

### Synjardy<sup>®</sup> XR (empagliflozin/metformin extended-release) – New Formulation Approval

- On December 12, 2016, [Eli Lilly](#) and [Boehringer-Ingelheim](#) announced the FDA approval of [Synjardy XR \(empagliflozin/metformin extended-release\)](#), as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (T2DM) when treatment with both empagliflozin and metformin is appropriate.
  - Synjardy XR is not recommended for patients with type 1 diabetes or for the treatment of diabetic ketoacidosis.
- [Synjardy<sup>®</sup> \(empagliflozin/metformin\)](#) was approved in August 2015 and shares the same indication as the XR formulation.
- There have been no clinical efficacy studies conducted with Synjardy XR; however, bioequivalence of Synjardy XR to empagliflozin and metformin extended-release coadministered as individual tablets was demonstrated in healthy subjects.
  - Multiple clinical trials examining the co-administration of empagliflozin and metformin, alone or in combination with a sulfonylurea in adults with T2DM, produced clinically and statistically significant improvements in HbA1c vs. placebo.
- Similar to metformin and metformin-containing products, Synjardy XR carries a boxed warning for lactic acidosis.
- Contraindications for Synjardy XR include moderate to severe renal impairment (eGFR less than 45 mL/min/1.73 m<sup>2</sup>), end stage renal disease, or dialysis; acute or chronic metabolic acidosis, including diabetic ketoacidosis; diabetic ketoacidosis should be treated with insulin; and history of serious hypersensitivity reaction to empagliflozin or metformin hydrochloride.
- Other warnings and precautions for Synjardy XR include hypotension, ketoacidosis, acute kidney injury and impairment in renal function, urosepsis and pyelonephritis, hypoglycemia with concomitant use with insulin and insulin secretagogues, genital mycotic infections, vitamin B12 levels, increased low-density lipoprotein cholesterol (LDL-C), and macrovascular outcomes.
- The most common adverse reactions ( $\geq 5\%$ ) with empagliflozin use were urinary tract infection and female genital mycotic infections.
- The most common adverse reactions ( $> 5\%$ ) with metformin use were diarrhea, nausea/vomiting, flatulence, abdominal discomfort, indigestion, asthenia, and headache.
- The recommended dose of Synjardy XR is individualized based on the patient's current regimen and is taken orally once daily with a meal in the morning.
  - The maximum recommended daily dose of Synjardy XR is 2000 mg of metformin and 25 mg of empagliflozin.
  - Synjardy XR should not be split, crushed, dissolved or chewed before swallowing.

- Eli Lilly and Boehringer Ingelheim plan to launch Synjardy XR as 5 mg/1000 mg, 10 mg/1000 mg, 12.5 mg/1000 mg, and 25 mg/1000 mg extended-release tablets in the second quarter of 2017.



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