose corticosteroids (prednisone \geq 40 mg per day or equivalent) for a median duration of 6 days
163 (1 day to 144 days) followed by a corticosteroid taper.

164 **5.3 Immune-Mediated Colitis**

165 TECENTRIQ can cause immune-mediated colitis or diarrhea, defined as requiring use of
166 systemic corticosteroids. Monitor patients for signs and symptoms of diarrhea or colitis.
167 Withhold treatment with TECENTRIQ for Grade 2 or 3 diarrhea or colitis. If symptoms persist
168 for longer than 5 days or recur, administer corticosteroids, prednisone 1–2 mg/kg/day or
169 equivalents, followed by a taper for Grade 2 diarrhea or colitis. Interrupt or permanently
170 discontinue TECENTRIQ based on the severity [see *Dosage and Administration (2.6)* and
171 *Adverse Reactions (6.1)*].

172 In clinical studies enrolling 2616 patients with various cancers who received TECENTRIQ as a
173 single-agent [see *Adverse Reactions (6.1)*], diarrhea or colitis occurred in 20% of patients,
174 including Grade 3 (1.4%) events. The median time to onset of diarrhea or colitis was 1.5 months
175 (1 day to 41 months). Diarrhea and colitis resolved in 85% of the patients. Diarrhea or colitis led
176 to discontinuation of TECENTRIQ in 0.2% of 2616 patients. Systemic corticosteroids were
177 required in 1.1% of patients and high-dose corticosteroids (prednisone \geq 40 mg per day or
178 equivalent) was required in 0.4% patients with a median duration of 3 days (1 day to 11 days)
179 followed by a corticosteroid taper.

180 In clinical studies enrolling 2421 patients with NSCLC and SCLC who received TECENTRIQ in
181 combination with platinum-based chemotherapy [see *Adverse Reactions (6.1)*], diarrhea or
182 colitis occurred in 29% of patients, including Grade 3-4 in 4.3% of patients. Systemic
183 corticosteroids were required in 4.7% of patients, including 2.9% who received high-dose
184 corticosteroids (prednisone \geq 40 mg per day or equivalent) for a median duration of 4 days (1
185 day to 170 days) followed by a corticosteroid taper.

186 **5.4 Immune-Mediated Endocrinopathies**

187 TECENTRIQ can cause immune-mediated endocrinopathies, including thyroid disorders,
188 adrenal insufficiency, and type 1 diabetes mellitus, including diabetic ketoacidosis, and
189 hypophysitis/hypopituitarism.

190 *Thyroid Disorders:* Monitor thyroid function prior to and periodically during treatment with
191 TECENTRIQ. Initiate hormone replacement therapy or medical management of hyperthyroidism
192 as clinically indicated. Continue TECENTRIQ for hypothyroidism and interrupt for
193 hyperthyroidism based on the severity [see *Dosage and Administration (2.6)*].

194 In clinical studies enrolling 2616 patients who received TECENTRIQ as a single-agent [see
195 *Adverse Reactions (6.1)*], hypothyroidism occurred in 4.6% of patients, and 3.8% of patients
196 required the use of hormone replacement therapy. Hyperthyroidism occurred in 1.6% of patients.
197 One patient experienced acute thyroiditis.

198 In clinical studies enrolling 2421 patients with NSCLC and SCLC who received TECENTRIQ
199 in combination with platinum-based chemotherapy [see *Adverse Reactions (6.1)*],
200 hypothyroidism occurred in 11% of patients, including Grades 3-4 in 0.3% of patients; 8.2% of
201 the 2421 patients required the use of hormone replacement therapy. The frequency and severity
202 of hyperthyroidism and thyroiditis were similar whether TECENTRIQ was given as a single-
203 agent in patients with various cancers or in combination with other antineoplastic drugs in
204 NSCLC and SCLC.

205 *Adrenal Insufficiency:* Monitor patients for clinical signs and symptoms of adrenal
206 insufficiency. For Grade 2 or higher adrenal insufficiency, initiate prednisone 1 to 2
207 mg/kg/day or equivalents, followed by a taper and hormone replacement as clinically
208 indicated. Interrupt TECENTRIQ based on the severity [*see Dosage and Administration*
209 (2.6)].

210 In clinical studies enrolling 2616 patients who received TECENTRIQ as a single-agent, adrenal
211 insufficiency occurred in 0.4% of patients, including Grade 3 (< 0.1%) adrenal insufficiency.
212 Median time to onset was 5.7 months (3 days to 19 months). There was insufficient information
213 to adequately characterize the median duration of adrenal insufficiency. Adrenal insufficiency
214 resolved in 27% of patients. Systemic corticosteroids were required in 0.3% of 2616 patients,
215 including 0.1% who required high-dose corticosteroids (prednisone \geq 40 mg per day or
216 equivalent). The frequency and severity of adrenal insufficiency were similar whether
217 TECENTRIQ was given as a single-agent in patients with various cancers or in combination
218 with other antineoplastic drugs in NSCLC and SCLC.

219 *Type 1 Diabetes Mellitus:* Monitor patients for hyperglycemia or other signs and symptoms of
220 diabetes. Initiate treatment with insulin as clinically indicated. Interrupt TECENTRIQ based on
221 the severity [*see Dosage and Administration* (2.6)].

222 In clinical studies enrolling 2616 patients who received TECENTRIQ as a single-agent, type 1
223 diabetes mellitus occurred in < 0.1% of patients. Insulin was required in one patient. The
224 frequency and severity of diabetes mellitus were similar whether TECENTRIQ was given as a
225 single-agent in patients with various cancers or in combination with other antineoplastic drugs in
226 NSCLC and SCLC.

227 *Hypophysitis:* For Grade 2 or higher hypophysitis, initiate prednisone 1–2 mg/kg/day or
228 equivalents, followed by a taper and hormone replacement therapy as clinically indicated.
229 Interrupt TECENTRIQ based on the severity [*see Dosage and Administration* (2.6)].

230 In clinical studies enrolling 2616 patients who received TECENTRIQ as a single-agent, Grade 2
231 hypophysitis occurred in < 0.1% of patients. The frequency and severity of hypophysitis were
232 similar whether TECENTRIQ was given as a single-agent in patients with various cancers or in
233 combination with other antineoplastic drugs in NSCLC and SCLC.

234 **5.5 Other Immune-Mediated Adverse Reactions**

235 TECENTRIQ can cause severe and fatal immune-mediated adverse reactions. These immune-
236 mediated reactions may involve any organ system. While immune-mediated reactions usually
237 manifest during treatment with TECENTRIQ, immune-mediated adverse reactions can also
238 manifest after discontinuation of TECENTRIQ.

239 For suspected Grade 2 immune-mediated adverse reactions, exclude other causes and initiate
240 corticosteroids as clinically indicated. For severe (Grades 3 or 4) adverse reactions, administer
241 corticosteroids, prednisone 1 to 2 mg/kg/day or equivalents, followed by a taper. Interrupt or
242 permanently discontinue TECENTRIQ, based on the severity of the reaction [*see Dosage and*
243 *Administration* (2.6)].

244 If uveitis occurs in combination with other immune-mediated adverse reactions, evaluate for
245 Vogt-Koyanagi-Harada syndrome, which has been observed with other products in this class and
246 may require treatment with systemic steroids to reduce the risk of permanent vision loss.

247 The following clinically significant, immune-mediated adverse reactions occurred at an
248 incidence of < 1% in 2616 patients who received TECENTRIQ as a single-agent and in 2421
249 patients who received TECENTRIQ in combination with platinum-based chemotherapy or were
250 reported in other products in this class [*see Adverse Reactions* (6.1)]:

251 *Cardiac:* myocarditis

- 252 *Dermatologic*: bullous dermatitis, pemphigoid, erythema multiforme, Stevens Johnson
253 Syndrome (SJS)/toxic epidermal necrolysis (TEN).
- 254 *Gastrointestinal*: pancreatitis, including increases in serum amylase or lipase levels
- 255 *General*: systemic inflammatory response syndrome, histiocytic necrotizing lymphadenitis
- 256 *Hematological*: autoimmune hemolytic anemia, immune thrombocytopenic purpura.
- 257 *Musculoskeletal*: myositis, rhabdomyolysis.
- 258 *Neurological*: Guillain-Barre syndrome, myasthenia syndrome/myasthenia gravis,
259 demyelination, immune-related meningoencephalitis, aseptic meningitis, encephalitis, facial and
260 abducens nerve paresis, polymyalgia rheumatica, autoimmune neuropathy, and Vogt-Koyanagi-
261 Harada syndrome.
- 262 *Ophthalmological*: uveitis, iritis.
- 263 *Renal*: nephrotic syndrome, nephritis.
- 264 *Vascular*: vasculitis

265 **5.6 Infections**

266 TECENTRIQ can cause severe infections including fatal cases. Monitor patients for signs and
267 symptoms of infection. For Grade 3 or higher infections, withhold TECENTRIQ and resume
268 once clinically stable [see *Dosage and Administration (2.6)* and *Adverse Reactions (6.1)*].

269 In clinical studies enrolling 2616 patients with various cancers who received TECENTRIQ as a
270 single-agent [see *Adverse Reactions (6.1)*], infections occurred in 42% of patients, including
271 Grade 3 (8.7%), Grade 4 (1.5%), and Grade 5 (1%). In patients with urothelial carcinoma, the
272 most common Grade 3 or higher infection was urinary tract infections, occurring in 6.5% of
273 patients. In patients with NSCLC, the most common Grade 3 or higher infection was pneumonia,
274 occurring in 3.8% of patients. The frequency and severity of infections were similar whether
275 TECENTRIQ was given as a single-agent in patients with various cancers or in combination with
276 other antineoplastic drugs in NSCLC and SCLC.

277 **5.7 Infusion-Related Reactions**

278 TECENTRIQ can cause severe or life-threatening infusion-related reactions. Monitor for signs
279 and symptoms of infusion-related reactions. Interrupt, slow the rate of, or permanently
280 discontinue TECENTRIQ based on the severity [see *Dosage and Administration (2.6)*]. For
281 Grade 1 or 2 infusion-related reactions, consider using pre-medications with subsequent doses.

282 In clinical studies enrolling 2616 patients with various cancers who received TECENTRIQ as a
283 single-agent [see *Adverse Reactions (6.1)*], infusion-related reactions occurred in 1.3% of
284 patients, including Grade 3 (0.2%). The frequency and severity of infusion-related reactions were
285 similar whether TECENTRIQ was given as a single-agent in patients with various cancers or in
286 combination with other antineoplastic drugs in NSCLC and SCLC.

287 **5.8 Embryo-Fetal Toxicity**

288 Based on its mechanism of action, TECENTRIQ can cause fetal harm when administered to a
289 pregnant woman. There are no available data on the use of TECENTRIQ in pregnant women.
290 Animal studies have demonstrated that inhibition of the PD-L1/PD-1 pathway can lead to
291 increased risk of immune-related rejection of the developing fetus resulting in fetal death.

292 Verify pregnancy status of females of reproductive potential prior to initiating TECENTRIQ.
293 Advise females of reproductive potential of the potential risk to a fetus. Advise females of
294 reproductive potential to use effective contraception during treatment with TECENTRIQ and for
295 at least 5 months after the last dose [see *Use in Specific Populations (8.1, 8.3)*].

296 **6 ADVERSE REACTIONS**

297 The following adverse reactions are discussed in greater detail in other sections of the label:

- 298 • Immune-Mediated Pneumonitis [*see Warnings and Precautions (5.1)*]
- 299 • Immune-Mediated Hepatitis [*see Warnings and Precautions (5.2)*]
- 300 • Immune-Mediated Colitis [*see Warnings and Precautions (5.3)*]
- 301 • Immune-Mediated Endocrinopathies [*see Warnings and Precautions (5.4)*]
- 302 • Other Immune-Mediated Adverse Reactions [*see Warnings and Precautions (5.5)*]
- 303 • Infections [*see Warnings and Precautions (5.6)*]
- 304 • Infusion-Related Reactions [*see Warnings and Precautions (5.7)*]

305 **6.1 Clinical Trials Experience**

306 Because clinical trials are conducted under widely varying conditions, adverse reaction rates
307 observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials
308 of another drug and may not reflect the rates observed in practice.

309 The data described in WARNINGS AND PRECAUTIONS reflect exposure to TECENTRIQ as
310 a single-agent in 2616 patients in two randomized, active-controlled studies (POPLAR, OAK)
311 and four open-label, single arm studies (PCD4989g, IMvigor210, BIRCH, FIR) which enrolled
312 524 patients with metastatic urothelial carcinoma, 1636 patients with metastatic NSCLC, and
313 456 patients with other tumor types. TECENTRIQ was administered at a dose of 1200 mg
314 intravenously every 3 weeks in all studies except PCD4989g. Among the 2616 patients who
315 received a single-agent TECENTRIQ, 36% were exposed for longer than 6 months and 20%
316 were exposed for longer than 12 months.

317 Using the dataset described for patients who received TECENTRIQ as a single-agent, the most
318 common adverse reactions in $\geq 20\%$ of patients were fatigue/asthenia (48%), decreased appetite
319 (25%), nausea (24%), cough (22%), and dyspnea (22%).

320 In addition, the data reflect exposure to TECENTRIQ in combination with other antineoplastic
321 drugs in 2421 patients with NSCLC (N = 2223) or SCLC (N = 198) enrolled in five randomized,
322 active-controlled trials, including IMpower150 and IMpower133. Among the 2421 patients, 53%
323 were exposed to TECENTRIQ for longer than 6 months and 29% were exposed to TECENTRIQ
324 for longer than 12 months.

325 Among the 2421 patients with NSCLC and SCLC who received TECENTRIQ in combination
326 with other antineoplastic drugs, the most common adverse reactions in $\geq 20\%$ of patients were
327 fatigue/asthenia (49%), nausea (38%), alopecia (35%), constipation (29%), diarrhea (28%) and
328 decreased appetite (27%).

329 The data described below in this section were obtained from one open-label, single arm, multiple
330 cohort study (IMvigor210) and three randomized open-label, active-controlled studies (OAK,
331 IMpower150 and IMpower133). In these trials, TECENTRIQ was administered at a dose of 1200
332 mg intravenously every 3 weeks. This section also describes data from one randomized, placebo-
333 controlled study (IMpassion130) in which TECENTRIQ was administered (at a dose of 840 mg

334 intravenously every 2 weeks) in combination with paclitaxel protein-bound to 452 patients with
335 metastatic TNBC.

