

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, 2.2, 2.3, 2.4, 2.5, 2.7)	5/2019
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

Administer TECENTRIQ as an intravenous infusion over 60 minutes. If the first infusion is tolerated, all subsequent infusions may be delivered over 30 minutes.

Urothelial Carcinoma (2.2)

- Administer TECENTRIQ as:
 - 840 mg every 2 weeks, 1200 mg every 3 weeks, or 1680 mg every 4 weeks

NSCLC (2.3)

- Administer TECENTRIQ as a single agent as:
 - 840 mg every 2 weeks, 1200 mg every 3 weeks, or 1680 mg every 4 weeks

- When administering in combination with bevacizumab and paclitaxel and carboplatin, administer TECENTRIQ 1200 mg every 3 weeks prior to chemotherapy or other antineoplastic drugs.
- Following completion of 4-6 cycles of paclitaxel and carboplatin, and if bevacizumab is discontinued, administer TECENTRIQ as:
 - 840 mg every 2 weeks, 1200 mg every 3 weeks, or 1680 mg every 4 weeks

Metastatic Treatment of TNBC (2.4)

Administer TECENTRIQ 840 mg, 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 (2.5)

- When administering with carboplatin and etoposide, administer TECENTRIQ 1200 mg every 3 weeks prior to chemotherapy.
- Following completion of 4 cycles of carboplatin and etoposide, administer TECENTRIQ as:
 - 840 mg every 2 weeks, 1200 mg every 3 weeks, or 1680 mg every 4 weeks

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)*].

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

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

2.2 Recommended Dosage for Urothelial Carcinoma

The recommended dosage of TECENTRIQ is:

- 840 mg every 2 weeks or
- 1200 mg every 3 weeks or
- 1680 mg every 4 weeks

administered intravenously over 60 minutes until disease progression or unacceptable toxicity. If the first infusion is tolerated, all subsequent infusions may be delivered over 30 minutes.

2.3 Recommended Dosage for NSCLC

The recommended dosage of TECENTRIQ as a single agent is:

- 840 mg every 2 weeks or
- 1200 mg every 3 weeks or
- 1680 mg every 4 weeks

administered intravenously until disease progression or unacceptable toxicity.

The recommended dosage of TECENTRIQ is 1200 mg every 3 weeks intravenously, when administered in combination with bevacizumab, paclitaxel, and carboplatin, until disease progression or unacceptable toxicity. Administer TECENTRIQ prior to chemotherapy or other antineoplastic drugs when given on the same day.

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

Following completion of 4-6 cycles of paclitaxel and carboplatin, and if bevacizumab is discontinued, the recommended dosage of TECENTRIQ is:

- 840 mg every 2 weeks or
- 1200 mg every 3 weeks or
- 1680 mg every 4 weeks

administered intravenously until disease progression or unacceptable toxicity.

Administer the initial infusion of TECENTRIQ over 60 minutes. If the first infusion is tolerated, all subsequent infusions may be delivered over 30 minutes.

2.4 Recommended Dosage for Locally Advanced or Metastatic TNBC

The recommended dosage of TECENTRIQ is 840 mg administered as an intravenous infusion 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 until disease progression or unacceptable toxicity.

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

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

84 **2.5 Recommended Dosage for SCLC**

85 The recommended dosage of TECENTRIQ is 1200 mg intravenously every 3 weeks, when
86 administered in combination with carboplatin and etoposide, until disease progression or
87 unacceptable toxicity. Administer TECENTRIQ prior to chemotherapy when given on the same
88 day.

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

91 Following completion of 4 cycles of carboplatin and etoposide, the recommended dosage of
92 TECENTRIQ is:

- 93 • 840 mg every 2 weeks or
- 94 • 1200 mg every 3 weeks or
- 95 • 1680 mg every 4 weeks

96 administered intravenously until disease progression or unacceptable toxicity.

97 Administer the initial infusion of TECENTRIQ over 60 minutes. If the first infusion is tolerated,
98 all subsequent infusions may be delivered over 30 minutes.

99 **2.6 Dosage Modifications for Adverse Reactions**

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

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Table 1: Recommended Dosage Modifications for Adverse Reactions

Adverse Reaction	Severity of Adverse Reaction ¹	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

Adverse Reaction	Severity of Adverse Reaction ¹	Dosage Modifications
Endocrinopathies (including but not limited to hypophysitis, adrenal insufficiency, hyperthyroidism, and type 1 diabetes mellitus) [see <i>Warnings and Precautions (5.4)</i>]	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 <i>Warnings and Precautions (5.5)</i>]	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 <i>Warnings and Precautions (5.6)</i>]	Grade 3 or 4	Withhold dose until Grade 1 or resolved
Infusion-Related Reactions [see <i>Warnings and Precautions (5.7)</i>]	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
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

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

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2.7 Preparation and Administration

Preparation

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

Prepare the solution for infusion as follows:

- Select the appropriate vial(s) based on the prescribed dose.
- Withdraw the required volume of TECENTRIQ from the vial(s).
- Dilute into a 250 mL polyvinyl chloride (PVC), polyethylene (PE), or polyolefin (PO) infusion bag containing 0.9% Sodium Chloride Injection, USP.
- Dilute with only 0.9% Sodium Chloride Injection, USP.

117 • Mix diluted solution by gentle inversion. Do not shake.

118 • Discard used or empty vials of TECENTRIQ.

119 Storage of Infusion Solution

120 This product does not contain a preservative.

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

123 • At room temperature for no more than 6 hours from the time of preparation. This includes
124 room temperature storage of the infusion in the infusion bag and time for administration of
125 the infusion, or

126 • Under refrigeration at 2°C to 8°C (36°F to 46°F) for no more than 24 hours from time of
127 preparation.

128 Do not freeze.

129 Do not shake.

130 Administration

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

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

135 Do not administer as an intravenous push or bolus.

136 **3 DOSAGE FORMS AND STRENGTHS**

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

139 **4 CONTRAINDICATIONS**

140 None.

141 **5 WARNINGS AND PRECAUTIONS**

142 **5.1 Immune-Mediated Pneumonitis**

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

149 In clinical studies enrolling 2616 patients with various cancers who received TECENTRIQ as a
150 single-agent [*see Adverse Reactions (6.1)*], pneumonitis occurred in 2.5% of patients, including
151 Grade 3 (0.6%), Grade 4 (0.1%), and Grade 5 (< 0.1%) immune-mediated pneumonitis. The
152 median time to onset of pneumonitis was 3.6 months (3 days to 20.5 months) and median
153 duration of pneumonitis was 1.4 months (1 day to 15.1 months). Pneumonitis resolved in 67% of
154 patients. Pneumonitis led to discontinuation of TECENTRIQ in 0.4% of the 2616 patients.
155 Systemic corticosteroids were required in 1.5% of patients, including 0.8% who received high-
156 dose corticosteroids (prednisone ≥ 40 mg per day or equivalent) for a median duration of 4 days
157 (1 day to 45 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 pneumonitis occurred in 5.5% of patients, including Grades 3-4 in 1.4% of patients.
161 Systemic corticosteroids were required in 4.2% of patients, including 3.1% who received high-
162 dose corticosteroids (prednisone \geq 40 mg per day or equivalent) for a median duration of 5 days
163 (1 day to 98 days) followed by a corticosteroid taper.

