Update on New Drugs

Michael Ernst, PharmD
April 14, 2015
2015 Refresher Course for the Family Physician
Disclosures

• None
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<th>Indications</th>
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**2014 FDA Approvals**

## 2014 approvals cont.

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<td>Nintedanib (Ofev)</td>
<td>Boehringer Ingelheim</td>
<td>Kinase inhibitor against PDGFRs, FGFRs, VEGFRs and FLT3</td>
<td>IPF</td>
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<td>Blinatumomab (Blinicyto)</td>
<td>Amgen</td>
<td>CD19- and CD3-bispecific antibody</td>
<td>B-ALL</td>
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<td>Finafloxacina (Xtorno)</td>
<td>Alcon</td>
<td>Fluoroquinolone antimicrobial</td>
<td>Acute otitis externa (swimmer’s ear)</td>
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<td>Olaparib (Lynparza)</td>
<td>AstraZeneca</td>
<td>PARP inhibitor</td>
<td>Advanced <em>BRCA</em>-mutated ovarian cancer</td>
<td>F, O, A</td>
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<tr>
<td>Ombitasvir plus paritaprevir plus dasabuvir plus ritonavir (Viekira Pak)</td>
<td>AbbVie</td>
<td>An NS5A inhibitor plus an NS3A- and NS4A-protease inhibitor plus a non-nucleoside NS5B-palm-polynase inhibitor plus a CYP3A inhibitor</td>
<td>Chronic HCV genotype 1 infection</td>
<td>F, B</td>
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<tr>
<td>Ceftolozane plus tazobactam (Zerbaxa)</td>
<td>Cubist</td>
<td>A cephalosporin antibacterial plus a ß-lactamase inhibitor</td>
<td>Complicated intra-abdominal infections and complicated urinary tract infections</td>
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<td>Peramivir (Rapivab)</td>
<td>BioCryst</td>
<td>Neuraminidase inhibitor</td>
<td>Influenza infection</td>
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<td>Nivolumab (Opdivo)</td>
<td>Bristol-Myers Squibb</td>
<td>PD1 inhibitor</td>
<td>Unresectable or metastatic melanoma</td>
<td>F, O, B, A</td>
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</table>

5-HT₁, serotonin type 3; A, accelerated approval; ABSSSI, acute bacterial skin and skin structure infection; ALK, anaplastic lymphoma kinase; B, breakthrough designation; B-ALL, B-cell acute lymphocytic leukaemia; CDER, Center for Drug Evaluation and Research; CLL, chronic lymphocytic leukaemia; COPD, chronic obstructive pulmonary disease; CYP3A, cytochrome P450 3A4; FGFR, fibroblast growth factor receptor; FLT3, receptor-type tyrosine-protein kinase FLT; GLP1, glucagon-like peptide 1; HCV, hepatitis C virus; IGF1R, insulin-like growth factor 1 receptor; IL-6, interleukin-6; IPF, idiopathic pulmonary fibrosis; MOA, mode of action; NK1, substance P; NS, non-structural protein; NSCLC, non-small-cell lung cancer; O, orphan designation; P, priority review; PD1, programmed cell death protein 1; PDGFR, platelet-derived growth factor receptor; PI3Kβ, phosphatidylinositol-3-OH kinase; ROS1, proto-oncogene tyrosine-protein kinase ROS; S, standard review; SGLT2, sodium–glucose cotransporter 2; SLL, small lymphocytic lymphoma; VEGFR, vascular endothelial growth factor receptor.
2014 Approvals by Therapeutic Area

Sampling of 2014/15
New FDA Approvals
Of Interest in Primary Care

• Dulaglutide (Trulicity®) – Sept 2014
• Albiglutide (Tanzeum®) – April 2014
• Dapagliflozin (Farxiga®) – Jan 2014
• Empagliflozin (Jardiance®) – Aug 2014
• Edoxaban (Savaysa®) – Jan 2015
• Dalbavancin (Dalvance®) – May 2014
• Oritivancin (Orbactiv®) – Aug 2014
GLP-1 Agonists
(Glucagon-like peptide-1 agonist)

