TECENTRIQ DOSING AND ADVERSE REACTION MANAGEMENT GUIDE

FOR HCC, NSCLC, AND ES-SCLC

Indications

TECENTRIQ is indicated in:

Unresectable or Metastatic Hepatocellular Carcinoma (HCC)

- In combination with bevacizumab, for the treatment of patients with unresectable or metastatic hepatocellular carcinoma (HCC) who have not received prior systemic therapy

Metastatic Non-Small Cell Lung Cancer (NSCLC)

- As as a single agent, for the first-line treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have high PD-L1 expression (PD-L1–stained ≥50% of tumor cells [TC ≥50%] or PD-L1–stained tumor-infiltrating immune cells [IC] covering ≥10% of the tumor area [IC ≥10%]), as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations
- 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
- In combination with paclitaxel protein-bound and carboplatin, for the first-line treatment of adult patients with metastatic non-squamous NSCLC with no EGFR or ALK genomic tumor aberrations
- As a single agent, 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

Extensive-Stage Small Cell Lung Cancer (ES-SCLC)

- In combination with carboplatin and etoposide, for the first-line treatment of adult patients with ES-SCLC

Select Important Safety Information

Serious and sometimes fatal adverse reactions occurred with TECENTRIQ treatment. Warnings and precautions include immune-mediated serious adverse reactions, including pneumonitis, hepatitis, colitis, endocrinopathies, and other immune-mediated adverse reactions. Other warnings and precautions include infections, infusion-related reactions, and embryo-fetal toxicity.

ALK=anaplastic lymphoma kinase;
EGFR=epidermal growth factor receptor;
PD-L1=programmed death-ligand 1.

Please see accompanying full Prescribing Information and additional Important Safety Information throughout this brochure.

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atezolizumab
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INTRODUCTION

This brochure provides guidelines for patients receiving treatment with TECENTRIQ for

- Unresectable or metastatic HCC
- Lung cancer (NSCLC and ES-SCLC)

It describes important dosing and administration information, as well as recommendations from the TECENTRIQ Prescribing Information, for the management of immune-mediated adverse reactions (ARs) that may occur in patients receiving treatment with TECENTRIQ.

The following pages will guide you through

- Preparing, administering, and storing TECENTRIQ
- Monitoring patients for signs and symptoms of immune-mediated ARs
- Managing ARs with step-by-step instructions
- Following up on management steps and knowing when to withhold, resume, and discontinue treatment with TECENTRIQ

Please see accompanying full Prescribing Information and additional Important Safety Information throughout this brochure.

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TECENTRIQ DOSING AND ADMINISTRATION
Unresectable or metastatic HCC

Recommended dosage schedule for HCC[1,2]

Indication	Recommended dosage	Schedule
1L unresectable or metastatic HCC	TECENTRIQ 1200 mg IV + bevacizumab* 15 mg/kg	q3w Until disease progression or unacceptable toxicity
	If bevacizumab is discontinued, TECENTRIQ can be administered at: 840 mg IV q2w, 1200 mg IV q3w, or 1680 mg† IV q4w	q2w, q3w, or q4w Until disease progression or unacceptable toxicity
TECENTRIQ infusion time	• 60-minute initial infusion • 30-minute subsequent infusions if initial infusion is tolerated	

Dosing information for bevacizumab is based on the IMbrave150 trial; TECENTRIQ was administered q3w in IMbrave150.
1L=first line; HCC=hepatocellular carcinoma; IV=intravenous; q2w=every 2 weeks; q3w=every 3 weeks; q4w=every 4 weeks.
*Refer to the Prescribing Information for bevacizumab prior to initiation.
†Administered with two 840-mg vials of TECENTRIQ.

- **Unresectable or metastatic HCC in patients who have not received prior systemic therapy:** TECENTRIQ should be administered prior to bevacizumab on Day 1 of the cycle
- TECENTRIQ can be administered with or without a sterile, nonpyrogenic, low-protein binding in-line filter (pore size of 0.2–0.22 micron)
- Do not administer TECENTRIQ as an IV push or bolus
- Do not co-administer other drugs through the same IV line
- Administer bevacizumab as an IV infusion
- First infusion of bevacizumab: administer infusion over 90 minutes
- Subsequent infusions: administer second infusion over 60 minutes if first infusion is tolerated. Administer all subsequent infusions over 30 minutes if second infusion over 60 minutes is tolerated
- Refer to the Prescribing Information for bevacizumab for bevacizumab dosage modifications for specific adverse reactions. No dose reductions for bevacizumab are recommended

Select Important Safety Information for bevacizumab[2]

- An evaluation for the presence of varices is recommended within 6 months of initiation of bevacizumab in patients with HCC
- There is a lack of clinical data to support the safety of bevacizumab in patients with history or risk of variceal bleeding

Please see accompanying full Prescribing Information and additional Important Safety Information throughout this brochure.