164 **5.2 Immune-Mediated Hepatitis**

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

172 In clinical studies enrolling 2616 patients with various cancers who received TECENTRIQ as a
173 single-agent [see *Adverse Reactions (6.1)*], hepatitis occurred in 9% of patients, including Grade
174 3 (2.3%), Grade 4 (0.6%), and Grade 5 (< 0.1%). The median time to onset of hepatitis was 1.4
175 months (1 day to 25.8 months) and median duration was 24 days (1 day to 13 months). Hepatitis
176 resolved in 71% of patients. Hepatitis led to discontinuation of TECENTRIQ in 0.4% of 2616
177 patients. Systemic corticosteroids were required in 2% of the patients, with 1.3% requiring high-
178 dose corticosteroids (prednisone \geq 40 mg per day or equivalent) for a median duration of 3 days
179 (1 day to 35 days) 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)*], immune-
182 mediated hepatitis occurred in 14% of patients, including Grades 3-4 in 4.1% of patients.
183 Systemic corticosteroids were required in 4.8% of patients, including 3.4% who received high-
184 dose corticosteroids (prednisone \geq 40 mg per day or equivalent) for a median duration of 6 days
185 (1 day to 144 days) followed by a corticosteroid taper.

186 **5.3 Immune-Mediated Colitis**

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

194 In clinical studies enrolling 2616 patients with various cancers who received TECENTRIQ as a
195 single-agent [see *Adverse Reactions (6.1)*], diarrhea or colitis occurred in 20% of patients,
196 including Grade 3 (1.4%) events. The median time to onset of diarrhea or colitis was 1.5 months
197 (1 day to 41 months). Diarrhea and colitis resolved in 85% of the patients. Diarrhea or colitis led
198 to discontinuation of TECENTRIQ in 0.2% of 2616 patients. Systemic corticosteroids were
199 required in 1.1% of patients and high-dose corticosteroids (prednisone \geq 40 mg per day or
200 equivalent) was required in 0.4% patients with a median duration of 3 days (1 day to 11 days)
201 followed by a corticosteroid taper.

202 In clinical studies enrolling 2421 patients with NSCLC and SCLC who received TECENTRIQ in
203 combination with platinum-based chemotherapy [see *Adverse Reactions (6.1)*], diarrhea or
204 colitis occurred in 29% of patients, including Grade 3-4 in 4.3% of patients. Systemic
205 corticosteroids were required in 4.7% of patients, including 2.9% who received high-dose

206 corticosteroids (prednisone \geq 40 mg per day or equivalent) for a median duration of 4 days (1
207 day to 170 days) followed by a corticosteroid taper.

208 **5.4 Immune-Mediated Endocrinopathies**

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

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

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

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

227 *Adrenal Insufficiency:* Monitor patients for clinical signs and symptoms of adrenal
228 insufficiency. For Grade 2 or higher adrenal insufficiency, initiate prednisone 1 to 2
229 mg/kg/day or equivalents, followed by a taper and hormone replacement as clinically
230 indicated. Interrupt TECENTRIQ based on the severity [see *Dosage and Administration*
231 *(2.6)*].

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

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

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

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

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

256 **5.5 Other Immune-Mediated Adverse Reactions**

257 TECENTRIQ can cause severe and fatal immune-mediated adverse reactions. These immune-
258 mediated reactions may involve any organ system. While immune-mediated reactions usually
259 manifest during treatment with TECENTRIQ, immune-mediated adverse reactions can also
260 manifest after discontinuation of TECENTRIQ.

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

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

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

273 *Cardiac:* myocarditis

274 *Dermatologic:* bullous dermatitis, pemphigoid, erythema multiforme, Stevens Johnson
275 Syndrome (SJS)/toxic epidermal necrolysis (TEN).

276 *Gastrointestinal:* pancreatitis, including increases in serum amylase or lipase levels

277 *General:* systemic inflammatory response syndrome, histiocytic necrotizing lymphadenitis

278 *Hematological:* autoimmune hemolytic anemia, immune thrombocytopenic purpura.

279 *Musculoskeletal:* myositis, rhabdomyolysis.

280 *Neurological:* Guillain-Barre syndrome, myasthenia syndrome/myasthenia gravis,
281 demyelination, immune-related meningoencephalitis, aseptic meningitis, encephalitis, facial and
282 abducens nerve paresis, polymyalgia rheumatica, autoimmune neuropathy, and Vogt-Koyanagi-
283 Harada syndrome.

284 *Ophthalmological:* uveitis, iritis.

285 *Renal:* nephrotic syndrome, nephritis.

286 *Vascular:* vasculitis

287 **5.6 Infections**

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

291 In clinical studies enrolling 2616 patients with various cancers who received TECENTRIQ as a
292 single-agent [*see Adverse Reactions (6.1)*], infections occurred in 42% of patients, including
293 Grade 3 (8.7%), Grade 4 (1.5%), and Grade 5 (1%). In patients with urothelial carcinoma, the
294 most common Grade 3 or higher infection was urinary tract infections, occurring in 6.5% of
295 patients. In patients with NSCLC, the most common Grade 3 or higher infection was pneumonia,

296 occurring in 3.8% of patients. The frequency and severity of infections were similar whether
297 TECENTRIQ was given as a single-agent in patients with various cancers or in combination with
298 other antineoplastic drugs in NSCLC and SCLC.

299 **5.7 Infusion-Related Reactions**

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

304 In clinical studies enrolling 2616 patients with various cancers who received TECENTRIQ as a
305 single-agent [see *Adverse Reactions (6.1)*], infusion-related reactions occurred in 1.3% of
306 patients, including Grade 3 (0.2%). The frequency and severity of infusion-related reactions were
307 similar whether TECENTRIQ was given as a single-agent in patients with various cancers, in
308 combination with other antineoplastic drugs in NSCLC and SCLC, and across the recommended
309 dose range (840 mg Q2W to 1680 mg Q4W).

