

## 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 (1.1)                        | 4/2017  |
| Indications and Usage (1.2)                        | 10/2016 |
| Warnings and Precautions (5.1, 5.2, 5.3, 5.4, 5.6) | 10/2016 |

### INDICATIONS AND USAGE

TECENTRIQ is a programmed death-ligand 1 (PD-L1) blocking antibody indicated for the treatment of patients with:

- Locally advanced or metastatic urothelial carcinoma who:
  - are not eligible for cisplatin-containing chemotherapy, 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 confirmatory trials. (1.1)

- Metastatic non-small cell lung cancer 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 these aberrations prior to receiving TECENTRIQ. (1.2)

### DOSAGE AND ADMINISTRATION

- Administer 1200 mg as an intravenous infusion over 60 minutes every 3 weeks. (2.1)
- Dilute prior to intravenous infusion. (2.3)

### DOSAGE FORMS AND STRENGTHS

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

### CONTRAINDICATIONS

None. (4)

### WARNINGS AND PRECAUTIONS

- Immune-Related Pneumonitis: Withhold for moderate and permanently discontinue for severe or life-threatening pneumonitis. (5.1)

- Immune-Related Hepatitis: Monitor for changes in liver function. Withhold for moderate and permanently discontinue for severe or life-threatening transaminase or total bilirubin elevation. (5.2)
- Immune-Related Colitis: Withhold for moderate or severe, and permanently discontinue for life-threatening colitis. (5.3)
- Immune-Related Endocrinopathies (5.4):
  - Hypophysitis: Withhold for moderate or severe and permanently discontinue for life-threatening hypophysitis.
  - Thyroid Disorders: Monitor for changes in thyroid function. Withhold for symptomatic thyroid disease.
  - Adrenal Insufficiency: Withhold for symptomatic adrenal insufficiency.
  - Type 1 Diabetes Mellitus: Withhold for  $\geq$  Grade 3 hyperglycemia.
- Immune-Related Myasthenic Syndrome/Myasthenia Gravis, Guillain-Barré or Meningoencephalitis: Permanently discontinue for any grade. (5.5)
- Ocular Inflammatory Toxicity: Withhold for moderate and permanently discontinue for severe ocular inflammatory toxicity. (5.5)
- Immune-Related Pancreatitis: Withhold for moderate or severe, and permanently discontinue for life-threatening pancreatitis, or any grade of recurring pancreatitis. (5.5)
- Infection: Withhold for severe or life-threatening infection. (5.6)
- Infusion Reaction: Interrupt or slow the rate of infusion for mild or moderate infusion reactions and discontinue for severe or life-threatening infusion reactions. (5.7)
- Embryo-Fetal Toxicity: TECENTRIQ 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 ( $\geq$  20%) in patients with locally advanced or metastatic urothelial carcinoma were fatigue, decreased appetite, nausea, constipation, urinary tract infection, diarrhea, and pyrexia. (6.1)

Most common adverse reactions ( $\geq$  20%) in patients with metastatic non-small cell lung cancer were fatigue, decreased appetite, dyspnea, cough, nausea, musculoskeletal pain, and constipation. (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](http://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: 4/2017

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# 1 FULL PRESCRIBING INFORMATION

## 2 1 INDICATIONS AND USAGE

### 3 1.1 Locally Advanced or Metastatic Urothelial Carcinoma

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

- 6 • are not eligible for cisplatin-containing chemotherapy, or
- 7 • have disease progression during or following any platinum-containing chemotherapy, or  
8 within 12 months of neoadjuvant or adjuvant chemotherapy

9 This indication is approved under accelerated approval based on tumor response rate and  
10 durability of response. Continued approval for this indication may be contingent upon  
11 verification and description of clinical benefit in confirmatory trials [see *Clinical Studies (14.1)*].

### 12 1.2 Metastatic Non-Small Cell Lung Cancer

13 TECENTRIQ is indicated for the treatment of patients with metastatic non-small cell lung cancer  
14 (NSCLC) who have disease progression during or following platinum-containing chemotherapy.  
15 Patients with EGFR or ALK genomic tumor aberrations should have disease progression on  
16 FDA-approved therapy for these aberrations prior to receiving TECENTRIQ [see *Clinical*  
17 *Studies (14.2)*].

## 18 2 DOSAGE AND ADMINISTRATION

### 19 2.1 Recommended Dosing

20 The recommended dose of TECENTRIQ is 1200 mg administered as an intravenous infusion  
21 over 60 minutes every 3 weeks until disease progression or unacceptable toxicity. If the first  
22 infusion is tolerated, all subsequent infusions may be delivered over 30 minutes. Do not  
23 administer TECENTRIQ as an intravenous push or bolus.

### 24 2.2 Dose Modifications

25 No dose reductions of TECENTRIQ are recommended.

26 Withhold TECENTRIQ for any of the following:

- 27 • Grade 2 pneumonitis [see *Warnings and Precautions (5.1)*]
- 28 • Aspartate aminotransferase (AST) or alanine aminotransferase (ALT) greater than 3 and  
29 up to 5 times upper limit of normal (ULN) or total bilirubin greater than 1.5 and up to  
30 3 times ULN [see *Warnings and Precautions (5.2)*]
- 31 • Grade 2 or 3 diarrhea or colitis [see *Warnings and Precautions (5.3)*]
- 32 • Symptomatic hypophysitis, adrenal insufficiency, hypothyroidism, hyperthyroidism, or  
33 Grade 3 or 4 hyperglycemia [see *Warnings and Precautions (5.4)*]
- 34 • Grade 2 ocular inflammatory toxicity [see *Warnings and Precautions (5.5)*]
- 35 • Grade 2 or 3 pancreatitis, or Grade 3 or 4 increases in amylase or lipase levels (greater  
36 than 2.0 times ULN) [see *Warnings and Precautions (5.5)*]
- 37 • Grade 3 or 4 infection [see *Warnings and Precautions (5.6)*]
- 38 • Grade 2 infusion-related reactions [see *Warnings and Precautions (5.7)*]
- 39 • Grade 3 rash

40 TECENTRIQ may be resumed in patients whose adverse reactions recover to Grade 0–1.

41 Permanently discontinue TECENTRIQ for any of the following:

- 42 • Grade 3 or 4 pneumonitis [see *Warnings and Precautions* (5.1)]
- 43 • AST or ALT greater than 5 times ULN or total bilirubin greater than 3 times ULN [see
- 44 *Warnings and Precautions* (5.2)]
- 45 • Grade 4 diarrhea or colitis [see *Warnings and Precautions* (5.3)]
- 46 • Grade 4 hypophysitis [see *Warnings and Precautions* (5.4)]
- 47 • Myasthenic syndrome/myasthenia gravis, Guillain-Barré or meningoencephalitis (all
- 48 grades) [see *Warnings and Precautions* (5.5)]
- 49 • Grade 3 or 4 ocular inflammatory toxicity [see *Warnings and Precautions* (5.5)]
- 50 • Grade 4 or any grade of recurrent pancreatitis [see *Warnings and Precautions* (5.5)]
- 51 • Grade 3 or 4 infusion-related reactions [see *Warnings and Precautions* (5.7)]
- 52 • Grade 4 rash

### 53 **2.3 Preparation and Administration**

#### 54 **Preparation**

55 Visually inspect drug product for particulate matter and discoloration prior to administration  
56 whenever solution and container permit. TECENTRIQ is a colorless to slightly yellow solution.  
57 Discard the vial if the solution is cloudy, discolored, or visible particles are observed. Do not  
58 shake the vial.

59 Prepare the solution for infusion as follows:

- 60 • Withdraw 20 mL of TECENTRIQ from the vial.
- 61 • Dilute into a 250 mL polyvinyl chloride (PVC), polyethylene (PE), or polyolefin (PO)
- 62 infusion bag containing 0.9% Sodium Chloride Injection, USP.
- 63 • Dilute with 0.9% Sodium Chloride Injection only.
- 64 • Mix diluted solution by gentle inversion. Do not shake.
- 65 • Discard used or empty vials of TECENTRIQ.

#### 66 **Storage of Infusion Solution**

67 This product does not contain a preservative.

68 Administer immediately once prepared. If diluted TECENTRIQ infusion solution is not used  
69 immediately, it can be stored either:

- 70 • At room temperature for no more than 6 hours from the time of preparation. This
- 71 includes room temperature storage of the infusion in the infusion bag and time for
- 72 administration for infusion.
- 73 • Under refrigeration at 2°C–8°C (36°F–46°F) for no more than 24 hours.

74 Do not freeze.

75 Do not shake.

76 **Administration**

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

80 Do not co-administer other drugs through the same intravenous line.

81 **3 DOSAGE FORMS AND STRENGTHS**

82 Injection: 1200 mg/20 mL (60 mg/mL) colorless to slightly yellow solution in a single-dose vial.

83 **4 CONTRAINDICATIONS**

84 None.

85 **5 WARNINGS AND PRECAUTIONS**

86 **5.1 Immune-Related Pneumonitis**

87 Immune-mediated pneumonitis or interstitial lung disease, defined as requiring use of  
88 corticosteroids and with no clear alternate etiology, occurred in patients receiving TECENTRIQ.  
89 Monitor patients for signs with radiographic imaging and for symptoms of pneumonitis.

90 Administer steroids at a dose of 1 to 2 mg/kg/day prednisone equivalents for Grade 2 or greater  
91 pneumonitis, followed by corticosteroid taper. Withhold TECENTRIQ until resolution for  
92 Grade 2 pneumonitis. Permanently discontinue TECENTRIQ for Grade 3 or 4 pneumonitis [*see*  
93 *Dosage and Administration (2.2)*].

94 Across clinical trials, 2.6% (51/1978) of patients developed pneumonitis. Fatal pneumonitis  
95 occurred in two patients.

