

WITH A PLUS  
ALL IN 1 PILL



**Generic Name:** Empagliflozin, Empagliflozin + Metformin **Dosage Form:** Film Coated tablets • **Empagliflozin** 10, 25 mg; **Empagliflozin/Metformin** (5 mg/500 mg, 5 mg/1000 mg, 12.5 mg/500 mg, and 12.5 mg/1000 mg). **Indications and Dosage:** Adult. **Empagliflozin:** Type II Diabetes: Initial: 10 mg once daily; may increase to 25 mg once daily after 4 to 12 weeks if needed to achieve glycemic goals. Atherosclerotic cardiovascular disease: 10 or 25 mg once daily. Diabetic kidney disease (off-label use): 10 mg once daily in patients with urinary albumin excretion >300 mg/day. Heart failure (off-label use): 10 mg once daily.

Heart failure with reduced ejection fraction (adjunct) (off-label use): 10 mg once daily (Packer 2020). **Empagliflozin/Metformin:** Diabetes mellitus, type 2, treatment: Oral: Initial: Individualize initial dose based on patient's current antidiabetic regimen. May gradually increase dose based on effectiveness and tolerability. **Patients on Metformin:** Empagliflozin 10 mg/day plus similar total daily dose of metformin, administered in 2 divided doses. **Patients on Empagliflozin:** Metformin 1 g/day plus similar total daily dose of empagliflozin, administered in 2 divided doses. **Maximum:** Empagliflozin 25 mg/metformin 2 g/day, administered in 2 divided doses. **Administration:** **Empagliflozin:** Administer once daily in the morning, with or without food. **Empagliflozin/Metformin:** Administer tablets twice daily with meals. **Adverse Effects: Empagliflozin:** >10%: Genitourinary: Urinary tract infection; females: 18%; males: 4%. 1% to 10%: Endocrine & metabolic: Dyslipidemia, increased thirst. Gastrointestinal: Nausea. Genitourinary: Increased urine output. Hematologic & oncologic: Increased hematocrit. Infection: Genitourinary fungal infection. **Metformin:** >10%: Gastrointestinal: Diarrhea: 10%, flatulence, nausea and vomiting. 1% to 10%: Cardiovascular: Chest discomfort, flushing, palpitations. Dermatologic: Diaphoresis, nail disease. Endocrine & Metabolic: Cyanocobalamin deficiency, hypoglycemia. Gastrointestinal: Abdominal distention, abdominal distress, abdominal pain, abnormal stools, dyspepsia, heartburn. Nervous system: Chills, dizziness, headache. Neuromuscular & skeletal: Asthenia, myalgia. Respiratory: Dyspnea, flu-like symptoms, upper respiratory tract infection. **Contraindications: Empagliflozin:** History of serious hypersensitivity to Empagliflozin or any component of the formulation; severe renal impairment (eGFR <30 mL/minute/1.73 m<sup>2</sup>), end-stage renal disease (ESRD), or dialysis. **Metformin:** Hypersensitivity to Metformin or any component of the formulation; severe renal dysfunction (eGFR <30 mL/minute/1.73 m<sup>2</sup>); acute or chronic metabolic acidosis with or without coma (including diabetic ketoacidosis). **Warnings/Precautions: Empagliflozin:** Bone fractures, Genital mycotic infections, Hypersensitivity, Hypotension, Ketoacidosis, Lower limb amputation, Necrotizing fasciitis, Acute kidney injury, Urinary tract infection, Bariatric surgery, Dehydration, Euglycemic diabetic ketoacidosis, Renal impairment, Elderly people, Hospitalized patients: Use of SGLT2 inhibitors is not routinely recommended for hospitalized patients, Surgical procedures. **Metformin:** Lactic acidosis, Vitamin B12 concentrations, Bariatric surgery, Heart failure, Hepatic impairment, Renal impairment, Stress-related states, Elderly patients, Ethanol use, Hospitalized patients, Iodinated contrast, Surgical procedure. **Pregnancy: Empagliflozin:** Use is not recommended during the second and third trimesters of pregnancy. **Metformin:** Human data suggests low risk. **Lactation: Empagliflozin:** Not recommended. **Metformin:** Compatible. **Pharmacokinetics and pharmacodynamics: Empagliflozin: Duration:** Following discontinuation, urinary glucose excretion returns to baseline within ~3 days for the 10 mg and 25 mg doses. **Distribution:** Vd: 73.8 L. **Protein binding:** 86.2%. **Metabolism:** Primarily through glucuronidation by UGT2B7, UGT1A3, UGT1A8, and UGT1A9 to minor metabolites. **Half-life Elimination:** 12.4 hours. **Time to Peak:** 1.5 hours. **Excretion:** Urine (54.4%; 50% as unchanged drug); feces (41.2%; majority as unchanged drug). **Metformin:** Onset of action: Within days; maximum effects up to 2 weeks. **Distribution:** Vd: 654 ± 358 L; partitions into erythrocytes; concentrates in liver, kidney, and GI tract. **Protein binding:** Negligible. **Metabolism:** Not metabolized by the liver. **Bioavailability:** Absolute: Fasting: 50% to 60%. **Half-life elimination: Plasma:** 4 to 9 hours; Blood ~17.6 hours. **Time to peak, serum: Immediate release:** 2 to 3 hours. **Excretion:** Urine (90% as unchanged drug; active secretion).