336 Urothelial Carcinoma

337 *Cisplatin-Ineligible Patients with Locally Advanced or Metastatic Urothelial Carcinoma*

338 The safety of TECENTRIQ was evaluated in IMvigor 210 (Cohort 1), a multicenter, open-label,
339 single-arm trial that included 119 patients with locally advanced or metastatic urothelial
340 carcinoma who were ineligible for cisplatin-containing chemotherapy and were either previously
341 untreated or had disease progression at least 12 months after neoadjuvant or adjuvant
342 chemotherapy [see *Clinical Studies (14.1)*]. Patients received TECENTRIQ 1200 mg
343 intravenously every 3 weeks until either unacceptable toxicity or disease progression. The
344 median duration of exposure was 15 weeks (0 to 87 weeks).

345 The most common Grades 3–4 adverse reactions ($\geq 2\%$) were fatigue, urinary tract infection,
346 anemia, diarrhea, blood creatinine increase, intestinal obstruction, ALT increase, hyponatremia,
347 decreased appetite, sepsis, back/neck pain, renal failure, and hypotension.

348 Five patients (4.2%) who were treated with TECENTRIQ experienced one of the following
349 events which led to death: sepsis, cardiac arrest, myocardial infarction, respiratory failure, or
350 respiratory distress. One additional patient (0.8%) was experiencing herpetic
351 meningoencephalitis and disease progression at the time of death.

352 Serious adverse reactions occurred in 37% of patients. The most frequent serious adverse
353 reactions ($\geq 2\%$) were diarrhea, intestinal obstruction, sepsis, acute kidney injury, and renal
354 failure.

355 TECENTRIQ was discontinued for adverse reactions in 4.2% of patients. The adverse reactions
356 leading to discontinuation were diarrhea/colitis (1.7%), fatigue (0.8%), hypersensitivity (0.8%),
357 and dyspnea (0.8%).

358 Adverse reactions leading to interruption occurred in 35% of patients; the most common ($\geq 1\%$)
359 were intestinal obstruction, fatigue, diarrhea, urinary tract infection, infusion-related reaction,
360 cough, abdominal pain, peripheral edema, pyrexia, respiratory tract infection, upper respiratory
361 tract infection, creatinine increase, decreased appetite, hyponatremia, back pain, pruritus, and
362 venous thromboembolism.

363 Tables 2 and 3 summarize the adverse reactions and Grades 3–4 selected laboratory
364 abnormalities, respectively, in patients who received TECENTRIQ in IMvigor210
365 (Cohort 1).

**Table 2: Adverse Reactions in $\geq 10\%$ of Patients with Urothelial Carcinoma
in IMvigor210 (Cohort 1)**

| Adverse Reaction | TECENTRIQ N = 119 | |
|-------------------------------|----------------------|-------------------|
| | All Grades (%) | Grades 3–4 (%) |
| General | | |
| Fatigue ¹ | 52 | 8 |
| Peripheral edema ² | 17 | 2 |
| Pyrexia | 14 | 0.8 |
| Gastrointestinal | | |
| Diarrhea ³ | 24 | 5 |

| Adverse Reaction | TECENTRIQ N = 119 | |
|---|----------------------|----------------|
| | All Grades (%) | Grades 3–4 (%) |
| Nausea | 22 | 2 |
| Vomiting | 16 | 0.8 |
| Constipation | 15 | 2 |
| Abdominal pain ⁴ | 15 | 0.8 |
| Metabolism and Nutrition | | |
| Decreased appetite ⁵ | 24 | 3 |
| Musculoskeletal and Connective Tissue | | |
| Back/Neck pain | 18 | 3 |
| Arthralgia | 13 | 0 |
| Skin and Subcutaneous Tissue | | |
| Pruritus | 18 | 0.8 |
| Rash ⁶ | 17 | 0.8 |
| Infections | | |
| Urinary tract infection ⁷ | 17 | 5 |
| Respiratory, Thoracic, and Mediastinal | | |
| Cough ⁸ | 14 | 0 |
| Dyspnea ⁹ | 12 | 0 |

¹ Includes fatigue, asthenia, lethargy, and malaise

² Includes edema peripheral, scrotal edema, lymphedema, and edema

³ Includes diarrhea, colitis, frequent bowel movements, autoimmune colitis

⁴ Includes abdominal pain, upper abdominal pain, lower abdominal pain, and flank pain

⁵ Includes decreased appetite and early satiety

⁶ Includes rash, dermatitis, dermatitis acneiform, rash maculo-papular, rash erythematous, rash pruritic, rash macular, and rash papular

⁷ Includes urinary tract infection, urinary tract infection bacterial, cystitis, and urosepsis

⁸ Includes cough and productive cough

⁹ Includes dyspnea and exertional dyspnea

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Table 3: Grades 3–4 Laboratory Abnormalities in ≥ 1% of Patients with Urothelial Carcinoma in IMvigor210 (Cohort 1)

| Laboratory Abnormality | Grades 3–4 (%) |
|--------------------------------|----------------|
| Chemistry | |
| Hyponatremia | 15 |
| Hyperglycemia | 10 |
| Increased Alkaline Phosphatase | 7 |
| Increased Creatinine | 5 |
| Hypophosphatemia | 4 |
| Increased ALT | 4 |

| Laboratory Abnormality | Grades 3–4 (%) |
|------------------------|----------------|
| Increased AST | 4 |
| Hyperkalemia | 3 |
| Hypermagnesemia | 3 |
| Hyperbilirubinemia | 3 |
| Hematology | |
| Lymphopenia | 9 |
| Anemia | 7 |

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371 *Previously Treated Locally Advanced or Metastatic Urothelial Carcinoma*

372 The safety of TECENTRIQ was evaluated in IMvigor210 (Cohort 2), a multicenter, open-label,
373 single-arm trial that included 310 patients with locally advanced or metastatic urothelial
374 carcinoma who had disease progression during or following at least one platinum-containing
375 chemotherapy regimen or who had disease progression within 12 months of treatment with a
376 platinum-containing neoadjuvant or adjuvant chemotherapy regimen [see *Clinical Studies*
377 (14.1)]. Patients received TECENTRIQ 1200 mg intravenously every 3 weeks until unacceptable
378 toxicity or either radiographic or clinical progression. The median duration of exposure was
379 12.3 weeks (0.1 to 46 weeks).

380 The most common Grades 3–4 adverse reactions ($\geq 2\%$) were urinary tract infection, anemia,
381 fatigue, dehydration, intestinal obstruction, urinary obstruction, hematuria, dyspnea, acute kidney
382 injury, abdominal pain, venous thromboembolism, sepsis, and pneumonia.

383 Three patients (1%) who were treated with TECENTRIQ experienced one of the following
384 events which led to death: sepsis, pneumonitis, or intestinal obstruction.

385 TECENTRIQ was discontinued for adverse reactions in 3.2% of patients. Sepsis led to
386 discontinuation in 0.6% of patients.

387 Serious adverse reactions occurred in 45% of patients. The most frequent serious adverse
388 reactions ($> 2\%$) were urinary tract infection, hematuria, acute kidney injury, intestinal
389 obstruction, pyrexia, venous thromboembolism, urinary obstruction, pneumonia, dyspnea,
390 abdominal pain, sepsis, and confusional state.

391 Adverse reactions leading to interruption occurred in 27% of patients; the most common ($> 1\%$)
392 were liver enzyme increase, urinary tract infection, diarrhea, fatigue, confusional state, urinary
393 obstruction, pyrexia, dyspnea, venous thromboembolism, and pneumonitis.

394 Tables 4 and 5 summarize the adverse reactions and Grades 3–4 selected laboratory
395 abnormalities, respectively, in patients who received TECENTRIQ in IMvigor210 (Cohort 2).

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Table 4: Adverse Reactions in $\geq 10\%$ of Patients with Urothelial Carcinoma in IMvigor210 (Cohort 2)

| Adverse Reaction | TECENTRIQ N = 310 | |
|------------------|----------------------|----------------|
| | All Grades (%) | Grades 3–4 (%) |
| General | | |
| Fatigue | 52 | 6 |
| Pyrexia | 21 | 1 |

| Adverse Reaction | TECENTRIQ N = 310 | |
|---|----------------------|----------------|
| | All Grades (%) | Grades 3–4 (%) |
| Peripheral edema | 18 | 1 |
| Metabolism and Nutrition | | |
| Decreased appetite | 26 | 1 |
| Gastrointestinal | | |
| Nausea | 25 | 2 |
| Constipation | 21 | 0.3 |
| Diarrhea | 18 | 1 |
| Abdominal pain | 17 | 4 |
| Vomiting | 17 | 1 |
| Infections | | |
| Urinary tract infection | 22 | 9 |
| Respiratory, Thoracic, and Mediastinal | | |
| Dyspnea | 16 | 4 |
| Cough | 14 | 0.3 |
| Musculoskeletal and Connective Tissue | | |
| Back/Neck pain | 15 | 2 |
| Arthralgia | 14 | 1 |
| Skin and Subcutaneous Tissue | | |
| Rash | 15 | 0.3 |
| Pruritus | 13 | 0.3 |
| Renal and Urinary | | |
| Hematuria | 14 | 3 |

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Table 5: Grades 3–4 Laboratory Abnormalities in ≥ 1% of Patients with Urothelial Carcinoma in IMvigor210 (Cohort 2)

| Laboratory Abnormality | Grades 3–4 (%) |
|--------------------------------|----------------|
| Chemistry | |
| Hyponatremia | 10 |
| Hyperglycemia | 5 |
| Increased Alkaline Phosphatase | 4 |
| Increased Creatinine | 3 |
| Increased ALT | 2 |
| Increased AST | 2 |

| Laboratory Abnormality | Grades 3–4 (%) |
|------------------------|----------------|
| Hypoalbuminemia | 1 |
| Hematology | |
| Lymphopenia | 10 |
| Anemia | 8 |

400 Non-small Cell Lung Cancer (NSCLC)

401 *Metastatic Non-Squamous NSCLC*

402 The safety of TECENTRIQ with bevacizumab, paclitaxel and carboplatin was evaluated in
403 IMpower150, a multicenter, international, randomized, open-label trial in which 393
404 chemotherapy-naïve patients with metastatic non-squamous NSCLC received TECENTRIQ
405 1200 mg with bevacizumab 15 mg/kg, paclitaxel 175 mg/m² or 200 mg/m², and carboplatin AUC
406 6 mg/mL/min every 3 weeks for a maximum of 4 or 6 cycles, followed by TECENTRIQ 1200
407 mg with bevacizumab 15 mg/kg every 3 weeks until disease progression or unacceptable toxicity
408 [see *Clinical Studies (14.2)*]. The median duration of exposure to TECENTRIQ was 8.3 months
409 in patients receiving TECENTRIQ with bevacizumab, paclitaxel, and carboplatin.

410 The most common Grades 3–4 adverse reactions (≥2%) in patients receiving TECENTRIQ were
411 fatigue/asthenia, hypertension, febrile neutropenia, diarrhea, pneumonia, nausea, decreased
412 appetite, dehydration, and pulmonary embolism.

413 Fatal adverse reactions occurred in 6% of patients receiving TECENTRIQ; these included
414 hemoptysis, febrile neutropenia, pulmonary embolism, pulmonary hemorrhage, death, cardiac
415 arrest, cerebrovascular accident, pneumonia, aspiration pneumonia, chronic obstructive
416 pulmonary disease, intracranial hemorrhage, intestinal angina, intestinal ischemia, intestinal
417 obstruction and aortic dissection.

418 Serious adverse reactions occurred in 44%. The most frequent serious adverse reactions (>2%)
419 were febrile neutropenia, pneumonia, diarrhea, and hemoptysis.

420 TECENTRIQ was discontinued due to adverse reactions in 15% of patients; the most common
421 adverse reaction leading to discontinuation was pneumonitis (1.8%).

422 Adverse reactions leading to interruption of TECENTRIQ occurred in 48%; the most common
423 (>1%) were neutropenia, thrombocytopenia, fatigue/asthenia, diarrhea, hypothyroidism, anemia,
424 pneumonia, pyrexia, hyperthyroidism, febrile neutropenia, increased ALT, dyspnea, dehydration
425 and proteinuria.

426 Tables 6 and 7 summarize adverse reactions and laboratory abnormalities in patients receiving
427 TECENTRIQ with bevacizumab, paclitaxel, and carboplatin in IMpower150. Study IMpower150
428 was not designed to demonstrate a statistically significant reduction in adverse reaction rates for
429 TECENTRIQ, as compared to the control arm, for any specified adverse reaction or laboratory
430 abnormality listed in Tables 6 and 7.

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Table 6: Adverse Reactions Occurring in ≥15% of Patients with NSCLC Receiving TECENTRIQ in IMpower150

| Adverse Reaction | TECENTRIQ with Bevacizumab, Paclitaxel, and Carboplatin N = 393 | | Bevacizumab, Paclitaxel and Carboplatin N = 394 | |
|--|--|-----------------|--|-----------------|
| | All Grades* (%) | Grades 3–4* (%) | All Grades* (%) | Grades 3–4* (%) |
| Nervous System | | | | |
| Neuropathy ¹ | 56 | 3 | 47 | 3 |
| Headache | 16 | 0.8 | 13 | 0 |
| General | | | | |
| Fatigue/Asthenia | 50 | 6 | 46 | 6 |
| Pyrexia | 19 | 0.3 | 9 | 0.5 |
| Skin and Subcutaneous Tissue | | | | |
| Alopecia | 48 | 0 | 46 | 0 |
| Rash ² | 23 | 2 | 10 | 0.3 |
| Musculoskeletal and Connective Tissue | | | | |
| Myalgia/Pain ³ | 42 | 3 | 34 | 2 |
| Arthralgia | 26 | 1 | 22 | 1 |
| Gastrointestinal | | | | |
| Nausea | 39 | 4 | 32 | 2 |
| Diarrhea ⁴ | 33 | 6 | 25 | 0.5 |
| Constipation | 30 | 0.3 | 23 | 0.3 |
| Vomiting | 19 | 2 | 18 | 1 |
| Metabolism and Nutrition | | | | |
| Decreased appetite | 29 | 4 | 21 | 0.8 |
| Vascular | | | | |
| Hypertension | 25 | 9 | 22 | 8 |
| Respiratory | | | | |
| Cough | 20 | 0.8 | 19 | 0.3 |
| Epistaxis | 17 | 1 | 22 | 0.3 |
| Renal | | | | |
| Proteinuria ⁵ | 16 | 3 | 15 | 3 |

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* Graded per NCI CTCAE v4.0
¹ Includes neuropathy peripheral, peripheral sensory neuropathy, hypoesthesia, paresthesia, dysesthesia, polyneuropathy.
² Includes rash, rash maculo-papular, drug eruption, eczema, eczema asteatotic, dermatitis, contact dermatitis, rash erythematous, rash macular, pruritic rash, seborrheic dermatitis, dermatitis psoriasiform.
³ Includes pain in extremity, musculoskeletal chest pain, musculoskeletal discomfort, neck pain, backpain, myalgia, and bone pain.
⁴ Includes diarrhea, gastroenteritis, colitis, enterocolitis.
⁵ Data based on Preferred Terms since laboratory data for proteinuria were not systematically collected.

