Potpourri of Pharmaceutical Pearls

Atenolol shortage--a blessing?
Ongoing manufacturing issues make it a good time to switch from atenolol that was never shown to improve outcomes in CHF, hypertension or post-MI. Go with carvediol IR BID ($4 at Walmart for 60 of the 25mg tabs) or metoprolol succinate (Toprol XL, 30 of the 25mg tabs for $14).

Daily vs Alternate Day Oral Iron Therapy
A small Swiss open label randomized controlled study (Lancet Haematol 2017 Oct 9) showed that in otherwise healthy iron depleted women providing iron supplements on alternative days and in single doses optimizes iron absorption. The presumed mechanism is that iron intake raises levels of hepcidin (which blocks the absorption of iron given the following day). This is an idea to consider while we wait for a bigger study in patients with substantial iron deficiency anemia.
A new, cheaper fluticasone

Armonair Respiclick uses the same inhaler as ProAir and AirDuo. Armonair Respiclick (55mcg, $167) has pharmacokinetic and dosing studies showing similar efficacy at significantly lower systemic exposures versus Flovent Diskus (110mcg, $175 down from $234, a month ago). This is an important advantage for both Armonair and AirDuo. No hand-mouth coordination is required.

<table>
<thead>
<tr>
<th>Available Doses</th>
<th>Starting Dose (naive)</th>
<th>Maximum Dose</th>
<th>Approved Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Armonair</td>
<td>55,113,232 mcg</td>
<td>55mcg BID</td>
<td>232mcg BID</td>
</tr>
<tr>
<td>Flovent Diskus</td>
<td>50, 100, 250 mcg</td>
<td>100mcg BID</td>
<td>1000mcg BID</td>
</tr>
</tbody>
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Two New Drugs to Avoid

Baxdela (delafloxacin) approved to treat skin infections, available in oral tablets (450 mg tabs BID for 14 days, $2,268 and IV formulations.)

- There are no efficacy data comparing delafloxacin with the four current fluoroquinolones. Infectious disease experts do not recommend fluoroquinolones for skin infections.
- Inappropriate broad-spectrum coverage can lead to increased bacterial resistance.
- Baxdela has a Black Box Warning as with all drugs in this class: tendinitis, tendon rupture, peripheral neuropathy and both psychiatric and neurologic syndromes.

Fiasp (insulin aspartate) $291 per 10ml vial with 100 units per ml.

- Niacinamide, vitamin B3, was added to Novolog to decrease the time to onset of action. Fiasp starts working about 5 minutes faster than Novolog. ($227 for 10ml vial of 100 units per ml).
- The niche for this “me too” may be that tiny sliver of patients who have meal time timing difficulties with the other rapid acting insulins.
- Good News: There are two new, less pricey, “follow-ons” to Novolog and Humalog close to launch!

Comparative Effectiveness Studies (CES)

CES drive the approval of most drugs in the UK and much of Europe. In the US, the FDA is programmed only to ascertain the safety and efficacy of new drugs (statistically better than a comparator drug, usually placebo). The price of new drugs in the US is driven by greed—what the market will bear. Therein, we suffer the sad tales of new third line oncology drugs that prolong life for an average of 22 emesis-filled days at a cost of $40,000!

The Institute for Clinical and Economic Review (ICER) is an independent nonprofit research institute that produces reports analyzing the evidence on the effectiveness and value of drugs. ICER’s reports include evidence-based calculations for prices for new drugs that reflect improvement expected in long-term patient outcomes.
On November 21, 2017, ICER released the following report on two drugs used to treat tardive dyskinesia (TD). Although this is a class of drugs that I’ve never prescribed, the concept is hopeful for the sanity of pharmacoeconomics.

ICER Report:
“Economic analyses found the cost-effectiveness of both valbenazine (Ingressa) and deutetrabenazine (Austedo) far exceed commonly cited thresholds of $50,000 – $150,000 per quality adjusted life year (QALY) at $752,000 and $1.1 million per QALY, respectively. To align with the benefits provided to patients, valbenazine’s annual wholesale acquisition cost (WAC) would need to fall to between $7600 and $11,260, a discount of 85% to 90% from its current price of $76,000. Deutetrabenazine’s annual WAC at $90,000 would need to be lowered by 90% – 93% to $6200 – $9200.”

Hopefully, we will see ICER evaluate some drugs commonly prescribed by primary care physicians.

**Management of the Acute Cough of the Common Cold**

I was excited when I delved into the meat of the research of the Chest Expert Panel Report (Chest 2017; 152 (5): 1021 – 1037). This systematic review of randomized controlled trials is an attempt to update the CHEST 2006 guideline on the topic. The authors found six new systematic reviews and four primary studies that reported data on 6,496 participants who received one or more interventions. The careful methods, relatively large “N” and the apparent lack of commercial bias create an air of credibility to this study.

Alas, the evidence supporting the management of coughs associated with the common cold is overall of low quality. The authors summarize with four, ungraded consensus based statements:

1. For adult and pediatric patients with cough due to the common cold, **suggest against the use of over-the-counter cough and cold medicines until they have been shown to make cough less severe or resolve sooner.**

2. In adult patients with cough due to the common cold, **suggest against the use of nonsteroidal anti-inflammatory agents until they have been shown to make cough less severe or resolve sooner.**

3. In pediatric patients (ages 1–18 years) with cough due to the common cold, **suggest honey may offer more relief for cold symptoms than no treatment, diphenhydramine, or placebo, but it is not better than dextromethorphan.**

4. In pediatric patients (age <18 years) with cough due to the common cold, **suggest avoiding use of codeine containing medications because of the potential for serious side effects including respiratory distress.**

Other thoughts from this expert panel on management of cough:

- **Zinc:** some small, very low quality studies in adults and children suggest some modest shortening of the period of cough. Bad taste.

- **Guaifenesin:** low quality studies with conflicting outcomes.

- **Vicks VapoRub:** Studies are lousy. Studies do show parents love this intervention. Menthol does improve nasal sensation of airflow.
- **Dextromethorphan**: is better than diphenhydramine, no treatment or placebo. Abuse potential, robo-tripping, euphoria and dissociative effects.
- **Narcotic combinations**: Vituz (hydrocodone and guaifenesin, $7.63 for 140ml 5mg/4mg/5ml oral solutions; Obredon 200ml of 2.5mg/200mg/5ml for $236. Prices all over the place. No new clinical studies required for these combination products. FDA says do not combine with benzodiazepines or other CNS depressants.

All drug prices researched on GoodRx on December 20, 2017 for the Grand Junction, Colorado area. Baxdela prices were estimates provided by the manufacturer, Melinta. ICER costs from their website on November 30, 2017.