96 **Urothelial Carcinoma**

97 In 523 patients with urothelial carcinoma who received TECENTRIQ, pneumonitis occurred in  
98 six (1.1%) patients. Of these patients, there was one patient with fatal pneumonitis, one patient  
99 with Grade 3, three patients with Grade 2, and one patient with Grade 1 pneumonitis.  
100 TECENTRIQ was held in all cases. Pneumonitis resolved in three patients. The median time to  
101 onset was 2.6 months (range: 15 days to 4.2 months). The median duration was 15 days (range:  
102 6 days to 3.1+ months). Immune-mediated pneumonitis occurred in 5 (1.0%) patients.

103 **NSCLC**

104 In 1027 patients with NSCLC who received TECENTRIQ, pneumonitis occurred in 38 (3.7%)  
105 patients. Of these patients, there was one patient with fatal pneumonitis, two patients with Grade  
106 4, thirteen patients with Grade 3, eleven patients with Grade 2, and eleven patients with Grade 1  
107 pneumonitis. TECENTRIQ was held in 24 patients and 21 patients were treated with  
108 corticosteroids. Pneumonitis resolved in 26 of the 38 patients. The median time to onset was 3.3  
109 months (range: 3 days to 18.7 months). The median duration was 1.4 months (range: 0 days to  
110 12.6+ months).

111 **5.2 Immune-Related Hepatitis**

112 Immune-mediated hepatitis, defined as requiring use of corticosteroids and with no clear  
113 alternate etiology, occurred in patients receiving TECENTRIQ treatment. Liver test  
114 abnormalities occurred in patients who received TECENTRIQ. Monitor patients for signs and  
115 symptoms of hepatitis. Monitor AST, ALT, and bilirubin prior to and periodically during  
116 treatment with TECENTRIQ. Administer corticosteroids at a dose of 1–2 mg/kg/day prednisone  
117 equivalents for Grade 2 or greater transaminase elevations, with or without concomitant  
118 elevation in total bilirubin, followed by corticosteroid taper. Withhold TECENTRIQ for Grade 2

119 and permanently discontinue TECENTRIQ for Grade 3 or 4 immune-mediated hepatitis [*see*  
120 *Dosage and Administration (2.2) and Adverse Reactions (6.1)*].

121 Across clinical trials (n=1978), Grade 3 or 4 elevation occurred in ALT (2.5%), AST (2.3%), and  
122 total bilirubin (1.6%).

### 123 **Urothelial Carcinoma**

124 In patients with urothelial carcinoma (n=523), Grade 3 or 4 elevation occurred in ALT (2.5%),  
125 AST (2.5%), and total bilirubin (2.1%). Immune-mediated hepatitis occurred in 1.3% (7/523) of  
126 patients. Of these cases, one patient died from hepatitis, five patients had Grade 3, and one  
127 patient had Grade 2 hepatitis. The median time to onset was 1.1 months (range: 0.4 to 7.7  
128 months). TECENTRIQ was temporarily interrupted in four patients; none of these patients  
129 developed recurrence of hepatitis after resuming TECENTRIQ.

### 130 **NSCLC**

131 In patients with NSCLC, Grade 3 or 4 elevation occurred in ALT (1.4%), AST (1.3%), and total  
132 bilirubin (0.6%). Immune-mediated hepatitis occurred in 0.9% (9/1027) of patients. Of these nine  
133 patients, one patient had Grade 4, four patients had Grade 3, three patients had Grade 2, and one  
134 patient had Grade 1 immune-mediated hepatitis. The median time to onset was 28 days (range:  
135 15 days to 4.2 months). TECENTRIQ was temporarily interrupted in seven patients; none of  
136 these patients developed recurrence of hepatitis after resuming TECENTRIQ.

### 137 **5.3 Immune-Related Colitis**

138 Immune-mediated colitis or diarrhea, defined as requiring use of corticosteroids and with no  
139 clear alternate etiology, occurred in patients receiving TECENTRIQ. Monitor patients for signs  
140 and symptoms of diarrhea or colitis. Withhold treatment with TECENTRIQ for Grade 2 diarrhea  
141 or colitis. If symptoms persist for longer than 5 days or recur, administer 1–2 mg/kg prednisone  
142 or equivalent per day. Withhold treatment with TECENTRIQ for Grade 3 diarrhea or colitis.  
143 Treat with IV methylprednisolone 1–2 mg/kg per day and convert to oral steroids once the  
144 patient has improved. For both Grade 2 and Grade 3 diarrhea or colitis, when symptoms  
145 improve to Grade 0 or Grade 1, taper steroids over  $\geq 1$  month. Resume treatment with  
146 TECENTRIQ if the event improves to Grade 0 or 1 within 12 weeks and corticosteroids have  
147 been reduced to the equivalent of  $\leq 10$  mg oral prednisone per day. Permanently discontinue  
148 TECENTRIQ for Grade 4 diarrhea or colitis [*see Dosage and Administration (2.2) and Adverse*  
149 *Reactions (6.1)*].

150 Across clinical trials, colitis or diarrhea occurred in 19.7% (389/1978) of all patients.

### 151 **Urothelial Carcinoma**

152 In 523 patients with urothelial carcinoma who received TECENTRIQ, colitis or diarrhea  
153 occurred in 98 (18.7%) patients. Ten patients (1.9%) developed Grade 3 or 4 diarrhea. Four  
154 patients (0.8%) had immune-mediated colitis or diarrhea with a median time to onset of 1.7  
155 months (range: 1.1 to 3.1 months). Immune-mediated colitis resolved with corticosteroid  
156 administration in three of these patients, while the other patient died without resolution of colitis  
157 in the setting of diarrhea-associated renal failure.

### 158 **NSCLC**

159 In 1027 patients with NSCLC who received TECENTRIQ, colitis or diarrhea occurred in 198  
160 (19.3%) patients. Twelve patients (1.2%) developed Grade 3 colitis or diarrhea. Five patients  
161 (0.5%) had immune-mediated colitis or diarrhea with a median time to onset of 21 days (range:  
162 12 days to 3.4 months). Of these patients, one had Grade 3, two had Grade 2, and two had Grade  
163 1 immune-mediated colitis or diarrhea. Immune-mediated colitis or diarrhea resolved with

164 corticosteroid administration in four of these patients, while the fifth patient died due to disease  
165 progression prior to resolution of colitis.

#### 166 **5.4 Immune-Related Endocrinopathies**

167 Immune-related thyroid disorders, adrenal insufficiency, and type 1 diabetes mellitus, including  
168 diabetic ketoacidosis, have occurred in patients receiving TECENTRIQ. Monitor patients for  
169 clinical signs and symptoms of endocrinopathies.

##### 170 ***Hypophysitis***

171 Hypophysitis occurred in 0.2% (1/523) of patients with urothelial cancer receiving  
172 TECENTRIQ. Monitor for signs and symptoms of hypophysitis. Administer corticosteroids and  
173 hormone replacement as clinically indicated. Withhold TECENTRIQ for Grade 2 or Grade 3  
174 and permanently discontinue for Grade 4 hypophysitis [*see Dosage and Administration (2.2) and*  
175 *Adverse Reactions (6.1)*].

##### 176 ***Thyroid Disorders***

177 Thyroid function was assessed routinely only at baseline and the end of the study. Monitor  
178 thyroid function prior to and periodically during treatment with TECENTRIQ. Asymptomatic  
179 patients with abnormal thyroid function tests can receive TECENTRIQ. For symptomatic  
180 hypothyroidism, withhold TECENTRIQ and initiate thyroid hormone replacement as needed.  
181 Manage isolated hypothyroidism with replacement therapy and without corticosteroids. For  
182 symptomatic hyperthyroidism, withhold TECENTRIQ and initiate an anti-thyroid drug as  
183 needed. Resume treatment with TECENTRIQ when symptoms of hypothyroidism or  
184 hyperthyroidism are controlled and thyroid function is improving [*see Dosage and*  
185 *Administration (2.2) and Adverse Reactions (6.1)*].

186 Across clinical trials, hypothyroidism and hyperthyroidism occurred in 3.9% (77/1978) and 1.0%  
187 (20/1978) of patients, respectively.

##### 188 **Urothelial Carcinoma**

189 In 523 patients with urothelial carcinoma who received TECENTRIQ, hypothyroidism occurred  
190 in 2.5% (13/523). One patient had Grade 3 and twelve patients had Grade 1–2 hypothyroidism.  
191 The median time to first onset was 5.4 months (range: 21 days to 11.3 months). Thyroid  
192 stimulating hormone (TSH) was elevated and above the patient's baseline in 16% (21/131) of  
193 patients with a follow-up measurement.

194 Hyperthyroidism occurred in 0.6% (3/523) of patients with urothelial carcinoma. Of the  
195 three urothelial carcinoma patients, one patient had Grade 2 and two patients had Grade 1  
196 hyperthyroidism. The median time to onset was 3.2 months (range: 1.4 to 5.8 months). TSH  
197 was decreased and below the patient's baseline in 3.8% (5/131) of patients with a follow-up  
198 measurement.

##### 199 **NSCLC**

200 In 1027 patients with NSCLC who received TECENTRIQ, hypothyroidism occurred in 4.2%  
201 (43/1027). Three patients had Grade 3 and forty patients had Grade 1–2 hypothyroidism. The  
202 median time to onset was 4.8 months (range 15 days to 31 months.) TSH was elevated and  
203 above the patient's baseline in 17% (54/315) of patients with follow-up measurement.

204 Hyperthyroidism occurred in 1.1% (11/1027) of patients with NSCLC. Eight patients had Grade  
205 2 and three patients had Grade 1 hyperthyroidism. The median time to onset was 4.9 months  
206 (range: 21 days to 31 months). TSH was decreased and below the patient's baseline in 7.6%  
207 (24/315) of patients with a follow-up measurement.

208 ***Adrenal Insufficiency***

209 Adrenal insufficiency occurred in 0.4% (7/1978) of patients across clinical trials, including two  
210 patients with Grade 3, four patients with Grade 2, and one patient with Grade 1. Adrenal  
211 insufficiency resolved in two patients.