Dulaglutide (Trulicity®)
Albiglutide (Tanzeum®)
GLP-1 Agonists
(Glucagon-like peptide-1 agonist)

• AKA: “incretin mimetics”

• Mechanism: Stimulates GLP-1 receptors (GLP = incretin hormone)
  – ↑ insulin production/secretion
  – ↓ glucagon release/glucose production
  – Slowing of gastric emptying
  – Increased satiety

Role of Incretins in Glucose Homeostasis

[Diagram showing the role of incretins in glucose homeostasis, including ingestion of food, release of gut hormones, increased insulin from beta cells, decreased glucagon from alpha cells, and decreased glucose production by liver.]
GLP-1 Agonists
(Glucagon-like peptide-1 agonist)

- All Subcutaneous **Injectables**

<table>
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<tr>
<th>Drug</th>
<th>Initial Dose</th>
<th>Max Dose</th>
<th>Supplied</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exenatide (Byetta®)</td>
<td>5 mcg twice daily</td>
<td>10 mcg twice daily</td>
<td>Prefilled pen</td>
</tr>
<tr>
<td>Exenatide ER (Bydureon®)</td>
<td>2 mg weekly</td>
<td>2 mg weekly</td>
<td>Kit* or prefilled pen</td>
</tr>
<tr>
<td>Liraglutide (Victoza®)</td>
<td>0.6 mg daily x 1 week 1.2 mg daily</td>
<td>1.8 mg/day</td>
<td>Prefilled pen</td>
</tr>
<tr>
<td>Albiglutide (Tanzeum®)</td>
<td>30 mg weekly</td>
<td>50 mg weekly</td>
<td>Prefilled pen/kit*</td>
</tr>
<tr>
<td>Dulaglutide (Trulicity®)</td>
<td>0.75 mg weekly</td>
<td>1.5 mg weekly</td>
<td>Prefilled pen</td>
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</table>

* Kit can be difficult for patient to use as it requires a number of steps to draw up medication.

- **Efficacy:** ↓ A1c by 1.0% to 1.5%
- **Adverse Effects:** Headache, **nausea, diarrhea**, pancreatitis(?)
  - Nausea may be less pronounced with liraglutide
  - Exenatide not recommended in CrCl < 30 mL/min

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<td>Low Risk</td>
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PL Detail-Document, Drugs for Type 2 Diabetes. Pharmacist’s Letter/Prescriber’s Letter. August 2013
GLP-1 Agonists
(Glucagon-like peptide-1 agonist)

**Black Box Warning**
Thyroid C-cell tumors have been observed in animal studies with glucagon-like peptide-1 (GLP-1) receptor agonists at clinically relevant exposures. If it unknown if any of the commercially available GLP-1 agonists cause thyroid C-cell tumors in humans, including medullary thyroid carcinoma (MTC). These are contraindicated in patients with a personal or family history of MTC or in patients with multiple endocrine neoplasia syndrome type 2.

Albiglutide (Tanzeum®)
Instructions for Use

TANZEUM (albiglutide) Pen 50 mg

Use 1 Time Each Week
Read all the instructions and follow the steps below to mix the medicine and prepare the pen for injection.

Failure to follow Steps A to C in the correct order may result in damage to your pen.

Information About This Pen
- This medicine is injected 1 time each week.
- The pen has medicine powder in 1 compartment and water in another compartment. You will need to mix them together by twisting the pen, then wait for 30 minutes for the medicine and water to fully mix.

CAUTION:
Do not allow the pen to freeze. Throw away the pen if frozen.

If stored in refrigerator, allow to sit at room temperature for 15 minutes before starting Step A.

