START Criteria

By Scott Wheeldon, R.Ph.

Most of us are familiar with the Beers List of medications considered potentially inappropriate for use in the elderly. Many of the medications are included on this list due to the high potential for anticholinergic side effects that can affect cognition and increase the risk of falls. But another less known list of medications that is also important is included in the STOPP/START criteria. STOPP criteria were previously discussed in the September/October 2018 edition of InformRx.

The second part of the STOPP criteria is the list of START guidelines (Screening Tool to Alert doctors to the Right Treatment), which is an evidence-based screening tool that can detect potential omissions in the therapy of elderly patients. It includes 22 scenarios, divided by physiological system (cardiovascular, respiratory, CNS, GI, locomotor and endocrine), where specific medications are recommended.

In one study of 600 consecutive hospital admissions, averaging five medications each, over half of the acutely-ill, newly hospitalized elderly patients—57.9%—had at least one appropriate medication omitted from their list of regular prescription medicines. The probability of not receiving an appropriate medication increased with age and female gender. Failure to prescribe appropriate medicines, which have a proven important role in primary and secondary disease prevention, could have a substantial clinical and economic impact over time.

The financial cost of the omitted medicines was not large; in this study, it was calculated at $128,241.00 per year for the 600 subjects, based on the wholesale cost of the omitted drugs in generic form (and not including extra costs such as pharmacists’ dispensing fees and use of non-generic drugs). This amount may not seem substantial until viewed from the perspective of secondary prevention. For example,

START guidelines (Screening Tool to Alert doctors to the Right Treatment) chart on page 2.
InformRx

**START medications (age ≥ 65 years)**

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Circumstances</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE Inhibitor</td>
<td>Chronic heart failure&lt;br&gt;Failing acute myocardial infarction&lt;br&gt;Diabetes with nephropathy (overt urinalysis, proteinuria or microalbuminuria) &gt;30mg/24 hours ± serum biochemical renal impairment</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>In presence of moderate to severe depressive symptoms lasting at least three months</td>
</tr>
<tr>
<td>Antihypertensives</td>
<td>Systolic blood pressure consistently &gt;160mm Hg</td>
</tr>
<tr>
<td>Aspirin</td>
<td>Documented history of atherosclerotic coronary, cerebral or peripheral vascular disease in patients with sinus rhythm&lt;br&gt;Following an acute MI</td>
</tr>
<tr>
<td>Beta-blocker (oral)</td>
<td>With chronic stable angina</td>
</tr>
<tr>
<td>Beta-agonist (inhaled)</td>
<td>Guidance at <a href="http://mm.wirral.nhs.uk/document">http://mm.wirral.nhs.uk/document</a> Uploads/Guidelines/COPDguidelinesv2.pdf&lt;br&gt;Review patients with mild, moderate or severe COPD at least twice a year as per NICE guidance - <a href="http://www.nice.org.uk/guidance/cg101">http://www.nice.org.uk/guidance/cg101</a></td>
</tr>
<tr>
<td>Bisphosphonates</td>
<td>In patients taking maintenance oral corticosteroid therapy with previous fragility fractures or incident fractures during glucocorticoid therapy. Ensure there are no absorption interactions e.g. Calcium. Counsel patient on the correct way to take a bisphosphonate.</td>
</tr>
<tr>
<td>Calcium and vitamin D</td>
<td>In patients with known osteoporosis (radiological evidence or previous fragility fracture) or acquired dorsal kyphosis</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>For ischemic stroke or PVD as per <a href="http://www.nice.org.uk/guidance/ta210">http://www.nice.org.uk/guidance/ta210</a></td>
</tr>
<tr>
<td>DMARD</td>
<td>With active moderate-severe rheumatoid disease lasting &gt;12 weeks</td>
</tr>
<tr>
<td>Fiber supplement</td>
<td>For chronic symptomatic diverticular disease with constipation</td>
</tr>
<tr>
<td>Laxatives</td>
<td>In patients taking opioids - to prevent constipation</td>
</tr>
<tr>
<td>PPI</td>
<td>For severe reflux or peptic stricture requiring dilatation&lt;br&gt;For patients over 80 years old on an antiplatelet and an SSRI</td>
</tr>
<tr>
<td>Statins</td>
<td>Documented history of coronary, cerebral or peripheral vascular disease, where the patient's functional status remains independent for activities of daily living and life expectancy &gt;5 years&lt;br&gt;Diabetes mellitus plus ≥ 1 co-existing major cardiovascular risk factor present</td>
</tr>
<tr>
<td>Anticoagulation</td>
<td>Chronic atrial fibrillation as per <a href="http://www.nice.org.uk/guidance/cg180">http://www.nice.org.uk/guidance/cg180</a> Following diagnosis of DVT and PE if benefit outweighs the risk of treatment</td>
</tr>
<tr>
<td>(warfarin or a NOAC)</td>
<td></td>
</tr>
<tr>
<td>Pneumococcal vaccination</td>
<td>At least once after age 65 according to national guidelines</td>
</tr>
<tr>
<td>Influenza vaccination</td>
<td>Seasonal influenza vaccination annually</td>
</tr>
</tbody>
</table>