212 For symptomatic adrenal insufficiency, withhold TECENTRIQ and administer  
213 methylprednisolone 1–2 mg/kg per day IV followed by oral prednisone 1–2 mg/kg per day or  
214 equivalent once symptoms improve. Start steroid taper when symptoms improve to  $\leq$  Grade 1  
215 and taper steroids over  $\geq$  1 month. Resume treatment with TECENTRIQ if the event improves  
216 to  $\leq$  Grade 1 within 12 weeks and corticosteroids have been reduced to the equivalent of  $\leq$  10 mg  
217 oral prednisone per day and the patient is stable on replacement therapy, if required [*see Dosage*  
218 *and Administration (2.2) and Adverse Reactions (6.1)*].

219 ***Diabetes Mellitus***

220 New onset diabetes with ketoacidosis has occurred in patients receiving TECENTRIQ. Diabetes  
221 mellitus without an alternative etiology occurred in one (0.2%) patient with urothelial carcinoma  
222 and three (0.3%) patients with NSCLC.

223 Initiate treatment with insulin for type 1 diabetes mellitus. For  $\geq$  Grade 3 hyperglycemia (fasting  
224 glucose  $>$ 250–500 mg/dL), withhold TECENTRIQ. Resume treatment with TECENTRIQ when  
225 metabolic control is achieved on insulin replacement therapy [*see Dosage and Administration*  
226 *(2.2) and Adverse Reactions (6.1)*].

227 **5.5 Other Immune-Related Adverse Reactions**

228 Other immune-related adverse reactions including meningoencephalitis, myasthenic  
229 syndrome/myasthenia gravis, Guillain-Barré, ocular inflammatory toxicity, and pancreatitis,  
230 including increases in serum amylase and lipase levels, have occurred in  $\leq$  1.0% of patients  
231 treated with TECENTRIQ.

232 ***Meningitis / Encephalitis***

233 Monitor patients for clinical signs and symptoms of meningitis or encephalitis. Permanently  
234 discontinue TECENTRIQ for any grade of meningitis or encephalitis. Treat with IV steroids (1–  
235 2 mg/kg/day methylprednisolone or equivalent) and convert to oral steroids (prednisone  
236 60 mg/day or equivalent) once the patient has improved. When symptoms improve to  $\leq$  Grade 1,  
237 taper steroids over  $\geq$  1 month [*see Dosage and Administration (2.2) and Adverse Reactions*  
238 *(6.1)*].

239 ***Motor and Sensory Neuropathy***

240 Monitor patients for symptoms of motor and sensory neuropathy. Permanently discontinue  
241 TECENTRIQ for any grade of myasthenic syndrome/myasthenia gravis or Guillain-Barré  
242 syndrome. Institute medical intervention as appropriate. Consider initiation of systemic  
243 corticosteroids at a dose of 1–2 mg/kg/day prednisone [*see Dosage and Administration (2.2) and*  
244 *Adverse Reactions (6.1)*].

245 ***Pancreatitis***

246 Symptomatic pancreatitis without an alternative etiology occurred in 0.1% (2/1978) of patients  
247 across clinical trials. Monitor patients for signs and symptoms of acute pancreatitis. Withhold  
248 TECENTRIQ for  $\geq$  Grade 3 serum amylase or lipase levels ( $>$  2.0 ULN), or Grade 2 or 3  
249 pancreatitis. Treat with 1–2 mg/kg IV methylprednisolone or equivalent per day. Once  
250 symptoms improve, follow with 1–2 mg/kg of oral prednisone or equivalent per day. Resume  
251 treatment with TECENTRIQ when serum amylase and lipase levels improve to  $\leq$  Grade 1 within

252 12 weeks or symptoms of pancreatitis have resolved, and corticosteroids have been reduced to  
253  $\leq 10$  mg oral prednisone or equivalent per day. Permanently discontinue TECENTRIQ for  
254 Grade 4 or any grade of recurrent pancreatitis [*see Dosage and Administration (2.2) and Adverse*  
255 *Reactions (6.1)*].

## 256 **5.6 Infection**

257 Severe infections, including sepsis, herpes encephalitis, and mycobacterial infection leading to  
258 retroperitoneal hemorrhage occurred in patients receiving TECENTRIQ. Monitor patients for  
259 signs and symptoms of infection and treat with antibiotics for suspected or confirmed bacterial  
260 infections. Withhold TECENTRIQ for  $\geq$  Grade 3 infection [*see Dosage and Administration*  
261 *(2.2) and Adverse Reactions (6.1)*].

262 Across clinical trials, infections occurred in 38.4% (759/1978) of patients.

## 263 **Urothelial Carcinoma**

264 In 523 patients with urothelial carcinoma who received TECENTRIQ, infection occurred in 197  
265 (37.7%) patients. Grade 3 or 4 infection occurred in sixty (11.5%) patients, while three patients  
266 died due to infections. Urinary tract infections were the most common cause of Grade 3 or  
267 higher infection, occurring in 37 (7.1%) patients.

## 268 **NSCLC**

269 In Study 3, a randomized trial in patients with NSCLC, infections were more common in patients  
270 treated with TECENTRIQ (43%) compared with those treated with docetaxel (34%). Grade 3 or  
271 4 infections occurred in 9.2% of patients treated with TECENTRIQ compared with 2.2% in  
272 patients treated with docetaxel. Two patients (1.4%) treated with TECENTRIQ and three patients  
273 (2.2%) treated with docetaxel died due to infection. Pneumonia was the most common cause of  
274 Grade 3 or higher infection, occurring in 7.7% of patients treated with TECENTRIQ.

## 275 **5.7 Infusion-Related Reactions**

276 Severe infusion reactions have occurred in patients in clinical trials of TECENTRIQ. Infusion-  
277 related reactions occurred in 1.3% (25/1978) of patients across clinical trials, 1.7% (9/523) of  
278 patients with urothelial carcinoma, and 1.6% (16/1027) of patients with NSCLC. Interrupt or  
279 slow the rate of infusion in patients with mild or moderate infusion reactions. Permanently  
280 discontinue TECENTRIQ in patients with Grade 3 or 4 infusion reactions [*see Dosage and*  
281 *Administration (2.2) and Adverse Reactions (6.1)*].

## 282 **5.8 Embryo-Fetal Toxicity**

283 Based on its mechanism of action, TECENTRIQ can cause fetal harm when administered to a  
284 pregnant woman. Animal studies have demonstrated that inhibition of the PD-L1/PD-1 pathway  
285 can lead to increased risk of immune-related rejection of the developing fetus resulting in fetal  
286 death. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this  
287 drug, advise the patient of the potential risk to a fetus. Advise females of reproductive potential  
288 to use effective contraception during treatment with TECENTRIQ and for at least 5 months after  
289 the last dose [*see Use in Specific Populations (8.1, 8.3)*].

## 290 **6 ADVERSE REACTIONS**

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

- 292 • Immune-Related Pneumonitis [*see Warnings and Precautions (5.1)*]
- 293 • Immune-Related Hepatitis [*see Warnings and Precautions (5.2)*]
- 294 • Immune-Related Colitis [*see Warnings and Precautions (5.3)*]



- 295 • Immune-Related Endocrinopathies [see Warnings and Precautions (5.4)]
- 296 • Other Immune-Related Adverse Reactions [see Warnings and Precautions (5.5)]
- 297 • Infection [see Warnings and Precautions (5.6)]
- 298 • Infusion-Related Reactions [see Warnings and Precautions (5.7)]

## 299 **6.1 Clinical Trials Experience**

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

### 303 **Urothelial Carcinoma**

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

305 The safety of TECENTRIQ was evaluated in Study 4, a multicenter, open-label, single-arm trial  
306 that included 119 patients with locally advanced or metastatic urothelial carcinoma who were  
307 ineligible for cisplatin-containing chemotherapy and were either previously untreated or had  
308 disease progression at least 12 months after neoadjuvant or adjuvant chemotherapy [see *Clinical*  
309 *Studies (14.1)*]. Patients received 1200 mg of TECENTRIQ intravenously every 3 weeks until  
310 either unacceptable toxicity or disease progression. The median duration of exposure was  
311 15.0 weeks (range 0, 87 weeks).

312 The most common adverse reactions ( $\geq 20\%$ ) were fatigue (52%), decreased appetite (24%),  
313 diarrhea (24%), and nausea (22%). The most common Grade 3–4 adverse reactions ( $\geq 2\%$ ) were  
314 fatigue, urinary tract infection, anemia, diarrhea, blood creatinine increase, intestinal obstruction,  
315 ALT increase, hyponatremia, decreased appetite, sepsis, back/neck pain, renal failure, and  
316 hypotension.

317 Five patients (4.2%) who were treated with TECENTRIQ experienced one of the following  
318 events which led to death: sepsis, cardiac arrest, myocardial infarction, respiratory failure, or  
319 respiratory distress. One additional patient (0.8%) was experiencing herpetic  
320 meningoencephalitis and disease progression at the time of death. TECENTRIQ was  
321 discontinued for adverse reactions in 4.2% (5/119) of patients. The adverse reactions leading to  
322 discontinuation were diarrhea/colitis (1.7%), fatigue (0.8%), hypersensitivity (0.8%), and  
323 dyspnea (0.8%). Adverse reactions leading to interruption of TECENTRIQ occurred in 35% of  
324 patients, the most common ( $\geq 1\%$ ) were intestinal obstruction, fatigue, diarrhea, urinary tract  
325 infection, infusion related reaction, cough, abdominal pain, peripheral edema, pyrexia,  
326 respiratory tract infection, upper respiratory tract infection, creatinine increase, decreased  
327 appetite, hyponatremia, back pain, pruritus, and venous thromboembolism. Serious adverse  
328 reactions occurred in 37% of patients. The most frequent serious adverse reactions ( $\geq 2\%$ ) were  
329 diarrhea, intestinal obstruction, sepsis, acute kidney injury, and renal failure.

330 Immune-related adverse reactions requiring systemic corticosteroids or hormone replacement  
331 therapy occurred in 19.3% (23/119) patients, including 12.6% (15/119) patients who required  
332 systemic corticosteroid therapy and 6.7% (8/119) patients who required only hormone  
333 replacement therapy.