**Abbreviations:**  
HF: Heart Failure, MI: Myocardial Infarction, CV: Cardiovascular, HbA1c: Hemoglobin A1c, BID: Bis in die (twice a day), QD: Quaque die (once a day)

**References:**  
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No.58, 8<sup>th</sup> St., Kooye Nasr (Gisha St.), Tehran, IR Iran  
Postal Code: 1446863914, Tel: +98(021)41637000  
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# Treating type 2 Diabetes with all your Heart

## Empagliflozin:

- Low risk of hypoglycemia
- Well-tolerated side effect profile<sup>(3,4)</sup>
- Weight reduction<sup>(1)</sup>
- Consistent 12-15% increase in life expectancy<sup>(5)</sup>
- Lowering systolic blood pressure<sup>(2)</sup>
- No risk of bone fracture<sup>(6)</sup>

### Cardiovascular Benefits<sup>(3)</sup>:

**No**

Increase in risk of MI and Stroke.

**32%**

Less deaths from any cause.

**38%**

Risk reduction in death from cardiovascular causes.

**35%**

Lower risk of hospitalization from HF.

### Renal Benefits<sup>(4)</sup>:

**39%**

Risk reduction for new or worsening kidney disease.

**44%**

Reduction in the chance of doubling serum creatinine.

**55%**

Lower risk of renal replacement compared to placebo.

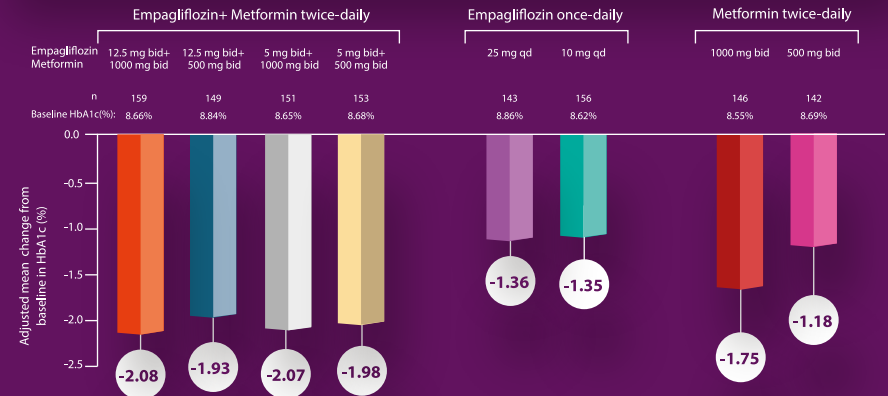
**No**

Increase in the Risk of Albuminuria.

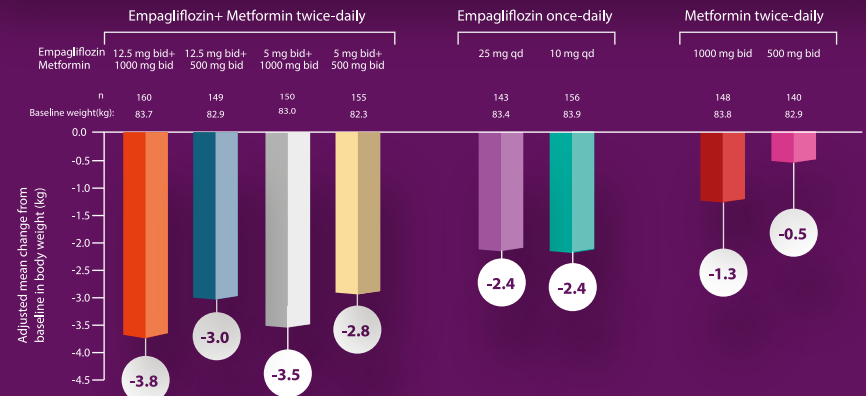


## THE POWER OF TWO ANTIDIABETICS IN ONE PILL

• About 2% reduction in HbA1c, more than Empagliflozin and Metformin alone<sup>(7)</sup>.



• 2-3% weight loss, more than Empagliflozin and Metformin alone<sup>(7)</sup>.



• Need for lower doses of insulin or insulin secretagogues (e.g. sulfonylureas) when added.

• Higher patients' compliance.