310 **5.8 Embryo-Fetal Toxicity**

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

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

319 **6 ADVERSE REACTIONS**

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

- 321 • Immune-Mediated Pneumonitis [see *Warnings and Precautions (5.1)*]
- 322 • Immune-Mediated Hepatitis [see *Warnings and Precautions (5.2)*]
- 323 • Immune-Mediated Colitis [see *Warnings and Precautions (5.3)*]
- 324 • Immune-Mediated Endocrinopathies [see *Warnings and Precautions (5.4)*]
- 325 • Other Immune-Mediated Adverse Reactions [see *Warnings and Precautions (5.5)*]
- 326 • Infections [see *Warnings and Precautions (5.6)*]
- 327 • Infusion-Related Reactions [see *Warnings and Precautions (5.7)*]

328 **6.1 Clinical Trials Experience**

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

332 The data described in WARNINGS AND PRECAUTIONS reflect exposure to TECENTRIQ as
333 a single-agent in 2616 patients in two randomized, active-controlled studies (POPLAR, OAK)
334 and four open-label, single arm studies (PCD4989g, IMvigor210, BIRCH, FIR) which enrolled
335 524 patients with metastatic urothelial carcinoma, 1636 patients with metastatic NSCLC, and
336 456 patients with other tumor types. TECENTRIQ was administered at a dose of 1200 mg
337 intravenously every 3 weeks in all studies except PCD4989g. Among the 2616 patients who

338 received a single-agent TECENTRIQ, 36% were exposed for longer than 6 months and 20%
339 were exposed for longer than 12 months.

340 Using the dataset described for patients who received TECENTRIQ as a single-agent, the most
341 common adverse reactions in $\geq 20\%$ of patients were fatigue/asthenia (48%), decreased appetite
342 (25%), nausea (24%), cough (22%), and dyspnea (22%).

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

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

352 The data described below in this section were obtained from one open-label, single arm, multiple
353 cohort study (IMvigor210) and three randomized open-label, active-controlled studies (OAK,
354 IMpower150 and IMpower133). In these trials, TECENTRIQ was administered at a dose of 1200
355 mg intravenously every 3 weeks. This section also describes data from one randomized, placebo-
356 controlled study (IMpassion130) in which TECENTRIQ was administered (at a dose of 840 mg
357 intravenously every 2 weeks) in combination with paclitaxel protein-bound to 452 patients with
358 metastatic TNBC.

359 Urothelial Carcinoma

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

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

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

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

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

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

381 Adverse reactions leading to interruption occurred in 35% of patients; the most common ($\geq 1\%$)
382 were intestinal obstruction, fatigue, diarrhea, urinary tract infection, infusion-related reaction,

383 cough, abdominal pain, peripheral edema, pyrexia, respiratory tract infection, upper respiratory
384 tract infection, creatinine increase, decreased appetite, hyponatremia, back pain, pruritus, and
385 venous thromboembolism.

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

389 **Table 2: Adverse Reactions in ≥ 10% of Patients with Urothelial Carcinoma**
390 **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
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

Adverse Reaction	TECENTRIQ N = 119	
	All Grades (%)	Grades 3-4 (%)

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
Increased AST	4
Hyperkalemia	3
Hypermagnesemia	3
Hyperbilirubinemia	3
Hematology	
Lymphopenia	9
Anemia	7

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Previously Treated Locally Advanced or Metastatic Urothelial Carcinoma

395 The safety of TECENTRIQ was evaluated in IMvigor210 (Cohort 2), a multicenter, open-label,
396 single-arm trial that included 310 patients with locally advanced or metastatic urothelial
397 carcinoma who had disease progression during or following at least one platinum-containing
398 chemotherapy regimen or who had disease progression within 12 months of treatment with a
399 platinum-containing neoadjuvant or adjuvant chemotherapy regimen [see *Clinical Studies*
400 (14.1)]. Patients received TECENTRIQ 1200 mg intravenously every 3 weeks until unacceptable
401 toxicity or either radiographic or clinical progression. The median duration of exposure was
402 12.3 weeks (0.1 to 46 weeks).

403 The most common Grades 3–4 adverse reactions (≥ 2%) were urinary tract infection, anemia,
404 fatigue, dehydration, intestinal obstruction, urinary obstruction, hematuria, dyspnea, acute kidney
405 injury, abdominal pain, venous thromboembolism, sepsis, and pneumonia.

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

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

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

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

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

419 **Table 4: Adverse Reactions in ≥ 10% of Patients with Urothelial Carcinoma in**
420 **IMvigor210 (Cohort 2)**

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

Adverse Reaction	TECENTRIQ N = 310	
	All Grades (%)	Grades 3-4 (%)
Hematuria	14	3

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Table 5: Grades 3–4 Laboratory Abnormalities in $\geq 1\%$ 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
Hypoalbuminemia	1
Hematology	
Lymphopenia	10
Anemia	8

423 Non-small Cell Lung Cancer (NSCLC)

424 *Metastatic Non-Squamous NSCLC*

425 The safety of TECENTRIQ with bevacizumab, paclitaxel and carboplatin was evaluated in
426 IMpower150, a multicenter, international, randomized, open-label trial in which 393
427 chemotherapy-naïve patients with metastatic non-squamous NSCLC received TECENTRIQ
428 1200 mg with bevacizumab 15 mg/kg, paclitaxel 175 mg/m² or 200 mg/m², and carboplatin AUC
429 6 mg/mL/min every 3 weeks for a maximum of 4 or 6 cycles, followed by TECENTRIQ 1200
430 mg with bevacizumab 15 mg/kg every 3 weeks until disease progression or unacceptable toxicity
431 [see *Clinical Studies (14.2)*]. The median duration of exposure to TECENTRIQ was 8.3 months
432 in patients receiving TECENTRIQ with bevacizumab, paclitaxel, and carboplatin.

433 The most common Grades 3–4 adverse reactions ($\geq 2\%$) in patients receiving TECENTRIQ were
434 fatigue/asthenia, hypertension, febrile neutropenia, diarrhea, pneumonia, nausea, decreased
435 appetite, dehydration, and pulmonary embolism.

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

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

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

445 Adverse reactions leading to interruption of TECENTRIQ occurred in 48%; the most common
446 (>1%) were neutropenia, thrombocytopenia, fatigue/asthenia, diarrhea, hypothyroidism, anemia,
447 pneumonia, pyrexia, hyperthyroidism, febrile neutropenia, increased ALT, dyspnea, dehydration
448 and proteinuria.

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

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Table 6: Adverse Reactions Occurring in $\geq 15\%$ 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		Bevacizumab, 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

468 NA = Not applicable.

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

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

473 Previously Treated Metastatic NSCLC

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

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

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

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

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

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

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

499 **Table 8: Adverse Reactions Occurring in $\geq 10\%$ of Patients with NSCLC Receiving**
500 **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

501 ¹ Graded per NCI CTCAE v4.0

502 ² Includes fatigue and asthenia

503 ³ Includes cough and exertional cough

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

505 ⁵ Includes rash, erythematous rash, generalized rash, maculopapular rash, papular rash, pruritic rash, pustular rash,
506 pemphigoid

507 **Table 9: Laboratory Abnormalities Worsening From Baseline Occurring in $\geq 20\%$ of**
508 **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

509 ¹ Graded according to NCI CTCAE version 4.0

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

512
513 Metastatic Triple Negative Breast Cancer (TNBC)