334 Six patients (5.0%) received an oral prednisone dose equivalent to  $\geq 40$  mg daily for an immune-  
335 mediated adverse reaction [see Warnings and Precautions (5)].

336 Table 1 summarizes the adverse reactions that occurred in  $\geq 10\%$  of patients and Table 2  
337 summarizes Grade 3–4 selected laboratory abnormalities that occurred in  $\geq 1\%$  of patients  
338 treated with TECENTRIQ in Study 4.

**Table 1: All Grade Adverse Reactions in  
≥ 10% of Patients with Urothelial Carcinoma in Study 4**

| Adverse Reaction  | TECENTRIQ<br>N = 119 |                |
|---|----------------------|----------------|
|   | All Grades (%)       | Grades 3–4 (%) |
| <b>General Disorders</b>                                |                      |                |
| Fatigue <sup>a</sup>                                    | 52                   | 8              |
| Peripheral edema <sup>b</sup>                           | 17                   | 2              |
| Pyrexia   | 14                   | 0.8            |
| <b>Gastrointestinal Disorders</b>                       |                      |                |
| Diarrhea <sup>c</sup>                                   | 24                   | 5              |
| Nausea  | 22                   | 2              |
| Vomiting  | 16                   | 0.8            |
| Constipation  | 15                   | 2              |
| Abdominal pain <sup>d</sup>                             | 15                   | 0.8            |
| <b>Metabolism and Nutrition Disorders</b>               |                      |                |
| Decreased appetite <sup>e</sup>                         | 24                   | 3              |
| <b>Musculoskeletal and Connective Tissue Disorders</b>  |                      |                |
| Back/Neck pain  | 18                   | 3              |
| Arthralgia  | 13                   | 0              |
| <b>Skin and Subcutaneous Tissue Disorders</b>           |                      |                |
| Pruritus  | 18                   | 0.8            |
| Rash <sup>f</sup>                                       | 17                   | 0.8            |
| <b>Infections</b>                                       |                      |                |
| Urinary tract infection <sup>g</sup>                    | 17                   | 5              |
| <b>Respiratory, Thoracic, and Mediastinal Disorders</b> |                      |                |
| Cough <sup>h</sup>                                      | 14                   | 0              |
| Dyspnea <sup>i</sup>                                    | 12                   | 0              |

<sup>a</sup> Includes fatigue, asthenia, lethargy, and malaise

<sup>b</sup> Includes edema peripheral, scrotal edema, lymphedema, and edema

<sup>c</sup> Includes diarrhea, colitis, frequent bowel movements, autoimmune colitis

<sup>d</sup> Includes abdominal pain, upper abdominal pain, lower abdominal pain, and flank pain

<sup>e</sup> Includes decreased appetite and early satiety

<sup>f</sup> Includes rash, dermatitis, dermatitis acneiform, rash maculo-papular, rash erythematous, rash pruritic, rash macular, and rash papular

<sup>g</sup> Includes urinary tract infection, urinary tract infection bacterial, cystitis, and urosepsis

<sup>h</sup> Includes cough and productive cough

<sup>i</sup> Includes dyspnea and exertional dyspnea

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**Table 2: Grade 3–4 Laboratory Abnormalities in Patients with Urothelial Carcinoma in Study 4 in  $\geq 1\%$  of Patients**

| Laboratory Test                | Grades 3–4 (%) |
|--------------------------------|----------------|
| Hyponatremia                   | 15             |
| Hyperglycemia                  | 10             |
| Lymphopenia                    | 9              |
| Anemia                         | 7              |
| Increased Alkaline phosphatase | 7              |
| Increased Creatinine           | 5              |
| Hypophosphatemia               | 4              |
| Increased ALT                  | 4              |
| Increased AST                  | 4              |
| Hyperkalemia                   | 3              |
| Hypermagnesemia                | 3              |
| Hyperbilirubinemia             | 3              |

344 **Previously Treated Patients with Locally Advanced or Metastatic Urothelial Carcinoma**

345 The safety of TECENTRIQ was evaluated in Study 1, a multicenter, open-label, single-arm trial  
346 that included 310 patients in a single arm trial with locally advanced or metastatic urothelial  
347 carcinoma who had disease progression during or following at least one platinum-containing  
348 chemotherapy regimen or who had disease progression within 12 months of treatment with a  
349 platinum-containing neoadjuvant or adjuvant chemotherapy regimen [see *Clinical Studies*  
350 (14.1)]. Patients received 1200 mg of TECENTRIQ intravenously every 3 weeks until  
351 unacceptable toxicity or either radiographic or clinical progression. The median duration of  
352 exposure was 12.3 weeks (range: 0.1, 46 weeks).

353 The most common adverse reactions ( $\geq 20\%$ ) were fatigue (52%), decreased appetite (26%),  
354 nausea (25%), urinary tract infection (22%), pyrexia (21%), and constipation (21%). The most  
355 common Grade 3–4 adverse reactions ( $\geq 2\%$ ) were urinary tract infection, anemia, fatigue,  
356 dehydration, intestinal obstruction, urinary obstruction, hematuria, dyspnea, acute kidney injury,  
357 abdominal pain, venous thromboembolism, sepsis, and pneumonia.

358 Three patients (1.0%) who were treated with TECENTRIQ experienced one of the following  
359 events which led to death: sepsis, pneumonitis, or intestinal obstruction. TECENTRIQ was  
360 discontinued for adverse reactions in 3.2% (10/310) of the 310 patients. Sepsis led to  
361 discontinuation in 0.6% (2/310) of patients. Adverse reactions leading to interruption of  
362 TECENTRIQ occurred in 27% of patients; the most common ( $> 1\%$ ) were liver enzyme  
363 increase, urinary tract infection, diarrhea, fatigue, confusional state, urinary obstruction, pyrexia,  
364 dyspnea, venous thromboembolism, and pneumonitis. Serious adverse reactions occurred in  
365 45% of patients. The most frequent serious adverse reactions ( $> 2\%$ ) were urinary tract  
366 infection, hematuria, acute kidney injury, intestinal obstruction, pyrexia, venous  
367 thromboembolism, urinary obstruction, pneumonia, dyspnea, abdominal pain, sepsis, and  
368 confusional state.

369 Immune-related adverse reactions requiring systemic corticosteroids or hormone replacement  
370 therapy occurred in 11.0% (34/310) patients, including 8.4% (26/310) patients who required  
371 systemic corticosteroid therapy and 2.6% (8/310) patients who required only hormone  
372 replacement therapy.

373 Eighteen patients (5.8%) received an oral prednisone dose equivalent to  $\geq 40$  mg daily for an  
374 immune-mediated adverse reaction [see *Warnings and Precautions* (5)].

375 Table 3 summarizes the adverse reactions that occurred in  $\geq 10\%$  of patients while Table 4  
 376 summarizes Grade 3–4 selected laboratory abnormalities that occurred in  $\geq 1\%$  of patients  
 377 treated with TECENTRIQ in Study 1.

378 **Table 3: All Grade Adverse Reactions in  $\geq 10\%$  of Patients with Urothelial**  
 379 **Carcinoma in Study 1**

| Adverse Reaction  | TECENTRIQ<br>N=310 |                |
|---|--------------------|----------------|
|   | All Grades (%)     | Grades 3–4 (%) |
| <b>Gastrointestinal Disorders</b>                       |                    |                |
| Nausea  | 25                 | 2              |
| Constipation  | 21                 | 0.3            |
| Diarrhea  | 18                 | 1              |
| Abdominal pain  | 17                 | 4              |
| Vomiting  | 17                 | 1              |
| <b>General Disorders</b>                                |                    |                |
| Fatigue   | 52                 | 6              |
| Pyrexia   | 21                 | 1              |
| Peripheral edema  | 18                 | 1              |
| <b>Infections</b>                                       |                    |                |
| Urinary tract infection                                 | 22                 | 9              |
| <b>Metabolism and Nutrition Disorders</b>               |                    |                |
| Decreased appetite                                      | 26                 | 1              |
| <b>Musculoskeletal and Connective Tissue Disorders</b>  |                    |                |
| Back/Neck pain  | 15                 | 2              |
| Arthralgia  | 14                 | 1              |
| <b>Renal and urinary disorders</b>                      |                    |                |
| Hematuria   | 14                 | 3              |
| <b>Respiratory, Thoracic, and Mediastinal Disorders</b> |                    |                |
| Dyspnea   | 16                 | 4              |
| Cough   | 14                 | 0.3            |
| <b>Skin and Subcutaneous Tissue Disorders</b>           |                    |                |
| Rash  | 15                 | 0.3            |
| Pruritus  | 13                 | 0.3            |

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**Table 4: Grade 3–4 Laboratory Abnormalities in Patients with Urothelial Carcinoma in Study 1 in  $\geq 1\%$  of Patients**

| Laboratory Test                | Grades 3–4 (%) |
|--------------------------------|----------------|
| Lymphopenia                    | 10             |
| Hyponatremia                   | 10             |
| Anemia                         | 8              |
| Hyperglycemia                  | 5              |
| Increased Alkaline phosphatase | 4              |
| Increased Creatinine           | 3              |
| Increased ALT                  | 2              |
| Increased AST                  | 2              |
| Hypoalbuminemia                | 1              |

382 **NSCLC**

383 The safety of TECENTRIQ was evaluated in Study 3, a multicenter, international, randomized,  
384 open-label trial in patients with metastatic NSCLC who progressed during or following a  
385 platinum-containing regimen, regardless of PD-L1 expression [see *Clinical Studies*  
386 (14.2)]. Patients received 1200 mg of TECENTRIQ (n=142) administered intravenously every 3  
387 weeks until unacceptable toxicity or either radiographic or clinical progression or docetaxel  
388 (n=135) administered intravenously at 75 mg/m<sup>2</sup> every 3 weeks until unacceptable toxicity or  
389 disease progression. The median duration of exposure was 3.7 months (range: 0–19 months) in  
390 TECENTRIQ-treated patients and 2.1 months (range: 0–17 months) in docetaxel-treated patients.

