Comparison of GLP-1 Agonists

*Trulicity* (dulaglutide) is the latest glucagon-like peptide-1 (GLP-1) receptor agonist (incretin mimetic) approved for type 2 diabetes. The first GLP-1 agonist, exenatide (*Byetta*), marketed in 2005, required twice-daily dosing. Since then, newer agents with longer half-lives have been developed allowing for once-daily, and more recently, once-weekly dosing. While all GLP-1 receptor agonists reduce A1C and fasting blood glucose concentrations, none have evidence of improved macrovascular outcomes. All of the agents carry a warning about the risk of worsening renal function, the rare occurrence of pancreatitis, and a possible association with thyroid C-cell tumors in rodents. Although the exact role in therapy for the GLP-1 receptor agonists has not been clearly established, according to the American Diabetes Association, they should not be used as initial monotherapy. For most patients GLP-1 agonists should be reserved for those who require two or more diabetes medications to maintain a desired A1C. See our *PL Algorithm, Stepwise Approach to Selecting Treatments for Type 2 Diabetes* (ADA), for more information. Choice of GLP-1 agonist should be based on efficacy, tolerability, ease of use, and cost. The table below compares the GLP-1 receptor agonists currently available in the U.S.

**Abbreviations:** BID-twice daily; g-gauge; GI-gastrointestinal; SC-subcutaneously

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<thead>
<tr>
<th>Drug</th>
<th>Cost/montha</th>
<th>Dosing</th>
<th>Availability</th>
<th>A1C reductionb</th>
<th>Rate of Nauseac</th>
<th>Rate of Injection Site Reactions</th>
<th>Warfarin Drug Interaction</th>
<th>Use in Renal/Hepatic Impairment</th>
<th>Avg. Weight Lossb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albiglutide</td>
<td>~$330</td>
<td>30 mg SC once weekly, at any time of the day, with or without meals. Dose can be increased to 50 mg once weekly, if needed for A1C control.</td>
<td>30 mg and 50 mg single-dose pens with 29 g needle. Reconstitute 15 minutes (30 mg dose) or 30 minutes (50 mg dose) prior to injection.</td>
<td>~1%</td>
<td>11.1% (placebo-controlled trials, monotherapy or add-on therapy)</td>
<td>18% (including injection site hematoma, erythema, rash, and injection site hypersensitivity).</td>
<td>None</td>
<td>As renal function declines, GI reactions increased. Adverse GI reactions may worsen renal function, so use caution when initiating or escalating doses. Hepatic impairment is not expected to affect blood concentrations.</td>
<td>~1 kg</td>
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3120 W. March Lane, Stockton, CA 95219 ~ Phone: 209-472-2240 ~ Fax: 209-472-2249
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<tr>
<th>Drug Cost/month</th>
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<tr>
<td>Dulaglutide (Trulicity)</td>
<td>~$500</td>
<td>0.75 mg SC, with or without meals, once weekly. Dose can be increased to 1.5 mg once weekly, if needed for A1C control.</td>
<td>0.75 mg and 1.5 mg single-dose pen with 29 g needle and ready-to-use liquid. No mixing needed.</td>
<td>~1.5%</td>
<td>12.4% (0.75 mg) to 21.1% (1.5 mg) (placebo-controlled trials, monotherapy or add-on therapy)</td>
<td>0.5%</td>
<td>None</td>
<td>No dosage changes necessary in patients with renal impairment. Monitor renal function in those with significant GI adverse effects. Hepatic impairment is not expected to affect blood concentrations.</td>
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<tr>
<td>Exenatide (Byetta)</td>
<td>~$430</td>
<td>5 mcg SC BID; increase to 10 mcg BID after one month, if needed for better A1C control. Inject within 60 minutes prior to morning and evening meals (or before the two main meals of the day, 6 hours or more apart).</td>
<td>5 mcg/dose: 60 doses, 1.2 mL prefilled multidose pen 10 mcg/dose: 60 doses, 2.4 mL prefilled multidose pen. Pen needles not supplied with pen. No mixing needed.</td>
<td>~1%</td>
<td>8% (monotherapy) Up to 44% (add-on therapy with other agents)</td>
<td>12.7%</td>
<td>May increase INR in patients taking warfarin. Monitor INR.</td>
<td>Not recommended in severe renal impairment or end-stage renal disease. Use with caution in patients with renal transplantation or moderate renal impairment. Hepatic impairment is not expected to affect blood concentrations.</td>
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<tr>
<td>Exenatide extended-release (Bydureon) ~$440</td>
<td>2 mg SC once weekly at any time of day, with or without meals.</td>
<td>2 mg injectable suspension vial with prefilled diluent syringe, vial connector, and 23 g needle OR Single-dose dual chamber pen (one chamber with medication and one with diluent) with 23 g needle. Both the vial and the pen dosage forms must be reconstituted immediately prior to use.</td>
<td>~1.5%</td>
<td>11.3% (pooled rate of mono-therapy or as add-on to other agents)</td>
<td>17.1% (post-marketing reports of serious injection site reactions with or without SC nodules).</td>
<td>May increase INR in patients taking warfarin. Monitor INR.</td>
<td>Not recommended in severe renal impairment or end-stage renal disease. Use with caution in patients with renal transplantation or moderate renal impairment. Hepatic impairment is not expected to affect blood concentrations.</td>
<td>~2.5 kg</td>
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<td>Liraglutide (Victoza)</td>
<td>~$400 for 1.2 mg daily</td>
<td>0.6 mg SC once daily for one week (to reduce incidence of nausea, dose not effective for glycemic control), then increase to 1.2 mg once daily. Can increase to 1.8 mg once daily if needed for A1C control. Administer at any time of day, with or without meals.</td>
<td>0.6 mg, 1.2 mg, 1.8 mg prefilled, ready-to-use multidose pen. Pen needles not supplied with pen. No mixing needed.</td>
<td>~1.5%</td>
<td>28.4%</td>
<td>2% (injection site rash, erythema)</td>
<td>None</td>
<td>Use caution when initiating or escalating doses in patients with renal impairment. Use caution in patients with hepatic impairment.</td>
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<td>~$600 for 1.8 mg daily</td>
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Because clinical trials are conducted under widely varying conditions, rates of efficacy and adverse effects seen in the clinical trials of a medication cannot be directly compared to those of another medication and may not reflect the rates seen in clinical practice.

a. Wholesale acquisition cost (WAC).
b. A1C reduction and weight loss based on results of FDA-approval clinical trials. A1C reduction and weight loss are average values and will vary among patients.
c. Nausea is transient and usually dissipates within the first few weeks of therapy. Incidence of nausea is the rate reported in placebo-controlled trials used for FDA approval. The exception is for extended-release exenatide, whose rate of nausea was only reported as pooled data of monotherapy or as add-on to other agents.


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Project Leader in preparation of this PL Detail-Document: Neeta Bahal O’Mara, Pharm.D., BCPS, Drug Information Consultant

References