Preparation of TECENTRIQ[1]

1. INSPECT

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.

2. WITHDRAW

- Select the appropriate vial(s) based on the prescribed dose
- Withdraw the required volume of TECENTRIQ from the vial(s)
- Dilute to a final concentration between 3.2 and 16.8 mg/mL in a 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

3. MIX

Mix diluted solution by gentle inversion. Do not shake.

4. DISCARD

Discard used or empty vials of TECENTRIQ.

Storage of TECENTRIQ[1]

This product does not contain a preservative. Administer immediately once prepared. If diluted TECENTRIQ infusion solution is not used immediately, it can be stored either

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

Do not freeze. Do not shake.

TECENTRIQ 840 mg is supplied in a 14-mL single-dose vial and TECENTRIQ 1200 mg is supplied in a 20-mL single-dose vial

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TECENTRIQ DOSING AND ADMINISTRATION
Lung (NSCLC and ES-SCLC)

Recommended dosage schedule for approved lung cancer indications[1]*

Indication	Recommended dosage	Schedule
TECENTRIQ combination therapy for 1L metastatic nsqNSCLC	**Induction** TECENTRIQ 1200 mg IV + bevacizumab 15 mg/kg IV + paclitaxel 200 mg/m^2† + carboplatin AUC 6 mg/mL/min **Post-induction** TECENTRIQ 1200 mg IV + bevacizumab 15 mg/kg IV	**Induction** q3w for 4 to 6 cycles **Post-induction** Until disease progression or unacceptable toxicity
TECENTRIQ monotherapy for metastatic NSCLC‡	TECENTRIQ 840 mg IV q2w, 1200 mg IV q3w, or 1680 mg§ IV q4w	Until disease progression or unacceptable toxicity
1L ES-SCLC	**Induction** Day 1 TECENTRIQ 1200 mg IV + carboplatin AUC 5 mg/mL/min + etoposide 100 mg/m^2 Days 2 and 3 Etoposide 100 mg/m^2 **Maintenance** TECENTRIQ 840 mg IV q2w, 1200 mg IV q3w, or 1680 mg§ IV q4w	**Induction** q3w for 4 cycles **Maintenance** Until disease progression or unacceptable toxicity
TECENTRIQ infusion time	• 60-minute initial infusion • 30-minute subsequent infusions if initial infusion is tolerated	

TECENTRIQ was administered q3w in the NSCLC trials IMpower110, IMpower150, and OAK and SCLC trial IMpower133.

1L=first line; 2L=second line; AUC=area under the concentration-time curve; IV=intravenous; nsqNSCLC=non-squamous non-small cell lung cancer; q2w=every 2 weeks; q3w=every 3 weeks; q4w=every 4 weeks.

*Please see full indications on front cover.
†In patients of Asian race/ethnicity, the paclitaxel starting dose has been lowered from 200 mg/m^2 to 175 mg/m^2.
‡TECENTRIQ monotherapy dosing applies to the IMpower110 and OAK trials.
§Administered with two 840-mg vials of TECENTRIQ.

- **TECENTRIQ combination therapy for first-line metastatic nsqNSCLC:** during induction phase, TECENTRIQ should be administered prior to bevacizumab, paclitaxel, and carboplatin on Day 1 of each cycle
- **First-line ES-SCLC:** during induction phase, TECENTRIQ should be administered first, followed by carboplatin, then etoposide
- Information on the dosing for agents other than TECENTRIQ is derived from clinical trial experiences. Refer to the respective Prescribing Information for bevacizumab, paclitaxel, carboplatin, and etoposide for recommended dosing information
- TECENTRIQ can be administered with or without a sterile, nonpyrogenic, low-protein binding in-line filter (pore size of 0.2–0.22 micron)
- Do not administer TECENTRIQ as an IV push or bolus
- Do not co-administer other drugs through the same IV line

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Preparation of TECENTRIQ[1]

1. INSPECT

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2. WITHDRAW

- Select the appropriate vial(s) based on the prescribed dose
- Withdraw the required volume of TECENTRIQ from the vial(s)
- Dilute to a final concentration between 3.2 and 16.8 mg/mL in a 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

3. MIX

Mix diluted solution by gentle inversion. Do not shake.

4. DISCARD

Discard used or empty vials of TECENTRIQ.

Storage of TECENTRIQ[1]

This product does not contain a preservative. Administer immediately once prepared. If diluted TECENTRIQ infusion solution is not used immediately, it can be stored either

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

Do not freeze. Do not shake.