391 The most common adverse reactions ( $\geq 20\%$ ) in patients receiving TECENTRIQ were fatigue  
392 (46%), decreased appetite (35%), dyspnea (32%), cough (30%), nausea (22%), musculoskeletal  
393 pain (22%), and constipation (20%). The most common Grade 3-4 adverse reactions ( $\geq 2\%$ ) were  
394 dyspnea, pneumonia, hypoxia, hyponatremia, fatigue, anemia, musculoskeletal pain, AST  
395 increase, ALT increase, dysphagia, and arthralgia.

396 Nine patients (6.3%) who were treated with TECENTRIQ experienced either pulmonary  
397 embolism (2), pneumonia (2), pneumothorax, ulcer hemorrhage, cachexia secondary to  
398 dysphagia, myocardial infarction, or large intestinal perforation which led to death.  
399 TECENTRIQ was discontinued due to adverse reactions in 4% (6/142) of patients. Adverse  
400 reactions leading to interruption of TECENTRIQ occurred in 24% of patients; the most common  
401 ( $>1\%$ ) were pneumonia, liver function test abnormality, upper respiratory tract infection,  
402 pneumonitis, acute kidney injury, hypoxia, hypothyroidism, dyspnea, anemia, and fatigue.  
403 Serious adverse reactions occurred in 37% of patients. The most frequent serious adverse  
404 reactions ( $> 2\%$ ) were pneumonia, dyspnea, pleural effusion, pyrexia, and venous  
405 thromboembolism.

406 Table 5 summarizes adverse reactions that occurred in at least 10% of TECENTRIQ-treated  
407 patients and at a higher incidence than in the docetaxel arm. Table 6 summarizes selected  
408 laboratory abnormalities worsening from baseline that occurred in  $\geq 10\%$  of TECENTRIQ-  
409 treated patients and at a higher incidence than in the docetaxel arm.

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**Table 5: Adverse Reactions Occurring in  $\geq 10\%$  of TECENTRIQ-Treated Patients with NSCLC and at a Higher Incidence than in the Docetaxel Arm (Between Arm Difference of  $\geq 5\%$  [All Grades] or  $\geq 2\%$  [Grades 3–4]) (Study 3)**

| Adverse Reaction                                       | TECENTRIQ<br>(n=142) |           | Docetaxel<br>(n=135) |           |
|--|----------------------|-----------|----------------------|-----------|
|  | All grades           | Grade 3–4 | All grades           | Grade 3–4 |
| <b>Percentage (%) of Patients</b>                      |                      |           |                      |           |
| <b>General Disorders</b>                               |                      |           |                      |           |
| Pyrexia  | 18                   | 0         | 13                   | 0         |
| <b>Infections</b>                                      |                      |           |                      |           |
| Pneumonia  | 18                   | 6         | 4                    | 2         |
| <b>Metabolism and nutrition disorders</b>              |                      |           |                      |           |
| Decreased appetite                                     | 35                   | 1         | 22                   | 0         |
| <b>Musculoskeletal and connective tissue disorders</b> |                      |           |                      |           |
| Arthralgia   | 16                   | 2         | 9                    | 2         |
| Back pain  | 14                   | 1         | 9                    | 1         |
| <b>Psychiatric Disorders</b>                           |                      |           |                      |           |
| Insomnia   | 14                   | 0         | 8                    | 2         |
| <b>Respiratory, thoracic and mediastinal disorders</b> |                      |           |                      |           |
| Dyspnea  | 32                   | 7         | 24                   | 2         |
| Cough  | 30                   | 1         | 25                   | 0         |

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**Table 6: Selected Laboratory Abnormalities Worsening from Baseline Occurring in  $\geq 10\%$  of TECENTRIQ-Treated Patients with NSCLC and at a Higher Incidence than in the Docetaxel Arm (Between Arm Difference of  $\geq 5\%$  [All Grades] or  $\geq 2\%$  [Grades 3–4]) (Study 3)**

| Test                                 | Percentage of Patients with Worsening<br>Laboratory Test from Baseline |                |                 |                |
|--------------------------------------|--|----------------|-----------------|----------------|
|                                      | TECENTRIQ  |                | Docetaxel       |                |
|                                      | All grades<br>%  | Grade 3–4<br>% | All grades<br>% | Grade 3–4<br>% |
| Hyponatremia                         | 48   | 13             | 28              | 8              |
| Hypoalbuminemia                      | 48   | 5              | 49              | 1              |
| Alkaline Phosphatase increased       | 42   | 2              | 24              | 1              |
| Aspartate aminotransferase increased | 33   | 2              | 15              | 0              |
| Alanine aminotransferase increased   | 31   | 2              | 9               | 1              |
| Creatinine increased                 | 19   | 1              | 14              | 2              |
| Hypokalemia                          | 18   | 2              | 11              | 4              |
| Hypercalcemia                        | 13   | 0              | 5               | 0              |
| Total Bilirubin increased            | 11   | 0              | 5               | 1              |

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## 6.2 Immunogenicity

As with all therapeutic proteins, there is a potential for immunogenicity. Among 275 patients in Study 1, 114 patients (41.5%) tested positive for treatment-emergent (treatment-induced or treatment-enhanced) anti-therapeutic antibodies (ATA) at one or more post-dose time points. Among 135 patients in Study 3, 73 patients (54.1%) tested positive for treatment-emergent ATAs at one or more post-dose time points. Among 111 patients in Study 4, 53 patients (47.7%)

423 tested positive for treatment-emergent ATAs at one or more post-dose time points. In Study 1,  
424 Study 3, and Study 4, the presence of ATAs did not appear to have a clinically significant impact  
425 on pharmacokinetics, safety or efficacy.

426 Immunogenicity assay results are highly dependent on several factors, including assay sensitivity  
427 and specificity, assay methodology, sample handling, timing of sample collection, concomitant  
428 medications and underlying disease. For these reasons, comparison of incidence of ATAs to  
429 TECENTRIQ with the incidence of antibodies to other products may be misleading.

## 430 **8 USE IN SPECIFIC POPULATIONS**

### 431 **8.1 Pregnancy**

#### 432 **Risk Summary**

433 Based on its mechanism of action, TECENTRIQ can cause fetal harm when administered to a  
434 pregnant woman [see *Clinical Pharmacology (12.1)*]. There are no available data on the use of  
435 TECENTRIQ in pregnant women. Animal studies have demonstrated that inhibition of the  
436 PD-L1/PD-1 pathway can lead to increased risk of immune-related rejection of the developing  
437 fetus resulting in fetal death [see *Data*]. If this drug is used during pregnancy, or if the patient  
438 becomes pregnant while taking this drug, advise the patient of the potential risk to a fetus.

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

#### 441 **Data**

##### 442 ***Animal Data***

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

### 454 **8.2 Lactation**

#### 455 **Risk Summary**

456 There is no information regarding the presence of atezolizumab in human milk, the effects on the  
457 breastfed infant, or the effects on milk production. As human IgG is excreted in human milk, the  
458 potential for absorption and harm to the infant is unknown. Because of the potential for serious  
459 adverse reactions in breastfed infants from TECENTRIQ, advise a lactating woman not to breastfeed  
460 during treatment and for at least 5 months after the last dose.

### 461 **8.3 Females and Males of Reproductive Potential**

#### 462 **Contraception**

##### 463 ***Females***

464 Based on its mechanism of action, TECENTRIQ can cause fetal harm when administered to a  
465 pregnant woman [see *Use in Specific Populations (8.1)*]. Advise females of reproductive

466 potential to use effective contraception during treatment with TECENTRIQ and for at least  
467 5 months following the last dose.

## 468 **Infertility**

### 469 ***Females***

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

### 472 **8.4 Pediatric Use**

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

### 474 **8.5 Geriatric Use**

475 Of the 310 previously-treated patients with urothelial carcinoma treated with TECENTRIQ in  
476 Study 1, 59% were 65 years or older. Of the 142 patients with NSCLC treated with  
477 TECENTRIQ in Study 3, 39% were 65 years or older. No overall differences in safety or  
478 efficacy were observed between patients  $\geq$  65 years of age and younger patients.

479 Of the 119 cisplatin-ineligible patients with urothelial carcinoma treated with TECENTRIQ in  
480 Study 4, 83% were 65 years or older and 41% were 75 years or older. The overall response rate  
481 in patients 65 years or older was 23% (23/99) and in patients 75 years or older was 29% (14/49).  
482 Grade 3 or 4 adverse reactions occurred in 53% (52/99) of patients 65 years or older and 51%  
483 (25/49) of patients 75 years or older. No overall differences in safety or efficacy were observed  
484 between patients  $\geq$  75 years of age and younger patients.

### 485 **8.6 Renal Impairment**

486 Based on a population pharmacokinetic analysis, no dose adjustment of TECENTRIQ is  
487 recommended for patients with renal impairment [see *Clinical Pharmacology (12.3)*].

### 488 **8.7 Hepatic Impairment**

489 Based on a population pharmacokinetic analysis, no dose adjustment of TECENTRIQ is  
490 recommended for patients with mild hepatic impairment. TECENTRIQ has not been studied in  
491 patients with moderate or severe hepatic impairment [see *Clinical Pharmacology (12.3)*].

## 492 **10 OVERDOSAGE**

493 There is no information on overdose with TECENTRIQ.

## 494 **11 DESCRIPTION**

495 Atezolizumab is an Fc-engineered, humanized, monoclonal antibody that binds to PD-L1 and  
496 blocks interactions with the PD-1 and B7.1 receptors. Atezolizumab is a non-glycosylated IgG1  
497 kappa immunoglobulin that has a calculated molecular mass of 145 kDa.

498 TECENTRIQ injection for intravenous infusion is a sterile, preservative-free, colorless to  
499 slightly yellow solution in single-dose vials. Each mL of TECENTRIQ contains 60 mg of  
500 atezolizumab and is formulated in glacial acetic acid (16.5 mg), L-histidine (62 mg), sucrose  
501 (821.6 mg), polysorbate 20 (8 mg), pH 5.8.