Dispose of the pen right away after injecting. Do not recap, remove, or reuse the needle.
Albiglutide (Tanzeum®)

Instructions for Use

- Gather a **clean, empty cup** to hold the pen while the medicine mixes, a **clock timer** to measure the time while the medicine mixes, and a large **sharps container** for pen disposal. See “Disposing of Your Used Pens and Needles” at the end of these instructions.

![Image of Needle and Tanzeum 50mg Disposable Pen]

**Tanzeum™ 50mg Disposable Pen**

This TANZEUM 50 mg pen needs **30 minutes** to let the medicine powder and water mix in Step A. This is different from the TANZEUM 30 mg pen you may have used before.

![Image of Clean, Empty Cup and Clock Timer and Large Sharps Container]

Tanzeum® [package insert]. Wilmington DE. GlaxoSmithKline LLC. 2014
Albiglutide (Tanzeum®)
Instructions for Use

STEP A
Inspect Your Pen and Mix Your Medicine

Inspect Your Pen
➢ Make sure that you have all of the supplies listed above (pen, needle, cup, timer, sharps container).
➢ Check the expiration date on the pen. **Do not use if expired.**

➢ Check that the pen has a [1] in the number window. **Do not use if the [1] is not showing.**
Albiglutide (Tanzeum®)

Instructions for Use

Twist Pen to Mix Your Medicine

➢ Hold the pen body with the clear cartridge pointing up so that you see the [1] in the window.

➢ With your other hand, twist the clear cartridge several times in the direction of the arrow (clockwise) until you feel and hear the pen “click” into place and you see the [2] in the number window. This will mix the medicine powder and liquid in the clear cartridge.

➢ Slowly and gently rock the pen side to side (like a windshield wiper) 5 times to mix the medicine. Do not shake the pen hard to avoid foaming; it may affect your dose.
Wait for Medicine to Dissolve

- Place the pen into the clean, empty cup to keep the clear cartridge pointing up.
- Set the clock timer for 30 minutes.

You must wait 30 minutes for the medicine to dissolve before continuing to Step B.
Albiglutide (Tanzeum®)
Instructions for Use

STEP B
Attach the Needle and Prepare the Pen for Injection
After the 30 minute wait, wash your hands and finish the rest of the steps right away.

Inspect Your Dissolved Medicine
➤ Again, slowly and gently rock the pen side to side (like a windshield wiper) 5 times to mix the medicine again. Do not shake the pen hard to avoid foaming; it may affect your dose.

![Repeat rocking 5 Times]

➤ Look through the viewing window to check that the liquid in the cartridge is clear and free of solid particles.

![Look for particles.]

➤ The liquid will have a yellow color and there will be large air bubbles on top of the liquid.

Tanzeum® [package insert]. Wilmington DE. GlaxoSmithKline LLC. 2014
Albiglutide (Tanzeum®)

Instructions for Use

- Hold the pen with the clear cartridge pointing up and push the needle straight down onto the clear cartridge until you hear a “click” and feel the needle “snap” down into place. This means the needle is attached.

![Image of pushing down firmly]

**Tap for Air Bubbles**

- With the needle point up, gently tap the clear cartridge 2 to 3 times to bring large air bubbles to the top.

![Image of tapping cartridge]

**Small bubbles are okay and do not need to rise to the top.**
Albiglutide (Tanzeum®)
Instructions for Use

Twist Pen to Prime the Needle

- Twist the clear cartridge several times in the direction of the arrow (clockwise) until you feel and hear the pen “click” and you see the [3] in the number window. This removes the large air bubbles from the clear cartridge. The injection button will also pop out from the bottom of the pen.

STEP C
Remove Both Needle Caps and Inject Your Medicine

Remove Needle Caps

- Carefully remove the outer needle cap, then the inner needle cap. A few drops of liquid may come out of the needle. This is normal.
Albiglutide (Tanzeum®)
Instructions for Use

Inject the Medicine

- Insert the needle into the skin on your abdomen, thigh, or upper arm and inject as shown to you by your healthcare provider.