TECENTRIQ 840 mg is supplied in a 14-mL single-dose vial and TECENTRIQ 1200 mg is supplied in a 20-mL single-dose vial

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TECENTRIQ ADVERSE REACTIONS PROFILE
Unresectable or metastatic HCC

ARs occurring at a frequency of ≥10% in patients receiving TECENTRIQ + Avastin® (bevacizumab)[1]

	TECENTRIQ + Avastin (n=329)		Sorafenib (n=156)	
Adverse reaction	**All grades* (%)**	**Grades 3-4* (%)**	**All grades* (%)**	**Grades 3-4* (%)**
Vascular disorders				
Hypertension	30	15	24	12
General disorders and administration site conditions				
Fatigue/asthenia†	26	2	32	6
Pyrexia	18	0	10	0
Renal and urinary disorders				
Proteinuria	20	3	7	0.6
Investigations				
Weight decreased	11	0	10	0
Skin and subcutaneous tissue disorders				
Pruritus	19	0	10	0
Rash	12	0	17	2.6
Gastrointestinal disorders				
Diarrhea	19	1.8	49	5
Constipation	13	0	14	0
Abdominal pain	12	0	17	0
Nausea	12	0	16	0
Vomiting	10	0	8	0
Metabolism and nutrition disorders				
Decreased appetite	18	1.2	24	3.8
Respiratory, thoracic and mediastinal disorders				
Cough	12	0	10	0
Epistaxis	10	0	4.5	0
Injury, poisoning and procedural complications				
Infusion-related reaction	11	2.4	0	0

Most common ARs

The most common ARs (rate ≥20%) in patients who received TECENTRIQ in combination with bevacizumab for HCC were hypertension (30%), fatigue/asthenia (26%), and proteinuria (20%).

*Graded per National Cancer Institute Common Terminology Criteria for Adverse Events version 4.0 (NCI CTCAE v4.0).
†Includes fatigue and asthenia.

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TECENTRIQ ADVERSE REACTIONS PROFILE
TECENTRIQ monotherapy and lung combinations (NSCLC and ES-SCLC)

Incidence of ARs in patients receiving TECENTRIQ monotherapy (N=2616) and combination therapy (N=2421)[1]

	All grades (%)	Grade 2 (%)	Grade 3 (%)	Grade 4 (%)	Grade 5 (%)
ARs (TECENTRIQ monotherapy, N=2616)					
Pneumonitis	2.5%	–	0.6%	0.1%	<0.1%
Hepatitis	9%	–	2.3%	0.6%	<0.1%
Diarrhea or colitis	20%	–	1.4%	–	–
Hypothyroidism	4.6%	–	–	–	–
Hyperthyroidism	1.6%	–	–	–	–
Adrenal insufficiency	0.4%	–	<0.1%	–	–
Diabetes	<0.1%	–	–	–	–
Hypophysitis	–	<0.1%	–	–	–
Infections	42%	–	8.7%	1.5%	1%
Infusion-related reaction	1.3%	–	0.2%	–	–
ARs (TECENTRIQ combination therapy, N=2421)*					
Pneumonitis	5.5%	–	1.4%	1.4%	–
Hepatitis	14%	–	4.1%	4.1%	–
Diarrhea or colitis	29%	–	4.3%	4.3%	–
Hypothyroidism	11%	–	0.3%	0.3%	–

– indicates data not reported in Prescribing Information.
*Immune-mediated ARs that occurred in patients with NSCLC and SCLC who received TECENTRIQ in combination with platinum-based chemotherapy (N=2421).

The frequency and severity of the following ARs were similar whether TECENTRIQ was given as a single agent in patients with various cancers or in combination with other antineoplastic drugs in NSCLC and SCLC

- Hyperthyroidism
- Thyroiditis
- Adrenal insufficiency
- Type 1 diabetes mellitus
- Hypophysitis
- Infections
- Infusion-related reactions

Please see accompanying full Prescribing Information and additional Important Safety Information throughout this brochure.

Median time to onset[1†]

In clinical studies enrolling 2616 patients who received TECENTRIQ monotherapy, median time to onset and median duration varied across select ARs

- Pneumonitis (3.6 months; range, 3 days to 20.5 months)
- Hepatitis (1.4 months; range, 1 day to 25.8 months)
- Diarrhea or colitis (1.5 months; range, 1 day to 41 months)
- Adrenal insufficiency (5.7 months; range, 3 days to 19 months)

Use of systemic corticosteroids and hormone replacement therapy across clinical trials[1]

In clinical studies enrolling 2616 patients who received TECENTRIQ monotherapy, systemic corticosteroids were required for the following immune-mediated ARs

- Pneumonitis (1.5%)
- Hepatitis (2%)
- Diarrhea or colitis (1.1%)
- Adrenal insufficiency (0.3%)

In clinical studies enrolling 2421 patients with NSCLC and SCLC who received TECENTRIQ in combination with platinum-based chemotherapy, systemic corticosteroids were required for the following immune-mediated ARs

- Pneumonitis (4.2%)
- Hepatitis (4.8%)
- Diarrhea or colitis (4.7%)

Hormone replacement therapy was used to treat hypothyroidism for

- 3.8% of patients who received TECENTRIQ monotherapy (N=2616)
- 8.2% of patients who received TECENTRIQ combination therapy (N=2421)

Most common ARs

The most common ARs (rate ≥20%) in patients who received TECENTRIQ alone were fatigue/asthenia (48%), decreased appetite (25%), nausea (24%), cough (22%), and dyspnea (22%).