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Table 7: Laboratory Abnormalities Worsening from Baseline Occurring in ≥20% of Patients with NSCLC Receiving TECENTRIQ in IMpower150

| Laboratory Abnormality | TECENTRIQ with Bevacizumab, Paclitaxel, and Carboplatin ² | | Beveracizumab, Paclitaxel and Carboplatin ² | |
|--------------------------------|--|----------------|--|----------------|
| | All Grades ¹ (%) | Grades 3–4 (%) | All Grades ¹ (%) | Grades 3–4 (%) |
| Hematology | | | | |
| Anemia | 83 | 10 | 83 | 9 |
| Neutropenia | 52 | 31 | 45 | 26 |
| Lymphopenia | 48 | 17 | 38 | 13 |
| Chemistry | | | | |
| Hyperglycemia | 61 | 0 | 60 | 0 |
| Increased BUN | 52 | NA | 44 | NA |
| Hypomagnesemia | 42 | 2 | 36 | 1 |
| Hypoalbuminemia | 40 | 3 | 31 | 2 |
| Increased AST | 40 | 4 | 28 | 0.8 |
| Hyponatremia | 38 | 10 | 36 | 9 |
| Increased Alkaline Phosphatase | 37 | 2 | 32 | 1 |
| Increased ALT | 37 | 6 | 28 | 0.5 |
| Increased TSH | 30 | NA | 20 | NA |
| Hyperkalemia | 28 | 3 | 25 | 2 |
| Increased Creatinine | 28 | 1 | 19 | 2 |
| Hypocalcemia | 26 | 3 | 21 | 3 |
| Hypophosphatemia | 25 | 4 | 18 | 4 |
| Hypokalemia | 23 | 7 | 14 | 4 |
| Hyperphosphatemia | 25 | N/A | 19 | N/A |

445 NA = Not applicable.

446 ¹ NCI CTCAE does not provide a Grades 3-4 definition for these laboratory abnormalities

447 ² Each test incidence is based on the number of patients who had both baseline and at least one on-study
448 laboratory measurement available: TECENTRIQ with bevacizumab, paclitaxel, and carboplatin range: 337-
449 380); bevacizumab, paclitaxel, and carboplatin (range: 337-382)

450 Previously Treated Metastatic NSCLC

451 The safety of TECENTRIQ was evaluated in OAK, a multicenter, international, randomized,
452 open-label trial in patients with metastatic NSCLC who progressed during or following a
453 platinum-containing regimen, regardless of PD-L1 expression [see *Clinical Studies (14.2)*]. A
454 total of 609 patients received TECENTRIQ 1200 mg intravenously every 3 weeks until
455 unacceptable toxicity, radiographic progression, or clinical progression or docetaxel (n=578) 75
456 mg/m² intravenously every 3 weeks until unacceptable toxicity or disease progression. The study
457 excluded patients with active or prior autoimmune disease or with medical conditions that
458 required systemic corticosteroids. The study population characteristics were: median age of 63
459 years (25 to 85 years), 46% age 65 years or older, 62% male, 71% White, 20% Asian, 68%
460 former smoker, 16% current smoker, and 63% had ECOG performance status of 1. The median

461 duration of exposure was 3.4 months (0 to 26 months) in TECENTRIQ-treated patients and 2.1
462 months (0 to 23 months) in docetaxel-treated patients.

463 The most common Grades 3–4 adverse reactions ($\geq 2\%$) were dyspnea, pneumonia, fatigue, and
464 pulmonary embolism.

465 Fatal adverse reactions occurred in 1.6% of patients; these included pneumonia, sepsis, septic
466 shock, dyspnea, pulmonary hemorrhage, sudden death, myocardial ischemia or renal failure.

467 Serious adverse reactions occurred in 33.5% of patients. The most frequent serious adverse
468 reactions ($>1\%$) were pneumonia, sepsis, dyspnea, pleural effusion, pulmonary embolism,
469 pyrexia and respiratory tract infection.

470 TECENTRIQ was discontinued due to adverse reactions in 8% of patients. The most common
471 adverse reactions leading to TECENTRIQ discontinuation were fatigue, infections and dyspnea.
472 Adverse reactions leading to interruption of TECENTRIQ occurred in 25% of patients; the most
473 common ($>1\%$) were pneumonia, liver function test abnormality, dyspnea, fatigue, pyrexia, and
474 back pain.

475 Tables 8 and 9 summarize adverse reactions and laboratory abnormalities, respectively, in OAK.

476 **Table 8: Adverse Reactions Occurring in $\geq 10\%$ of Patients with NSCLC Receiving**
477 **TECENTRIQ in OAK**

| Adverse Reaction ¹ | TECENTRIQ N = 609 | | Docetaxel N = 578 | |
|---------------------------------|----------------------|-------------------|----------------------|-------------------|
| | All Grades (%) | Grades 3-4 (%) | All Grades (%) | Grades 3-4 (%) |
| General | | | | |
| Fatigue/Asthenia ² | 44 | 4 | 53 | 6 |
| Pyrexia | 18 | <1 | 13 | <1 |
| Respiratory | | | | |
| Cough ³ | 26 | <1 | 21 | <1 |
| Dyspnea | 22 | 2.8 | 21 | 2.6 |
| Metabolism and Nutrition | | | | |
| Decreased appetite | 23 | <1 | 24 | 1.6 |
| Musculoskeletal | | | | |
| Myalgia/pain ⁴ | 20 | 1.3 | 20 | <1 |
| Arthralgia | 12 | 0.5 | 10 | 0.2 |
| Gastrointestinal | | | | |
| Nausea | 18 | <1 | 23 | <1 |
| Constipation | 18 | <1 | 14 | <1 |
| Diarrhea | 16 | <1 | 24 | 2 |
| Skin | | | | |
| Rash ⁵ | 12 | <1 | 10 | 0 |

478 ¹ Graded per NCI CTCAE v4.0

479 ² Includes fatigue and asthenia

480 ³ Includes cough and exertional cough

481 ⁴ Includes musculoskeletal pain, musculoskeletal stiffness, musculoskeletal chest pain, myalgia

482 ⁵ Includes rash, erythematous rash, generalized rash, maculopapular rash, papular rash, pruritic rash, pustular rash,
483 pemphigoid

484 **Table 9: Laboratory Abnormalities Worsening From Baseline Occurring in $\geq 20\%$ of**
485 **Patients with NSCLC Receiving TECENTRIQ in OAK**

| Laboratory Abnormality | TECENTRIQ | | Docetaxel | |
|--------------------------------|---|-------------------|---|-------------------|
| | All Grades ¹ (%) ² | Grades 3-4 (%) | All Grades ¹ (%) ² | Grades 3-4 (%) |
| Hematology | | | | |
| Anemia | 67 | 3 | 82 | 7 |
| Lymphocytopenia | 49 | 14 | 60 | 21 |
| Chemistry | | | | |
| Hypoalbuminemia | 48 | 4 | 50 | 3 |
| Hyponatremia | 42 | 7 | 31 | 6 |
| Increased Alkaline Phosphatase | 39 | 2 | 25 | 1 |
| Increased AST | 31 | 3 | 16 | 0.5 |
| Increased ALT | 27 | 3 | 14 | 0.5 |
| Hypophosphatemia | 27 | 5 | 23 | 4 |
| Hypomagnesemia | 26 | 1 | 21 | 1 |
| Increased Creatinine | 23 | 2 | 16 | 1 |

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¹ Graded according to NCI CTCAE version 4.0

² Each test incidence is based on the number of patients who had both baseline and at least one on-study laboratory measurement available: TECENTRIQ (range: 546–585) and docetaxel (range: 532–560)

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Metastatic Triple Negative Breast Cancer (TNBC)

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The safety of TECENTRIQ in combination with paclitaxel protein-bound was evaluated in IMpassion130, a multicenter, international, randomized, double-blinded placebo-controlled trial in patients with locally advanced or metastatic TNBC who have not received prior chemotherapy for metastatic disease [see *Clinical Studies (14.3)*]. Patients received 840 mg of TECENTRIQ (n=452) or placebo (n=438) intravenously followed by paclitaxel protein-bound (100 mg/m²) intravenously. For each 28 day cycle, TECENTRIQ was administered on days 1 and 15 and paclitaxel protein-bound was administered on days 1, 8, and 15 until disease progression or unacceptable toxicity. In the safety-evaluable population, the median duration of exposure to TECENTRIQ was 5.5 months (range: 0-32 months) and paclitaxel protein-bound was 5.1 months (range: 0 – 31.5 months) in the TECENTRIQ plus paclitaxel protein-bound arm. The median duration of exposure to placebo was 5.1 months (range: 0-25.1 months) and paclitaxel protein-bound was 5.0 months (range: 0-23.7 months) in the placebo plus paclitaxel protein-bound arm.

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The most common Grades 3-4 adverse reactions occurring in ≥2%, were neutropenia (8%), peripheral neuropathies (9%), neutrophil count decreased (4.6%), fatigue (4%), anemia (2.9%), hypokalemia (2.2%), pneumonia (2.2%), and aspartate aminotransferase increased (2.0%). Adverse reactions leading to discontinuation of TECENTRIQ occurred in 6% (29/452) of patients in the TECENTRIQ and paclitaxel protein-bound arm. The most common adverse reaction leading to TECENTRIQ discontinuation was peripheral neuropathy (<1%). Fatal adverse reactions occurred in 1.3% (6/452) of patients in the TECENTRIQ and paclitaxel protein-bound arm; these included septic shock, mucosal inflammation, auto-immune hepatitis, aspiration, pneumonia, pulmonary embolism. Adverse reactions leading to interruption of TECENTRIQ occurred in 31% of patients; the most common (≥ 2%) were neutropenia, neutrophil count decreased, hyperthyroidism, and pyrexia. Serious adverse reactions occurred in 23% (103/452) of patients. The most frequent serious adverse reactions were pneumonia (2%), urinary tract infection (1%), dyspnea (1%), and pyrexia (1%).

517 Immune-related adverse reactions requiring systemic corticosteroid therapy occurred in 13%
518 (59/452) of patients in the TECENTRIQ and paclitaxel protein-bound arm.

519 Table 10 summarizes adverse reactions that occurred in at least 10% of patients treated with
520 TECENTRIQ and paclitaxel protein-bound. Table 11 summarizes selected laboratory
521 abnormalities worsening from baseline that occurred in at least 20% of patients in the
522 TECENTRIQ treated patients.

523 **Table 10: Adverse Reactions Occurring in ≥10% of Patients with TNBC (IMpassion130)**

| Adverse Reaction ¹ | TECENTRIQ in combination with paclitaxel protein-bound (n=452) | | Placebo in combination with paclitaxel protein-bound (n=438) | |
|---|--|----------------|--|----------------|
| | All Grades (%) | Grades 3–4 (%) | All Grades (%) | Grades 3–4 (%) |
| Percentage (%) of Patients | | | | |
| Skin and Subcutaneous Tissue Disorders | | | | |
| Alopecia | 56 | <1 | 58 | <1 |
| Rash | 17 | <1 | 16 | <1 |
| Pruritus | 14 | 0 | 10 | 0 |
| Nervous System | | | | |
| Peripheral neuropathies ² | 47 | 9 | 44 | 5 |
| Headache | 23 | <1 | 22 | <1 |
| Dysgeusia | 14 | 0 | 14 | 0 |
| Dizziness | 14 | 0 | 11 | 0 |
| General Disorders and administration site conditions | | | | |
| Fatigue | 47 | 4 | 45 | 3.4 |
| Pyrexia | 19 | <1 | 11 | 0 |
| Peripheral Edema | 15 | <1 | 16 | 1.4 |
| Asthenia | 12 | <1 | 11 | <1 |
| Gastrointestinal Disorders | | | | |
| Nausea | 46 | 1.1 | 38 | 1.8 |
| Diarrhea | 33 | 1.3 | 34 | 2.1 |
| Constipation | 25 | <1 | 25 | <1 |
| Vomiting | 20 | <1 | 17 | 1.1 |
| Abdominal pain | 10 | <1 | 12 | <1 |
| Respiratory, Thoracic, and Mediastinal Disorders | | | | |
| Cough | 25 | 0 | 19 | 0 |
| Dyspnea | 16 | <1 | 15 | <1 |
| Metabolism and Nutrition Disorders | | | | |
| Decreased Appetite | 20 | <1 | 18 | <1 |
| Musculoskeletal and Connective Tissue Disorders | | | | |
| Arthralgia | 18 | <1 | 16 | <1 |
| Back pain | 15 | 1.3 | 13 | <1 |
| Myalgia | 14 | <1 | 15 | <1 |

| | | | | |
|------------------------------------|----|-----|-----|----|
| Pain in extremity | 11 | <1 | 10 | <1 |
| Endocrine Disorders | | | | |
| Hypothyroidism | 14 | 0 | 3.4 | 0 |
| Infections and infestations | | | | |
| Urinary tract infection | 12 | <1 | 11 | <1 |
| Upper respiratory tract infection | 11 | 1.1 | 9 | 0 |
| Nasopharyngitis | 11 | 0 | 8 | 0 |

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¹ Graded per NCI CTCAE v4.0

² Includes peripheral neuropathy, peripheral sensory neuropathy, paresthesia, and polyneuropathy

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Table 11: Laboratory Abnormalities Worsening from Baseline Occurring in ≥20% of Patients with TNBC (IMpassion130)

| Laboratory Abnormality Test | Percentage of Patients with Worsening Laboratory Test from Baseline | | | |
|--------------------------------|---|----------------|--|----------------|
| | TECENTRIQ in combination with paclitaxel protein-bound (n=452) | | Placebo in combination with paclitaxel protein-bound (n=438) | |
| | All Grades ¹ (%) ² | Grades 3–4 (%) | All Grades ¹ (%) ² | Grades 3–4 (%) |
| Chemistry | | | | |
| Increased ALT | 43 | 6 | 34 | 2.7 |
| Increased AST | 42 | 4.9 | 34 | 3.4 |
| Decreased Calcium | 28 | 1.1 | 26 | <1 |
| Decreased Sodium | 27 | 4.2 | 25 | 2.7 |
| Decreased Albumin | 27 | <1 | 25 | <1 |
| Increased Alkaline Phosphatase | 25 | 3.3 | 22 | 2.7 |
| Decreased Phosphate | 22 | 3.6 | 19 | 3.7 |
| Increased Creatinine | 21 | <1 | 16 | <1 |
| Hematology | | | | |
| Decreased Hemoglobin | 79 | 3.8 | 73 | 3 |
| Decreased Leukocytes | 76 | 14 | 71 | 9 |
| Decreased Neutrophils | 58 | 13 | 54 | 13 |
| Decreased Lymphocytes | 54 | 13 | 47 | 8 |
| Increased Prothrombin INR | 25 | <1 | 25 | <1 |

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¹ Graded per NCI CTCAE v4.0, except for increased creatinine which only includes patients with creatinine increase based on upper limit of normal definition for grade 1 events (NCI CTCAE v5.0).