![Injection Sites](image)

- With your thumb, press the injection button slowly and steadily to inject your medicine. The slower you press the button, the less pressure you will feel.

- Keep the injection button pressed down until you hear a “click”. After hearing the click, continue holding your thumb down on the button and then slowly count to 5 to deliver the full dose of the medicine.

![“Click”](image)

- After hearing the “click” and then slowly counting to 5, pull the needle out of your skin.
Dulaglutide (Trulicity®)

• Single-dose pen

1 Uncap the Pen
- Make sure the Pen is locked.
- Pull the Base Cap straight off and throw it away in your household trash.
- Do not put the Base Cap back on—this could damage the needle. Do not touch the needle.

2 Place and Unlock
- Place the Clear Base flat and firmly against your skin at the injection site.
- Unlock by turning the Lock Ring.

3 Press and Hold
- Press and hold the green Injection Button; you will hear a loud click.
- Continue holding the Clear Base firmly against your skin until you hear a second click. This happens when the needle starts retracting in about 5-10 seconds.
- Remove the Pen from your skin.

You will know your injection is complete when the gray plunger is visible.
SGL-2 Inhibitor
(Sodium-glucose Co-transporter 2 Inhibitor)

• Dapagliflozin (Farxiga®)
• Empagliflozin (Jardiance®)

• SGL-2 is a low-affinity, high-capacity glucose transporter located in the proximal tubule of the kidneys. It is responsible for 90% of glucose reabsorption.
SGLT-2 Inhibitor
(Sodium-glucose Co-transporter 2 Inhibitor)

• **Efficacy:** ↓A1c by 0.7% to 1.0%

• **Available Medications:**
  - Canagliflozin (Invokana®): 100 mg daily (up to 300 mg/day)
  - Dapagliflozin (Farxiga®): 5 mg daily (up to 10 mg/day) – approved 1/8/14
  - Empagliflozin (Jardiance®): 10 mg daily (up to 25 mg/day) – approved 8/1/14

• **Adverse Effects:** genital fungal infections, UTI, increased urination, hypotension, increased LDL, volume depletion
  - Small association of:
    - Increased stroke (canagliflozin), Bladder cancer (dapagliflozin)
  - Avoid in renal dysfunction
    - GFR < 60 mL/min: avoid dapagliflozin
    - GFR < 45 mL/min: avoid canagliflozin

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SGLT-2 Inhibitor ADEs

• **LDL Elevation**: dose-related increase ¹
  – Canagliflozin 100 mg: ↑ LDL 2.9%
  – Canagliflozin 300 mg: ↑ LDL 7.1%
  – Empagliflozin 10 mg: ↑ LDL 4.6%
  – Empagliflozin 25 mg: ↑ LDL 6.5%
  – Dapagliflozin 10 mg: ↑ LDL 2.9%

• **Stroke**
  – High number of CV events during the first 30 days of treatment with canagliflozin ²
  – Subsequent meta-analysis showed no further significant increase in cardiovascular adverse events during extended use ³

• **Cancer**
  – In a post-marketing surveillance program, a disproportionate amount of breast and bladder cancers were noted in patients receiving dapagliflozin
  – Neither types of cancer were previously identified as possible ADE’s in randomized trials ⁴

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Antihyperglycemic therapy in type 2 diabetes: general recommendations.

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<tr>
<td><strong>Side effects</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Costs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| Combination injectable therapy | | | |
|---|---|---|---|---| 
| **Efficacy** |
| **Hypo risk** |
| **Weight** |
| **Side effects** |
| **Costs** |

---

American Diabetes Association Dia Care 2015;38:S41-S48

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Novel Oral Anticoagulants (NOACs)