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

527 The most common Grades 3-4 adverse reactions occurring in ≥2%, were neutropenia (8%),
528 peripheral neuropathies (9%), neutrophil count decreased (4.6%), fatigue (4%), anemia (2.9%),
529 hypokalemia (2.2%), pneumonia (2.2%), and aspartate aminotransferase increased (2.0%).
530 Adverse reactions leading to discontinuation of TECENTRIQ occurred in 6% (29/452) of
531 patients in the TECENTRIQ and paclitaxel protein-bound arm. The most common adverse
532 reaction leading to TECENTRIQ discontinuation was peripheral neuropathy (<1%). Fatal
533 adverse reactions occurred in 1.3% (6/452) of patients in the TECENTRIQ and paclitaxel
534 protein-bound arm; these included septic shock, mucosal inflammation, auto-immune hepatitis,
535 aspiration, pneumonia, pulmonary embolism. Adverse reactions leading to interruption of
536 TECENTRIQ occurred in 31% of patients; the most common (≥ 2%) were neutropenia,
537 neutrophil count decreased, hyperthyroidism, and pyrexia. Serious adverse reactions occurred in
538 23% (103/452) of patients. The most frequent serious adverse reactions were pneumonia (2%),
539 urinary tract infection (1%), dyspnea (1%), and pyrexia (1%).

540 Immune-related adverse reactions requiring systemic corticosteroid therapy occurred in 13%
541 (59/452) of patients in the TECENTRIQ and paclitaxel protein-bound arm.

542 Table 10 summarizes adverse reactions that occurred in at least 10% of patients treated with
543 TECENTRIQ and paclitaxel protein-bound. Table 11 summarizes selected laboratory
544 abnormalities worsening from baseline that occurred in at least 20% of patients in the
545 TECENTRIQ treated patients.

546 **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

547 ¹ Graded per NCI CTCAE v4.0

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

549 **Table 11: Laboratory Abnormalities Worsening from Baseline Occurring in**
550 **≥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

551 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).

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

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554 Small Cell Lung Cancer (SCLC)

555 The safety of TECENTRIQ with carboplatin and etoposide was evaluated in IMpower133, a
556 randomized, multicenter, double-blind, placebo-controlled trial in which 198 patients with ES-
557 SCLC received TECENTRIQ 1200 mg and carboplatin AUC 5 mg/mL/min on Day 1 and
558 etoposide 100 mg/m² intravenously on Days 1, 2 and 3 of each 21-day cycle for a maximum of 4
559 cycles, followed by TECENTRIQ 1200 mg every 3 weeks until disease progression or
560 unacceptable toxicity [see *Clinical Studies (14.4)*]. Among 198 patients receiving TECENTRIQ,
561 32% were exposed for 6 months or longer and 12% were exposed for 12 months or longer.

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

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

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

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

573 Adverse reactions leading to interruption of TECENTRIQ occurred in 59% of patients; the most
574 common (>1%) were neutropenia (22%), anemia (9%), leukopenia (7%), thrombocytopenia
575 (5%), fatigue (4.0%), infusion-related reaction (3.5%), pneumonia (2.0%), febrile neutropenia
576 (1.5%), increased ALT (1.5%), and nausea (1.5%).

577 Tables 12 and 13 summarize adverse reactions and laboratory abnormalities, respectively, in
578 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

581 ¹ Graded per NCI CTCAE v4.0

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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

608 IMvigor210 (Cohort 1), 48% tested positive for treatment-emergent ADA at one or more post-
609 dose time points. Patients who tested positive for treatment-emergent ADA also had decreased
610 systemic atezolizumab exposures. The presence of ADA did not have a clinically significant
611 effect on the incidence or severity of adverse reactions.

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

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

628 **8 USE IN SPECIFIC POPULATIONS**

629 **8.1 Pregnancy**

630 Risk Summary

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

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

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

639 Data

640 *Animal Data*

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

652 **8.2 Lactation**

653 Risk Summary

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

659 **8.3 Females and Males of Reproductive Potential**

660 Pregnancy Testing

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

663 Contraception

664 *Females*

665 Based on its mechanism of action, TECENTRIQ can cause fetal harm when administered to a
666 pregnant woman [*see Use in Specific Populations (8.1)*]. Advise females of reproductive
667 potential to use effective contraception during treatment with TECENTRIQ and for at least
668 5 months following the last dose.

669 Infertility

670 *Females*

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

673 **8.4 Pediatric Use**

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

675 **8.5 Geriatric Use**

676 Of 2481 patients with urothelial carcinoma, lung cancer, and triple-negative breast cancer who
677 were treated with TECENTRIQ in clinical studies, 45% were 65 years and over and 11% were
678 75 years and over. No overall differences in safety or effectiveness were observed between
679 patients aged 65 years or older, and younger patients.

680 **11 DESCRIPTION**

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

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

690 **12 CLINICAL PHARMACOLOGY**

691 **12.1 Mechanism of Action**

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

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

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

701 **12.3 Pharmacokinetics**

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

710 Specific Populations

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

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

722 Drug Interaction Studies

723 The drug interaction potential of atezolizumab is unknown.

724 **13 NONCLINICAL TOXICOLOGY**

725 **13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility**

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

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

735 **13.2 Animal Toxicology and/or Pharmacology**

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

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

742 **14 CLINICAL STUDIES**

743 **14.1 Urothelial Carcinoma**

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

745 The efficacy of TECENTRIQ was investigated in IMvigor210 (Cohort 1) (NCT02951767), a
746 multicenter, open-label, single-arm trial that included 119 patients with locally advanced or
747 metastatic urothelial carcinoma who were ineligible for cisplatin-containing chemotherapy and
748 were either previously untreated or had disease progression at least 12 months after neoadjuvant
749 or adjuvant chemotherapy. Patients were considered cisplatin-ineligible if they met any one of
750 the following criteria at study entry: impaired renal function [creatinine clearance (CLcr) of 30 to
751 59 mL/min], Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 2,
752 hearing loss of ≥ 25 decibels (dB) at two contiguous frequencies, or Grades 2-4 peripheral
753 neuropathy. This study excluded patients who had: a history of autoimmune disease; active or
754 corticosteroid-dependent brain metastases; administration of a live, attenuated vaccine within
755 28 days prior to enrollment; or administration of systemic immunostimulatory agents within 6
756 weeks or systemic immunosuppressive medications within 2 weeks prior to enrollment. Patients
757 received TECENTRIQ 1200 mg as an intravenous infusion every 3 weeks until unacceptable
758 toxicity or disease progression. Tumor response assessments were conducted every 9 weeks for
759 the first 54 weeks and every 12 weeks thereafter. Major efficacy outcome measures included
760 confirmed overall response rate (ORR) as assessed by independent review facility (IRF) using
761 Response Evaluation Criteria in Solid Tumors (RECIST v1.1), duration of response (DoR) and
762 overall survival (OS).

