1. Dosage [*]

Adults
Incretin hormones such as glucagon-like peptide (GLP-1) are peptides released from gastrointestinal tract cells in response to food ingestion that stimulate glucose-dependent insulin release from the pancreas, decrease glucagon production, and slow gastric emptying. **Incretin mimetics also known as GLP-1 agonists, are FDA-approved as adjunct therapy to diet and exercise to improve glycemic control in adult type 2 diabetics.** **GLP-1 agonists** are not recommended for use as first-line therapy in type 2 diabetes mellitus due to development of malignant thyroid C-cell tumors in rats; these compounds should be used in diabetic patients only when the therapeutic benefits exceed treatment risks.

**GLP-1 agonists** should not be administered to patients:
- with type 1 diabetes
- experiencing diabetic ketoacidosis
- receiving prandial insulin therapy
- with a history of pancreatitis
- experiencing hypersensitivity reactions to exenatide or its components
- with severe gastrointestinal disease, including gastroparesis

**GLP-1 agonist** recommended dosages are summarized in Table 1. Patient profiles containing prescriptions with **GLP-1 agonist** dosages that exceed these recommendations will be reviewed.
<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosage Form</th>
<th>Maximum Recommended Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>albiglutide</td>
<td>extended-release SC solution (Tanzeum®) 30 mg, 50 mg single-dose pens</td>
<td>50 mg once weekly at any time of day with or without meals</td>
</tr>
<tr>
<td>dulaglutide</td>
<td>extended-release SC solution (Trulicity®) 0.75/0.5 ml, 1.5/0.5 ml as single-dose pens or pre-filled syringes</td>
<td>1.5 mg once weekly at any time of day with or without meals</td>
</tr>
<tr>
<td>exenatide</td>
<td>regular-release SC solution (Byetta®) 5 mcg/0.02 ml pen, 10 mcg/0.04 ml pen*</td>
<td>5 mcg SC twice daily initially within 60 minutes prior to the morning and evening meals, or prior to the two main meals of the day spaced six hours or more apart; dose may be increased to 10 mcg twice daily prior to the morning and evening meals (or the two main meals of the day, spaced six hours or more apart) after one month of therapy based on clinical response</td>
</tr>
<tr>
<td></td>
<td>extended-release SC suspension (Bydureon®) 2 mg/0.65 ml mixed in syringe</td>
<td>2 mg once every 7 days (weekly) at any time of day, with or without meals</td>
</tr>
<tr>
<td>liraglutide</td>
<td>SC solution (Victoza®) multi-dose pen (18 mg/3 ml) that delivers 0.6 mg, 1.2 mg, or 1.8 mg</td>
<td>1.8 mg/day at any time of day with or without meals</td>
</tr>
<tr>
<td>lixisenatide#</td>
<td>SC solution (Adlyxin®) 150 mcg/3 ml (starter pen) - delivers 14 doses of 10 mcg; 300 mcg/3 ml (maintenance pre-filled pen) – delivers 14 doses of 20 mcg</td>
<td>20 mcg/day at any time of day with or without meals</td>
</tr>
</tbody>
</table>

SC = subcutaneous
*each pen provides 60 doses of medication
+each pen is single-use pen; supplied in carton of 4 pens
#approved July 2016; anticipated availability not determined
Pediatrics

GLP-1 agonists are not recommended for use in children as safety and efficacy in pediatric patients have not been established.

2. Duration of Therapy

GLP-1 agonists are indicated for the management of type 2 diabetes mellitus and may be continued indefinitely, as control of blood glucose is a chronic, lifelong process.

3. Duplicative Therapy [*]

Adjunctive administration of multiple GLP-1 agonists is not recommended due to increased risk for adverse events with no additional therapeutic benefit. Exenatide regular-release should be discontinued prior to initiating exenatide extended-release therapy. Patient profiles containing prescriptions for multiple GLP-1 agonists will be reviewed.