• Edoxaban (Savaysa®)
  – Oral Factor Xa inhibitor
  – Approved to reduce risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation
  – Approved to treat VTE
  – Once-daily dosing
Figure adapted from: Dipiro et al. Pharmacotherapy: A Pathophysiologic Approach, 3rd Ed. 1997.
## NOACs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Factor Inhibition</th>
<th>Indications</th>
<th>Manufacturer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dabigatran etexilate (Pradaxa®)</td>
<td>IIa (Thrombin)</td>
<td>(Oct 2010 - AFib)</td>
<td>Boehringer-Ingelheim</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(April 2014 – DVT/PE)</td>
<td></td>
</tr>
<tr>
<td>Rivaroxaban (Xarelto®)</td>
<td>Xa</td>
<td>(July 2011 - VTE px TKR/THR)</td>
<td>Janssen/Bayer</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(Nov 2011 – AFib)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(Nov 2012 – DVT/PE)</td>
<td></td>
</tr>
<tr>
<td>Apixaban (Eliquis®)</td>
<td>Xa</td>
<td>(Dec 2012 - Afib)</td>
<td>Bristol-Myers Squibb/Pfizer</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(Mar 2014 – VTE px TKR/THR)</td>
<td></td>
</tr>
<tr>
<td>Edoxaban (Savaysa®)</td>
<td>Xa</td>
<td>Jan 2015 – afib, DVT and PE</td>
<td>Daiichi Sankyo</td>
</tr>
</tbody>
</table>
Edoxaban (Savaysa®)

- **Efficacy** – similar to warfarin
- Slightly lower rate of major bleeding (afib: 6 fewer bleeds per 1000 patients/year; DVT/PE: 18 fewer bleeds per 1000 patients/year)
- **Dose**: advantage of once-daily 60 mg/d (30 mg if CrCl 15-50 ml/min)
- **Black box warning** regarding reduced efficacy in nonvalvular afib with CrCL >95 ml/min
- $280/mo (cheapest of NOACs)

### ENGAGE AF-TIMI 48

<table>
<thead>
<tr>
<th>Events</th>
<th>SAVAYS A 30 mg</th>
<th>SAVAYS A 60 mg</th>
<th>Warfarin (N=7012)</th>
<th>SAVAYS A 30 mg vs. warfarin HR (CI) p-value</th>
<th>SAVAYS A 60 mg vs. warfarin HR (CI) p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>First Stroke or SEE</td>
<td>253 (1.6)</td>
<td>182 (1.2)</td>
<td>232 (1.5)</td>
<td>1.07 (0.87, 1.31) p=0.44</td>
<td>0.79 (0.63, 0.99) p=0.017</td>
</tr>
<tr>
<td>Ischemic Stroke</td>
<td>225 (1.4)</td>
<td>135 (0.9)</td>
<td>144 (0.9)</td>
<td>1.54 (1.25, 1.90)</td>
<td>0.94 (0.75, 1.19)</td>
</tr>
<tr>
<td>Hemorrhagic Stroke</td>
<td>18 (0.1)</td>
<td>30 (0.3)</td>
<td>75 (0.5)</td>
<td>0.24 (0.14, 0.39)</td>
<td>0.52 (0.36, 0.77)</td>
</tr>
<tr>
<td>Systemic Embolism</td>
<td>10 (&lt;0.1)</td>
<td>8 (&lt;0.1)</td>
<td>13 (&lt;0.1)</td>
<td>0.75 (0.33, 1.72)</td>
<td>0.62 (0.26, 1.50)</td>
</tr>
</tbody>
</table>

Abbreviations: HR = Hazard Ratio versus Warfarin, CI = Confidence Interval, n = number of events, mITT = Modified Intent-to-Treat, N=number of patients in mITT population, SEE = Systemic Embolic Event, yr = year.