² Based on the number of patients with available baseline and at least one on-treatment laboratory test.

531 Small Cell Lung Cancer (SCLC)

532 The safety of TECENTRIQ with carboplatin and etoposide was evaluated in IMpower133, a
533 randomized, multicenter, double-blind, placebo-controlled trial in which 198 patients with ES-
534 SCLC received TECENTRIQ 1200 mg and carboplatin AUC 5 mg/mL/min on Day 1 and
535 etoposide 100 mg/m² intravenously on Days 1, 2 and 3 of each 21-day cycle for a maximum of 4
536 cycles, followed by TECENTRIQ 1200 mg every 3 weeks until disease progression or
537 unacceptable toxicity [see *Clinical Studies (14.4)*]. Among 198 patients receiving TECENTRIQ,
538 32% were exposed for 6 months or longer and 12% were exposed for 12 months or longer.

539 The most common Grades 3–4 adverse reactions (≥2%) were fatigue/asthenia (5%), febrile
540 neutropenia (3.5%), pneumonia (3.0%), asthenia (2.5%), diarrhea (2.0%), and infusion related
541 reaction (2.0%).

542 Fatal adverse reactions occurred in 2% of patients receiving TECENTRIQ. These included
543 pneumonia, respiratory failure, neutropenia, and death (1 patient each).

544 Serious adverse reactions occurred in 37% of patients receiving TECENTRIQ. Serious adverse
545 reactions in >2% were pneumonia (4.5%), neutropenia (3.5%), febrile neutropenia (2.5%), and
546 thrombocytopenia (2.5%).

547 TECENTRIQ was discontinued due to adverse reactions in 11% of patients. The most frequent
548 adverse reaction requiring permanent discontinuation in >2% of patients was infusion-related
549 reactions (2.5%).

550 Adverse reactions leading to interruption of TECENTRIQ occurred in 59% of patients; the most
551 common (>1%) were neutropenia (22%), anemia (9%), leukopenia (7%), thrombocytopenia
552 (5%), fatigue (4.0%), infusion-related reaction (3.5%), pneumonia (2.0%), febrile neutropenia
553 (1.5%), increased ALT (1.5%), and nausea (1.5%).

554 Tables 12 and 13 summarize adverse reactions and laboratory abnormalities, respectively, in
555 patients who received TECENTRIQ with carboplatin and etoposide in IMpower133.

**Table 12: Adverse Reactions Occurring in ≥20% of Patients with SCLC
Receiving TECENTRIQ in IMpower133**

| Adverse Reaction | TECENTRIQ with Carboplatin and Etoposide N = 198 | | Placebo with Carboplatin and Etoposide N = 196 | |
|-------------------------------------|---|--------------------------------|---|--------------------------------|
| | All Grades ¹ (%) | Grades 3–4 ¹ (%) | All Grades ¹ (%) | Grades 3–4 ¹ (%) |
| General | | | | |
| Fatigue/asthenia | 39 | 5 | 33 | 3 |
| Gastrointestinal | | | | |
| Nausea | 38 | 1 | 33 | 1 |
| Constipation | 26 | 1 | 30 | 1 |
| Vomiting | 20 | 2 | 17 | 3 |
| Skin and Subcutaneous Tissue | | | | |
| Alopecia | 37 | 0 | 35 | 0 |
| Metabolism and Nutrition | | | | |
| Decreased appetite | 27 | 1 | 18 | 0 |

¹ Graded per NCI CTCAE v4.0

**Table 13: Laboratory Abnormalities Worsening from Baseline Occurring in
≥20% of Patients with SCLC Receiving TECENTRIQ in IMpower133**

| Laboratory Abnormality | TECENTRIQ with Carboplatin and Etoposide ² | | Placebo with Carboplatin and Etoposide ² | |
|--------------------------------|---|--|---|--|
| | All Grades ¹ (%) ² | Grades 3–4 ¹ (%) ² | All Grades ¹ (%) ² | Grades 3–4 ¹ (%) ² |
| Hematology | | | | |
| Anemia | 94 | 17 | 93 | 19 |
| Neutropenia | 73 | 45 | 76 | 48 |
| Thrombocytopenia | 58 | 20 | 53 | 17 |
| Lymphopenia | 46 | 14 | 38 | 11 |
| Chemistry | | | | |
| Hyperglycemia | 67 | 10 | 65 | 8 |
| Increased Alkaline Phosphatase | 38 | 1 | 35 | 2 |
| Hyponatremia | 34 | 15 | 33 | 11 |
| Hypoalbuminemia | 32 | 1 | 30 | 0 |
| Decreased TSH ³ | 28 | NA ³ | 15 | NA ³ |
| Hypomagnesemia | 31 | 5 | 35 | 6 |
| Hypocalcemia | 26 | 3 | 28 | 5 |
| Increased ALT | 26 | 3 | 31 | 1 |
| Increased AST | 22 | 1 | 21 | 2 |
| Increased Blood Creatinine | 22 | 4 | 15 | 1 |
| Hyperphosphatemia ³ | 21 | NA ³ | 23 | NA ³ |
| Increased TSH ³ | 21 | NA ³ | 7 | NA ³ |

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¹ Graded per NCI CTCAE v4.0

² Each test incidence is based on the number of patients who had both baseline and at least one on-study laboratory measurement available: TECENTRIQ (range: 181-193); Placebo (range: 181-196)

³ NA= Not applicable. NCI CTCAE v4.0 does not include these laboratories.

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6.2 Immunogenicity

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As with all therapeutic proteins, there is a potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to atezolizumab in the studies described above with the incidence of antibodies in other studies or to other products may be misleading.

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Among 565 patients with NSCLC in OAK, 30% tested positive for treatment-emergent anti-drug antibodies (ADA) at one or more post-dose time points. The median onset time to ADA formation was 3 weeks. The ability of these binding ADA to neutralize atezolizumab is unknown. Patients who tested positive for treatment-emergent ADA also had decreased systemic atezolizumab exposure [see *Clinical Pharmacology (12.3)*]. Exploratory analyses showed that the subset of patients who were ADA positive by week 4 (21%; 118/560) appeared to have less efficacy (effect on overall survival) as compared to patients who tested negative for treatment-emergent ADA by week 4 [see *Clinical Studies (14.2)*]. The presence of ADA did not have a clinically significant effect on the incidence or severity of adverse reactions.

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Among 275 patients with urothelial carcinoma in IMvigor210 (Cohort 2), 42% tested positive for treatment-emergent ADA at one or more post-dose time points. Among 111 patients in IMvigor210 (Cohort 1), 48% tested positive for treatment-emergent ADA at one or more post-dose time points. Patients who tested positive for treatment-emergent ADA also had decreased

587 systemic atezolizumab exposures. The presence of ADA did not have a clinically significant
588 effect on the incidence or severity of adverse reactions.

589 Among 364 ADA-evaluable patients with NSCLC who received TECENTRIQ with
590 bevacizumab, paclitaxel and carboplatin in IMpower150, 36% (n=132) tested positive for
591 treatment-emergent ADA at one or more post-dose time points and 83% of these 132 patients
592 tested ADA positive prior to receiving the second dose of atezolizumab. The ability of these
593 binding ADA to neutralize atezolizumab is unknown. Patients who tested positive for treatment-
594 emergent ADA had lower systemic atezolizumab exposure as compared to patients who were
595 ADA negative [see *Clinical Pharmacology (12.3)*]. The presence of ADA did not increase the
596 incidence or severity of adverse reactions [see *Clinical Studies (14.2)*].

597 Among 434 patients with TNBC in IMpassion130, 13% tested positive for treatment-emergent
598 ADA at one or more post-dose time points. Among 178 patients in PD-L1 positive subgroup
599 with TNBC in IMpassion130, 12% tested positive for treatment-emergent ADA at one or more
600 post-dose time points. Patients who tested positive for treatment-emergent ADA had decreased
601 systemic atezolizumab exposure [see *Clinical Pharmacology (12.3)*]. There are insufficient
602 numbers of patients in the PD-L1 positive subgroup with ADA to determine whether ADA alters
603 the efficacy of atezolizumab. The presence of ADA did not have a clinically significant effect on
604 the incidence or severity of adverse reactions.

605 **8 USE IN SPECIFIC POPULATIONS**

606 **8.1 Pregnancy**

607 Risk Summary

608 Based on its mechanism of action [see *Clinical Pharmacology (12.1)*], TECENTRIQ can cause
609 fetal harm when administered to a pregnant woman. There are no available data on the use of
610 TECENTRIQ in pregnant women.

611 Animal studies have demonstrated that inhibition of the PD-L1/PD-1 pathway can lead to
612 increased risk of immune-related rejection of the developing fetus resulting in fetal death (see
613 *Data*). Advise females of reproductive potential of the potential risk to a fetus.

614 In the U.S. general population, the estimated background risk of major birth defects and
615 miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

616 Data

617 *Animal Data*

618 Animal reproduction studies have not been conducted with TECENTRIQ to evaluate its effect on
619 reproduction and fetal development. A literature-based assessment of the effects on reproduction
620 demonstrated that a central function of the PD-L1/PD-1 pathway is to preserve pregnancy by
621 maintaining maternal immune tolerance to a fetus. Blockage of PD-L1 signaling has been shown
622 in murine models of pregnancy to disrupt tolerance to a fetus and to result in an increase in fetal
623 loss; therefore, potential risks of administering TECENTRIQ during pregnancy include increased
624 rates of abortion or stillbirth. As reported in the literature, there were no malformations related to
625 the blockade of PD-L1/PD-1 signaling in the offspring of these animals; however, immune-
626 mediated disorders occurred in PD-1 and PD-L1 knockout mice. Based on its mechanism of
627 action, fetal exposure to atezolizumab may increase the risk of developing immune-mediated
628 disorders or altering the normal immune response.

629 **8.2 Lactation**

630 Risk Summary

631 There is no information regarding the presence of atezolizumab in human milk, the effects on the
632 breastfed infant, or the effects on milk production. As human IgG is excreted in human milk, the
633 potential for absorption and harm to the infant is unknown. Because of the potential for serious
634 adverse reactions in breastfed infants from TECENTRIQ, advise women not to breastfeed during
635 treatment and for at least 5 months after the last dose.

636 **8.3 Females and Males of Reproductive Potential**

637 Pregnancy Testing

638 Verify pregnancy status in females of reproductive potential prior to initiating TECENTRIQ [*see*
639 *Use in Specific Populations (8.1)*].

640 Contraception

641 *Females*

642 Based on its mechanism of action, TECENTRIQ can cause fetal harm when administered to a
643 pregnant woman [*see Use in Specific Populations (8.1)*]. Advise females of reproductive
644 potential to use effective contraception during treatment with TECENTRIQ and for at least
645 5 months following the last dose.

646 Infertility

647 *Females*

648 Based on animal studies, TECENTRIQ may impair fertility in females of reproductive potential
649 while receiving treatment [*see Nonclinical Toxicology (13.1)*].

650 **8.4 Pediatric Use**

651 The safety and effectiveness of TECENTRIQ have not been established in pediatric patients.

652 **8.5 Geriatric Use**

653 Of 2481 patients with urothelial carcinoma, lung cancer, and triple-negative breast cancer who
654 were treated with TECENTRIQ in clinical studies, 45% were 65 years and over and 11% were
655 75 years and over. No overall differences in safety or effectiveness were observed between
656 patients aged 65 years or older, and younger patients.

657 **11 DESCRIPTION**

658 Atezolizumab is a programmed cell death ligand 1 (PD-L1) blocking antibody. Atezolizumab is
659 an Fc-engineered, humanized, non-glycosylated IgG1 kappa immunoglobulin that has a
660 calculated molecular mass of 145 kDa.

661 TECENTRIQ (atezolizumab) injection for intravenous use is a sterile, preservative-free,
662 colorless to slightly yellow solution in single-dose vials. Each 20 mL vial contains 1200 mg of
663 atezolizumab and is formulated in glacial acetic acid (16.5 mg), L-histidine (62 mg),
664 polysorbate 20 (8 mg), and sucrose (821.6 mg), with a pH of 5.8. Each 14 mL vial contains 840
665 mg of atezolizumab and is formulated in glacial acetic acid (11.5 mg), L-histidine (43.4 mg),
666 polysorbate 20 (5.6 mg), and sucrose (575.1 mg) with a pH of 5.8.

667 **12 CLINICAL PHARMACOLOGY**

668 **12.1 Mechanism of Action**

669 PD-L1 may be expressed on tumor cells and/or tumor infiltrating immune cells and can
670 contribute to the inhibition of the anti-tumor immune response in the tumor microenvironment.

671 Binding of PD-L1 to the PD-1 and B7.1 receptors found on T cells and antigen presenting cells
672 suppresses cytotoxic T-cell activity, T-cell proliferation and cytokine production.

673 Atezolizumab is a monoclonal antibody that binds to PD-L1 and blocks its interactions with both
674 PD-1 and B7.1 receptors. This releases the PD-L1/PD-1 mediated inhibition of the immune
675 response, including activation of the anti-tumor immune response without inducing antibody-
676 dependent cellular cytotoxicity. In syngeneic mouse tumor models, blocking PD-L1 activity
677 resulted in decreased tumor growth.

678 **12.3 Pharmacokinetics**

679 Patients' exposure to atezolizumab increased dose proportionally over the dose range of 1 mg/kg
680 to 20 mg/kg, including a dose of 1200 mg administered every 3 weeks. The clearance (CV%)
681 was 0.20 L/day (29%), the volume of distribution at steady state was 6.9 L, and the terminal half-
682 life was 27 days. Steady state was achieved after 6 to 9 weeks following multiple doses. The
683 systemic accumulation ratio for every 2 weeks administration and every 3 weeks administration
684 was 3.3- and 1.9- fold, respectively. Atezolizumab clearance was found to decrease over time,
685 with a mean maximal reduction (CV%) from baseline value of approximately 17% (41%);
686 however, the decrease in clearance was not considered clinically relevant.