4. Drug-Drug Interactions [*]

Patient profiles will be assessed to identify those drug regimens which may result in clinically significant drug-drug interactions. Drug-drug interactions considered clinically relevant for GLP-1 agonists are summarized in Table 2. Only those drug-drug interactions identified as clinical significance level 1 or those considered life-threatening which have not yet been classified will be reviewed:
### Table 2: GLP-1 Receptor Agonist Drug-Drug Interactions

<table>
<thead>
<tr>
<th>Target Drug</th>
<th>Interacting Drug</th>
<th>Interaction</th>
<th>Recommendations</th>
<th>Clinical Significance+</th>
</tr>
</thead>
<tbody>
<tr>
<td>antidiabetic agents</td>
<td>fluoroquinolones</td>
<td>adjunctive administration may result in blood glucose disturbances and increased risk for hyper- or hypoglycemia due to an unknown mechanism</td>
<td>closely monitor blood glucose levels and adjust antidiabetic doses as needed; doses may also require adjustments with fluoroquinolone discontinuation</td>
<td>major (DrugReax) 3-moderate (CP)</td>
</tr>
<tr>
<td>antidiabetic agents</td>
<td>somatostatin analogues (SAs) (e.g., octreotide, pasireotide)</td>
<td>concurrent use may impair glucose regulation as SAs inhibit insulin and glucagon secretion; substantially increased blood glucose levels may result</td>
<td>monitor closely for changes in blood glucose control before and throughout SA therapy; adjust antidiabetic doses as needed</td>
<td>major (DrugReax) 2-major (CP)</td>
</tr>
<tr>
<td>exenatide</td>
<td>oral medications requiring threshold concentrations for effect (e.g., acetaminophen, oral contraceptives)</td>
<td>concurrent administration may reduce serum levels of drugs with threshold concentrations as exenatide delays gastric emptying</td>
<td>use cautiously together; administer medications having threshold levels for effect at least 1 hour before exenatide</td>
<td>3-moderate (CP)</td>
</tr>
<tr>
<td>exenatide</td>
<td>warfarin</td>
<td>concurrent administration may result in increased international normalized ratio (INR), sometimes with associated bleeding; mechanism unknown</td>
<td>closely monitor for changes in INR and bleeding with exenatide/warfarin drug combination</td>
<td>moderate (DrugReax) 3-moderate (CP)</td>
</tr>
<tr>
<td>GLP-1 agonists</td>
<td>alpha glucosidase inhibitors (AGIs) (e.g., acarbose, miglitol)</td>
<td>AGIs slow nutritive absorption; adjunctive administration may potentiate GLP-1 agonist pharmacologic effects, including additional blood glucose reductions and hypoglycemia risk</td>
<td>use cautiously together and monitor for additive hypoglycemia</td>
<td>undetermined</td>
</tr>
<tr>
<td>GLP-1 agonists</td>
<td>gastric stimulants (e.g., metoclopramide, tegaserod)</td>
<td>concurrent administration may attenuate pharmacologic effects due to competing effects from both agents</td>
<td>monitor blood glucose levels and adjust antidiabetic doses as needed</td>
<td>3-moderate (CP)</td>
</tr>
</tbody>
</table>
### Table 2: Exenatide Drug-Drug Interactions (continued)

<table>
<thead>
<tr>
<th>Target Drug</th>
<th>Interacting Drug</th>
<th>Interaction</th>
<th>Recommendations</th>
<th>Significance Level†</th>
</tr>
</thead>
<tbody>
<tr>
<td>GLP-1 agonists</td>
<td>oral medications with hypoglycemic effects (e.g., oral antidiabetic agents, angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, disopyramide, fibric acid derivatives, salicylates, sulfonamide antibiotics)</td>
<td>concomitant administration may result in enhanced hypoglycemic pharmacologic and adverse effects</td>
<td>monitor blood glucose levels closely and adjust dosages as necessary if drug combination required to minimize excessive hypoglycemia and associated adverse events</td>
<td>3-moderate (CP)</td>
</tr>
<tr>
<td>GLP-1 agonists</td>
<td>oral medications that slow gastrointestinal motility (e.g., opiate agonists, tricyclic antidepressants, antimuscarinics, diphenoxylate)</td>
<td>adjunctive administration may potentiate GLP-1 agonist pharmacologic effects, including additional blood glucose reductions and hypoglycemia risk</td>
<td>use cautiously together</td>
<td>undetermined</td>
</tr>
</tbody>
</table>

*Clinical Pharmacology

### References

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