* Includes patients dose-reduced to 15 mg for the 30 mg treatment group and 30 mg for the 60 mg treatment group

† The event rate (%/yr) is calculated as number of events/subject-year exposure

‡ 97.5% CI for primary endpoint of First Stroke or SEE. 95% CI for Ischemic Stroke, Hemorrhagic Stroke or Systemic Embolism

NEJM 2013;369:2093-2104.
Edoxaban (Savaysa®)

<table>
<thead>
<tr>
<th>Category</th>
<th>SAVAYSA n/N (%/yr)</th>
<th>Warfarin n/N (%/yr)</th>
<th>Hazard Ratio and 95% CI</th>
<th>HR (96% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Overall</strong></td>
<td>296/7035 (1.57)</td>
<td>337/7036 (1.80)</td>
<td></td>
<td>0.87</td>
</tr>
<tr>
<td><strong>VKA use at randomization</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.74, 1.02</td>
</tr>
<tr>
<td>Naive (41%)</td>
<td>114/2895 (1.49)</td>
<td>158/2896 (2.12)</td>
<td></td>
<td>0.71</td>
</tr>
<tr>
<td>Experienced (59%)</td>
<td>182/4410 (1.62)</td>
<td>179/4138 (1.60)</td>
<td></td>
<td>1.01</td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;65 (26%)</td>
<td>53/1337 (1.05)</td>
<td>57/1870 (1.11)</td>
<td></td>
<td>0.94</td>
</tr>
<tr>
<td>≥65 to &lt;75 (33%)</td>
<td>101/2350 (1.53)</td>
<td>1/2346 (1.78)</td>
<td></td>
<td>0.89</td>
</tr>
<tr>
<td>≥75 (40%)</td>
<td>142/2849 (1.91)</td>
<td>168/2820 (2.31)</td>
<td></td>
<td>0.83</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male (62%)</td>
<td>171/4366 (1.45)</td>
<td>1964395 (1.68)</td>
<td></td>
<td>0.87</td>
</tr>
<tr>
<td>Female (38%)</td>
<td>125/2669 (1.76)</td>
<td>141/2641 (2.00)</td>
<td></td>
<td>0.87</td>
</tr>
<tr>
<td><strong>Weight (kg)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤60 (10%)</td>
<td>44/684 (2.53)</td>
<td>50/702 (2.31)</td>
<td></td>
<td>0.87</td>
</tr>
<tr>
<td>&gt;60 (90%)</td>
<td>252/6351 (1.47)</td>
<td>287/6335 (1.69)</td>
<td></td>
<td>0.88</td>
</tr>
<tr>
<td><strong>Prior stroke/TIA</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes (28%)</td>
<td>125/1976 (2.44)</td>
<td>145/1991 (2.85)</td>
<td></td>
<td>0.96</td>
</tr>
<tr>
<td>No (72%)</td>
<td>171/5059 (1.24)</td>
<td>192/5045 (1.41)</td>
<td></td>
<td>0.88</td>
</tr>
<tr>
<td><strong>Prior diabetes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes (36%)</td>
<td>97/2559 (1.42)</td>
<td>102/2521 (1.52)</td>
<td></td>
<td>0.94</td>
</tr>
<tr>
<td>No (64%)</td>
<td>199/4476 (1.65)</td>
<td>235/4515 (1.96)</td>
<td></td>
<td>0.84</td>
</tr>
<tr>
<td><strong>CHADS2 score</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 (47%)</td>
<td>107/3235 (1.19)</td>
<td>110/3335 (1.20)</td>
<td></td>
<td>0.99</td>
</tr>
<tr>
<td>3 (53%)</td>
<td>189/3795 (1.91)</td>
<td>227/3696 (2.39)</td>
<td></td>
<td>0.80</td>
</tr>
<tr>
<td><strong>Creatinine clearance (mL/min)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤30 (1%)</td>
<td>4/70 (2.41)</td>
<td>3/52 (2.61)</td>
<td></td>
<td>0.87</td>
</tr>
<tr>
<td>30 to 50 (19%)</td>
<td>78/1309 (2.34)</td>
<td>85/1311 (2.70)</td>
<td></td>
<td>0.87</td>
</tr>
<tr>
<td>&gt;50 to 80 (43%)</td>
<td>122/3030 (1.49)</td>
<td>176/3085 (2.17)</td>
<td></td>
<td>0.88</td>
</tr>
<tr>
<td>&gt;80 (37%)</td>
<td>92/2626 (1.28)</td>
<td>70/2607 (0.97)</td>
<td></td>
<td>1.33</td>
</tr>
<tr>
<td><strong>Geographic region</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>US (18%)</td>
<td>46/1268 (1.27)</td>
<td>55/1302 (1.53)</td>
<td></td>
<td>0.82</td>
</tr>
<tr>
<td>Outside the US (82%)</td>
<td>250/5747 (1.64)</td>
<td>282/5734 (1.87)</td>
<td></td>
<td>0.88</td>
</tr>
<tr>
<td><strong>Aspirin at randomization</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes (30%)</td>
<td>85/2070 (1.54)</td>
<td>122/2092 (2.23)</td>
<td></td>
<td>0.70</td>
</tr>
<tr>
<td>No (70%)</td>
<td>211/4985 (1.53)</td>
<td>215/4944 (1.63)</td>
<td></td>
<td>0.97</td>
</tr>
</tbody>
</table>