763 In this study, the median age was 73 years, 81% were male, and 91% were White. Thirty-five
764 percent of patients had non-bladder urothelial carcinoma and 66% had visceral metastases.
765 Eighty percent of patients had an ECOG PS of 0 or 1. Reasons for ineligibility for cisplatin-
766 containing chemotherapy were: 70% had impaired renal function, 20% had an ECOG PS of 2,
767 14% had a hearing loss of ≥ 25 dB, and 6% had Grades 2-4 peripheral neuropathy at baseline.
768 Twenty percent of patients had disease progression following prior platinum-containing
769 neoadjuvant or adjuvant chemotherapy.

770 Tumor specimens were evaluated prospectively using the VENTANA PD-L1 (SP142) Assay at a
771 central laboratory, and the results were used to define subgroups for pre-specified analyses. Of
772 the 119 patients, 27% were classified as having PD-L1 expression of $\geq 5\%$ (defined as PD-L1
773 stained tumor-infiltrating immune cells [IC] covering $\geq 5\%$ of the tumor area). The remaining
774 73% of patients were classified as having PD-L1 expression of $< 5\%$ (PD-L1 stained tumor-
775 infiltrating IC covering $< 5\%$ of the tumor area).

776 Among the 32 patients with PD-L1 expression of $\geq 5\%$, median age was 67 years, 81% were
777 male, 19% female, and 88% were White. Twenty-eight percent of patients had non-bladder
778 urothelial carcinoma and 56% had visceral metastases. Seventy-two percent of patients had an
779 ECOG PS of 0 or 1. Reasons for ineligibility for cisplatin-containing chemotherapy were: 66%
780 had impaired renal function, 28% had an ECOG PS of 2, 16% had a hearing loss ≥ 25 dB, and
781 9% had Grades 2-4 peripheral neuropathy at baseline. Thirty-one percent of patients had disease
782 progression following prior platinum-containing neoadjuvant or adjuvant chemotherapy.

783 Confirmed ORR in all patients and the two PD-L1 subgroups are summarized in Table 14. The
784 median follow-up time for this study was 14.4 months. In 24 patients with disease progression
785 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)			

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

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Previously Treated Locally Advanced or Metastatic Urothelial Carcinoma

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

816

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

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

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

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

828 Confirmed ORR and median DOR in all patients and the two PD-L1 subgroups are summarized
829 in Table 15. The median follow-up time for this study was 32.9 months. In 59 patients with
830 disease progression following neoadjuvant or adjuvant therapy, the ORR was 22.0% (95% CI:
831 12.3%, 34.7%).

832 **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	27.7	20.9	29.7
(range)	(2.1+, 33.4+)	(2.1+, 33.4+)	(4.2, 31.2+)
+ Denotes a censored value			
¹ PD-L1 expression in tumor-infiltrating immune cells (IC)			

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834 **14.2 Non-Small Cell Lung Cancer**

835 Metastatic Chemotherapy-Naive Non-Squamous NSCLC

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

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

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

- 851 • Arm A: TECENTRIQ 1200 mg, paclitaxel 175 mg/m² or 200 mg/m² and carboplatin AUC 6
852 mg/mL/min on Day 1 of each 21-day cycle for a maximum of 4 or 6 cycles
- 853 • Arm B: TECENTRIQ 1200 mg, bevacizumab 15 mg/kg, paclitaxel 175 mg/m² or 200 mg/m²,
854 and carboplatin AUC 6 mg/mL/min on Day 1 of each 21-day cycle for a maximum of 4 or 6
855 cycles
- 856 • Arm C: bevacizumab 15 mg/kg, paclitaxel 175 mg/m² or 200 mg/m², and carboplatin AUC 6
857 mg/mL/min on Day 1 of each 21-day cycle for a maximum of 4 or 6 cycles

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

- 860 • Arm A: TECENTRIQ 1200 mg intravenously on Day 1 of each 21-day cycle until disease
861 progression or unacceptable toxicity
- 862 • Arm B: TECENTRIQ 1200 mg and bevacizumab 15 mg/kg intravenously on Day 1 of each
863 21-day cycle until disease progression or unacceptable toxicity
- 864 • Arm C: bevacizumab 15 mg/kg intravenously on Day 1 of each 21-day cycle until disease
865 progression or unacceptable toxicity

866 Tumor assessments were conducted every 6 weeks for the first 48 weeks following Cycle 1, Day
867 1 and then every 9 weeks thereafter. Tumor specimens were evaluated prior to randomization for
868 PD-L1 tumor expression using the VENTANA PD-L1 (SP142) assay at a central laboratory.
869 Tumor tissue was collected at baseline for expression of tGE signature and evaluation was
870 performed using a clinical trial assay in a central laboratory prior to the analysis of efficacy
871 outcome measures.

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

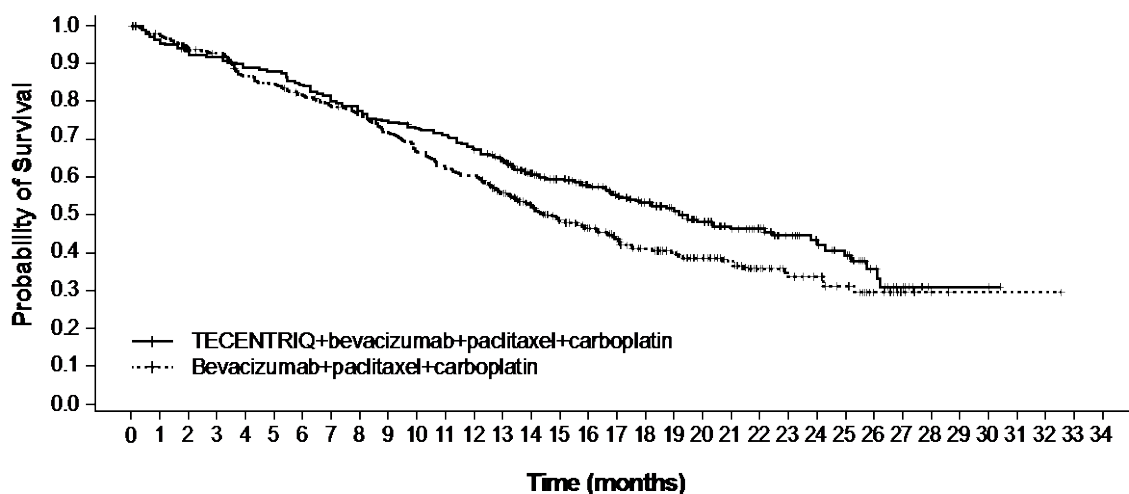
879 A total of 1202 patients were enrolled across the three arms of whom 1045 were in the ITT-WT
880 subpopulation and 447 were in the tGE-WT subpopulation. The demographic information is
881 limited to the 800 patients enrolled in Arms B and C where efficacy has been demonstrated. The
882 median age was 63 years (range: 31 to 90), and 60% of patients were male. The majority of
883 patients were White (82%), 13% of patients were Asian, 10% were Hispanic, and 2% of patients
884 were Black. Clinical sites in Asia (enrolling 13% of the study population) received paclitaxel at a
885 dose of 175 mg/m² while the remaining 87% received paclitaxel at a dose of 200 mg/m².
886 Approximately 14% of patients had liver metastases at baseline, and most patients were current
887 or previous smokers (80%). Baseline ECOG performance status was 0 (43%) or 1 (57%). PD-L1
888 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
889 demographics for the 696 patients in the ITT-WT subpopulation were similar to the ITT
890 population except for the absence of patients with EGFR- or ALK-positive NSCLC.