The most common ARs (rate ≥20%) in patients who received TECENTRIQ in combination with other antineoplastic drugs for NSCLC and SCLC were fatigue/asthenia (49%), nausea (38%), alopecia (35%), constipation (29%), diarrhea (28%), and decreased appetite (27%).

†While immune-mediated ARs usually manifest during treatment with TECENTRIQ, immune-mediated ARs can also manifest after discontinuation of TECENTRIQ.

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MONITORING SELECT TECENTRIQ ADVERSE REACTIONS

ARs that may occur during treatment with TECENTRIQ

Adverse reaction	Monitoring patients	Counsel patients to inform their healthcare provider immediately if they experience
Immune-mediated pneumonitis	Monitor patients for signs and symptoms of pneumonitis Evaluate patients with suspected pneumonitis with radiographic imaging	• New or worsening cough • Shortness of breath • Chest pain
Immune-mediated hepatitis	Monitor patients for signs and symptoms of hepatitis, during and after discontinuation of TECENTRIQ, including clinical chemistry monitoring	• Yellowing of the skin or whites of the eyes • Severe nausea or vomiting • Pain on the right side of the stomach area (abdomen) • Drowsiness • Dark urine (tea colored) • Bleeding or bruising more easily than normal • Feeling less hungry than usual
Immune-mediated colitis	Monitor patients for signs and symptoms of colitis or diarrhea	• Diarrhea (loose stools) or more bowel movements than usual • Blood or mucus in stools or dark, tarry, sticky stools • Severe stomach area (abdomen) pain or tenderness
Immune-mediated endocrinopathies	Monitor thyroid function prior to and periodically during treatment with TECENTRIQ Monitor patients for clinical signs and symptoms of adrenal insufficiency Monitor patients for hyperglycemia or other signs and symptoms of diabetes	• Headaches that will not go away or unusual headaches • Extreme tiredness • Weight gain or weight loss • Dizziness or fainting • Feeling more hungry or thirsty than usual • Hair loss • Changes in mood or behavior, such as decreased sex drive, irritability, or forgetfulness • Feeling cold • Constipation • Voice gets deeper • Urinating more often than usual • Nausea or vomiting • Stomach area (abdomen) pain
Other immune-mediated adverse reactions*	Monitor patients for signs and symptoms of immune-mediated adverse reactions involving a major organ*	• Severe muscle weakness • Numbness or tingling in hands or feet • Confusion • Blurry vision, double vision, or other vision problems • Changes in mood or behavior • Extreme sensitivity to light • Neck stiffness • Eye pain or redness • Skin blisters or peeling • Chest pain, irregular heartbeat, shortness of breath, or swelling of the ankles
Infections	Monitor patients for signs and symptoms of infection	• Fever • Cough • Flu-like symptoms • Pain when urinating, frequent urination, or back pain
Infusion-related reactions	Monitor patients for signs and symptoms of infusion-related reactions	• Chills or shaking • Itching or rash • Flushing • Shortness of breath or wheezing • Swelling of the face or lips • Dizziness • Fever • Feeling like passing out • Back or neck pain

*Immune-mediated ARs include cardiac, dermatologic, gastrointestinal, general, hematological, musculoskeletal, neurological, ophthalmological, renal, and vascular.

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MANAGING SELECT TECENTRIQ ADVERSE REACTIONS

Immune-mediated pneumonitis[1]

MANAGE		FOLLOW UP	
Grade 2 pneumonitis	**Withhold TECENTRIQ** **Administer corticosteroids, prednisone 1-2 mg/kg/day or equivalents**	**Taper corticosteroids**	*When adverse reaction recovers to grade 1 or is resolved* **and** *corticosteroid dose is less than or equal to prednisone 10 mg per day (or equivalent)* **resume TECENTRIQ**
Grade 3 or 4 pneumonitis	**Permanently discontinue TECENTRIQ** **Administer corticosteroids, prednisone 1-2 mg/kg/day or equivalents**	**Taper corticosteroids**	

Pneumonitis grading[3]*

- Grade 2: symptomatic; medical intervention indicated; limiting instrumental ADL
- Grade 3: severe symptoms; limiting self-care ADL; oxygen indicated
- Grade 4: life-threatening respiratory compromise; urgent intervention indicated (eg, tracheotomy or intubation)

ADL=activities of daily living.
*Grading per National Cancer Institute Common Terminology Criteria for Adverse Events version 4.0 (NCI CTCAE v4.0).