Savaysa package insert
Table 14.2: Primary Endpoint, Ischemic and Hemorrhagic Stroke Results

<table>
<thead>
<tr>
<th>STROKE TYPE</th>
<th>Renal Function Subgroups*</th>
<th>Treatment Arm</th>
<th>n (N)</th>
<th>Event Rate (%/yr)</th>
<th>SAVAYSA 60 mg vs. Warfarin HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRIMARY ENDPOINT (STROKE/SEE)</td>
<td>≤ 50 (Indicated Population)</td>
<td>Warfarin</td>
<td>211 (6485)</td>
<td>1.8</td>
<td>0.68 (0.55, 0.84)</td>
</tr>
<tr>
<td></td>
<td>&gt; 50 to ≤ 80</td>
<td>Warfarin</td>
<td>45 (1377)</td>
<td>1.8</td>
<td>0.90 (0.60, 1.34)</td>
</tr>
<tr>
<td></td>
<td>&gt; 80 to &lt; 95</td>
<td>Warfarin</td>
<td>135 (3033)</td>
<td>2.0</td>
<td></td>
</tr>
<tr>
<td>&gt; &gt; 95 **</td>
<td>Warfarin</td>
<td>21 (1227)</td>
<td>0.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ISCHEMIC STROKE</td>
<td>≤ 50 (Indicated Population)</td>
<td>Warfarin</td>
<td>129 (5485)</td>
<td>1.1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt; 50 to ≤ 80</td>
<td>Warfarin</td>
<td>31 (1372)</td>
<td>1.2</td>
<td>0.66 (0.46, 1.04)</td>
</tr>
<tr>
<td></td>
<td>&gt; 80 to &lt; 95</td>
<td>Warfarin</td>
<td>83 (3033)</td>
<td>1.2</td>
<td></td>
</tr>
<tr>
<td>&gt; &gt; 95 **</td>
<td>Warfarin</td>
<td>15 (1227)</td>
<td>0.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HEMORRHAGIC STROKE</td>
<td>≤ 50 (Indicated Population)</td>
<td>Warfarin</td>
<td>70 (6485)</td>
<td>0.6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt; 50 to ≤ 80</td>
<td>Warfarin</td>
<td>12 (1372)</td>
<td>0.5</td>
<td>0.66 (0.32, 1.36)</td>
</tr>
<tr>
<td></td>
<td>&gt; 80 to &lt; 95</td>
<td>Warfarin</td>
<td>45 (3033)</td>
<td>0.7</td>
<td></td>
</tr>
<tr>
<td>&gt; &gt; 95 **</td>
<td>Warfarin</td>
<td>6 (1029)</td>
<td>0.2</td>
<td>0.76 (0.24, 2.38)</td>
<td></td>
</tr>
</tbody>
</table>