891 The trial demonstrated a statistically significant improvement in PFS between Arms B and C in
892 both the tGE-WT and ITT-WT subpopulations, but did not demonstrate a significant difference
893 for either subpopulation between Arms A and C based on the final PFS analyses. In the interim
894 analysis of OS, a statistically significant improvement was observed for Arm B compared to
895 Arm C, but not for Arm A compared to Arm C. Efficacy results for the ITT-WT subpopulation
896 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			

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



No. at Risk	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34
TECENTRIQ+bevacizumab+paclitaxel+carboplatin	359	339	328	323	314	310	296	284	273	264	256	250	235	218	188	167	147	133	119	103	84	66	57	41	34	28	16	9	2	2	2				
Bevacizumab+paclitaxel+carboplatin	337	326	315	308	287	280	268	255	247	233	216	203	196	174	152	129	115	101	87	77	66	56	40	32	29	22	13	6	3	1	1	1	1		

899 Exploratory analyses showed that the subset of patients in the four drug regimen arm who were
 900 ADA positive by week 4 (30%) appeared to have similar efficacy (effect on overall survival) as
 901 compared to patients who tested negative for treatment-emergent ADA by week 4 (70%) [see
 902 *Adverse Reactions* (6.2), *Clinical Pharmacology* (12.3)]. In an exploratory analysis, propensity
 903 score matching was conducted to compare ADA positive patients in the TECENTRIQ,
 904 bevacizumab, paclitaxel, and carboplatin arm with a matched population in the bevacizumab,
 905 paclitaxel, and carboplatin arm. Similarly ADA negative patients in the TECENTRIQ,
 906 bevacizumab, paclitaxel, and carboplatin arm were compared with a matched population in the
 907 bevacizumab, paclitaxel, and carboplatin arm. Propensity score matching factors were: baseline
 908 sum of longest tumor size (BSLD), baseline ECOG, baseline albumin, baseline LDH, sex, tobacco
 909 history, metastatic site, TC level, and IC level. The hazard ratio comparing the ADA-positive
 910 subgroup with its matched control was 0.69 (95% CI: 0.44, 1.07). The hazard ratio comparing the
 911 ADA-negative subgroup with its matched control was 0.64 (95% CI: 0.46, 0.90).
 912

913 Previously Treated Metastatic NSCLC

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

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

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

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

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

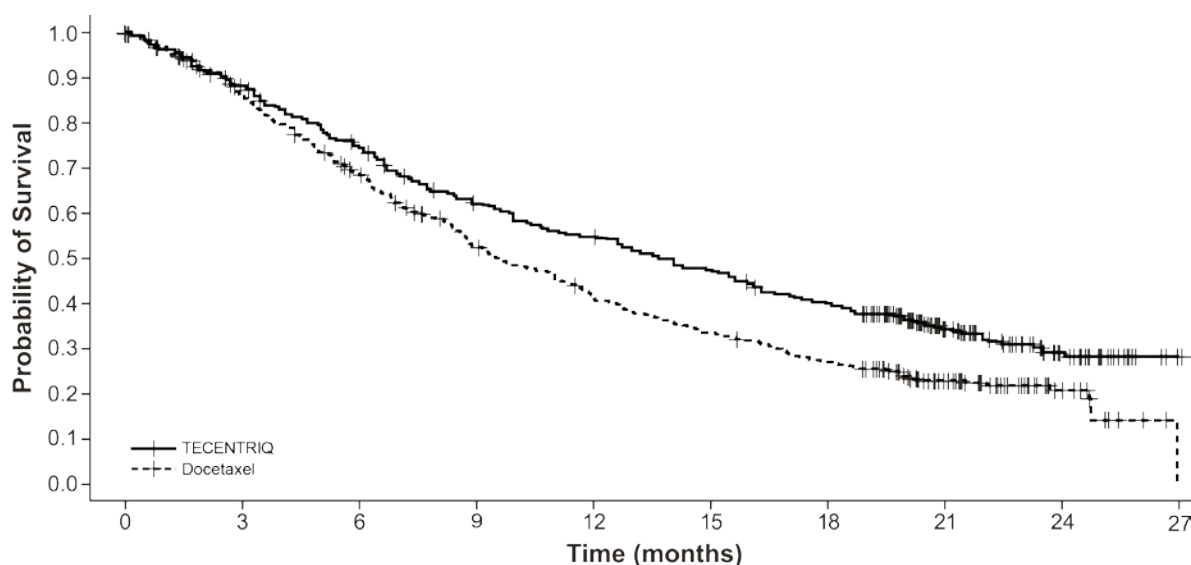
939 **Table 17: Efficacy Results in OAK**

	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)	16.3	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

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



No. Patients at Risk																												
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	

942
943 Tumor specimens were evaluated prospectively using the VENTANA PD-L1 (SP142) Assay at a
944 central laboratory and the results were used to define the PD-L1 expression subgroups for pre-
945 specified analyses. Of the 850 patients, 16% were classified as having high PD-L1 expression,
946 defined as having PD-L1 expression on $\geq 50\%$ of TC or $\geq 10\%$ of IC. In an exploratory efficacy
947 subgroup analysis of OS based on PD-L1 expression, the hazard ratio was 0.41 (95% CI: 0.27,
948 0.64) in the high PD-L1 expression subgroup and 0.82 (95% CI: 0.68, 0.98) in patients who did
949 not have high PD-L1 expression.

950 Exploratory analyses showed that the subset of patients who were ADA positive by week 4
951 (21%) appeared to have less efficacy (effect on overall survival) as compared to patients who
952 tested negative for treatment-emergent ADA by week 4 (79%) [see Adverse Reactions (6.2),
953 Clinical Pharmacology (12.3)]. ADA positive patients by week 4 appeared to have similar OS
954 compared to docetaxel-treated patients. In an exploratory analysis, propensity score matching
955 was conducted to compare ADA positive patients in the atezolizumab arm with a matched
956 population in the docetaxel arm and ADA negative patients in the atezolizumab arm with a
957 matched population in the docetaxel arm. Propensity score matching factors were: baseline sum
958 of longest tumor size (BSLD), baseline ECOG, histology (squamous vs. non-squamous),
959 baseline albumin, baseline LDH, gender, tobacco history, metastases status (advanced or local),
960 metastatic site, TC level, and IC level. The hazard ratio comparing the ADA positive subgroup