71 subjects with chronic atrial fibrillation did not receive warfarin or aspirin, despite the absence of clear-cut contra-indications to these medicines. Among this age group of patients not receiving thrombo-embolic prophylaxis, the annual risk of stroke is approximately 10–15%. Therefore, in the 71 patients with chronic atrial fibrillation and intrinsic heart disease, approximately seven–eleven stroke events would be expected each year. Warfarin therapy would be expected to reduce the annual stroke risk by approximately 60% (preventing four–seven cases of avoidable stroke). The total cost of treating these four–seven stroke cases in a teaching hospital in 2006 was calculated at $43,223.00 (four cases) to $75,641 (seven cases) alone, without considering the additional cost of treatment for adverse events that may have occurred without appropriate START criteria interventions.

As always, treatment should be individualized for each long-term care resident, but the STOPP and also the START criteria are examples of evidence-based guidelines for improved medication-related outcomes in our elderly population.
Medication administration via tube has always been a focus for survey teams. The Tube Feeding Status Critical Element Pathway (CMS form 22093) and Medication Administration Observation (CMS form 22056) are new survey tools to assist us in ensuring regulatory compliance. Here are just a few of the F-tags that can be cited for residents with tube feedings:

FTAG 552, 578, 572, 580, 636, 637, 641, 655, 656, 657, 658, 693, 710, 715, 750, 755, 759, 841, 880

To ensure successful medication oversight, pharmacists must be informed when residents are placed on enteral nutrition or dietary supplements. There are potential food-drug interactions that could occur due to inappropriate timing of medication administration, feeding tube occlusion, and medication binding to feeding tubes, resulting in the potential for suboptimal clinical response.

**KEY TERMS:**

Enteral feeding tubes are used when a resident is unable to take adequate oral intake. The tubes are classified by location of the tube distal tip (gastric, duodenal, or jejunal), site of insertion (oral, nasal, percutaneous) and size of tube (small 5-12 French or large 14 French or greater).

- **Bolus feeding:** The administration of a limited volume of enteral formula over brief periods of time
- **Continuous feeding:** The administration of enteral formula over extended periods of time
- **Enteral nutrition (tube feeding):** The delivery of nutrients via a feeding tube directly into the stomach, duodenum, or jejunum
- **Feeding tube:** A medical device used to provide enteral nutrition to a resident in place of oral food
- **Gastrostomy tube (G tube):** A feeding tube placed directly into the stomach through an abdominal wall incision
- **Jejunostomy tube (J tube):** A feeding tube placed directly into the small intestine
- **Nasogastric tube (NG tube):** A feeding tube placed through the nose, nasopharynx, esophagus and into stomach
- **PEG (percutaneous endoscopic gastronomy) tube:** A common type of a gastrostomy tube
- **PEJ (percutaneous endoscopic jejunostomy) tube:** A common type of jejunostomy tube
- **Transgastric jejunal feeding tube (GJ tube):** A feeding tube placed through the stomach into the jejunum with dual ports to access both the stomach and small intestine

continued on page 4
PREPARE ORDER:
- Physician order to administer medication via feeding tube and MAR states via tube
- Physician order to crush medications and care planned accordingly
- Medications are crushable per manufacturer’s guidelines; do NOT crush enteric coated, sustained-release, enzyme specific, buccal, sublingual
- Physician order to change to liquid medication form whenever possible

PREPARE MEDICATIONS:
- Wash hands
- Crush medications individually
- Use gloves to open capsules
- Tablets, powders and beaded (never crushed) from opened capsules - mix each crushed immediate release medication or capsule content with at least 5-15ml water
- Dilute liquid medications with at least 30ml of water to prevent stomach irritation
- Use 60ml water to dilute GI irritants such as KCL solution
- Use syringe type that does NOT have a needle

