HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use MOUNJARO safely and effectively. See full prescribing information for MOUNJARO.

MOUNJARO® (tirzepatide) Injection, for subcutaneous use
Initial U.S. Approval: 2022

WARNING: RISK OF THYROID C-CELL TUMORS

See full prescribing information for complete boxed warning.

- **Tirzepatide causes thyroid C-cell tumors in rats. It is unknown whether MOUNJARO causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans as the human relevance of tirzepatide-induced rodent thyroid C-cell tumors has not been determined (5.1, 13.1).**
- **MOUNJARO is contraindicated in patients with a personal or family history of MTC or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). Counsel patients regarding the potential risk of MTC and symptoms of thyroid tumors (4, 5.1).**

---------- RECENT MAJOR CHANGES ----------

Contraindications (4)	04/2023
Warnings and Precautions	
Hypersensitivity Reactions (5.4)	04/2023

---------- INDICATIONS AND USAGE ----------

MOUNJARO® is a glucose-dependent insulinotropic polypeptide (GIP) receptor and glucagon-like peptide-1 (GLP-1) receptor agonist indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. (1)

Limitations of Use:

- Has not been studied in patients with a history of pancreatitis (1, 5.2)
- Is not indicated for use in patients with type 1 diabetes mellitus (1)

----------DOSAGE AND ADMINISTRATION----------

- The recommended starting dosage is 2.5 mg injected subcutaneously once weekly (2.1)
- After 4 weeks, increase to 5 mg injected subcutaneously once weekly (2.1)
- If additional glycemic control is needed, increase the dosage in 2.5 mg increments after at least 4 weeks on the current dose.
- The maximum dosage is 15 mg subcutaneously once weekly (2.1).
- Administer once weekly at any time of day, with or without meals. (2.2)
- Inject subcutaneously in the abdomen, thigh, or upper arm. (2.2)
- Rotate injection sites with each dose.

----------DOSAGE FORMS AND STRENGTHS----------

Injection: 2.5 mg, 5 mg, 7.5 mg, 10 mg, 12.5 mg, or 15 mg per 0.5 mL in single-dose pen or single-dose vial (3)

---------- CONTRAINDICATIONS ----------

- Personal or family history of medullary thyroid carcinoma or in patients with Multiple Endocrine Neoplasia syndrome type 2 (4, 5.1)
- Known serious hypersensitivity to tirzepatide or any of the excipients in MOUNJARO (4, 5.4)

----------WARNINGS AND PRECAUTIONS----------

- *Pancreatitis:* Has been reported in clinical trials. Discontinue promptly if pancreatitis is suspected. (5.2)
- *Hypoglycemia with Concomitant Use of Insulin Secretagogues or Insulin:* Concomitant use with an insulin secretagogue or insulin may increase the risk of hypoglycemia, including severe hypoglycemia. Reducing dose of insulin secretagogue or insulin may be necessary. (5.3)
- *Hypersensitivity Reactions:* Serious hypersensitivity reactions (e.g., anaphylaxis and angioedema) have been reported. Discontinue MOUNJARO if suspected and promptly seek medical advice. (5.4)
- *Acute Kidney Injury:* Monitor renal function in patients with renal impairment reporting severe adverse gastrointestinal reactions. (5.5)
- *Severe Gastrointestinal Disease:* Use may be associated with gastrointestinal adverse reactions, sometimes severe. Has not been studied in patients with severe gastrointestinal disease and is not recommended in these patients. (5.6)
- *Diabetic Retinopathy Complications in Patients with a History of Diabetic Retinopathy:* Has not been studied in patients with non-proliferative diabetic retinopathy requiring acute therapy, proliferative diabetic retinopathy, or diabetic macular edema. Monitor patients with a history of diabetic retinopathy for progression. (5.7)
- *Acute Gallbladder Disease:* Has occurred in clinical trials. If cholelithiasis is suspected, gallbladder studies and clinical follow-up are indicated. (5.8)

----------ADVERSE REACTIONS----------

The most common adverse reactions, reported in ≥5% of patients treated with MOUNJARO are: nausea, diarrhea, decreased appetite, vomiting, constipation, dyspepsia, and abdominal pain. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Eli Lilly and Company at 1-800-LillyRx (1-800-545-5979) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

---------- DRUG INTERACTIONS ----------

MOUNJARO delays gastric emptying and has the potential to impact the absorption of concomitantly administered oral medications. (7.2)

----------USE IN SPECIFIC POPULATIONS----------

- *Pregnancy:* Based on animal study, may cause fetal harm. (8.1)
- *Females of Reproductive Potential:* Advise females using oral contraceptives to switch to a non-oral contraceptive method, or add a barrier method of contraception for 4 weeks after initiation and for 4 weeks after each dose escalation. (7.2, 8.3, 12.3)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved Medication Guide.

