Metformin ER (generics for Fortamet® & Glumetza®)

Indications:

Glucophage® XR, Fortamet®, and Glumetza® are "indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus."[1, 2, 3]

Dosage Form/Strength:

- Fortamet Extended Release Tablet: 500mg, 1000mg
- Glucophage XR Extended Release Tablet: 500mg, 750mg
- Glumetza Extended Release Tablet: 500mg, 1000mg

Pharmacokinetics:

Glucophage XR: [1]

- Peak plasma concentration is achieved at an average of approximately 7 hours (range is 4—8 hours) post-dose.
- The peak plasma level is approximately 80% that of a comparative dose of metformin immediate-release, but the AUC (total drug exposure over time) is similar.
- When Glucophage XR is given with food, the extent of metformin absorption was increased by approximately 50%.

Fortamet: [2]

- Peak plasma concentration is achieved at an average of approximately 6 hours (range is 3—10 hours).
- Peak plasma concentrations are higher with Fortamet compared to immediate-release metformin, but the bioavailability of an equal total daily dose of Fortamet is similar to metformin immediate-release, measured by the AUC.
- When administered with food, the AUC is increased by approximately 60%; the peak plasma level is increased by 30%; and Tmax is prolonged (6.1 hours with food versus 4 hours in the fasting state).
- Following doses of 1000mg to 2500mg, the increase in metformin exposure was dose-proportional.

Glumetza: [3]

- Glumetza should be taken immediately after a meal to achieve maximal therapeutic benefit. When Glumetza is given with food, systemic exposure increased by 38%-73%, depending on the fat content of the meal, compared to the systemic exposure with a fasting dose.
- Peak plasma concentration of Glumetza which was dosed after a meal, occurs in approximately 7—8 hours.
- Compared to equivalent metformin immediate-release doses, use of Glumetza results in equivalent systemic drug exposure, and a 35% higher peak plasma concentration.
- Following doses of Glumetza 500 mg to 2500mg, there was a less than dose-proportional growth in total drug exposure and peak plasma concentration.

Criteria for Approval:

Grandfathering for patients who are currently using brand or generic Fortamet or Glumetza will not be permitted.

- Patient has tried metformin ER (generic Glucophage XR); **AND,**
- The patient has a documented allergy to an inert ingredient in metformin ER (generic Glucophage XR) which is not an ingredient present in Fortamet or Glumetza (or the respective generics); **AND,**
- A FDA MedWatch report has been completed and submitted to report the adverse event with metformin ER (generic Glucophage XR).

Criteria for Reauthorization Approval:

- Patient meets all of the criteria for the initial authorization; **AND,**
- There is documented evidence of a positive clinical response to metformin ER (generic for Fortamet or Glumetza) therapy; **AND,**
- The patient tolerates the requested generic for Fortamet or Glumetza better than the patient had tolerated the generic Glucophage XR.

Criteria for Denial:

- The patient has not tried metformin ER (generic for Glucophage XR); **OR,**
- The patient does not have a documented allergy to an inert ingredient in metformin ER (generic Glucophage XR) which is not an ingredient present in Fortamet or Glumetza (or the respective generics); **OR,**
- A FDA MedWatch report has not been completed and submitted to report the adverse event with metformin ER (generic Glucophage XR).

Criteria for Reauthorization Denial:

- Patient does not meet all of the criteria for the initial authorization; **OR,**
- There is no documented evidence of a positive clinical response to metformin ER (generic for Fortamet or Glumetza) therapy; **OR,**
- There is no documentation that the patient tolerates Fortamet or Glumetza (or their generic) better than the patient had tolerated the generic Glucophage XR.

Length of Authorization – Initial coverage:

- May be authorized for up to 6 months

Length of Authorization – Reauthorization:

- May be reauthorized for up to 1 year

Quantity Limit:

- Fortamet: Quantity of 2 tablets per day.
- Glumetza: Quantity of 2 tablets per day.

Mechanism of Action:

Metformin is a biguanide antihyperglycemic medication which "improves glucose tolerance in patients with type 2 diabetes, lowering both basal and postprandial plasma glucose." [1, 2, 3] "Metformin decreases hepatic glucose production, decreases intestinal absorption of glucose, and improves insulin sensitivity by increasing peripheral glucose uptake and utilization. " [1, 2, 3] Except in certain situations, metformin will not cause hypoglycemia in patients with a diagnosis of type 2 diabetes, and use of metformin does not result in hyperinsulinemia. "With metformin therapy, insulin secretion remains unchanged while fasting insulin levels and day-long plasma insulin response may actually decrease." [1, 2, 3]

References / Footnotes:

[1] Glucophage XR® package insert:Btistol-Myers Squibb Company. Princeton, NJ. June 2015. http://packageinserts.bms.com/pi/pi_glucophage_xr.pdf. Accessed 4/7/2016.

[2]Fortamet® package insert: Shionogi, Inc. Florham Park, NJ. April 2012. http://www.shionogi.com/pdf/pi/fortamet.pdf. Accessed 4/7/16.

[3] Glumetza® package insert: Salix Pharmactuticals. Raleigh, NC. September 2014. https://shared.salix.com/shared/pi/glumetza-pi.pdf?id=8251081. Accessed 4/7/2016.