Clinical Policy: Metformin ER (Glumetza)
Reference Number: ERX.NPA.43
Effective Date: 12.01.15
Last Review Date: 05.18

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Metformin extended-release [ER] (Glumetza®) is an oral biguanide antidiabetic agent.

FDA Approved Indication(s)
Glumetza is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (DM).

Limitation(s) of use: Glumetza should not be used in patients with type 1 DM or for the treatment of diabetic ketoacidosis, as it would not be effective in these settings.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Glumetza is medically necessary when the following criteria are met:

I. Initial Approval Criteria
   A. Type 2 Diabetes Mellitus (must meet all):
      1. Diagnosis of type 2 DM;
      2. Member has experienced clinically significant adverse effects to immediate-release metformin or has contraindication(s) to its excipients;
      3. Member has experienced clinically significant adverse effects to extended-release metformin tablets (Glucophage® XR, Fortamet®) or has contraindication(s) to its excipients;
      4. If request is for brand Glumetza, member has experienced clinically significant adverse effects to generic Glumetza or has contraindication(s) to its excipients;
      5. Dose does not exceed 2000 mg/day.
   
   Approval duration: 12 months

   B. Other diagnoses/indications
      1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy
   A. Type 2 Diabetes Mellitus (must meet all):
      1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
      2. Member is responding positively to therapy;
      3. If request is for a dose increase, new dose does not exceed 2000 mg/day.
   
   Approval duration: 12 months

   B. Other diagnoses/indications (must meet 1 or 2):
      1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   
   Approval duration: Duration of request or 12 months (whichever is less); or

      2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).
CLINICAL POLICY
Metformin ER

III. Diagnoses/Indications for which coverage is NOT authorized:
   A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient
documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or
evidence of coverage documents;
   B. Type 1 DM;
   C. Diabetic ketoacidosis.

IV. Appendices/General Information
   Appendix A: Abbreviation/Acronym Key
   DM: diabetes mellitus
   ER: extended-release
   FDA: Food and Drug Administration
   GPI: generic product identifier

   Appendix B: Therapeutic Alternatives
   This table provides a listing of preferred alternative therapy recommended in the approval criteria.
The drugs listed here may not be a formulary agent and may require prior authorization.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>metformin</td>
<td>500 mg PO twice daily or 850 mg PO once daily, given with meals. Dosage increases</td>
<td></td>
</tr>
<tr>
<td>(Glucophage®)</td>
<td>should be made in increments of 500 mg weekly or 850 mg every 2 weeks, up to 2000</td>
<td></td>
</tr>
<tr>
<td></td>
<td>mg/day PO, given in divided doses</td>
<td>2550 mg/day</td>
</tr>
<tr>
<td>metformin ER</td>
<td>Glucophage XR: 500 mg PO once daily with the evening meal; may increase daily</td>
<td></td>
</tr>
<tr>
<td>(Glucophage® XR,</td>
<td>dose by 500 mg/week as needed</td>
<td>Glucophage XR: 2000</td>
</tr>
<tr>
<td>Fortamet®)</td>
<td>Fortamet: 1000 mg PO once daily; may titrate in increments of no more than 500</td>
<td></td>
</tr>
<tr>
<td></td>
<td>mg/week</td>
<td>Fortamet: 2500 mg/day</td>
</tr>
</tbody>
</table>

   Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic
   (Brand name®) when the drug is available by both brand and generic.

   Appendix C: General Information
   • Generic Glucophage XR (GPI 27250050007520 or 27250050007530) and generic Fortamet (GPI 27250050007560 or 27250050007570) are identified with different GPI 14.
   • Glucophage XR uses dual hydrophilic polymer matrix systems, Fortamet uses single-composition osmotic technology, and Glumetza uses gastric retention technology.

V. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 2 DM</td>
<td>500 mg PO QD with the evening meal; may increase the dose in 500 mg increments</td>
<td></td>
</tr>
<tr>
<td></td>
<td>every 1-2 weeks as needed</td>
<td>2000 mg/day</td>
</tr>
</tbody>
</table>

VI. Product Availability
Extended-release tablets: 500 mg and 1000 mg

VII. References
1. Glumetza Prescribing Information. Bridgewater, NJ: Salix Pharmaceuticals; April 2017. Available at:
2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2017. Available at:

Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Policy created.</td>
<td>09.15</td>
</tr>
<tr>
<td>Updated to new template. Added background and references.</td>
<td>07.16</td>
</tr>
</tbody>
</table>
Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Description</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Converted to new template. For initial, added requirements related to 1) immediate release metformin and 2) contraindication related to severe renal impairment (excluding hypersensitivity) per PI; modified generalized FDA max dose to specific max dose of drug; On re-auth, added that member is responding positively to therapy; Section III-added indications (type 1 DM and diabetic ketoacidosis) for which coverage is not authorized per limitations of use/PI; updated references.</td>
<td>06.17</td>
<td>08.17</td>
</tr>
<tr>
<td>2Q 2018 annual review: Removed age limit and contraindication since other formulations of metformin are available freely on PDL without such restrictions. Added that members requesting brand Glumetza must have contraindication/intolerance to generic Glumetza. References reviewed and updated.</td>
<td>02.27.18</td>
<td>05.18</td>
</tr>
</tbody>
</table>

**Important Reminder**
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.

This policy is the property of Envolve Pharmacy Solutions. Unauthorized copying, use, and distribution of this Policy or any information contained herein is strictly prohibited. By accessing this policy, you agree to be bound by the foregoing terms and conditions, in addition to the Site Use Agreement for Health Plans associated with Envolve Pharmacy Solutions.

©2015 Envolve Pharmacy Solutions. All rights reserved. All materials are exclusively owned by Envolve Pharmacy Solutions and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Envolve Pharmacy Solutions. You may not alter or remove any trademark, copyright or other notice contained herein.