Revised: 07/2023

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescr bing information are not listed.

FULL PRESCRIBING INFORMATION

WARNING: RISK OF THYROID C-CELL TUMORS

- **In both male and female rats, tirzepatide causes dose-dependent and treatment-duration-dependent thyroid C-cell tumors at clinically relevant exposures. It is unknown whether MOUNJARO causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans as human relevance of tirzepatide-induced rodent thyroid C-cell tumors has not been determined *[see Warnings and Precautions (5.1) and Nonclinical Toxicology (13.1)]*.**
- **MOUNJARO is contraindicated in patients with a personal or family history of MTC or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2) *[see Contraindications (4)]*. Counsel patients regarding the potential risk for MTC with the use of MOUNJARO and inform them of symptoms of thyroid tumors (e.g., a mass in the neck, dysphagia, dyspnea, persistent hoarseness). Routine monitoring of serum calcitonin or using thyroid ultrasound is of uncertain value for early detection of MTC in patients treated with MOUNJARO *[see Contraindications (4) and Warnings and Precautions (5.1)]*.**

1 INDICATIONS AND USAGE

MOUNJARO® is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use

- MOUNJARO has not been studied in patients with a history of pancreatitis *[see Warnings and Precautions (5.2)]*.
- MOUNJARO is not indicated for use in patients with type 1 diabetes mellitus.

2 DOSAGE AND ADMINISTRATION

2.1 Dosage

- The recommended starting dosage of MOUNJARO is 2.5 mg injected subcutaneously once weekly. The 2.5 mg dosage is for treatment initiation and is not intended for glycemic control.
- After 4 weeks, increase the dosage to 5 mg injected subcutaneously once weekly.
- If additional glycemic control is needed, increase the dosage in 2.5 mg increments after at least 4 weeks on the current dose.
- The maximum dosage of MOUNJARO is 15 mg injected subcutaneously once weekly.
- If a dose is missed, instruct patients to administer MOUNJARO as soon as possible within 4 days (96 hours) after the missed dose. If more than 4 days have passed, skip the missed dose and administer the next dose on the regularly scheduled day. In each case, patients can then resume their regular once weekly dosing schedule.

- The day of weekly administration can be changed, if necessary, as long as the time between the two doses is at least 3 days (72 hours).

2.2 Important Administration Instructions

- Prior to initiation, train patients and caregivers on proper injection technique *[see Instructions for Use]*.
- Instruct patients using the single-dose vial to use a syringe appropriate for dose administration (e.g., a 1 mL syringe capable of measuring a 0.5 mL dose).
- Administer MOUNJARO once weekly, any time of day, with or without meals.
- Inject MOUNJARO subcutaneously in the abdomen, thigh, or upper arm.
- Rotate injection sites with each dose.
- Inspect MOUNJARO visually before use. It should appear clear and colorless to slightly yellow. Do not use MOUNJARO if particulate matter or discoloration is seen.
- When using MOUNJARO with insulin, administer as separate injections and never mix. It is acceptable to inject MOUNJARO and insulin in the same body region, but the injections should not be adjacent to each other.

3 DOSAGE FORMS AND STRENGTHS

Injection: Clear, colorless to slightly yellow solution in pre-filled single-dose pens or single-dose vials, each available in the following strengths:

- 2.5 mg/0.5 mL
- 5 mg/0.5 mL
- 7.5 mg/0.5 mL
- 10 mg/0.5 mL
- 12.5 mg/0.5 mL
- 15 mg/0.5 mL

4 CONTRAINDICATIONS

MOUNJARO is contraindicated in patients with:

- A personal or family history of medullary thyroid carcinoma (MTC) or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2) *[see Warnings and Precautions (5.1)]*.
- Known serious hypersensitivity to tirzepatide or any of the excipients in MOUNJARO. Serious hypersensitivity reactions, including anaphylaxis and angioedema, have been reported with MOUNJARO *[see Warnings and Precautions (5.4)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Risk of Thyroid C-Cell Tumors

In both sexes of rats, tirzepatide caused a dose-dependent and treatment-duration-dependent increase in the incidence of thyroid C-cell tumors (adenomas and carcinomas) in a 2-year study at clinically relevant plasma exposures *[see Nonclinical Toxicology (13.1)]*. It is unknown whether MOUNJARO causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans as human relevance of tirzepatide-induced rodent thyroid C-cell tumors has not been determined.