Immune-mediated hepatitis (non-HCC)[1]

MANAGE		FOLLOW UP
≥Grade 2 elevations of ALT, AST, and/or total bilirubin	**Administer corticosteroids, prednisone 1-2 mg/kg/day or equivalents**	**Taper corticosteroids**
AST or ALT >3 and ≤8 times the ULN or total bilirubin >1.5 and ≤3 times the ULN	**Withhold TECENTRIQ**	*When adverse reaction recovers to grade 1 or is resolved* **and** *corticosteroid dose is less than or equal to prednisone 10 mg per day (or equivalent)* **resume TECENTRIQ**
AST or ALT >8 times the ULN or total bilirubin >3 times the ULN	**Permanently discontinue TECENTRIQ**	

Immune-mediated hepatitis (HCC)[1]

MANAGE	FOLLOW UP
• AST or ALT is within normal limits at baseline and increases to >3 and ≤10 times the ULN • AST or ALT >1 and ≤3 times ULN at baseline and increases to >5 and ≤10 times the ULN • AST or ALT >3 and ≤5 times ULN at baseline and increases to >8 and ≤10 times the ULN	**Withhold TECENTRIQ** *When adverse reaction recovers to grade 1 or is resolved* **and** *corticosteroid dose is less than or equal to prednisone 10 mg per day (or equivalent)* **resume TECENTRIQ**
AST or ALT increases to >10 times the ULN or total bilirubin increases to >3 times the ULN	**Permanently discontinue TECENTRIQ**

ALT=alanine aminotransferase; AST=aspartate aminotransferase; ULN=upper limit of normal.

Liver function test grading[3]*

- ALT grade ≥2: >3.0 x ULN
- AST grade ≥2: >3.0 x ULN
- Bilirubin grade ≥2: >1.5 x ULN

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MANAGING SELECT TECENTRIQ ADVERSE REACTIONS (CONT'D)

Immune-mediated colitis[1]

MANAGE			FOLLOW UP
Grade 2* or 3 colitis or diarrhea	**Withhold TECENTRIQ** *If symptoms persist for >5 days or recur* **administer corticosteroids, prednisone 1-2 mg/kg/day or equivalents**	**Taper corticosteroids**	*When adverse reaction recovers to grade 1 or is resolved* **and** *corticosteroid dose is less than or equal to prednisone 10 mg per day (or equivalent)* **resume TECENTRIQ**
Grade 4 colitis or diarrhea	**Permanently discontinue TECENTRIQ**		

*If symptoms persist for >5 days or recur, administer corticosteroids, prednisone 1 to 2 mg/kg/day or equivalents, **followed by a taper for grade 2 colitis or diarrhea**.

Colitis grading[3†]
- Grade 2: abdominal pain; mucus or blood in stool
- Grade 3: severe abdominal pain; change in bowel habits; medical intervention indicated; peritoneal signs
- Grade 4: life-threatening consequences; urgent intervention indicated

Diarrhea grading[3†]
- Grade 2: increase of 4 to 6 stools per day over baseline; moderate increase in ostomy output compared to baseline
- Grade 3: increase of ≥7 stools per day over baseline; incontinence; hospitalization indicated; severe increase in ostomy output compared to baseline; limiting self-care ADL
- Grade 4: life-threatening consequences; urgent intervention indicated

Hyperthyroidism grading[3†]
- Grade 2: symptomatic; thyroid-suppression therapy indicated; limiting instrumental ADL
- Grade 3: severe symptoms; limiting self-care ADL; hospitalization indicated
- Grade 4: life-threatening consequences; urgent intervention indicated

Hypothyroidism grading[3†]
- Grade 2: symptomatic; thyroid replacement indicated; limiting instrumental ADL
- Grade 3: severe symptoms; limiting self-care ADL; hospitalization indicated
- Grade 4: life-threatening consequences; urgent intervention indicated

Adrenal insufficiency grading[3†]
- Grade 2: moderate symptoms; medical intervention indicated
- Grade 3: severe symptoms; hospitalization indicated
- Grade 4: life-threatening consequences; urgent intervention indicated

Hypophysitis grading[3†]
- Grade 2: moderate symptoms; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL
- Grade 3: severe or medically significant but not immediately life-threatening; hospitalization or prolongation of existing hospitalization indicated; disabling; limiting self-care ADL
- Grade 4: life-threatening consequences; urgent intervention indicated

†Grading per NCI CTCAE v4.0.

Please see accompanying full Prescribing Information and additional Important Safety Information throughout this brochure.