## 502 **12 CLINICAL PHARMACOLOGY**

### 503 **12.1 Mechanism of Action**

504 PD-L1 may be expressed on tumor cells and/or tumor-infiltrating immune cells and can  
505 contribute to the inhibition of the anti-tumor immune response in the tumor microenvironment.  
506 Binding of PD-L1 to the PD-1 and B7.1 receptors found on T cells and antigen presenting cells  
507 suppresses cytotoxic T-cell activity, T-cell proliferation and cytokine production.



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

### 513 **12.3 Pharmacokinetics**

514 Patients' exposures to atezolizumab increased dose proportionally over the dose range of  
515 1 mg/kg to 20 mg/kg, including the fixed dose 1200 mg administered every 3 weeks. Based on a  
516 population analysis that included 472 patients in the dose range, the typical population clearance  
517 was 0.20 L/day, volume of distribution at steady state was 6.9 L, and the terminal half-life was  
518 27 days. The population PK analysis suggests steady state is obtained after 6 to 9 weeks (2 to 3  
519 cycles) of repeated dosing. The systemic accumulation in area under the curve (AUC), maximum  
520 concentration (C<sub>max</sub>) and trough concentration (C<sub>min</sub>) was 1.91, 1.46 and 2.75-fold,  
521 respectively. In a post hoc analysis, atezolizumab clearance was found to decrease over time,  
522 with a mean maximal reduction (% coefficient of variation [CV%]) from baseline value of  
523 approximately 17.1% (40.6%). However, the decrease in CL was not considered clinically  
524 relevant.

525 *Specific Populations:* Age (21–89 years), body weight, gender, positive anti-therapeutic  
526 antibody (ATA) status, albumin levels, tumor burden, region or race, mild or moderate renal  
527 impairment (estimated glomerular filtration rate (eGFR) 30 to 89 mL/min/1.73 m<sup>2</sup>), mild hepatic  
528 impairment (bilirubin ≤ ULN and AST > ULN or bilirubin < 1.0 to 1.5 × ULN and any AST),  
529 level of PD-L1 expression, or ECOG status had no clinically significant effect on the systemic  
530 exposure of atezolizumab.

531 The effect of severe renal impairment (eGFR 15 to 29 mL/min/1.73 m<sup>2</sup>) or moderate or severe  
532 hepatic impairment (bilirubin > ULN and AST > ULN or bilirubin ≥ 1.0 to 1.5 × ULN and any  
533 AST) on the pharmacokinetics of atezolizumab is unknown.

### 534 *Drug Interaction Studies*

535 The drug interaction potential of atezolizumab is unknown.

## 536 **13 NONCLINICAL TOXICOLOGY**

### 537 **13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility**

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

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

### 547 **13.2 Animal Toxicology and/or Pharmacology**

548 In animal models, inhibition of PD-L1/PD-1 signaling increased the severity of some infections  
549 and enhanced inflammatory responses. *M. tuberculosis*-infected PD-1 knockout mice exhibit  
550 markedly decreased survival compared with wild-type controls, which correlated with increased  
551 bacterial proliferation and inflammatory responses in these animals. PD-L1 and PD-1 knockout  
552 mice and mice receiving PD-L1 blocking antibody have also shown decreased survival following  
553 infection with lymphocytic choriomeningitis virus.

554 **14 CLINICAL STUDIES**

555 **14.1 Urothelial Carcinoma**

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

557 The efficacy of TECENTRIQ was investigated in Study 4, a multicenter, open-label, single-arm  
558 trial that included 119 patients with locally advanced or metastatic urothelial carcinoma who  
559 were ineligible for cisplatin-containing chemotherapy and were either previously untreated or  
560 had disease progression at least 12 months after neoadjuvant or adjuvant chemotherapy. Patients  
561 were considered cisplatin-ineligible if they met any one of the following criteria at study entry:  
562 impaired renal function (creatinine clearance of > 30 but < 60 mL/min), ECOG score of 2,  
563 hearing loss of  $\geq 25$  dB at two contiguous frequencies, or  $\geq$  Grade 2 peripheral neuropathy. This  
564 study excluded patients who had: a history of autoimmune disease; active or corticosteroid-  
565 dependent brain metastases; administration of a live, attenuated vaccine within 28 days prior to  
566 enrollment; or administration of systemic immunostimulatory agents within 6 weeks or systemic  
567 immunosuppressive medications within 2 weeks prior to enrollment. Patients received an  
568 intravenous infusion of 1200 mg of TECENTRIQ every 3 weeks until unacceptable toxicity or  
569 disease progression. Tumor response assessments were conducted every 9 weeks for the first  
570 54 weeks and every 12 weeks thereafter. Major efficacy outcome measures included confirmed  
571 objective response rate (ORR) as assessed by independent review facility (IRF) using Response  
572 Evaluation Criteria in Solid Tumors (RECIST v1.1), duration of response (DoR) and overall  
573 survival (OS).

574 In this study, the median age was 73 years, 81% were male, and 91% were Caucasian. Thirty-  
575 five percent of patients had non-bladder urothelial carcinoma and 66% had visceral metastases.  
576 Eighty percent of patients had an ECOG score of 0-1. Reasons for patients' ineligibility for  
577 cisplatin-containing chemotherapy were: 70% had impaired renal function, 20% had an ECOG  
578 score of 2, 14% had a hearing loss of  $\geq 25$ db, and 6% had  $\geq$  Grade 2 peripheral neuropathy at  
579 baseline. Twenty percent of patients had disease progression following prior platinum-  
580 containing neoadjuvant or adjuvant chemotherapy.

581 Tumor specimens were evaluated prospectively using the Ventana PD-L1 (SP142) Assay at a  
582 central laboratory, and the results were used to define subgroups for pre-specified analyses. Of  
583 the 119 patients, 27% were classified as having PD-L1 expression of  $\geq 5\%$  (defined as PD-L1  
584 stained tumor-infiltrating immune cells [IC] covering  $\geq 5\%$  of the tumor area). The remaining  
585 73% of patients were classified as having PD-L1 expression of  $< 5\%$  (PD-L1 stained tumor-  
586 infiltrating IC covering  $< 5\%$  of the tumor area).

587 Confirmed ORR in all patients and the two PD-L1 subgroups are summarized in Table 7. The  
588 median follow-up time for this study was 14.4 months. In 24 patients with disease progression  
589 following neoadjuvant or adjuvant therapy, the ORR was 33.0% (95% CI: 16%, 55%).

**Table 7: Summary of Efficacy from Study 4**

|  | All Patients              | PD-L1 Expression Subgroups                          |   |
|--|---------------------------|---|---|
|  | N=119                     | PD-L1 Expression of < 5% in ICs <sup>1</sup> (N=87) | PD-L1 Expression of ≥ 5% in ICs <sup>1</sup> (N=32) |
| <b>Number of IRF-assessed Confirmed Responders</b>   | 28                        | 19  | 9   |
| <b>ORR % (95% CI)</b>  | <b>23.5% (16.2, 32.2)</b> | <b>21.8% (13.7, 32.0)</b>                           | <b>28.1% (13.8, 46.8)</b>                           |
| Complete Response (CR) (%)   | 6.7%                      | 6.9%  | 6.3%  |
| Partial Response (PR) (%)  | 16.8%                     | 14.9%   | 21.9%   |
| <b>Median DoR, months (range)</b>  | NR<br>(3.7, 16.6+)        | NR<br>(3.7, 16.6+)                                  | NR<br>(8.1, 15.6+)                                  |
| NR = Not reached<br>+ Denotes a censored value<br><sup>1</sup> PD-L1 expression in tumor-infiltrating immune cells (ICs) |                           |   |   |

### 591 **Previously Treated Patients with Locally Advanced or Metastatic Urothelial Carcinoma**

592 The efficacy of TECENTRIQ was investigated in Study 1, a multicenter, open-label, single-arm  
593 trial that included 310 patients with locally advanced or metastatic urothelial carcinoma who had  
594 disease progression during or following a platinum-containing chemotherapy regimen or who  
595 had disease progression within 12 months of treatment with a platinum-containing neoadjuvant  
596 or adjuvant chemotherapy regimen. This study excluded patients who had: a history of  
597 autoimmune disease, active or corticosteroid-dependent brain metastases, administration of a  
598 live, attenuated vaccine within 28 days prior to enrollment, or administration of systemic  
599 immunostimulatory agents within 6 weeks or systemic immunosuppressive medications within 2  
600 weeks prior to enrollment. Patients received an intravenous infusion of 1200 mg of  
601 TECENTRIQ every 3 weeks until unacceptable toxicity or either radiographic or clinical  
602 progression. Tumor response assessments were conducted every 9 weeks for the first 54 weeks  
603 and every 12 weeks thereafter. Major efficacy outcome measures included confirmed objective  
604 response rate (ORR) as assessed by independent review facility (IRF) using Response Evaluation  
605 Criteria in Solid Tumors (RECIST v1.1) and duration of response (DOR).

606 In this study, the median age was 66 years, 78% were male, 91% of patients were Caucasian.  
607 Twenty-six percent had non-bladder urothelial carcinoma and 78% of patients had visceral  
608 metastases. Sixty-two percent of patients had an ECOG score of 1 and 35% of patients had a  
609 baseline creatinine clearance of < 60 mL/min. Nineteen percent of patients had disease  
610 progression following prior platinum-containing neoadjuvant or adjuvant chemotherapy. Forty-  
611 one percent of patients had received ≥ 2 prior systemic regimens in the metastatic setting.  
612 Seventy-three percent of patients received prior cisplatin, 26% had prior carboplatin, and 1%  
613 were treated with other platinum-based regimens.