687 Specific Populations

688 Age (21 to 89 years), body weight, sex, albumin levels, tumor burden, region or race, mild or
689 moderate renal impairment [estimated glomerular filtration rate (eGFR) 30 to 89 mL/min/1.73
690 m²], mild hepatic impairment (bilirubin ≤ ULN and AST > ULN or bilirubin > 1 to 1.5 × ULN
691 and any AST), level of PD-L1 expression, or performance status had no clinically significant
692 effect on the systemic exposure of atezolizumab. In OAK, IMpower150 (TECENTRIQ,
693 bevacizumab, paclitaxel, carboplatin arm only), and IMpassion130 (TECENTRIQ and paclitaxel
694 protein-bound) atezolizumab clearance in patients who tested positive for treatment-emergent
695 anti-drug antibodies (ADA) was 25%, 18%, and 22% higher, respectively, as compared to
696 clearance in patients who tested negative for treatment-emergent ADA.

697 The effect of severe renal impairment or moderate or severe hepatic impairment on the
698 pharmacokinetics of atezolizumab is unknown.

699 Drug Interaction Studies

700 The drug interaction potential of atezolizumab is unknown.

701 **13 NONCLINICAL TOXICOLOGY**

702 **13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility**

703 No studies have been performed to test the potential of atezolizumab for carcinogenicity or
704 genotoxicity.

705 Animal fertility studies have not been conducted with atezolizumab; however, an assessment of
706 the male and female reproductive organs was included in a 26-week, repeat-dose toxicity study
707 in cynomolgus monkeys. Weekly administration of atezolizumab to female monkeys at the
708 highest dose tested caused an irregular menstrual cycle pattern and a lack of newly formed
709 corpora lutea in the ovaries. This effect occurred at an estimated AUC approximately 6 times the
710 AUC in patients receiving the recommended dose and was reversible. There was no effect on the
711 male monkey reproductive organs.

712 **13.2 Animal Toxicology and/or Pharmacology**

713 In animal models, inhibition of PD-L1/PD-1 signaling increased the severity of some infections
714 and enhanced inflammatory responses. M. tuberculosis-infected PD-1 knockout mice exhibit
715 markedly decreased survival compared with wild-type controls, which correlated with increased

716 bacterial proliferation and inflammatory responses in these animals. PD-L1 and PD-1 knockout
717 mice and mice receiving PD-L1 blocking antibody have also shown decreased survival following
718 infection with lymphocytic choriomeningitis virus.

719 **14 CLINICAL STUDIES**

720 **14.1 Urothelial Carcinoma**

721 Cisplatin-Ineligible Patients with Locally Advanced or Metastatic Urothelial Carcinoma

722 The efficacy of TECENTRIQ was investigated in IMvigor210 (Cohort 1) (NCT02951767), a
723 multicenter, open-label, single-arm trial that included 119 patients with locally advanced or
724 metastatic urothelial carcinoma who were ineligible for cisplatin-containing chemotherapy and
725 were either previously untreated or had disease progression at least 12 months after neoadjuvant
726 or adjuvant chemotherapy. Patients were considered cisplatin-ineligible if they met any one of
727 the following criteria at study entry: impaired renal function [creatinine clearance (CLcr) of 30 to
728 59 mL/min], Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 2,
729 hearing loss of ≥ 25 decibels (dB) at two contiguous frequencies, or Grades 2-4 peripheral
730 neuropathy. This study excluded patients who had: a history of autoimmune disease; active or
731 corticosteroid-dependent brain metastases; administration of a live, attenuated vaccine within
732 28 days prior to enrollment; or administration of systemic immunostimulatory agents within 6
733 weeks or systemic immunosuppressive medications within 2 weeks prior to enrollment. Patients
734 received TECENTRIQ 1200 mg as an intravenous infusion every 3 weeks until unacceptable
735 toxicity or disease progression. Tumor response assessments were conducted every 9 weeks for
736 the first 54 weeks and every 12 weeks thereafter. Major efficacy outcome measures included
737 confirmed overall response rate (ORR) as assessed by independent review facility (IRF) using
738 Response Evaluation Criteria in Solid Tumors (RECIST v1.1), duration of response (DoR) and
739 overall survival (OS).

740 In this study, the median age was 73 years, 81% were male, and 91% were White. Thirty-five
741 percent of patients had non-bladder urothelial carcinoma and 66% had visceral metastases.
742 Eighty percent of patients had an ECOG PS of 0 or 1. Reasons for ineligibility for cisplatin-
743 containing chemotherapy were: 70% had impaired renal function, 20% had an ECOG PS of 2,
744 14% had a hearing loss of ≥ 25 dB, and 6% had Grades 2-4 peripheral neuropathy at baseline.
745 Twenty percent of patients had disease progression following prior platinum-containing
746 neoadjuvant or adjuvant chemotherapy.

747 Tumor specimens were evaluated prospectively using the VENTANA PD-L1 (SP142) Assay at a
748 central laboratory, and the results were used to define subgroups for pre-specified analyses. Of
749 the 119 patients, 27% were classified as having PD-L1 expression of $\geq 5\%$ (defined as PD-L1
750 stained tumor-infiltrating immune cells [IC] covering $\geq 5\%$ of the tumor area). The remaining
751 73% of patients were classified as having PD-L1 expression of $< 5\%$ (PD-L1 stained tumor-
752 infiltrating IC covering $< 5\%$ of the tumor area).

753 Among the 32 patients with PD-L1 expression of $\geq 5\%$, median age was 67 years, 81% were
754 male, 19% female, and 88% were White. Twenty-eight percent of patients had non-bladder
755 urothelial carcinoma and 56% had visceral metastases. Seventy-two percent of patients had an
756 ECOG PS of 0 or 1. Reasons for ineligibility for cisplatin-containing chemotherapy were: 66%
757 had impaired renal function, 28% had an ECOG PS of 2, 16% had a hearing loss ≥ 25 dB, and
758 9% had Grades 2-4 peripheral neuropathy at baseline. Thirty-one percent of patients had disease
759 progression following prior platinum-containing neoadjuvant or adjuvant chemotherapy.

760 Confirmed ORR in all patients and the two PD-L1 subgroups are summarized in Table 14. The
761 median follow-up time for this study was 14.4 months. In 24 patients with disease progression
762 following neoadjuvant or adjuvant therapy, the ORR was 33% (95% CI: 16%, 55%).

Table 14: Efficacy Results in IMvigor210 (Cohort 1)

| | All Patients | PD-L1 Expression Subgroups | |
|--|--------------------|--|--|
| | N = 119 | PD-L1 Expression of < 5% in ICs ¹ N = 87 | PD-L1 Expression of ≥ 5% in ICs ¹ N = 32 |
| Number of IRF-assessed Confirmed Responders | 28 | 19 | 9 |
| ORR % (95% CI) | 23.5% (16.2, 32.2) | 21.8% (13.7, 32) | 28.1% (13.8, 46.8) |
| Complete Response (CR) (%) | 6.7% | 6.9% | 6.3% |
| Partial Response (PR) (%) | 16.8% | 14.9% | 21.9% |
| Median DoR, months (range) | NR (3.7, 16.6+) | NR (3.7, 16.6+) | NR (8.1, 15.6+) |
| NR = Not reached + Denotes a censored value ¹ PD-L1 expression in tumor-infiltrating immune cells (ICs) | | | |

764

765 IMvigor130 (NCT02807636) is an ongoing multicenter, randomized study in previously
766 untreated patients with metastatic urothelial carcinoma who are eligible for platinum-containing
767 chemotherapy. The study contains three arms: TECENTRIQ monotherapy, TECENTRIQ with
768 platinum-based chemotherapy (i.e., cisplatin or carboplatin with gemcitabine), and platinum-
769 based chemotherapy alone (comparator). Both cisplatin-eligible and cisplatin-ineligible patients
770 are included in the study. Tumor specimens were evaluated prospectively using the VENTANA
771 PD-L1 (SP142) Assay at a central laboratory. The independent Data Monitoring Committee
772 (iDMC) for the study conducted a review of early data and found that patients classified as
773 having PD-L1 expression of <5% when treated with TECENTRIQ monotherapy had decreased
774 survival compared to those who received platinum-based chemotherapy. The iDMC
775 recommended closure of the monotherapy arm to further accrual of patients with low PD-L1
776 expression, however, no other changes were recommended for the study, including any change
777 of therapy for patients who had already been randomized to and were receiving treatment in the
778 monotherapy arm.

779

Previously Treated Locally Advanced or Metastatic Urothelial Carcinoma

780

781 The efficacy of TECENTRIQ was investigated in IMvigor210 (Cohort 2) (NCT02108652), a
782 multicenter, open-label, single-arm trial that included 310 patients with locally advanced or
783 metastatic urothelial carcinoma who had disease progression during or following a platinum-
784 containing chemotherapy regimen or who had disease progression within 12 months of treatment
785 with a platinum-containing neoadjuvant or adjuvant chemotherapy regimen. This study excluded
786 patients who had: a history of autoimmune disease, active or corticosteroid-dependent brain
787 metastases, administration of a live, attenuated vaccine within 28 days prior to enrollment, or
788 administration of systemic immunostimulatory agents within 6 weeks or systemic
789 immunosuppressive medications within 2 weeks prior to enrollment. Patients received
790 TECENTRIQ 1200 mg intravenously every 3 weeks until unacceptable toxicity or either
791 radiographic or clinical progression. Tumor response assessments were conducted every 9 weeks
792 for the first 54 weeks and every 12 weeks thereafter. Major efficacy outcome measures included
792 confirmed ORR as assessed by IRF using RECIST v1.1 and DoR.

793

In this study, the median age was 66 years, 78% were male, 91% of patients were White.

794

Twenty-six percent had non-bladder urothelial carcinoma and 78% of patients had visceral

795 metastases. Sixty-two percent of patients had an ECOG PS of 1 and 35% of patients had a
796 baseline CLcr < 60 mL/min. Nineteen percent of patients had disease progression following prior
797 platinum-containing neoadjuvant or adjuvant chemotherapy. Forty-one percent of patients had
798 received 2 or more prior systemic regimens in the metastatic setting. Seventy-three percent of
799 patients received prior cisplatin, 26% had prior carboplatin, and 1% were treated with other
800 platinum-based regimens.

801 Tumor specimens were evaluated prospectively using the VENTANA PD-L1 (SP142) Assay at a
802 central laboratory and the results were used to define subgroups for pre-specified analyses. Of
803 the 310 patients, 32% were classified as having PD-L1 expression of ≥ 5%. The remaining 68%
804 of patients were classified as having PD-L1 expression of < 5%.

805 Confirmed ORR and median DOR in all patients and the two PD-L1 subgroups are summarized
806 in Table 15. The median follow-up time for this study was 32.9 months. In 59 patients with
807 disease progression following neoadjuvant or adjuvant therapy, the ORR was 22.0% (95% CI:
808 12.3%, 34.7%).

809 **Table 15: Efficacy Results in IMvigor210 (Cohort 2)**

| | All Patients | PD-L1 Expression Subgroups | |
|---|-----------------------|--|--|
| | N = 310 | PD-L1 Expression of < 5% in IC ¹ N = 210 | PD-L1 Expression of ≥ 5% in IC ¹ N = 100 |
| Number of IRF-assessed Confirmed Responders | 46 | 20 | 26 |
| ORR % (95% CI) | 14.8% (11.2, 19.3) | 9.5% (5.9, 14.3) | 26% (17.7, 35.7) |
| Complete Response (CR) (%) | 5.5% | 2.4% | 12.0% |
| Partial Response (PR) (%) | 9.4% | 7.1% | 14.0% |
| Median DOR, months (range) | 27.7 (2.1+, 33.4+) | 20.9 (2.1+, 33.4+) | 29.7 (4.2, 31.2+) |
| + Denotes a censored value | | | |
| ¹ PD-L1 expression in tumor-infiltrating immune cells (IC) | | | |

810

811 **14.2 Non-Small Cell Lung Cancer**

812 Metastatic Chemotherapy-Naive Non-Squamous NSCLC

813 The efficacy of TECENTRIQ with bevacizumab, paclitaxel, and carboplatin was evaluated in
814 IMpower150 (NCT02366143), a multicenter, international, randomized (1:1:1), open-label trial
815 in 1202 patients with metastatic non-squamous NSCLC. IMpower150 enrolled patients with
816 stage IV non-squamous NSCLC who had received no prior chemotherapy for metastatic disease,
817 but could have received prior EGFR or ALK kinase inhibitor if appropriate, regardless of PD-L1
818 or T-effector gene (tGE) status and ECOG performance status 0 or 1. The trial excluded patients
819 with a history of autoimmune disease, administration of a live attenuated vaccine within 28 days
820 prior to randomization, active or untreated CNS metastases, administration of systemic
821 immunostimulatory agents within 4 weeks or systemic immunosuppressive medications within 2
822 weeks prior to randomization, or clear tumor infiltration into the thoracic great vessels or clear
823 cavitation of pulmonary lesions as seen on imaging.

824 Randomization was stratified by sex, presence of liver metastases, and PD-L1 expression status
825 on tumor cells (TC) and tumor-infiltrating immune cells (IC) as follows: TC3 and any IC vs.

826 TC0/1/2 and IC2/3 vs. TC0/1/2 and IC0/1. Patients were randomized to one of the following
827 three treatment arms.

- 828 • Arm A: TECENTRIQ 1200 mg, paclitaxel 175 mg/m² or 200 mg/m² and carboplatin AUC 6
829 mg/mL/min on Day 1 of each 21-day cycle for a maximum of 4 or 6 cycles
- 830 • Arm B: TECENTRIQ 1200 mg, bevacizumab 15 mg/kg, paclitaxel 175 mg/m² or 200 mg/m²,
831 and carboplatin AUC 6 mg/mL/min on Day 1 of each 21-day cycle for a maximum of 4 or 6
832 cycles
- 833 • Arm C: bevacizumab 15 mg/kg, paclitaxel 175 mg/m² or 200 mg/m², and carboplatin AUC 6
834 mg/mL/min on Day 1 of each 21-day cycle for a maximum of 4 or 6 cycles

835 Patients who had not experienced disease progression following the completion or cessation of
836 platinum-based chemotherapy, received:

- 837 • Arm A: TECENTRIQ 1200 mg intravenously on Day 1 of each 21-day cycle until disease
838 progression or unacceptable toxicity
- 839 • Arm B: TECENTRIQ 1200 mg and bevacizumab 15 mg/kg intravenously on Day 1 of each
840 21-day cycle until disease progression or unacceptable toxicity
- 841 • Arm C: bevacizumab 15 mg/kg intravenously on Day 1 of each 21-day cycle until disease
842 progression or unacceptable toxicity

843 Tumor assessments were conducted every 6 weeks for the first 48 weeks following Cycle 1, Day
844 1 and then every 9 weeks thereafter. Tumor specimens were evaluated prior to randomization for
845 PD-L1 tumor expression using the VENTANA PD-L1 (SP142) assay at a central laboratory.
846 Tumor tissue was collected at baseline for expression of tGE signature and evaluation was
847 performed using a clinical trial assay in a central laboratory prior to the analysis of efficacy
848 outcome measures.