Immune-mediated endocrinopathies[1]

MANAGE			FOLLOW UP
For **grade 2, 3, or 4** endocrinopathies, **withhold TECENTRIQ** until grade 1 or resolved **and** clinically stable on hormone replacement therapies. See below for information on the management of select endocrinopathies.			
Grade 2, 3, or 4 hyperthyroidism	**Withhold TECENTRIQ based on severity** **Initiate hormone replacement therapy or medical management of hyperthyroidism as clinically indicated**		*When adverse reaction recovers to grade 1 or is resolved* **and** *clinically stable on hormone replacement therapy* **resume TECENTRIQ**
Hypothyroidism	**Continue TECENTRIQ**		
Grade 2, 3, or 4 adrenal insufficiency	**Withhold TECENTRIQ based on severity** **Initiate prednisone 1-2 mg/kg/day or equivalents**	**Follow with a taper and hormone replacement therapy as clinically indicated**	*When adverse reaction recovers to grade 1 or is resolved* **and** *clinically stable on hormone replacement therapy* **resume TECENTRIQ**
Grade 2, 3, or 4 type 1 diabetes mellitus	**Withhold TECENTRIQ based on severity** **Initiate treatment with insulin as clinically indicated**		*When adverse reaction recovers to grade 1 or is resolved* **and** *clinically stable on hormone replacement therapy* **resume TECENTRIQ**
Grade 2, 3, or 4 hypophysitis	**Withhold TECENTRIQ based on severity** **Initiate prednisone 1-2 mg/kg/day or equivalents**	**Follow with a taper and hormone replacement therapy as clinically indicated**	*When adverse reaction recovers to grade 1 or is resolved* **and** *clinically stable on hormone replacement therapy* **resume TECENTRIQ**

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MANAGING SELECT TECENTRIQ ADVERSE REACTIONS (CONT'D)

Other immune-mediated ARs[1]*

	MANAGE		FOLLOW UP
Grade 2 immune-mediated adverse reactions involving a major organ	**For suspected grade 2 immune-mediated adverse reactions, exclude other causes and initiate corticosteroids as clinically indicated**		
Grade 3 immune-mediated adverse reactions involving a major organ	**Withhold TECENTRIQ** **Administer corticosteroids, prednisone 1-2 mg/kg/day or equivalents**	**Taper corticosteroids**	*When adverse reaction recovers to grade 1 or is resolved* **and** *corticosteroid dose is less than or equal to prednisone 10 mg per day (or equivalent)* **resume TECENTRIQ**
Grade 4 immune-mediated adverse reactions involving a major organ	**Permanently discontinue TECENTRIQ** **Administer corticosteroids, prednisone 1-2 mg/kg/day or equivalents followed by a taper**		
Uveitis occurring in combination with other immune-mediated adverse reactions	**Evaluate for Vogt-Koyanagi-Harada syndrome, which has been observed with other products in this class and may require treatment with systemic steroids to reduce the risk of permanent vision loss**		

*Immune-mediated ARs include cardiac, dermatologic, gastrointestinal, general, hematological, musculoskeletal, neurological, ophthalmological, renal, and vascular.

Infections[1]

MANAGE		FOLLOW UP
Grade 3 or 4 infections	**Withhold TECENTRIQ**	*When adverse reaction recovers to grade 1 or is resolved* **resume TECENTRIQ**

Infection grading[3†]

- Grade 3: IV antibiotic, antifungal, or antiviral intervention indicated; radiologic or operative intervention indicated
- Grade 4: life-threatening consequences; urgent intervention indicated

†Grading information for most, but not all, types of infections listed in the NCI CTCAE v4.0.

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MANAGING SELECT TECENTRIQ ADVERSE REACTIONS (CONT'D)

Infusion-related reactions[1]

MANAGE		FOLLOW UP
Grade 1 or 2 infusion-related reactions	**Interrupt or slow the rate of infusion**	*Consider using premedications with subsequent doses*
Grade 3 or 4 infusion-related reactions	**Permanently discontinue TECENTRIQ**	

Infusion-related reaction grading[3]*

- Grade 1: mild transient reaction; infusion interruption not indicated; intervention not indicated
- Grade 2: therapy or infusion interruption indicated but responds promptly to symptomatic treatment (eg, antihistamines, NSAIDs, narcotics, IV fluids); prophylactic medications indicated for ≤24 hours
- Grade 3: prolonged (eg, not rapidly responsive to symptomatic medication and/or brief interruption of infusion); recurrence of symptoms following initial improvement; hospitalization indicated for clinical sequelae
- Grade 4: life-threatening consequences; urgent intervention indicated

NSAID=nonsteroidal anti-inflammatory drug.
*Grading per NCI CTCAE v4.0.

Additional dosage modifications for ARs[1]

MANAGE		FOLLOW UP
Persistent grade 2 or 3 adverse reactions (excluding endocrinopathies)	*If grade 2 or 3 adverse reaction does not recover to grade 1 or is not resolved within 12 weeks after last TECENTRIQ dose*	**Permanently discontinue TECENTRIQ**
Inability to taper corticosteroid	*If corticosteroid cannot be reduced to less than or equal to prednisone 10 mg per day (or equivalent) within 12 weeks after last TECENTRIQ dose*	**Permanently discontinue TECENTRIQ**
Recurrent grade 3 or 4 adverse reactions	*If grade 3 or 4 (severe or life-threatening) adverse reactions recur*	**Permanently discontinue TECENTRIQ**

Please see accompanying full Prescribing Information and additional Important Safety Information throughout this brochure.