PREPARE ADMINISTRATION:
- Provide privacy
- Position the resident at 30-45 degrees
- Clean stethoscope per policy and ensure all areas have proper infection control barrier for placing medications down on a solid surface during individual medication administration
- Wash hands and wear gloves
- Verify tube placement/check residual per facility policy
- Flush tube with 15-30ml of water (all amounts and type water per facility policy)
- Never mix medications with enteral formula
- Administer medications separately (liquids first, thick medications last), allow medications to flow by gravity, flush tube with 5-15ml water between each medication

PREPARE TO PREVENT POTENTIAL DRUG-ENTERAL FEEDING INTERACTIONS:
- Check manufacturer recommendations for hold parameters before administration of these common medications (hold time varies from 1-2 hours before and after medication administered):
  - phenytoin
  - Fluoroquinolone antibiotics(Cipro®/Levaquin®)
  - Theophylline
  - Sucralfate (should be avoided - consider alternatives)
  - Levothyroxine
  - Warfarin
  - Carbamazepine
  - hydralazine
  - penicillin VK
  - tetracycline
HOLD nutrition for thirty minutes before medications that should be given on empty stomach (does not apply to jejunal administration). Antacids should not be given at the same time as many medications and antibiotics; hold feeding for 30 minutes before and after antacids. Some medications are not recommended in jejunal administration due to pH for absorption.
ENTERAL TUBE KEY REGULATIONS:

F759/760 Medication Error Rate  F880 Infection control  F755 Pharmacy Services

- The administration of medications with adequate fluid as manufacturer specifies
- Staff did not crush tablets/capsules that manufacturer states “do not crush”
- Staff did not crush and combine medications and then give medications all at once via feeding tube
- Prior to medication administration, ng or g tube placement is confirmed (F693)
- NG or G tube flushed with the required amount of water before and after each medication unless physician orders indicate a different flush schedule due to the resident’s clinical condition
- Staff must separate the administration of enteral nutrition formula and phenytoin to minimize interactions. Simultaneous administration of enteral nutrition formula and phenytoin is considered a medication error.

Does the facility ensure that it is free of medication error rates of 5 percent or greater? NO = F759
Does the facility ensure that residents are free of any significant medication errors? NO = F760
Did the staff use appropriate hand hygiene practices and implement appropriate standard precautions when assisting with tube feeding? NO = F880
Did the facility have a system to account for the receipt, usage, disposition, and reconciliation of all controlled medications? Does your facility have a policy on tube feeding and medication administration via tube? NO = F755

For more information on Enteral Tube administration contact your PharMerica consultant pharmacist
ASCVD and Diabetes

By Bridgette Sullivan Piefer, PharmD

The prevalence of diabetes has been steadily increasing, particularly in older populations, with approximately 25 to 34% of those living in long-term care facilities suffering from the disease. The leading cause of morbidity and mortality in diabetic patients is atherosclerotic cardiovascular disease (ASCVD). ASCVD also carries significant costs, both direct and indirect. Therefore, it is important to ensure optimal care for diabetic patients with ASCVD or at risk for ASCVD to prevent these devastating consequences.

In 2018, the ADA released updated guidelines regarding patients with diabetes and ASCVD. A summary of the recommendations are as follows.

**HYPERTENSION:**

Blood pressure should be monitored daily. The goal blood pressure for most diabetic patients is 140/90 mmHg. A more stringent goal of less than 130/80 mmHg may be considered for patients with high risk for CVD.

<table>
<thead>
<tr>
<th>Blood Pressure</th>
<th>Treatment Strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Greater than 120/80</td>
<td>Begin with lifestyle modifications such as diet, exercise, and restricting sodium intake</td>
</tr>
<tr>
<td>Greater than 140/90</td>
<td>Start pharmacological therapy with 1 medication; lifestyle modifications</td>
</tr>
<tr>
<td>Greater than 160/90</td>
<td>Start dual pharmacological therapy with 2 medications; lifestyle modifications</td>
</tr>
</tbody>
</table>

Preferred medications shown to reduce cardiovascular events in diabetic patients:

<table>
<thead>
<tr>
<th>Class of Medication</th>
<th>Examples</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE inhibitors or ARBs</td>
<td>• Lisinopril • Enalapril • Ramipril • Benazepril • Losartan • Valsartan • Irbesartan</td>
<td>First-line therapy for patients with albuminuria Monitor serum creatinine and potassium at least once a year</td>
</tr>
<tr>
<td>Thiazide-like diuretics</td>
<td>• Indapamide • Chlorothalidone</td>
<td>Thiazide-like diuretics have been shown to have greater cardiovascular benefit than thiazide diuretics (hydrochlorothiazide, chlorothiazide)</td>
</tr>
<tr>
<td>Dihydropyridine calcium channel blockers</td>
<td>• Amlodipine • Nifedepine</td>
<td></td>
</tr>
</tbody>
</table>

continued on page 7
ASCVD and Diabetes, cont.