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

963 **14.3 Locally Advanced or Metastatic Triple-Negative Breast Cancer**

964 The efficacy of TECENTRIQ in combination with paclitaxel protein-bound was investigated in
965 IMpassion130 (NCT02425891), a multicenter, international, double-blinded, placebo-controlled,
966 randomized trial that included 902 unresectable locally advanced or metastatic triple-negative
967 breast cancer patients that had not received prior chemotherapy for metastatic disease. Patients
968 were stratified by presence of liver metastases, prior taxane treatment, and by PD-L1 expression
969 status in tumor infiltrating immune cells (IC) (PD-L1 stained tumor-infiltrating immune cells
970 [IC] <1% of tumor area vs. ≥ 1% of the tumor area) by the VENTANA PD-L1 (SP142) Assay.
971 Of the 902 patients in the intent to treat population (ITT), 41% (369 patients) were classified as
972 PD-L1 expression ≥ 1%. Patients were randomized (1:1) to receive either TECENTRIQ (840
973 mg) or placebo intravenous infusions on Days 1 and 15 of every 28-day cycle, plus paclitaxel
974 protein-bound (100 mg/m²) administered via intravenous infusion on Days 1, 8 and 15 of every
975 28-day cycle. Patients received treatment until radiographic disease progression per RECIST
976 v1.1, or unacceptable toxicity.

977 Patients were excluded if they had a history of autoimmune disease, administration of a live
978 attenuated vaccine within 4 weeks prior to randomization, administration of systemic
979 immunostimulatory agents within 4 weeks or systemic immunosuppressive medications within 2
980 weeks prior to randomization; or untreated or corticosteroid-dependent brain metastases. Tumor
981 assessments were performed every 8 weeks (± 1 week) for the first 12 months after Cycle 1, day
982 1 and every 12 weeks (± 1 week) thereafter.

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

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

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

1000 **Table 18: Efficacy Results from IMpassion130 in Patients with PD-L1 Expression ≥ 1%**

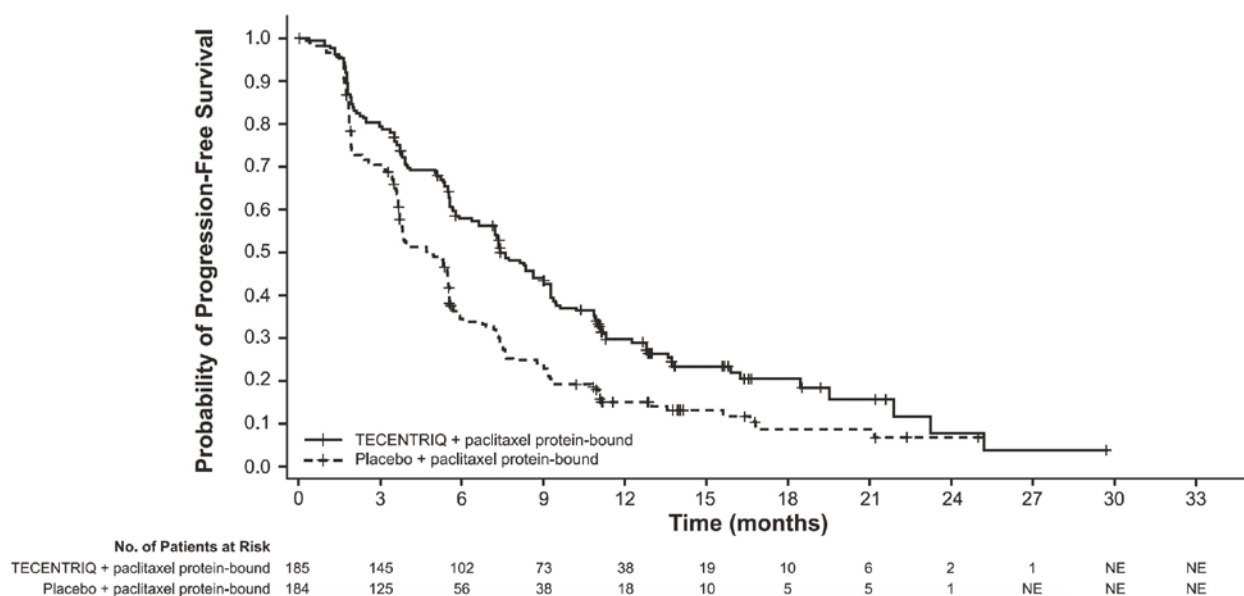
	PD-L1 Expression ≥ 1% ¹	
	TECENTRIQ in combination with paclitaxel protein-bound	Placebo in combination with paclitaxel protein-bound
Progression-Free Survival^{2,3}	(n=185)	(n=184)
Events (%)	136 (74)	151 (82)
Median, months	7.4 (6.6, 9.2)	4.8 (3.8, 5.5)
Stratified Hazard ratio (95% CI) ⁴	0.60 (0.48,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

1001

1002 **Figure 3: Kaplan-Meier Plot of Progression-Free-Survival in IMpassion130 in Patients**
1003 **with PD-L1 Expression $\geq 1\%$**



1004

1005

1006 14.4 Small Cell Lung Cancer

1007 The efficacy of TECENTRIQ with carboplatin and etoposide was investigated in IMpower133
1008 (NCT02763579), a randomized (1:1), multicenter, double-blind, placebo-controlled trial in 403
1009 patients with ES-SCLC. IMpower133 enrolled patients with ES-SCLC who had received no
1010 prior chemotherapy for extensive stage disease and ECOG performance status 0 or 1. The trial
1011 excluded patients with active or untreated CNS metastases, history of autoimmune disease,
1012 administration of a live, attenuated vaccine within 4 weeks prior to randomization, or
1013 administration of systemic immunosuppressive medications within 1 week prior to randomization.

1014 Randomization was stratified by sex, ECOG performance status, and presence of brain
1015 metastases. Patients were randomized to receive one of the following two treatment arms:

- 1016 • TECENTRIQ 1200 mg and carboplatin AUC 5 mg/mL/min on Day 1 and etoposide 100
1017 mg/m² intravenously on Days 1, 2 and 3 of each 21-day cycle for a maximum of 4 cycles
1018 followed by TECENTRIQ 1200 mg once every 3 weeks until disease progression or
1019 unacceptable toxicity, or
- 1020 • placebo and carboplatin AUC 5 mg/mL/min on Day 1 and etoposide 100 mg/m²
1021 intravenously on Days 1, 2, and 3 of each 21-day cycle for a maximum of 4 cycles followed
1022 by placebo once every 3 weeks until disease progression or unacceptable toxicity.

1023 Administration of TECENTRIQ was permitted beyond RECIST-defined disease progression.
1024 Tumor assessments were conducted every 6 weeks for the first 48 weeks following Cycle 1, Day
1025 1 and then every 9 weeks thereafter. Patients treated beyond disease progression had tumor
1026 assessment conducted every 6 weeks until treatment discontinuation.