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IMPORTANT SAFETY INFORMATION

Serious Adverse Reactions

Please refer to the full Prescribing Information for important dose management information specific to adverse reactions.

Immune-Mediated Pneumonitis

- Immune-mediated pneumonitis or interstitial lung disease, including fatal cases, have occurred with TECENTRIQ treatment
- In clinical studies of TECENTRIQ as a single agent, 2.5% of patients developed pneumonitis, including Grade 3 (0.6%), Grade 4 (0.1%), and Grade 5 (<0.1%) events
- In clinical studies of TECENTRIQ in combination with platinum-based chemotherapy for NSCLC and SCLC, pneumonitis occurred in 5.5% of patients, including Grades 3 to 4 (1.4%) events
- Monitor patients for signs and symptoms of pneumonitis. Evaluate patients with suspected pneumonitis with radiographic imaging. Administer corticosteroids followed by a taper. Withhold TECENTRIQ for Grade 2 and permanently discontinue for Grade 3 or 4 pneumonitis

Immune-Mediated Hepatitis

- Liver test abnormalities and immune-mediated hepatitis, including fatal cases, have occurred with TECENTRIQ treatment
- In clinical studies of TECENTRIQ as a single agent, hepatitis occurred in 9% of patients, including Grade 3 (2.3%), Grade 4 (0.6%), and Grade 5 (<0.1%) events
- In clinical studies of TECENTRIQ in combination with platinum-based chemotherapy for NSCLC and SCLC, hepatitis occurred in 14% of patients, including Grades 3 to 4 (4.1%) events
- Monitor patients for signs and symptoms of hepatitis, during and after discontinuation of TECENTRIQ, including clinical chemistry monitoring. Administer corticosteroids followed by a taper for immune-mediated hepatitis. Withhold TECENTRIQ for AST or ALT elevations 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. Permanently discontinue TECENTRIQ for AST or ALT elevations more than 8 times the upper limit of normal or total bilirubin more than 3 times the upper limit of normal

Immune-Mediated Colitis

- Immune-mediated diarrhea or colitis have occurred with TECENTRIQ treatment
- In clinical studies of TECENTRIQ as a single agent, diarrhea or colitis occurred in 20% of patients, including Grade 3 (1.4%) events
- In clinical studies of TECENTRIQ in combination with platinum-based chemotherapy for NSCLC and SCLC, diarrhea or colitis occurred in 29% of patients, including Grades 3 to 4 (4.3%) events
- Monitor patients for signs and symptoms of diarrhea or colitis. Withhold TECENTRIQ for Grade 2 or 3 and permanently discontinue for Grade 4 diarrhea or colitis

Please see accompanying full Prescribing Information and additional Important Safety Information throughout this brochure.

Immune-Mediated Endocrinopathies

- TECENTRIQ can cause immune-mediated endocrinopathies, including thyroid disorders; adrenal insufficiency; type 1 diabetes mellitus, including diabetic ketoacidosis; and hypophysitis/hypopituitarism
- Withhold TECENTRIQ for Grades 2 to 4 endocrinopathies
- Thyroid Disorders
  - In clinical studies of TECENTRIQ as a single agent, hypothyroidism occurred in 4.6% of patients and hyperthyroidism occurred in 1.6% of patients
  - In clinical studies of TECENTRIQ in combination with platinum-based chemotherapy for NSCLC and SCLC, hypothyroidism occurred in 11% of patients, including Grades 3 to 4 (0.3%) events
  - Monitor thyroid function prior to and during treatment with TECENTRIQ. Initiate hormone replacement therapy or medical management of hyperthyroidism as clinically indicated
- Adrenal Insufficiency
  - In clinical studies of TECENTRIQ as a single agent, adrenal insufficiency occurred in 0.4% of patients, including Grade 3 (<0.1%) events
  - Monitor patients for clinical signs and symptoms of adrenal insufficiency. For Grade 2 or higher adrenal insufficiency, initiate corticosteroids and hormone replacement therapy as clinically indicated
- Type 1 Diabetes Mellitus
  - In clinical studies of TECENTRIQ as a single agent, type 1 diabetes mellitus occurred in <0.1% of patients
  - Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Initiate treatment with insulin as clinically indicated
- Hypophysitis
  - In clinical studies of TECENTRIQ as a single agent, Grade 2 hypophysitis occurred in <0.1% of patients
  - For Grades 2 to 4 hypophysitis, initiate corticosteroids and hormone replacement therapy as clinically indicated
- The frequency and severity of hyperthyroidism, thyroiditis, adrenal insufficiency, diabetes mellitus, and hypophysitis were similar whether TECENTRIQ was given as a single agent or in combination with other antineoplastic drugs in NSCLC and SCLC