849 The major efficacy outcome measures for comparison of Arms B and C were progression free
850 survival (PFS) by RECIST v1.1 in the tGE-WT (patients with high expression of T-effector gene
851 signature [tGE], excluding those with EGFR- and ALK-positive NSCLC [WT]) and in the ITT-
852 WT subpopulations and overall survival (OS) in the ITT-WT subpopulation. Additional efficacy
853 outcome measures for comparison of Arms B and C or Arms A and C were PFS and OS in the
854 ITT population, OS in the tGE-WT subpopulation, and ORR/DoR in the tGE-WT and ITT-WT
855 subpopulations.

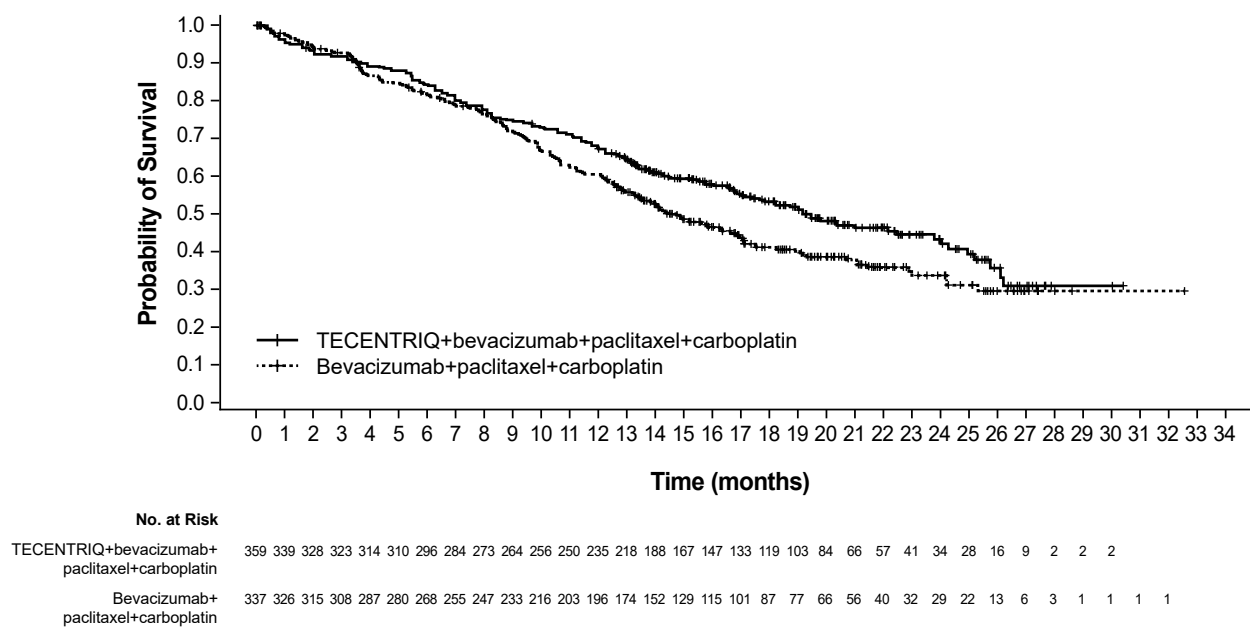
856 A total of 1202 patients were enrolled across the three arms of whom 1045 were in the ITT-WT
857 subpopulation and 447 were in the tGE-WT subpopulation. The demographic information is
858 limited to the 800 patients enrolled in Arms B and C where efficacy has been demonstrated. The
859 median age was 63 years (range: 31 to 90), and 60% of patients were male. The majority of
860 patients were White (82%), 13% of patients were Asian, 10% were Hispanic, and 2% of patients
861 were Black. Clinical sites in Asia (enrolling 13% of the study population) received paclitaxel at a
862 dose of 175 mg/m² while the remaining 87% received paclitaxel at a dose of 200 mg/m².
863 Approximately 14% of patients had liver metastases at baseline, and most patients were current
864 or previous smokers (80%). Baseline ECOG performance status was 0 (43%) or 1 (57%). PD-L1
865 was TC3 and any IC in 12%, TC0/1/2 and IC2/3 in 13%, and TC0/1/2 and IC0/1 in 75%. The
866 demographics for the 696 patients in the ITT-WT subpopulation were similar to the ITT
867 population except for the absence of patients with EGFR- or ALK-positive NSCLC.

868 The trial demonstrated a statistically significant improvement in PFS between Arms B and C in
869 both the tGE-WT and ITT-WT subpopulations, but did not demonstrate a significant difference
870 for either subpopulation between Arms A and C based on the final PFS analyses. In the interim
871 analysis of OS, a statistically significant improvement was observed for Arm B compared to
872 Arm C, but not for Arm A compared to Arm C. Efficacy results for the ITT-WT subpopulation
873 are presented in Table 16 and Figure 1.

Table 16: Efficacy Results in ITT-WT Population in IMpower150

| | Arm C: Bevacizumab, Paclitaxel and Carboplatin N = 337 | Arm B: TECENTRIQ with Bevacizumab, Paclitaxel, and Carboplatin N = 359 | Arm A: TECENTRIQ with Paclitaxel, and Carboplatin N = 349 |
|---|--|--|---|
| Overall Survival¹ | | | |
| Deaths (%) | 197 (59%) | 179 (50%) | 179 (51%) |
| Median, months | 14.7 | 19.2 | 19.4 |
| (95% CI) | (13.3, 16.9) | (17.0, 23.8) | (15.7, 21.3) |
| Hazard ratio ² (95% CI) | --- | 0.78 (0.64, 0.96) | 0.84 (0.72, 1.08) |
| p-value ³ | --- | 0.016 ⁴ | 0.204 ⁵ |
| Progression-Free Survival⁶ | | | |
| Number of events (%) | 247 (73%) | 247 (69%) | 245 (70%) |
| Median, months | 7.0 | 8.5 | 6.7 |
| (95% CI) | (6.3, 7.9) | (7.3, 9.7) | (5.6, 6.9) |
| Hazard ratio ² (95% CI) | --- | 0.71 (0.59, 0.85) | 0.94 (0.79, 1.13) |
| p-value ³ | --- | 0.0002 ⁷ | 0.5219 |
| Objective Response Rate⁶ | | | |
| Number of responders (%) | 142 (42%) | 196 (55%) | 150 (43%) |
| (95% CI) | (37, 48) | (49, 60) | (38, 48) |
| Complete response | 3 (1%) | 14 (4%) | 9 (3%) |
| Partial response | 139 (41%) | 182 (51%) | 141 (40%) |
| Duration of Response⁶ | n = 142 | n = 196 | n = 150 |
| Median (months) | 6.5 | 10.8 | 9.5 |
| (95% CI) | (5.6, 7.6) | (8.4, 13.9) | (7.0, 13.0) |
| ¹ Based on OS interim analysis . ² Stratified by sex, presence of liver metastases, and PD-L1 expression status on TC and IC ³ Based on the stratified log-rank test compared to Arm C ⁴ Compared to the allocated $\alpha=0.0174$ (two sided) for this interim analysis. ⁵ Compared to the allocated $\alpha=0.0128$ (two sided) for this interim analysis. ⁶ As determined by independent review facility (IRF) per RECIST v1.1 (Response Evaluation Criteria in Solid Tumors v1.1) ⁷ Compared to the allocated $\alpha=0.006$ (two sided) for the final PFS analysis. CI=confidence interval | | | |

875 **Figure 1: Kaplan-Meier Curves for Overall Survival in ITT-WT Population in IMpower150**



876 Exploratory analyses showed that the subset of patients in the four drug regimen arm who were
 877 ADA positive by week 4 (30%) appeared to have similar efficacy (effect on overall survival) as
 878 compared to patients who tested negative for treatment-emergent ADA by week 4 (70%) [see
 879 *Adverse Reactions (6.2), Clinical Pharmacology (12.3)*]. In an exploratory analysis, propensity
 880 score matching was conducted to compare ADA positive patients in the TECENTRIQ,
 881 bevacizumab, paclitaxel, and carboplatin arm with a matched population in the bevacizumab,
 882 paclitaxel, and carboplatin arm. Similarly ADA negative patients in the TECENTRIQ,
 883 bevacizumab, paclitaxel, and carboplatin arm were compared with a matched population in the
 884 bevacizumab, paclitaxel, and carboplatin arm. Propensity score matching factors were: baseline
 885 sum of longest tumor size (BSLD), baseline ECOG, baseline albumin, baseline LDH, sex, tobacco
 886 history, metastatic site, TC level, and IC level. The hazard ratio comparing the ADA-positive
 887 subgroup with its matched control was 0.69 (95% CI: 0.44, 1.07). The hazard ratio comparing the
 888 ADA-negative subgroup with its matched control was 0.64 (95% CI: 0.46, 0.90).
 889

890 Previously Treated Metastatic NSCLC

891 The efficacy of TECENTRIQ was evaluated in a multicenter, international, randomized (1:1),
 892 open-label study (OAK; NCT02008227) conducted in patients with locally advanced or
 893 metastatic NSCLC whose disease progressed during or following a platinum-containing regimen.
 894 Patients with a history of autoimmune disease, symptomatic or corticosteroid-dependent brain
 895 metastases, or requiring systemic immunosuppression within 2 weeks prior to enrollment were
 896 ineligible. Randomization was stratified by PD-L1 expression tumor-infiltrating immune cells
 897 (IC), the number of prior chemotherapy regimens (1 vs. 2), and histology (squamous vs. non-
 898 squamous).

899 Patients were randomized to receive TECENTRIQ 1200 mg intravenously every 3 weeks until
 900 unacceptable toxicity, radiographic progression, or clinical progression or docetaxel 75 mg/m²
 901 intravenously every 3 weeks until unacceptable toxicity or disease progression. Tumor
 902 assessments were conducted every 6 weeks for the first 36 weeks and every 9 weeks thereafter.
 903 The major efficacy outcome measure was overall survival (OS) in the first 850 randomized
 904 patients and OS in the subgroup of patients with PD-L1-expressing tumors (defined as ≥ 1% PD-
 905 L1 expression on tumor cells [TC] or immune cells [IC]). Additional efficacy outcome measures

906 were OS in all randomized patients (n = 1225), OS in subgroups based on PD-L1 expression,
907 overall response rate (ORR), and progression free survival as assessed by the investigator per
908 RECIST v.1.1.

909 Among the first 850 randomized patients, the median age was 64 years (33 to 85 years) and 47%
910 were ≥ 65 years old; 61% were male; 70% were White and 21% were Asian; 15% were current
911 smokers and 67% were former smokers; and 37% had baseline ECOG PS of 0 and 63% had a
912 baseline ECOG PS of 1. Nearly all (94%) had metastatic disease, 74% had non-squamous
913 histology, 75% had received only one prior platinum-based chemotherapy regimen, and 55% of
914 patients had PD-L1-expressing tumors.

915 Efficacy results are presented in Table 17 and Figure 2.

916

Table 17: Efficacy Results in OAK

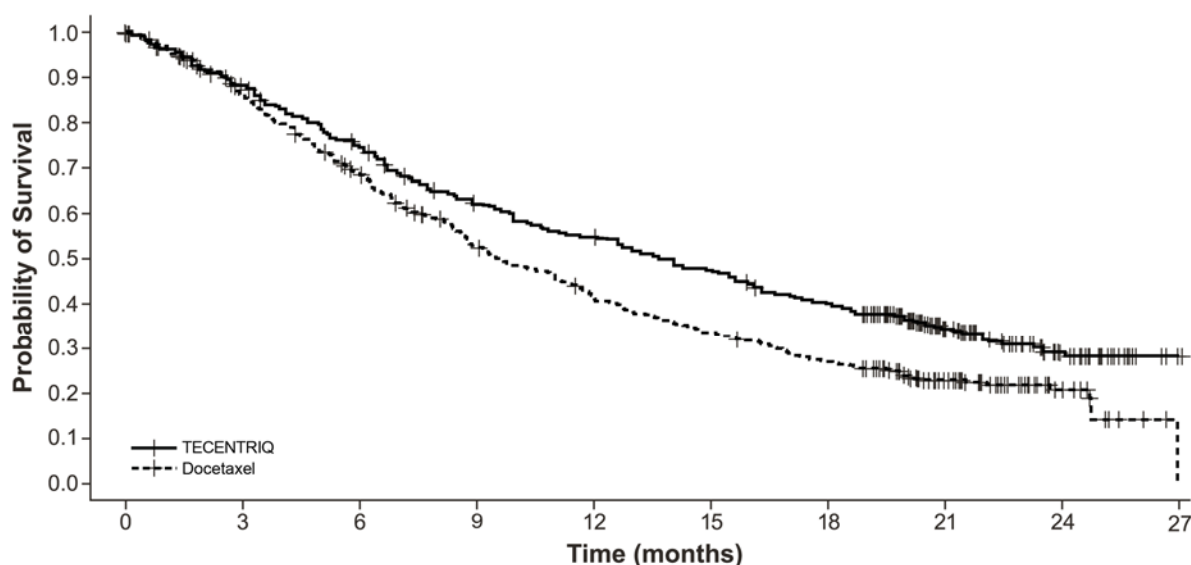
| | TECENTRIQ | Docetaxel |
|---|---------------------|------------------|
| Overall Survival in first 850 patients | | |
| Number of patients | N=425 | N=425 |
| Deaths (%) | 271 (64%) | 298 (70%) |
| Median, months | 13.8 | 9.6 |
| (95% CI) | (11.8, 15.7) | (8.6, 11.2) |
| Hazard ratio ¹ (95% CI) | 0.74 (0.63, 0.87) | |
| p-value ² | 0.0004 ³ | |
| Progression-Free Survival | | |
| Number of Patients | N=425 | N=425 |
| Events (%) | 380 (89%) | 375 (88%) |
| Progression (%) | 332 (78%) | 290 (68%) |
| Deaths (%) | 48 (11%) | 85 (20%) |
| Median, months | 2.8 | 4.0 |
| (95% CI) | (2.6, 3.0) | (3.3, 4.2) |
| Hazard ratio ¹ (95% CI) | 0.95 (0.82, 1.10) | |
| Overall Response Rate⁴ | | |
| Number of Patients | N=425 | N=425 |
| ORR, n (%) | 58 (14%) | 57 (13%) |
| (95% CI) | (11%, 17%) | (10%, 17%) |
| Complete response | 6 (1%) | 1 (0.2%) |
| Partial response | 52 (12%) | 56 (13%) |
| Duration of Response³ | | |
| Median (months) | N=58 16.3 | N=57 6.2 |
| (95% CI) | (10.0, NE) | (4.9, 7.6) |
| Overall Survival in all 1225 patients | | |
| Number of patients | N=613 | N=612 |
| Deaths (%) | 384 (63%) | 409 (67%) |
| Median, months | 13.3 | 9.8 |
| (95% CI) | (11.3, 14.9) | (8.9, 11.3) |

| | TECENTRIQ | Docetaxel |
|------------------------------------|---------------------|-----------|
| Hazard ratio ¹ (95% CI) | 0.79 (0.69, 0.91) | |
| p-value ² | 0.0013 ⁵ | |