MOUNJARO is contraindicated in patients with a personal or family history of MTC or in patients with MEN 2. Counsel patients regarding the potential risk for MTC with the use of MOUNJARO and inform them of symptoms of thyroid tumors (e.g., a mass in the neck, dysphagia, dyspnea, persistent hoarseness).

Routine monitoring of serum calcitonin or using thyroid ultrasound is of uncertain value for early detection of MTC in patients treated with MOUNJARO. Such monitoring may increase the risk of unnecessary procedures, due to the low test specificity for serum calcitonin and a high background incidence of thyroid disease. Significantly elevated serum calcitonin values may indicate MTC and patients with MTC usually have calcitonin values >50 ng/L. If serum calcitonin is measured and found to be elevated, the patient should be further evaluated. Patients with thyroid nodules noted on physical examination or neck imaging should also be further evaluated.

5.2 Pancreatitis

Acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis, has been observed in patients treated with GLP-1 receptor agonists.

In clinical studies, 14 events of acute pancreatitis were confirmed by adjudication in 13 MOUNJARO-treated patients (0.23 patients per 100 years of exposure) versus 3 events in 3 comparator-treated patients (0.11 patients per 100 years of exposure). MOUNJARO has not been studied in patients with a prior history of pancreatitis. It is unknown if patients with a history of pancreatitis are at higher risk for development of pancreatitis on MOUNJARO.

After initiation of MOUNJARO, observe patients carefully for signs and symptoms of pancreatitis (including persistent severe abdominal pain, sometimes radiating to the back and which may or may not be accompanied by vomiting). If pancreatitis is suspected, discontinue MOUNJARO and initiate appropriate management.

5.3 Hypoglycemia with Concomitant Use of Insulin Secretagogues or Insulin

Patients receiving MOUNJARO in combination with an insulin secretagogue (e.g., sulfonylurea) or insulin may have an increased risk of hypoglycemia, including severe hypoglycemia *[see Adverse Reactions (6.1), Drug Interactions (7.1)]*.

The risk of hypoglycemia may be lowered by a reduction in the dose of sulfonylurea (or other concomitantly administered insulin secretagogue) or insulin. Inform patients using these concomitant medications of the risk of hypoglycemia and educate them on the signs and symptoms of hypoglycemia.

5.4 Hypersensitivity Reactions

Serious hypersensitivity reactions (e.g., anaphylaxis, angioedema) have been reported in patients treated with MOUNJARO. If hypersensitivity reactions occur, discontinue use of MOUNJARO; treat promptly per standard of care, and monitor until signs and symptoms resolve. Do not use in patients with a previous serious hypersensitivity reaction to tirzepatide or any of the excipients in MOUNJARO *[see Contraindications (4), Adverse Reactions (6.2)]*.

Anaphylaxis and angioedema have been reported with GLP-1 receptor agonists. Use caution in patients with a history of angioedema or anaphylaxis with a GLP-1 receptor agonist because it is unknown whether such patients will be predisposed to these reactions with MOUNJARO.

5.5 Acute Kidney Injury

MOUNJARO has been associated with gastrointestinal adverse reactions, which include nausea, vomiting, and diarrhea *[see Adverse Reactions (6.1)]*. These events may lead to dehydration, which if severe could cause acute kidney injury.

In patients treated with GLP-1 receptor agonists, there have been postmarketing reports of acute kidney injury and worsening of chronic renal failure, which may sometimes require hemodialysis. Some of these events have been reported in patients without known underlying renal disease. A majority of the reported events occurred in patients who had experienced nausea, vomiting, diarrhea, or dehydration. Monitor renal function when initiating or escalating doses of MOUNJARO in patients with renal impairment reporting severe gastrointestinal adverse reactions.

5.6 Severe Gastrointestinal Disease

Use of MOUNJARO has been associated with gastrointestinal adverse reactions, sometimes severe *[see Adverse Reactions 6.1]*. MOUNJARO has not been studied in patients with severe gastrointestinal disease, including severe gastroparesis, and is therefore not recommended in these patients.

5.7 Diabetic Retinopathy Complications in Patients with a History of Diabetic Retinopathy

Rapid improvement in glucose control has been associated with a temporary worsening of diabetic retinopathy. MOUNJARO has not been studied in patients with non-proliferative diabetic retinopathy requiring acute therapy, proliferative diabetic retinopathy, or diabetic macular edema. Patients with a history of diabetic retinopathy should be monitored for progression of diabetic retinopathy.