For patients who have uncontrolled hypotension on three different types of medications, including a diuretic, consider adding a mineralocorticoid receptor agonist (spironolactone, eplerenone).

For patients with a history of MI, consider adding a beta blocker for at least two years. Beta blockers may also be considered for patients with angina or heart failure.

New studies suggest that bedtime administration of hypertensive medications may help to control blood pressure and reduce cardiovascular events.

HYPERLIPIDEMIA:

For diabetic patients over the age of 40, both those with and without ACVD, the addition of statin therapy is recommended. Older adults may get more benefit from statin therapy due to the increased risk of ASCVD. However, the risk versus benefit in this population needs to be considered.

<table>
<thead>
<tr>
<th>Age and ASCVD Status</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients between 40 to 75 years without ACSVD</td>
<td>Moderate intensity statin</td>
</tr>
<tr>
<td>Patients between 40 to 75 years with ASCVD</td>
<td>High intensity statin</td>
</tr>
<tr>
<td>Patients over 75 years</td>
<td>Moderate intensity statin; downward titration if needed based on patient risk versus benefit</td>
</tr>
</tbody>
</table>

Moderate intensity statin

• Atorvastatin 10-20mg daily
• Rosuvastatin 5-10mg daily
• Simvastatin 20-40mg daily
• Pravastatin 40-80mg daily
• Lovastatin 40mg daily

High intensity statin

• Atorvastatin 40-80mg daily
• Rosuvastatin 20-40mg daily

For patients on high intensity statin but who still have an LDL over 70mg/dl, consider adding Ezetimibe (Zetia) or a Proprotein convertase subtilisin/kexin type 9 inhibitor such as Evolovumab (Repatha) or alirocumab (Praluent).

Combinations of medications to avoid:

• Statins with fibric acid derivatives did not show any improvements to ASCVD outcomes but did carry a greater risk of side effects.

• Statins with niacin did not show any ASCVD benefits greater than statin alone but increased the risk of stroke.

ANTIPLATELET THERAPY:

Aspirin low dose (81mg daily) is recommended for diabetic patients with ASCVD. Aspirin low dose therapy may also be considered for patients over 50 years old without ASCVD but with increased cardiovascular risk. For patients with an aspirin allergy, Plavix may be considered.

continued on page 8
ASCVD and Diabetes, cont.

**DIABETIC THERAPY:**

The following medications have been shown to provide potential benefit to diabetic patients with ASCVD:

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Generic Name</th>
<th>Drug Class</th>
<th>Typical initial dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucophage</td>
<td>Metformin</td>
<td>Biguanide</td>
<td>250 to 500mg by mouth twice daily</td>
</tr>
<tr>
<td>Jardiance</td>
<td>Empagliflozin</td>
<td>SGLT2 inhibitor</td>
<td>10mg by mouth once daily</td>
</tr>
<tr>
<td>Invokana</td>
<td>Canagliflozin</td>
<td>SGLT2 inhibitor</td>
<td>100mg by mouth once daily</td>
</tr>
<tr>
<td>Victoza</td>
<td>Liraglutide</td>
<td>GLP-1 RA</td>
<td>0.6mg subcutaneously once daily for 1 week, then 1.2mg daily</td>
</tr>
</tbody>
</table>

For type 2 diabetic patients with ASCVD, metformin is recommended as a first-line treatment with lifestyle and diet modifications.

The goal for older adults with few chronic illnesses and intact cognitive function should be a hemoglobin A1C less than 7.5. For older adults with multiple chronic illnesses or cognitive impairment, the goal should be less than 8.0 to 8.5.

If the patient cannot meet hemoglobin A1C goals with metformin alone, consider adding either Jardiance, Invokana, or Victoza, which have all shown to improve cardiovascular outcomes in patients with ASCVD.