614 Tumor specimens were evaluated prospectively using the VENTANA PD-L1 (SP142) Assay at a  
615 central laboratory and the results were used to define subgroups for pre-specified analyses. Of  
616 the 310 patients, 32% were classified as having PD-L1 expression of ≥ 5% (defined as PD-L1  
617 stained tumor-infiltrating immune cells [IC] covering ≥ 5% of the tumor area). The remaining  
618 68% of patients were classified as having PD-L1 expression of < 5% (PD-L1 stained tumor-  
619 infiltrating IC covering < 5% of the tumor area).

620 Confirmed ORR in all patients and the two PD-L1 subgroups are summarized in Table 8. The  
 621 median follow-up time for this study was 14.4 months. In 59 patients with disease progression  
 622 following neoadjuvant or adjuvant therapy, the ORR was 22.0% (95% CI: 12.3%, 34.7%).

623 **Table 8: Summary of Efficacy from Study 1**

|   | All Patients              | PD-L1 Expression Subgroups                                   |  |
|---|---------------------------|--|--|
|   | N=310                     | PD-L1<br>Expression of<br>< 5% in IC <sup>1</sup><br>(N=210) | PD-L1<br>Expression of<br>≥ 5% in IC <sup>1</sup><br>(N=100) |
| <b>Number of IRF-assessed<br/>Confirmed Responders</b>  | 46                        | 20   | 26   |
| <b>ORR % (95% CI)</b>   | <b>14.8% (11.1, 19.3)</b> | <b>9.5% (5.9, 14.3)</b>                                      | <b>26.0% (17.7, 35.7)</b>                                    |
| Complete Response (CR) (%)  | 5.5%                      | 2.4%   | 12.0%  |
| Partial Response (PR) (%)   | 9.4%                      | 7.1%   | 14.0%  |
| <b>Median DOR, months<br/>(range)</b>   | NR<br>(2.1+, 13.8+)       | 12.7<br>(2.1+, 12.7)   | NR<br>(4.2, 13.8+)   |
| NR = Not reached<br>+ Denotes a censored value<br><sup>1</sup> PD-L1 expression in tumor-infiltrating immune cells (IC) |                           |  |  |

624 **14.2 Metastatic Non-Small Cell Lung Cancer**

625 **Previously Treated Patients with Metastatic NSCLC**

626 The efficacy of TECENTRIQ was investigated in two multicenter, international, randomized,  
 627 open-label trials in patients with metastatic NSCLC who progressed during or following a  
 628 platinum-containing regimen. Study 2 was a trial in 1225 patients with the primary analysis  
 629 population consisting of the first 850 randomized patients and Study 3 was a trial in 287 patients.  
 630 In both studies, eligible patients were stratified by PD-L1 expression status in tumor-infiltrating  
 631 immune cells (IC), by the number of prior chemotherapy regimens, and by histology. Patients  
 632 were randomized (1:1) to receive either TECENTRIQ administered intravenously at 1200 mg  
 633 every 3 weeks until unacceptable toxicity or either radiographic or clinical progression or  
 634 docetaxel administered intravenously at 75 mg/m<sup>2</sup> every 3 weeks until unacceptable toxicity or  
 635 disease progression. These studies excluded patients who had: a history of autoimmune disease,  
 636 had active or corticosteroid-dependent brain metastases, administration of a live, attenuated  
 637 vaccine within 28 days prior to enrollment, administration of systemic immunostimulatory  
 638 agents within 4 weeks or systemic immunosuppressive medications within 2 weeks prior to  
 639 enrollment. Tumor assessments were conducted every 6 weeks for the first 36 weeks, and every  
 640 9 weeks thereafter. In Study 2, tumor specimens were evaluated prospectively for PD-L1  
 641 expression on tumor cells (TC) and IC using the VENTANA PD-L1 (SP142) Assay and the  
 642 results were used to define the PD-L1 expression subgroups for the analyses described below.

643 In Study 2, among patients in the primary analysis population, the median age was 64 years  
 644 (range: 33 to 85), and 61% of patients were male. The majority of patients were white (70%).  
 645 Approximately three-fourths of patients had non-squamous disease (74%), 10% had known  
 646 EGFR mutation, 0.2% had known ALK rearrangements, and most patients were current or  
 647 previous smokers (82%). Baseline ECOG performance status was 0 (37%) or 1 (63%). Seventy  
 648 five percent of patients received only one prior platinum-based therapeutic regimen. In Study 3,

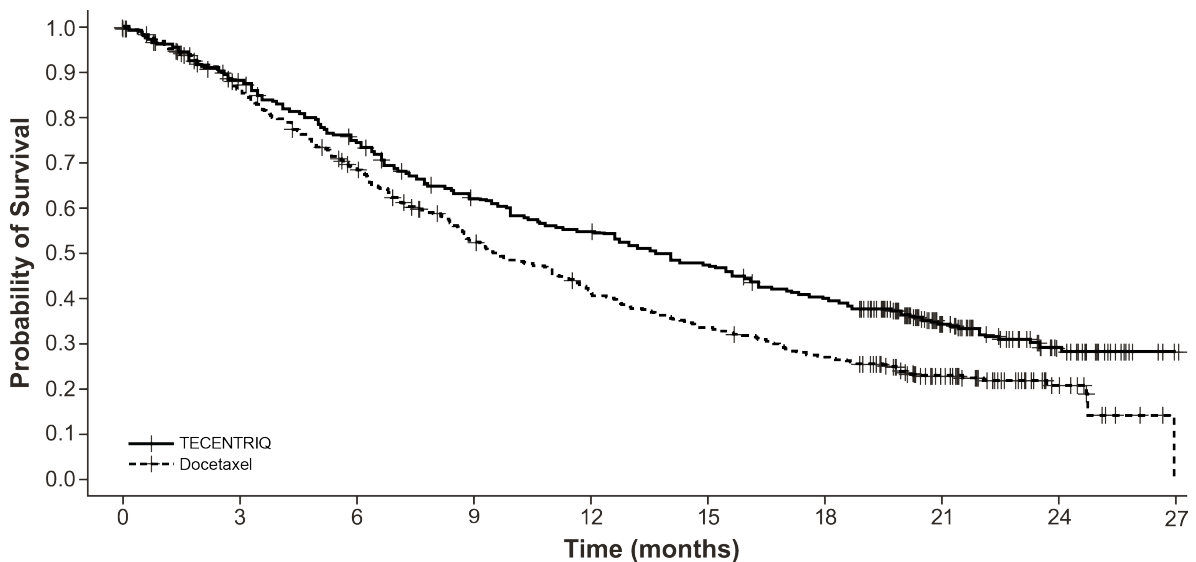
649 the median age was 62 years (range: 36 to 84), and 59% of patients were male. The majority of  
 650 patients were white (79%). Approximately two-thirds of patients had non-squamous disease  
 651 (66%), 7% had known EGFR mutation, 1% had ALK rearrangements, and most patients were  
 652 current or previous smokers (80%). Baseline ECOG performance status was 0 (33%) or 1 (67%).  
 653 Approximately two-thirds of patients received only one prior platinum-based therapeutic  
 654 regimen.

655 The major efficacy outcome measure of Study 2 was overall survival (OS) in the primary  
 656 analysis population (first 850 randomized patients). The major efficacy outcome measure of  
 657 Study 3 was overall survival (OS). Other efficacy outcome measures for Study 3 included  
 658 investigator-assessed objective response rates and duration of response per RECIST v1.1. The  
 659 results of Study 2 with a median follow up of 21 months are presented in Table 9 and Figure 1.

660 **Table 9: Efficacy Results in the Primary Analysis Population from Study 2**

|  | <b>TECENTRIQ<br/>(n=425)</b> | <b>Docetaxel<br/>(n=425)</b> |
|--|------------------------------|------------------------------|
| <b>Overall Survival</b>  |                              |                              |
| Deaths (%)   | 271 (64%)                    | 298 (70%)                    |
| Median, months<br>(95% CI)   | 13.8<br>(11.8, 15.7)         | 9.6<br>(8.6, 11.2)           |
| Hazard ratio <sup>1</sup> (95% CI)   | 0.74 (0.63, 0.87)            |                              |
| p-value <sup>2</sup>   | 0.0004                       |                              |
| <sup>1</sup> Stratified by PD-L1 expression in tumor infiltrating immune cells, the number of prior chemotherapy regimens, and histology |                              |                              |
| <sup>2</sup> Based on the stratified log-rank test   |                              |                              |
| CI=confidence interval   |                              |                              |

661 **Figure 1: Kaplan-Meier Plot of Overall Survival in the Primary Analysis Population in**  
 662 **Study 2**



| No. Patients at Risk | 0   | 3   | 6   | 9   | 12  | 15  | 18  | 21  | 24  | 27  |     |     |     |     |     |     |     |     |     |     |     |    |    |    |    |    |   |   |
|----------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|----|----|----|----|----|---|---|
| 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 |   |

663  
 664 Tumor specimens were evaluated prospectively using the VENTANA PD-L1 (SP142) Assay at a  
 665 central laboratory and the results were used to define the PD-L1 expression subgroups for pre-  
 666 specified analyses. Of the 850 patients, 16% were classified as having high PD-L1 expression,  
 667 defined as having PD-L1 expression on  $\geq 50\%$  of TC or  $\geq 10\%$  of IC. In an exploratory efficacy

668 subgroup analysis of OS based on PD-L1 expression, the hazard ratio was 0.41 (95% CI: 0.27,  
 669 0.64) in the high PD-L1 expression subgroup and 0.82 (95% CI: 0.68, 0.98) in patients who did  
 670 not have high PD-L1 expression.