¹ Stratified by PD-L1 expression in tumor infiltrating immune cells, the number of prior chemotherapy regimens, and histology
² Based on the stratified log-rank test
³ Compared to the pre-specified allocated α of 0.03 for this analysis
⁴ Per RECIST v1.1 (Response Evaluation Criteria in Solid Tumors v1.1)
⁵ Compared to the allocated α of 0.0177 for this interim analysis based on 86% information using O'Brien-Fleming boundary
CI=confidence interval; NE=not estimable

917
918

Figure 2: Kaplan-Meier Curves of Overall Survival in the First 850 Patients Randomized in OAK



| No. Patients at Risk | 425 | 407 | 382 | 363 | 342 | 326 | 305 | 279 | 260 | 248 | 234 | 223 | 218 | 205 | 198 | 188 | 175 | 163 | 157 | 141 | 116 | 74 | 54 | 41 | 28 | 15 | 4 | 1 |
|----------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|----|----|----|----|----|---|---|
| TECENTRIQ | 425 | 407 | 382 | 363 | 342 | 326 | 305 | 279 | 260 | 248 | 234 | 223 | 218 | 205 | 198 | 188 | 175 | 163 | 157 | 141 | 116 | 74 | 54 | 41 | 28 | 15 | 4 | 1 |
| Docetaxel | 425 | 390 | 365 | 336 | 311 | 286 | 263 | 236 | 219 | 195 | 179 | 168 | 151 | 140 | 132 | 123 | 116 | 104 | 98 | 90 | 70 | 51 | 37 | 28 | 16 | 6 | 3 | |

919

920 Tumor specimens were evaluated prospectively using the VENTANA PD-L1 (SP142) Assay at a
921 central laboratory and the results were used to define the PD-L1 expression subgroups for pre-
922 specified analyses. Of the 850 patients, 16% were classified as having high PD-L1 expression,
923 defined as having PD-L1 expression on $\geq 50\%$ of TC or $\geq 10\%$ of IC. In an exploratory efficacy
924 subgroup analysis of OS based on PD-L1 expression, the hazard ratio was 0.41 (95% CI: 0.27,
925 0.64) in the high PD-L1 expression subgroup and 0.82 (95% CI: 0.68, 0.98) in patients who did
926 not have high PD-L1 expression.

927 Exploratory analyses showed that the subset of patients who were ADA positive by week 4
928 (21%) appeared to have less efficacy (effect on overall survival) as compared to patients who
929 tested negative for treatment-emergent ADA by week 4 (79%) [see Adverse Reactions (6.2),
930 Clinical Pharmacology (12.3)]. ADA positive patients by week 4 appeared to have similar OS
931 compared to docetaxel-treated patients. In an exploratory analysis, propensity score matching
932 was conducted to compare ADA positive patients in the atezolizumab arm with a matched
933 population in the docetaxel arm and ADA negative patients in the atezolizumab arm with a
934 matched population in the docetaxel arm. Propensity score matching factors were: baseline sum
935 of longest tumor size (BSLD), baseline ECOG, histology (squamous vs. non-squamous),
936 baseline albumin, baseline LDH, gender, tobacco history, metastases status (advanced or local),
937 metastatic site, TC level, and IC level. The hazard ratio comparing the ADA positive subgroup

938 with its matched control was 0.89 (95% CI: 0.61, 1.3). The hazard ratio comparing the ADA
939 negative subgroup with its matched control was 0.68 (95% CI: 0.55, 0.83).

940 **14.3 Locally Advanced or Metastatic Triple-Negative Breast Cancer**

941 The efficacy of TECENTRIQ in combination with paclitaxel protein-bound was investigated in
942 IMpassion130 (NCT02425891), a multicenter, international, double-blinded, placebo-controlled,
943 randomized trial that included 902 unresectable locally advanced or metastatic triple-negative
944 breast cancer patients that had not received prior chemotherapy for metastatic disease. Patients
945 were stratified by presence of liver metastases, prior taxane treatment, and by PD-L1 expression
946 status in tumor infiltrating immune cells (IC) (PD-L1 stained tumor-infiltrating immune cells
947 [IC] <1% of tumor area vs. ≥ 1% of the tumor area) by the VENTANA PD-L1 (SP142) Assay.
948 Of the 902 patients in the intent to treat population (ITT), 41% (369 patients) were classified as
949 PD-L1 expression ≥ 1%. Patients were randomized (1:1) to receive either TECENTRIQ (840
950 mg) or placebo intravenous infusions on Days 1 and 15 of every 28-day cycle, plus paclitaxel
951 protein-bound (100 mg/m²) administered via intravenous infusion on Days 1, 8 and 15 of every
952 28-day cycle. Patients received treatment until radiographic disease progression per RECIST
953 v1.1, or unacceptable toxicity.

954 Patients were excluded if they had a history of autoimmune disease, administration of a live
955 attenuated vaccine within 4 weeks prior to randomization, administration of systemic
956 immunostimulatory agents within 4 weeks or systemic immunosuppressive medications within 2
957 weeks prior to randomization; or untreated or corticosteroid-dependent brain metastases. Tumor
958 assessments were performed every 8 weeks (± 1 week) for the first 12 months after Cycle 1, day
959 1 and every 12 weeks (± 1 week) thereafter.

960 In IMpassion130, the median age was 55 years (range: 20-86). Overall, most patients were
961 women (99.6%) and the majority of patients were white (68%), Asian (18%), Black or African
962 American (7%), and American Indian or Alaskan Native (4.4%). The demographic and baseline
963 disease characteristics of the study population were well balanced between the treatment arms.
964 Baseline ECOG performance status was 0 (58%) or 1 (41%). Overall, 41% of enrolled patients
965 had PD-L1 expression ≥ 1%, 27% had liver metastases and 7% brain metastases at baseline.
966 Approximately half the patients had received a taxane (51%) or anthracycline (54%) in the
967 (neo)adjuvant setting. Patient demographics and baseline tumor disease in the PD-L1 expressing
968 population were generally representative of the broader study population.

969 Tumor specimens (archival or fresh) were evaluated prospectively using the VENTANA PD-L1
970 (SP142) Assay at a central laboratory and the results were used as a stratification factor for
971 randomization and to define the PD-L1 expression subgroups for pre-specified analyses.

972 The major efficacy outcomes were investigator-assessed progression free survival (PFS) in the
973 ITT and PD-L1 expressing patient population per RECIST v1.1 and overall survival (OS) in the
974 ITT population. Overall survival data were immature with 43% deaths in the ITT population. The
975 efficacy results of IMpassion130 for the patient population with PD-L1 expression ≥ 1% are
976 presented in Table 18 and Figure 3.

977 **Table 18: Efficacy Results from IMpassion130 in Patients with PD-L1 Expression ≥ 1%**

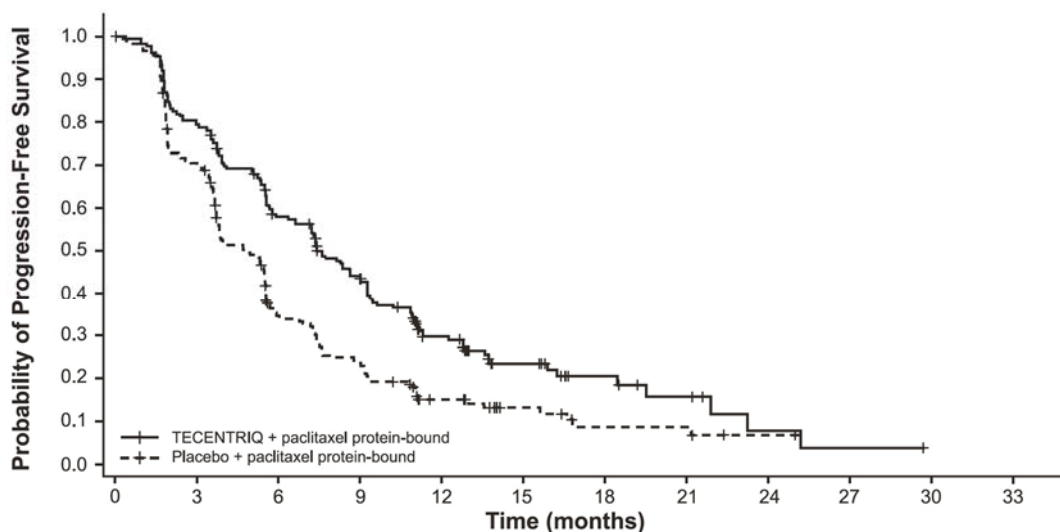
| | PD-L1 Expression ≥ 1% ¹ | |
|--|--|--|
| | TECENTRIQ in combination with paclitaxel protein-bound | Placebo in combination with paclitaxel protein-bound |
| Progression-Free Survival^{2,3} | (n=185) | (n=184) |
| Events (%) | 136 (74) | 151 (82) |
| Median, months | 7.4 (6.6, 9.2) | 4.8 (3.8, 5.5) |
| Stratified Hazard ratio (95% CI) ⁴ | 0.60 (0.48, 0.77) | |

| p-value | <0.0001 | |
|---|--------------|--------------|
| Objective Response Rate ^{2,3,5,6} | n=185 | n=183 |
| Number of responders (%) | 98 (53) | 60 (33) |
| (95% CI) | (45.5, 60.3) | (26.0, 40.1) |
| Complete response (%) | 17 (9) | 1 (<1) |
| Partial response (%) | 81 (44) | 59 (32) |
| Duration of Response ^{2,3,6} | n=98 | n=60 |
| Median (months) | 9.2 | 6.2 |
| (95% CI) | (7.5, 11.9) | (5.5, 8.8) |

¹ PD-L1 expression in tumor-infiltrating immune cells (IC)
² As determined by investigator assessment
³ per RECIST v1.1 (Response Evaluation Criteria in Solid Tumors v1.1)
⁴ Stratified by presence of liver metastases, and by prior taxane treatment
⁵ patients with measurable disease at baseline
⁶ confirmed responses
PFS=Progression-Free Survival; CI=Confidence Interval; ORR=Objective Response Rate; DOR=Duration of Response; NE=Not Estimable

978

979 **Figure 3: Kaplan-Meier Plot of Progression-Free-Survival in IMpassion130 in Patients**
980 **with PD-L1 Expression $\geq 1\%$**



| | No. of Patients at Risk | | | | | | | | | | | |
|--------------------------------------|-------------------------|-----|-----|----|----|----|----|----|----|----|----|----|
| | 0 | 3 | 6 | 9 | 12 | 15 | 18 | 21 | 24 | 27 | 30 | 33 |
| TECENTRIQ + paclitaxel protein-bound | 185 | 145 | 102 | 73 | 38 | 19 | 10 | 6 | 2 | 1 | NE | NE |
| Placebo + paclitaxel protein-bound | 184 | 125 | 56 | 38 | 18 | 10 | 5 | 5 | 1 | NE | NE | NE |

981

982

983 **14.4 Small Cell Lung Cancer**

984 The efficacy of TECENTRIQ with carboplatin and etoposide was investigated in IMpower133
985 (NCT02763579), a randomized (1:1), multicenter, double-blind, placebo-controlled trial in 403
986 patients with ES-SCLC. IMpower133 enrolled patients with ES-SCLC who had received no
987 prior chemotherapy for extensive stage disease and ECOG performance status 0 or 1. The trial
988 excluded patients with active or untreated CNS metastases, history of autoimmune disease,
989 administration of a live, attenuated vaccine within 4 weeks prior to randomization, or
990 administration of systemic immunosuppressive medications within 1 week prior to randomization.

991 Randomization was stratified by sex, ECOG performance status, and presence of brain
992 metastases. Patients were randomized to receive one of the following two treatment arms:

- 993 • TECENTRIQ 1200 mg and carboplatin AUC 5 mg/mL/min on Day 1 and etoposide 100
994 mg/m² intravenously on Days 1, 2 and 3 of each 21-day cycle for a maximum of 4 cycles
995 followed by TECENTRIQ 1200 mg once every 3 weeks until disease progression or
996 unacceptable toxicity, or
- 997 • placebo and carboplatin AUC 5 mg/mL/min on Day 1 and etoposide 100 mg/m²
998 intravenously on Days 1, 2, and 3 of each 21-day cycle for a maximum of 4 cycles followed
999 by placebo once every 3 weeks until disease progression or unacceptable toxicity.

1000 Administration of TECENTRIQ was permitted beyond RECIST-defined disease progression.
1001 Tumor assessments were conducted every 6 weeks for the first 48 weeks following Cycle 1, Day
1002 1 and then every 9 weeks thereafter. Patients treated beyond disease progression had tumor
1003 assessment conducted every 6 weeks until treatment discontinuation.

1004 Major efficacy outcome measures were OS and PFS as assessed by investigator per RECIST
1005 v1.1 in the intent-to-treat population. Additional efficacy outcome measures included ORR and
1006 DoR as assessed by investigator per RECIST v1.1.

1007 A total of 403 patients were randomized, including 201 to the TECENTRIQ arm and 202 to the
1008 chemotherapy alone arm. The median age was 64 years (range 26 to 90) and 65% were male.
1009 The majority of patients were White (80%); 17% were Asian, 4% were Hispanic and 1% were
1010 Black. Baseline ECOG performance status was 0 (35%) or 1 (65%); 9% of patients had a history
1011 of brain metastases, and 97% were current or previous smokers.