For patients with renal disease, options may be more limited. Metformin and Jardiance are contraindicated in patients with a creatinine clearance less than 30ml/min. Invokana is contraindicated in those with a creatinine clearance less than 45ml/min. Victoza does not require any dosing adjustments for patients with renal impairment.

**SUMMARY:**

Diabetes and ASCVD are multi-faceted diseases that require multiple approaches to therapy. Several pharmacologic therapies have been shown to provide a benefit to diabetics with ASCVD or at risk for ASCVD. ACE inhibitors or ARBS, thiazide-like diuretics, and dihydropyridine calcium channel blockers have been shown to improve cardiovascular outcomes. For diabetic patients with albuminuria, ACE inhibitors or ARBs are considered first-line therapy. Statin medications are recommended for all diabetic patients over the age of 40. Aspirin is recommended for patients with ASCVD and may also be considered for patients over 50 without ASCVD but who have additional risk factors. For type 2 diabetic patients, metformin is considered first-line therapy. Jardiance, Invokana, and Victoza have also been shown to provide cardiovascular benefit in type 2 diabetics with ASCVD. Please keep in mind contraindications, risk versus benefit, and patient preference before initiating pharmacologic therapy.
Medication Spotlight: NUEDEXTA

By Judd Carpenter, PharmD, MBA

NUEDEXTA (dextromethorphan HBr and quinidine sulfate) is the first and only FDA-approved treatment for pseudobulbar affect (PBA). PBA is characterized by involuntary, sudden, and frequent episodes of laughing and/or crying. It occurs secondary to a variety of otherwise unrelated neurologic conditions, including:

- Dementias, including Alzheimer’s disease (AD)
- Stroke
- Traumatic brain injury (TBI)
- Multiple sclerosis (MS)
- Parkinson’s disease (PD)
- Amyotrophic lateral sclerosis (ALS)

PBA episodes typically occur out of proportion or incongruent with the underlying emotional state. PBA is a specific condition, distinct from other types of emotional lability that may occur in patients with neurological disease or injury.

NUEDEXTA capsules contain 20 mg dextromethorphan hydrobromide and 10 mg quinidine sulfate. Dextromethorphan (DM) is a sigma-1 receptor agonist and an uncompetitive NMDA receptor antagonist. Quinidine is used to block the rapid metabolism of dextromethorphan, thereby increasing serum concentrations. The mechanism by which dextromethorphan exerts therapeutic effects in patients with pseudobulbar affect is unknown.

*Note: The dose of quinidine in this combination product provides serum concentrations 1% to 3% of those needed to treat cardiac arrhythmias.

The recommended starting dose of NUEDEXTA is one capsule daily by mouth for the initial seven days of therapy. On the eighth day of therapy, and thereafter, the daily dose should be a total of two capsules a day, given as one capsule every 12 hours. The need for continued treatment should be reassessed periodically, as spontaneous improvement of PBA occurs in some patients.

No dosage adjustment is necessary for patients with mild to moderate renal or hepatic impairment. There are no dosage adjustments provided in the manufacturer’s labeling for patients with severe renal or hepatic impairment (has not been studied); however, increases in dextromethorphan/quinidine levels are likely to be observed.

Geriatric Considerations
Given the use of quinidine in this product, careful assessment of the medication regimen for drug-drug interactions is paramount in the older adult population. Limited clinical evidence exists in the general older adult population and even less data exists to support dextromethorphan/quinidine in the population residing in long-term care facilities. The data that exists shows a significant increased risk for falls, even with short-term use.

Assessment of the QTc interval is prudent in older adults prior to initiating dextromethorphan/quinidine, and avoidance of this medication may be advisable if other QTc prolonging medications are present on the drug profile.

Monitoring Parameters
QT interval at baseline and three to four hours after the first dose in patients at risk for QTc prolongation; potassium and magnesium prior to and during therapy; CBC, liver and renal function tests; periodically assess risk factors for arrhythmias during treatment; periodically reassess the need for treatment (spontaneous improvement of PBA may occur); worsening myasthenia gravis or other sensitive conditions due to anticholinergic effects.

Adverse Reactions
The most common adverse reactions (incidence of ≥3% and two-fold greater than placebo) in patients taking NUEDEXTA are diarrhea, dizziness, cough, vomiting, asthenia, peripheral edema, urinary tract infection, influenza, increased gamma-glutamyltransferase, and flatulence.

For more information on NUEDEXTA, please contact your PharMerica Consultant Pharmacist.