### Care Step Pathway - Type 1 Diabetes Mellitus (immune destruction of beta cells in pancreas)

#### Nursing Assessment

<table>
<thead>
<tr>
<th>Look:</th>
<th>Listen:</th>
<th>Recognize:</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Does the patient appear fatigued?</td>
<td>- Frequent urination?</td>
<td>- Symptoms of diabetes</td>
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<tr>
<td>- Does the patient appear dehydrated?</td>
<td>- Increased thirst?</td>
<td>- Serum glucose levels</td>
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<td>- Does the breath have a sweet/fruity smell?</td>
<td>- Increased hunger?</td>
<td>- Other immune-related toxicity (and any corticosteroids given)</td>
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<tr>
<td>- Is the patient tachycardic?</td>
<td>- Increased fatigue?</td>
<td>- Infections</td>
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<td>- Confusion, altered level of consciousness with advanced cases</td>
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</tbody>
</table>

#### Grading Toxicity

<table>
<thead>
<tr>
<th>Mild hyperglycemia</th>
<th>Moderate or worse hyperglycemia (Likely New-onset Type 1 Diabetes); No DKA</th>
<th>Moderate or worse hyperglycemia (Likely New Onset Type 1 Diabetes); DKA</th>
</tr>
</thead>
<tbody>
<tr>
<td>New-onset hyperglycemia glucose &gt;ULN –200 mg OR history of type 2 DM with low suspicion of DKA</td>
<td>New onset fasting glucose &gt;200 mg/dL or random blood glucose &gt;250 mg/dL OR history of type 2 DM with fasting/random glucose &gt;250 mg/dL; DKA workup negative</td>
<td>New onset fasting glucose &gt;200 mg/dL or random blood glucose &gt;250 mg/dL OR history of type 2 DM with fasting/random glucose &gt;250 mg/dL; DKA workup positive</td>
</tr>
</tbody>
</table>

#### Management

**Overall Strategy**
- Evaluate for symptoms of DKA in patients with new onset fasting glucose >200 mg/dL or random blood glucose >250 mg/dL OR history of type 2 DM with fasting/random glucose >250 mg/dL: excessive thirst, frequent urination, general weakness, vomiting, confusion, abdominal pain, dry skin, dry mouth, increased heart rate, and fruity odor on the breath
- If DKA is suspected, evaluate per institutional guidelines, including blood pH, basic metabolic panel, urine or serum ketones/anion gap positive. Consider C-peptide if urine or serum ketones/anion gap is positive
- If Type 1 DM is suspected, also consider anti-GAD, anti-islet cell antibodies
- High-dose corticosteroid* use for other immune-related adverse events may induce or exacerbate hyperglycemia; if corticosteroid-induced hyperglycemia is suspected, evaluate benefit: risk ratio of tapering corticosteroid for glucose control vs management of the immune-related adverse event

**Mild hyperglycemia**
- Continue pembrolizumab, nivolumab, or ipilimumab
- Monitor serial blood glucose at each dose
- Institute diet/lifestyle modification
- If necessary, provide antidiabetes medication per institutional protocol
- Consider endocrine consultation if patient is symptomatic/hyperglycemia cannot be controlled

**Moderate or worse hyperglycemia (Likely New-onset Type 1 Diabetes); No DKA**
- Continue pembrolizumab, nivolumab, or ipilimumab
- Monitor serial blood glucose at each dose
- Institute diet/lifestyle modification
- Provide antidiabetes medication per institutional protocol

**Moderate or worse hyperglycemia (Likely New Onset Type 1 Diabetes); DKA**
- Hold pembrolizumab, nivolumab, or ipilimumab
- Obtain endocrinology consultation
- Provide inpatient care
- Insulin to be provided as directed by inpatient team and/or endocrinologist
- DKA to be managed per institutional guidelines (e.g., intravenous fluids, potassium supplementation, intravenous insulin, hourly glucose, serum ketones, blood pH, and anion gap)
- Consider resuming immune checkpoint inhibitor therapy once DKA has been corrected and glucose level has been stabilized

#### Implementation:
- For patients with new-onset Type 1 diabetes, discuss that it will most likely be permanent
- Review signs and symptoms of hyper/hypoglycemia
- Follow patients closely with checks on blood glucose levels, signs of DKA (fruity breath, confusion, nausea, etc.), and other symptoms (e.g., increased infections)
- Provide insulin education (or refer)
- Discuss possibility of other immune-related AEs, including others of endocrine origin
- Discuss dietary modification

*Administering Corticosteroids:*
Steroid taper instructions/calendar as a guide but not an absolute
- Taper should consider patient’s current symptom profile
- Close follow-up in person or by phone, based on individual need & symptomatology
- Steroids cause indigestion; provide antacid therapy daily as gastric ulcer prevention while on steroids (e.g., proton pump inhibitor or H2 blocker if prednisone dosage is >20 mg/day)
- Review steroid medication side effects: mood changes (angry, reactive, hyperraware, euphoric, manic), increased appetite, interrupted sleep, oral thrush, fluid retention
- Be alert to recurring symptoms as steroids taper down & report them (taper may need to be adjusted)

**Long-term high-dose steroids:***
- Consider antimicrobial prophylaxis (sulfamethoxazole/trimethoprim double dose MWF: single dose if used daily) or alternative if sulfa-allergic (e.g., atovaquone [Mepron®] 1500 mg po daily)
- Consider additional antiviral and antifungal coverage
- Avoid alcohol/acetaminophen or other hepatotoxins
- If extended steroid use, risk for osteoporosis; initiate calcium and vitamin D supplements

DKA = diabetic ketoacidosis; DM = diabetes mellitus; GAD = glutamic acid decarboxylase; po = by mouth; ULN = upper limit of normal

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