1027 Major efficacy outcome measures were OS and PFS as assessed by investigator per RECIST
1028 v1.1 in the intent-to-treat population. Additional efficacy outcome measures included ORR and
1029 DoR as assessed by investigator per RECIST v1.1.

1030 A total of 403 patients were randomized, including 201 to the TECENTRIQ arm and 202 to the
1031 chemotherapy alone arm. The median age was 64 years (range 26 to 90) and 65% were male.
1032 The majority of patients were White (80%); 17% were Asian, 4% were Hispanic and 1% were
1033 Black. Baseline ECOG performance status was 0 (35%) or 1 (65%); 9% of patients had a history
1034 of brain metastases, and 97% were current or previous smokers.

1035 Efficacy results are presented in Table 19 and Figure 4.

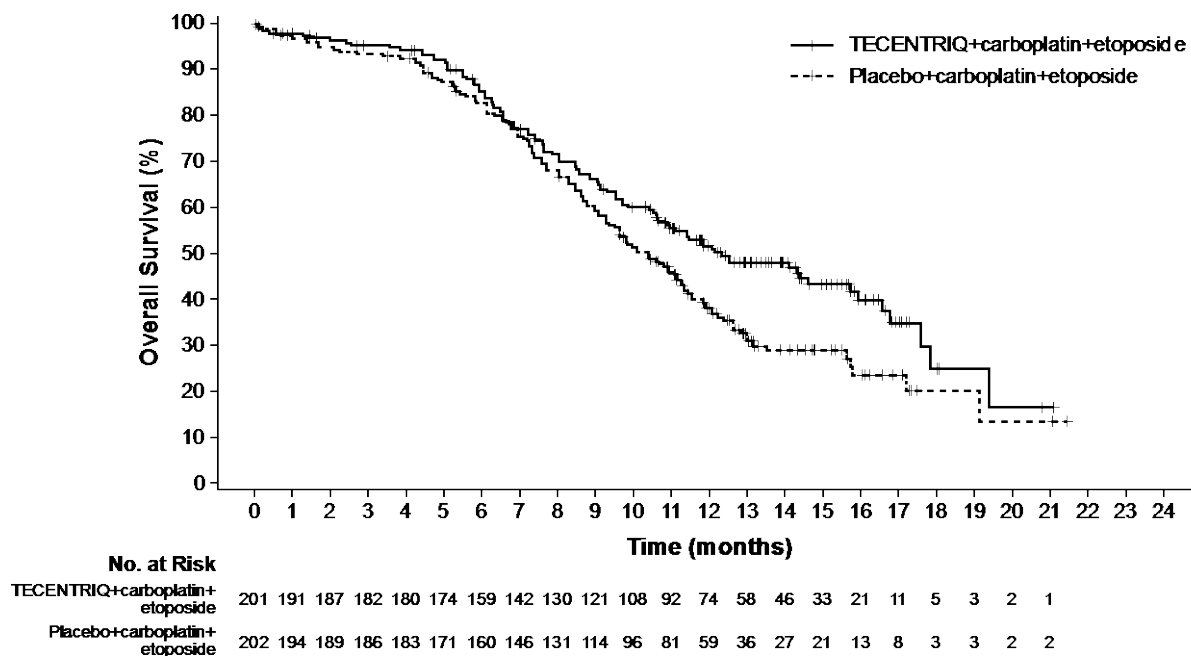
1036

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		

1037

1038 **Figure 4: Kaplan-Meier Plot of Overall Survival in IMpower133**



1039

1040 **16 HOW SUPPLIED/STORAGE AND HANDLING**

1041 TECENTRIQ injection is a sterile, preservative-free, and colorless to slightly yellow solution for
1042 intravenous infusion supplied as a carton containing one 840 mg/14 mL single-dose vial (NDC
1043 50242-918-01) or 1200 mg/20 mL single-dose vial (NDC 50242-917-01).

1044 Store vials under refrigeration at 2°C to 8°C (36°F to 46°F) in original carton to protect from
1045 light. Do not freeze. Do not shake.

1046 **17 PATIENT COUNSELING INFORMATION**

1047 Advise the patient to read the FDA-approved patient labeling (Medication Guide).

1048 Immune-Mediated Adverse Reactions

1049 Inform patients of the risk of immune-mediated adverse reactions that may require corticosteroid
1050 treatment and interruption or discontinuation of TECENTRIQ, including:

1051 • Pneumonitis: Advise patients to contact their healthcare provider immediately for any new
1052 or worsening cough, chest pain, or shortness of breath [see Warnings and Precautions
1053 (5.1)].

1054 • Hepatitis: Advise patients to contact their healthcare provider immediately for jaundice,
1055 severe nausea or vomiting, pain on the right side of abdomen, lethargy, or easy bruising or
1056 bleeding [see Warnings and Precautions (5.2)].

1057 • Colitis: Advise patients to contact their healthcare provider immediately for diarrhea, blood
1058 or mucus in stools, or severe abdominal pain [see Warnings and Precautions (5.3)].

1059 • Endocrinopathies: Advise patients to contact their healthcare provider immediately for signs
1060 or symptoms of hypophysitis, hyperthyroidism, hypothyroidism, adrenal insufficiency, or
1061 type 1 diabetes mellitus, including diabetic ketoacidosis [see *Warnings and Precautions*
1062 (5.4)].

1063 • Other Immune-Mediated Adverse Reactions: Advise patients to contact their healthcare
1064 provider immediately for signs or symptoms of other potential immune-mediated adverse
1065 reactions [see *Warnings and Precautions* (5.5)].

1066 Infections

1067 Advise patients to contact their healthcare provider immediately for signs or symptoms of
1068 infection [see *Warnings and Precautions* (5.6)].

1069 Infusion-Related Reactions

1070 Advise patients to contact their healthcare provider immediately for signs or symptoms of
1071 infusion-related reactions [see *Warnings and Precautions* (5.7)].

1072 Embryo-Fetal Toxicity

1073 Advise females of reproductive potential that TECENTRIQ can cause harm to a fetus and to
1074 inform their healthcare provider of a known or suspected pregnancy [see *Warnings and*
1075 *Precautions* (5.8), *Use in Specific Populations* (8.1, 8.3)].

1076 Advise females of reproductive potential to use effective contraception during treatment and for
1077 at least 5 months after the last dose of TECENTRIQ [see *Use in Specific Populations* (8.3)].

1078 Lactation

1079 Advise female patients not to breastfeed while taking TECENTRIQ and for at least 5 months
1080 after the last dose [see *Use in Specific Populations* (8.2)].
1081

1082

1083 Manufactured by:
1084 Genentech, Inc.
1085 A Member of the Roche Group
1086 1 DNA Way
1087 South San Francisco, CA 94080-4990

1088 U.S. License No. 1048

1089 TECENTRIQ is a registered trademark of Genentech, Inc.

1090 ©2019 Genentech, Inc.

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 alone 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, 3, or 4 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 or weak
- 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, polysorbate 20 and sucrose,

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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