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IMPORTANT SAFETY INFORMATION (CONT'D)

Other Immune-Mediated Adverse Reactions

- TECENTRIQ can cause severe and fatal immune-mediated adverse reactions. These immune-mediated reactions may involve any organ system
- In clinical studies of TECENTRIQ as a single agent and in combination with platinum-based chemotherapy, or were reported in other products in this class, the immune-mediated adverse reactions occurring at an incidence of <1% were cardiac, dermatologic, gastrointestinal, general, hematological, musculoskeletal, neurological, ophthalmological, renal, and vascular
- For suspected Grade 2 immune-mediated adverse reactions, exclude other causes and initiate corticosteroids as clinically indicated. For severe (Grade 3 or 4) adverse reactions, withhold TECENTRIQ and administer corticosteroids. Permanently discontinue TECENTRIQ for Grade 4 immune-mediated adverse reactions involving a major organ
- Evaluate for Vogt-Koyanagi-Harada syndrome if uveitis occurs in combination with other immune-mediated adverse reactions

Infections

- TECENTRIQ can cause severe infections including fatal cases
- In clinical studies of TECENTRIQ as a single agent, infections occurred in 42% of patients, including Grade 3 (8.7%), Grade 4 (1.5%), and Grade 5 (1%) events
- The frequency and severity of infections were similar whether TECENTRIQ was given as a single agent or in combination with other antineoplastic drugs in NSCLC and SCLC
- Monitor patients for signs and symptoms of infection. For Grade 3 or higher infections, withhold TECENTRIQ and resume once clinically stable

Infusion-Related Reactions

- TECENTRIQ can cause severe or life-threatening infusion-related reactions
- In clinical studies of TECENTRIQ as a single agent, infusion-related reactions occurred in 1.3% of patients, including Grade 3 (0.2%) events
- The frequency and severity of infusion-related reactions were similar whether TECENTRIQ was given as a single agent or in combination with other antineoplastic drugs in NSCLC and SCLC
- Monitor patients for signs and symptoms of infusion-related reactions. Interrupt or slow the rate of infusion in patients with Grade 1 or 2 infusion-related reactions. Permanently discontinue TECENTRIQ in patients with Grade 3 or 4 infusion-related reactions

Embryo-Fetal Toxicity

- Based on its mechanism of action, TECENTRIQ can cause fetal harm when administered to a pregnant woman. Verify pregnancy status of females of reproductive potential prior to initiating TECENTRIQ. Advise females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with TECENTRIQ and for at least 5 months after the last dose

Nursing Mothers/Fertility

- Because of the potential for serious adverse reactions in breastfed infants from TECENTRIQ, advise female patients not to breastfeed while taking TECENTRIQ and for at least 5 months after the last dose
- Based on animal studies, TECENTRIQ may impair fertility in females of reproductive potential while receiving treatment

Most Common Adverse Reactions

The most common adverse reactions (rate ≥20%) in patients who received TECENTRIQ alone were fatigue/asthenia (48%), decreased appetite (25%), nausea (24%), cough (22%), and dyspnea (22%).

The most common adverse reactions (rate ≥20%) in patients who received TECENTRIQ in combination with other antineoplastic drugs for NSCLC and SCLC were fatigue/asthenia (49%), nausea (38%), alopecia (35%), constipation (29%), diarrhea (28%), and decreased appetite (27%).

The most common adverse reactions (rate ≥20%) in patients who received TECENTRIQ in combination with bevacizumab for HCC were hypertension (30%), fatigue/asthenia (26%), and proteinuria (20%).

You may report side effects to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Genentech at 1-888-835-2555.

Please see accompanying full Prescribing Information for additional Important Safety Information.

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Advice for patients

- Contact their healthcare provider right away if they experience any symptoms, including those listed in this brochure, or if those symptoms worsen
- Seeking medical treatment right away may help keep these problems from becoming more serious

For more information on HCC:

Visit **TECENTRIQ-HCP.com/uHCC**

For more information on NSCLC:

Visit **TECENTRIQ-HCP.com/mNSCLC**

For more information on ES-SCLC:

Visit **TECENTRIQ-HCP.com/esSCLC**

- This information should not be a substitute for the treating healthcare provider's medical judgment and should be individualized for each patient
- These are not all the possible side effects of TECENTRIQ. Please see the full Prescribing Information for additional Important Safety Information
- Side effects may be reported to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch or to Genentech at 1-888-835-2555

Please see accompanying full Prescribing Information and additional Important Safety Information throughout this brochure.

References: 1. TECENTRIQ Prescribing Information. Genentech, Inc. **2.** Avastin (bevacizumab) Prescribing Information. Genentech, Inc. **3.** US Department of Health and Human Services. National Institutes of Health. National Cancer Institute. Common Terminology Criteria for Adverse Events (CTCAE), version 4.0. Published May 28, 2009.

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