5.8 Acute Gallbladder Disease

Acute events of gallbladder disease such as cholelithiasis or cholecystitis have been reported in GLP-1 receptor agonist trials and postmarketing.

In MOUNJARO placebo-controlled clinical trials, acute gallbladder disease (cholelithiasis, biliary colic, and cholecystectomy) was reported by 0.6% of MOUNJARO-treated patients and 0% of placebo-treated patients. If cholelithiasis is suspected, gallbladder diagnostic studies and appropriate clinical follow-up are indicated.

6 ADVERSE REACTIONS

The following serious adverse reactions are described below or elsewhere in the prescribing information:

- Risk of Thyroid C-cell Tumors *[see Warnings and Precautions (5.1)]*
- Pancreatitis *[see Warnings and Precautions (5.2)]*
- Hypoglycemia with Concomitant Use of Insulin Secretagogues or Insulin *[see Warnings and Precautions (5.3)]*
- Hypersensitivity Reactions *[see Warnings and Precautions (5.4)]*
- Acute Kidney Injury *[see Warnings and Precautions (5.5)]*
- Severe Gastrointestinal Disease *[see Warnings and Precautions (5.6)]*
- Diabetic Retinopathy Complications *[see Warnings and Precautions (5.7)]*
- Acute Gallbladder Disease *[see Warnings and Precautions (5.8)]*

6.1 Clinical Trials Experience

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

Pool of Two Placebo-Controlled Clinical Trials

The data in Table 1 are derived from 2 placebo-controlled trials [1 monotherapy trial (SURPASS-1) and 1 trial in combination with basal insulin with or without metformin (SURPASS-5)] in adult patients with type 2 diabetes mellitus *[see Clinical Studies (14.2, 14.4)]*. These data reflect exposure of 718 patients to MOUNJARO and a mean duration of exposure to MOUNJARO of 36.6 weeks. The mean age of patients was 58 years, 4% were 75 years or older and 54% were male. The population was 57% White, 27% Asian, 13% American Indian or Alaska Native, and 3% Black or African American; 25% identified as Hispanic or Latino ethnicity. At baseline, patients had type 2 diabetes mellitus for an average of 9.1 years with a mean HbA1c of 8.1%. As assessed by baseline fundoscopic examination, 13% of the population had retinopathy. At baseline, eGFR was ≥90 mL/min/1.73 m^2 in 53%, 60 to 90 mL/min/1.73 m^2 in 39%, 45 to 60 mL/min/1.73 m^2 in 7%, and 30 to 45 mL/min/1.73 m^2 in 1% of patients.

Pool of Seven Controlled Clinical Trials

Adverse reactions were also evaluated in a larger pool of adult patients with type 2 diabetes mellitus participating in seven controlled clinical trials which included two placebo-controlled trials (SURPASS-1 and -5), three trials of MOUNJARO in combination with metformin, sulfonylureas, and/or SGLT2 Inhibitors (SURPASS-2, -3, -4) *[see Clinical Studies (14.3)]* and two additional trials conducted in Japan. In this pool, a total of 5119 adult patients with type 2 diabetes mellitus were treated with MOUNJARO for a mean duration of 48.1 weeks. The mean age of patients was 58 years, 4% were 75 years or older and 58% were male. The population was 65% White, 24% Asian, 7% American Indian or Alaska Native, and 3% Black or African American; 38% identified as Hispanic or Latino ethnicity. At baseline, patients had type 2 diabetes mellitus for an average of 9.1 years with a mean HbA1c of 8.3%. As assessed by baseline fundoscopic examination, 15% of the population had retinopathy. At baseline, eGFR was ≥90 mL/min/1.73 m^2 in 52%, 60 to 90 mL/min/1.73 m^2 in 40%, 45 to 60 mL/min/1.73 m^2 in 6%, and 30 to 45 mL/min/1.73 m^2 in 1% of patients.

Common Adverse Reactions

Table 1 shows common adverse reactions, not including hypoglycemia, associated with the use of MOUNJARO in the pool of placebo-controlled trials. These adverse reactions occurred more commonly on MOUNJARO than on placebo and occurred in at least 5% of patients treated with MOUNJARO.

Table 1: Adverse Reactions in Pool of Placebo-Controlled Trials Reported in ≥5% of MOUNJARO-treated Adult Patients with Type 2 Diabetes Mellitus

Adverse Reaction	Placebo (N=235) %	MOUNJARO 5 mg (N=237) %	MOUNJARO 10 mg (N=240) %	MOUNJARO 15 mg (N=241) %
Nausea	4	12	15	18
Diarrhea	9	12	13	17
Decreased Appetite	1	5	10	11

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