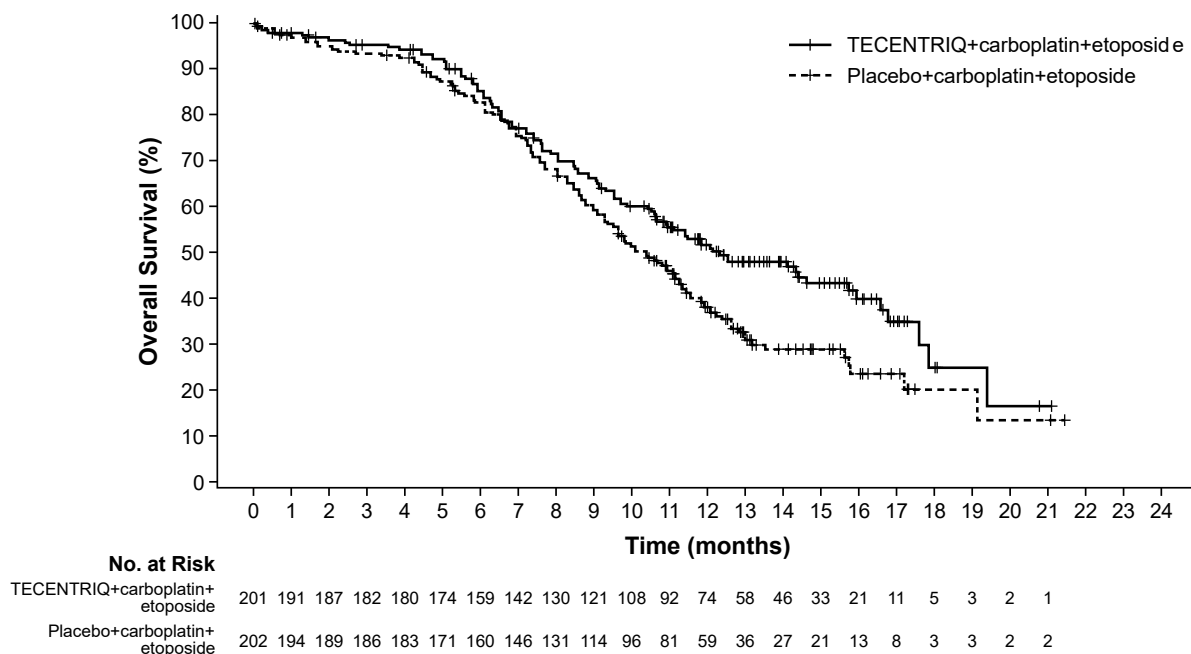
1012 Efficacy results are presented in Table 19 and Figure 4.

1013 **Table 19: Efficacy Results from IMpower133**

| | TECENTRIQ with Carboplatin and Etoposide | Placebo with Carboplatin and Etoposide |
|---|---|---|
| Overall Survival | N=201 | N=202 |
| Deaths (%) | 104 (52%) | 134 (66%) |
| Median, months (95% CI) | 12.3 (10.8, 15.9) | 10.3 (9.3, 11.3) |
| Hazard ratio ³ (95% CI) | 0.70 (0.54, 0.91) | |
| p-value ^{4, 5} | 0.0069 | |
| Progression-Free Survival^{1,2} | N=201 | N=202 |
| Number of events (%) | 171 (85%) | 189 (94%) |
| Median, months (95% CI) | 5.2 (4.4, 5.6) | 4.3 (4.2, 4.5) |
| Hazard ratio ³ (95% CI) | 0.77 (0.62, 0.96) | |
| p-value ^{4, 6} | 0.0170 | |
| Objective Response Rate^{1,2,7} | N=201 | N=202 |
| Number of responders (%) (95% CI) | 121 (60%) (53, 67) | 130 (64%) (57, 71) |
| Complete response | 5 (2%) | 2 (1%) |
| Partial response | 116 (58%) | 128 (63%) |
| Duration of Response^{1,2,7} | N=121 | N=130 |
| Median (months) (95% CI) | 4.2 (4.1, 4.5) | 3.9 (3.1, 4.2) |
| ¹ As determined by investigator assessment ² per RECIST v1.1 (Response Evaluation Criteria in Solid Tumors v1.1) ³ Stratified by sex and ECOG performance status ⁴ Based on the stratified log-rank test ⁵ Compared to the allocated α of 0.0193 for this interim analysis based on 78% information using O'Brien-Fleming boundary ⁶ Compared to the allocated α of 0.05 for this analysis. ⁷ Confirmed response CI=confidence interval | | |

1014

1015 **Figure 4: Kaplan-Meier Plot of Overall Survival in IMpower133**



1016

1017 **16 HOW SUPPLIED/STORAGE AND HANDLING**

1018 TECENTRIQ injection is a sterile, preservative-free, and colorless to slightly yellow solution for
1019 intravenous infusion supplied as a carton containing one 840 mg/14 mL single-dose vial (NDC
1020 50242-918-01) or 1200 mg/20 mL single-dose vial (NDC 50242-917-01).

1021 Store vials under refrigeration at 2°C to 8°C (36°F to 46°F) in original carton to protect from
1022 light. Do not freeze. Do not shake.

1023 **17 PATIENT COUNSELING INFORMATION**

1024 Advise the patient to read the FDA-approved patient labeling (Medication Guide).

1025 Immune-Mediated Adverse Reactions

1026 Inform patients of the risk of immune-mediated adverse reactions that may require corticosteroid
1027 treatment and interruption or discontinuation of TECENTRIQ, including:

- 1028 • Pneumonitis: Advise patients to contact their healthcare provider immediately for any new
1029 or worsening cough, chest pain, or shortness of breath [see Warnings and Precautions
1030 (5.1)].
- 1031 • Hepatitis: Advise patients to contact their healthcare provider immediately for jaundice,
1032 severe nausea or vomiting, pain on the right side of abdomen, lethargy, or easy bruising or
1033 bleeding [see Warnings and Precautions (5.2)].
- 1034 • Colitis: Advise patients to contact their healthcare provider immediately for diarrhea, blood
1035 or mucus in stools, or severe abdominal pain [see Warnings and Precautions (5.3)].

1036 • Endocrinopathies: Advise patients to contact their healthcare provider immediately for signs
1037 or symptoms of hypophysitis, hyperthyroidism, hypothyroidism, adrenal insufficiency, or
1038 type 1 diabetes mellitus, including diabetic ketoacidosis [see *Warnings and Precautions*
1039 (5.4)].

1040 • Other Immune-Mediated Adverse Reactions: Advise patients to contact their healthcare
1041 provider immediately for signs or symptoms of other potential immune-mediated adverse
1042 reactions [see *Warnings and Precautions* (5.5)].

1043 Infections

1044 Advise patients to contact their healthcare provider immediately for signs or symptoms of
1045 infection [see *Warnings and Precautions* (5.6)].

1046 Infusion-Related Reactions

1047 Advise patients to contact their healthcare provider immediately for signs or symptoms of
1048 infusion-related reactions [see *Warnings and Precautions* (5.7)].

1049 Embryo-Fetal Toxicity

1050 Advise females of reproductive potential that TECENTRIQ can cause harm to a fetus and to
1051 inform their healthcare provider of a known or suspected pregnancy [see *Warnings and*
1052 *Precautions* (5.8), *Use in Specific Populations* (8.1, 8.3)].

1053 Advise females of reproductive potential to use effective contraception during treatment and for
1054 at least 5 months after the last dose of TECENTRIQ [see *Use in Specific Populations* (8.3)].

1055 Lactation

1056 Advise female patients not to breastfeed while taking TECENTRIQ and for at least 5 months
1057 after the last dose [see *Use in Specific Populations* (8.2)].
1058

1059

1060 Manufactured by:
1061 Genentech, Inc.
1062 A Member of the Roche Group
1063 1 DNA Way
1064 South San Francisco, CA 94080-4990

1065 U.S. License No. 1048

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MEDICATION GUIDE
TECENTRIQ® (te-SEN-trik)
(atezolizumab)
Injection

What is the most important information I should know about TECENTRIQ?

TECENTRIQ is a medicine that may treat certain cancers by working with your immune system. TECENTRIQ can cause your immune system to attack normal organs and tissues and can affect the way they work. These problems can sometimes become serious or life-threatening and can lead to death.

Call or see your healthcare provider right away if you get any symptoms of the following problems or these symptoms get worse:

Lung problems (pneumonitis). Signs and symptoms of pneumonitis may include:

- new or worsening cough
- shortness of breath
- chest pain

Liver problems (hepatitis). Signs and symptoms of hepatitis may include:

- yellowing of your skin or the whites of your eyes
- dark urine (tea colored)
- severe nausea or vomiting
- bleeding or bruising more easily than normal
- pain on the right side of your stomach area (abdomen)
- feeling less hungry than usual
- drowsiness

Intestinal problems (colitis). Signs and symptoms of colitis may include:

- diarrhea (loose stools) or more bowel movements than usual
- blood or mucus in your stools or dark, tarry, sticky stools
- severe stomach area (abdomen) pain or tenderness

Hormone gland problems (especially the thyroid, adrenal glands, pancreas, and pituitary). Signs and symptoms that your hormone glands are not working properly may include:

- headaches that will not go away or unusual headaches
- feeling cold
- extreme tiredness
- constipation
- weight gain or weight loss
- your voice gets deeper
- dizziness or fainting
- urinating more often than usual
- feeling more hungry or thirsty than usual
- nausea or vomiting
- hair loss
- stomach area (abdomen) pain
- changes in mood or behavior, such as decreased sex drive, irritability, or forgetfulness

Problems in other organs. Signs and symptoms may include:

- severe muscle weakness
- neck stiffness
- numbness or tingling in hands or feet
- eye pain or redness
- confusion
- skin blisters or peeling
- blurry vision, double vision, or other vision problems
- chest pain, irregular heartbeat, shortness of breath or swelling of the ankles
- changes in mood or behavior
- extreme sensitivity to light

Severe infections. Signs and symptoms of infection may include:

- fever
- flu-like symptoms
- cough
- pain when urinating, frequent urination or back pain

Severe infusion reactions. Signs and symptoms of infusion reactions may include:

- chills or shaking
- dizziness
- itching or rash
- fever
- flushing
- feeling like passing out
- shortness of breath or wheezing
- back or neck pain
- swelling of your face or lips

Getting medical treatment right away may help keep these problems from becoming more serious.

Your healthcare provider will check you for these problems during your treatment with TECENTRIQ. Your healthcare provider may treat you with corticosteroid or hormone replacement medicines. Your healthcare provider may delay or completely stop treatment with TECENTRIQ if you have severe side effects.

What is TECENTRIQ?

TECENTRIQ is a prescription medicine used to treat adults with:

- **a type of bladder and urinary tract cancer called urothelial carcinoma.** TECENTRIQ may be used when your bladder cancer has spread or cannot be removed by surgery, **and if you have any one of the following conditions:**
 - you are not able to take chemotherapy that contains a medicine called cisplatin, and your cancer tests positive for “PD-L1”, **or**
 - you are not able to take chemotherapy that contains any platinum regardless of “PD-L1” status, **or**
 - you have tried chemotherapy that contains platinum, and it did not work or is no longer working.
- **a type of lung cancer called non-small cell lung cancer (NSCLC).**
 - **TECENTRIQ may be used with bevacizumab and the chemotherapy medicines carboplatin and paclitaxel as your first treatment when your lung cancer:**
 - has spread or grown, **and**
 - is a type of lung cancer called “non-squamous NSCLC
 - your tumor does not have an abnormal “EGFR” or “ALK” gene
 - **TECENTRIQ may be used when your lung cancer:**
 - has spread or grown, **and**
 - you have tried chemotherapy that contains platinum, and it did not work or is no longer working.
 - if your tumor has an abnormal “EGFR” or “ALK” gene, you should have also tried an FDA-approved therapy for tumors with these abnormal genes, and it did not work or is no longer working.
- **a type of breast cancer called triple-negative breast cancer (TNBC).** TECENTRIQ may be used with the medicine paclitaxel protein-bound when your breast cancer:
 - has spread or cannot be removed by surgery, **and**
 - your cancer tests positive for “PD-L1”.
- **a type of lung cancer called small cell lung cancer (SCLC).**

TECENTRIQ may be used with the chemotherapy medicines carboplatin and etoposide as your first treatment when your lung cancer

is a type called “extensive-stage SCLC,” which means that it has spread or grown.

It is not known if TECENTRIQ is safe and effective in children.

Before you receive TECENTRIQ, tell your healthcare provider about all of your medical conditions, including if you:

- have immune system problems such as Crohn’s disease, ulcerative colitis, or lupus
- have had an organ transplant
- have lung or breathing problems
- have liver problems
- have a condition that affects your nervous system, such as myasthenia gravis or Guillain-Barré syndrome
- are being treated for an infection
- are pregnant or plan to become pregnant. TECENTRIQ can harm your unborn baby. Tell your healthcare provider right away if you become pregnant or think you may be pregnant during treatment with TECENTRIQ.

Females who are able to become pregnant:

- Your healthcare provider should do a pregnancy test before you start treatment with TECENTRIQ.
- You should use an effective method of birth control during your treatment and for at least 5 months after the last dose of TECENTRIQ.
- are breastfeeding or plan to breastfeed. It is not known if TECENTRIQ passes into your breast milk. Do not breastfeed during treatment and for at least 5 months after the last dose of TECENTRIQ.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

How will I receive TECENTRIQ?

- Your healthcare provider will give you TECENTRIQ into your vein through an intravenous (IV) line over 30 to 60 minutes.
- TECENTRIQ is usually given every 2 or 3 weeks.
- Your healthcare provider will decide how many treatments you need.
- Your healthcare provider will test your blood to check you for certain side effects.
- If you miss any appointments, call your healthcare provider as soon as possible to reschedule your appointment.

What are the possible side effects of TECENTRIQ?

TECENTRIQ can cause serious side effects, including:

- See “What is the most important information I should know about TECENTRIQ?”

The most common side effects of TECENTRIQ when used alone include:

- feeling tired
- nausea
- cough
- shortness of breath
- decreased appetite

The most common side effects of TECENTRIQ when used in lung cancer with other anti-cancer medicines include:

- feeling tired or weak
- nausea
- hair loss
- constipation
- diarrhea
- decreased appetite

The most common side effects of TECENTRIQ when used in triple-negative breast cancer with paclitaxel protein-bound include:

- hair loss
- tingling or numbness in hands or feet
- feeling tired
- nausea
- diarrhea
- low red blood cells (anemia)
- constipation
- cough
- headache
- low white blood cells
- vomiting
- decreased appetite

TECENTRIQ may cause fertility problems in females, which may affect the ability to have children. Talk to your healthcare provider if you have concerns about fertility.

These are not all the possible side effects of TECENTRIQ. Ask your healthcare provider or pharmacist for more information. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of TECENTRIQ.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. If you would like more information about TECENTRIQ, talk with your healthcare provider. You can ask your healthcare provider for information about TECENTRIQ that is written for health professionals.

What are the ingredients in TECENTRIQ?

Active ingredient: atezolizumab

Inactive ingredients: glacial acetic acid, L-histidine, sucrose, polysorbate 20

Manufactured by: **Genentech, Inc.**, A Member of the Roche Group, 1 DNA Way, South San Francisco, CA 94080-4990 USA

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For more information, call 1-844-832-3687 or go to www.TECENTRIQ.com.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

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