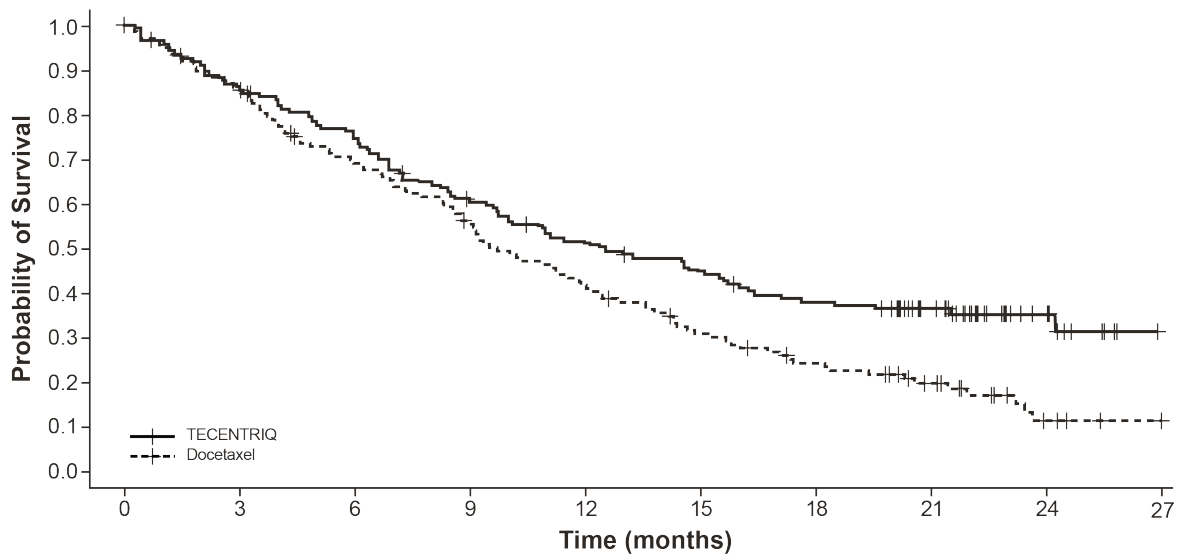
671 Results of an updated survival analysis in Study 3 with a median follow-up of 22 months are  
 672 provided for all randomized patients (Table 10 and Figure 2).

673 **Table 10: Efficacy Results from Study 3**

|  | <b>TECENTRIQ<br/>(n=144)</b> | <b>Docetaxel<br/>(n=143)</b> |
|--|------------------------------|------------------------------|
| <b>Overall Survival</b>                          |                              |                              |
| Deaths (%)                                       | 90 (63%)                     | 110 (77%)                    |
| Median, months<br>(95% CI)                       | 12.6<br>(9.7, 16.0)          | 9.7<br>(8.6, 12.0)           |
| Hazard ratio <sup>1</sup> (95% CI)               | 0.69 (0.52, 0.92)            |                              |
| <b>Objective Response Rate<sup>2</sup> n (%)</b> | 22 (15%)                     | 21 (15%)                     |
| (95% CI)   | (10%, 22%)                   | (9%, 22%)                    |
| Complete response                                | 1 (0.7%)                     | 0                            |
| Partial response                                 | 21 (15%)                     | 21 (15%)                     |
| <b>Duration of Response<sup>2</sup></b>          | n=22                         | n=21                         |
| Median (months)<br>(95% CI)                      | 18.6<br>(11.6, NE)           | 7.2<br>(5.6, 12.5)           |

<sup>1</sup> Stratified by PD-L1 expression in tumor-infiltrating immune cells, the number of prior chemotherapy regimens, and histology  
<sup>2</sup> per RECIST v1.1 (Response Evaluation Criteria in Solid Tumors v1.1)  
 CI=confidence interval; NE=not estimable

674 **Figure 2: Kaplan-Meier Plot of updated Overall Survival in Study 3**



| No. of Patients at Risk | 0   | 3   | 6   | 9   | 12  | 15  | 18  | 21 | 24 | 27 |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |   |   |
|-------------------------|-----|-----|-----|-----|-----|-----|-----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|---|---|
| TECENTRIQ               | 144 | 139 | 131 | 123 | 117 | 110 | 106 | 95 | 90 | 84 | 78 | 73 | 70 | 67 | 64 | 60 | 54 | 52 | 50 | 49 | 46 | 34 | 24 | 14 | 11 | 5 | 1 |
| Docetaxel               | 143 | 130 | 123 | 118 | 106 | 97  | 92  | 87 | 82 | 73 | 65 | 61 | 55 | 49 | 46 | 39 | 36 | 33 | 29 | 27 | 24 | 18 | 12 | 9  | 5  | 2 | 1 |

675 **16 HOW SUPPLIED/STORAGE AND HANDLING**

677 TECENTRIQ injection is a sterile, preservative-free, and colorless to slightly yellow solution for  
 678 intravenous infusion supplied as a carton containing one 1200 mg/20 mL single-dose vial (NDC  
 679 50242-917-01).

680 **Storage:** Store vials under refrigeration at 2°C to 8°C (36°F to 46°F) in original carton to protect  
681 from light. Do not freeze. Do not shake.

## 682 **17 PATIENT COUNSELING INFORMATION**

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

684 Inform patients of the risk of immune-related adverse reactions that may require corticosteroid  
685 treatment and interruption or discontinuation of TECENTRIQ, including:

- 686 • Pneumonitis: Advise patients to contact their healthcare provider immediately for any  
687 new or worsening cough, chest pain, or shortness of breath [*see Warnings and*  
688 *Precautions (5.1)*].
- 689 • Hepatitis: Advise patients to contact their healthcare provider immediately for jaundice,  
690 severe nausea or vomiting, pain on the right side of abdomen, lethargy, or easy bruising  
691 or bleeding [*see Warnings and Precautions (5.2)*].
- 692 • Colitis: Advise patients to contact their healthcare provider immediately for diarrhea or  
693 severe abdominal pain [*see Warnings and Precautions (5.3)*].
- 694 • Endocrinopathies: Advise patients to contact their healthcare provider immediately for  
695 signs or symptoms of hypophysitis, hyperthyroidism, hypothyroidism, adrenal  
696 insufficiency, or type 1 diabetes mellitus, including diabetic ketoacidosis [*see Warnings*  
697 *and Precautions (5.4)*].
- 698 • Meningoencephalitis, Myasthenic syndrome/Myasthenia Gravis, and Guillain-Barré  
699 syndrome: Advise patients to contact their healthcare provider immediately for signs or  
700 symptoms of meningitis, myasthenic syndrome/myasthenia gravis, or Guillain-Barré  
701 syndrome [*see Warnings and Precautions (5.5)*].
- 702 • Ocular Inflammatory Toxicity: Advise patients to contact their healthcare provider  
703 immediately for signs or symptoms of ocular inflammatory toxicity [*see Warnings and*  
704 *Precautions (5.5)*].
- 705 • Pancreatitis: Advise patients to contact their healthcare provider immediately for signs  
706 and symptoms of pancreatitis [*see Warnings and Precautions (5.5)*].
- 707 • Infection: Advise patients to contact their healthcare provider immediately for signs or  
708 symptoms of infection [*see Warnings and Precautions (5.6)*].
- 709 • Infusion-Related Reactions: Advise patients to contact their healthcare provider  
710 immediately for signs or symptoms of infusion-related reactions [*see Warnings and*  
711 *Precautions (5.7)*].
- 712 • Rash: Advise patients to contact their healthcare provider immediately for signs or  
713 symptoms of rash [*see Dosage and Administration (2.2)*].

### 714 Embryo-Fetal Toxicity

715 Advise female patients that TECENTRIQ can cause fetal harm. Instruct females of  
716 reproductive potential to use effective contraception during treatment and for at least  
717 5 months after the last dose of TECENTRIQ [*see Use in Specific Populations (8.1, 8.3)*].

### 718 Lactation

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

---

**TECENTRIQ<sup>®</sup> [atezolizumab]**

Manufactured by:

**Genentech, Inc.**

A Member of the Roche Group

1 DNA Way

South San Francisco, CA 94080-4990

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Inc.

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**MEDICATION GUIDE**  
**TECENTRIQ® (te-SEN-trik)**  
**(atezolizumab)**  
**injection**

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

TECENTRIQ is a medicine that may treat your bladder cancer or lung cancer by working with your immune system. TECENTRIQ can cause your immune system to attack normal organs and tissues in many areas of your body 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 in your stools or dark, tarry, sticky stools
- severe stomach area (abdomen) pain or tenderness

**Hormone gland problems (especially the pituitary, thyroid, adrenal glands, and pancreas).** 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

**Nervous system problems (neuropathy, meningitis, encephalitis).** Signs and symptoms of nervous system problems may include:

- severe muscle weakness
- changes in mood or behavior
- numbness or tingling in hands or feet
- extreme sensitivity to light
- fever
- neck stiffness
- confusion

**Inflammation of the eyes.** Signs and symptoms may include:

- blurry vision, double vision, or other vision problems
- eye pain or redness

**Severe infections.** Signs and symptoms of infection may include:

- fever
- flu-like symptoms
- cough
- pain when urinating
- frequent urination

**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:

### 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 (advanced urothelial carcinoma), **and**
- you are not able to take chemotherapy that contains a medicine called cisplatin, **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 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.

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. If you are able to become pregnant, 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 3 weeks.
- Your healthcare provider will decide how many treatments you need.
- Your healthcare provider will test your blood to check you for certain side effects.  
If you miss any appointments, call your healthcare provider as soon as possible to reschedule your appointment.

## What are the possible side effects of TECENTRIQ?

### TECENTRIQ can cause serious side effects, including:

- **See "What is the most important information I should know about TECENTRIQ?"**

The most common side effects of TECENTRIQ in people with urothelial carcinoma include:

- feeling tired
- decreased appetite
- nausea
- constipation
- urinary tract infection
- diarrhea
- fever

The most common side effects of TECENTRIQ in people with non-small cell lung cancer include:

- feeling tired
- decreased appetite
- shortness of breath
- cough
- nausea
- muscle or bone pain
- constipation

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

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

## General information about the safe and effective use of TECENTRIQ.

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

**What are the ingredients in TECENTRIQ?**

**Active ingredient:** atezolizumab

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

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

U.S. License No. 1048 TECENTRIQ is a registered trademark of Genentech, Inc.

For more information, call 1-844-832-3687 or go to [www.TECENTRIQ.com](http://www.TECENTRIQ.com).

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

Revised: 4/2017