*SAVAYSA 60 mg

**SAVAYSA 60 mg vs. Warfarin HR (95% CI)
### Transition to SAVAYSA

<table>
<thead>
<tr>
<th>From</th>
<th>To</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warfarin or other Vitamin K Antagonists</td>
<td>SAVAYSA</td>
<td>Discontinue warfarin and start SAVAYSA when the INR is $\leq 2.5$</td>
</tr>
<tr>
<td>Oral anticoagulants other than warfarin or other Vitamin K Antagonists</td>
<td>SAVAYSA</td>
<td>Discontinue current oral anticoagulant and start SAVAYSA at the time of the next scheduled dose of the other oral anticoagulant</td>
</tr>
<tr>
<td>Low Molecular Weight Heparin (LMWH)</td>
<td>SAVAYSA</td>
<td>Discontinue LMWH and start SAVAYSA at the time of the next scheduled administration of LMWH</td>
</tr>
<tr>
<td>Unfractionated heparin</td>
<td>SAVAYSA</td>
<td>Discontinue the infusion and start SAVAYSA 4 hours later</td>
</tr>
</tbody>
</table>

### Transition from SAVAYSA

<table>
<thead>
<tr>
<th>From</th>
<th>To</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAVAYSA</td>
<td>Warfarin</td>
<td><strong>Oral option:</strong> For patients taking 60 mg of SAVAYSA, reduce the dose to 30 mg and begin warfarin concomitantly. For patients receiving 30 mg of SAVAYSA, reduce the dose to 15 mg and begin warfarin concomitantly. INR must be measured at least weekly and just prior to the daily dose of SAVAYSA to minimize the influence of SAVAYSA on INR measurements. Once a stable INR $\geq 2.0$ is achieved, SAVAYSA should be discontinued and the warfarin continued</td>
</tr>
<tr>
<td>SAVAYSA</td>
<td>Warfarin</td>
<td><strong>Parenteral option:</strong> Discontinue SAVAYSA and administer a parenteral anticoagulant and warfarin at the time of the next scheduled SAVAYSA dose. Once a stable INR $\geq 2.0$ is achieved the parenteral anticoagulant should be discontinued and the warfarin continued</td>
</tr>
<tr>
<td>SAVAYSA</td>
<td>Non-Vitamin-K-Dependent Oral anticoagulants</td>
<td>Discontinue SAVAYSA and start the other oral anticoagulant at the time of the next dose of SAVAYSA</td>
</tr>
<tr>
<td>SAVAYSA</td>
<td>Parenteral anticoagulants</td>
<td>Discontinue SAVAYSA and start the parenteral anticoagulant at the time of the next dose of SAVAYSA</td>
</tr>
</tbody>
</table>

Abbreviations: INR=International Normalized Ratio
<table>
<thead>
<tr>
<th></th>
<th>Warfarin (Coumadin*)</th>
<th>Dabigatran (Pradaxa*)</th>
<th>Rivaroxaban (Xarelto*)</th>
<th>Apixaban (Eliquis*)</th>
<th>Edoxaban (Savaysa*)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Factor Inhibition</strong></td>
<td>II, VII, IX, X Proteins C and S</td>
<td>IIa (Thrombin)</td>
<td>Xa</td>
<td>Xa</td>
<td>Xa</td>
</tr>
</tbody>
</table>
| **FDA-Labeled Indications** | • Atrial fibrillation  
• AVR/MVR  
• Prevent systemic embolism post-MI  
• VTE treatment | • Atrial fibrillation  
• Post-op VTE prophylaxis (TKR/THR)  
• VTE treatment | • Atrial fibrillation  
• Post-op VTE prophylaxis (TKR/THR) | • Atrial fibrillation  
• VTE treatment |
| **Dosing** | Daily | BID | Daily (BID x 3 wks for VTE) | BID | Daily |
| **Reversibility** | Vitamin K, Kcentra™ | None | None | None | None |
| **Questionable or Poor Candidates** | • Erratic INR  
• Alcoholism  
• Significant drug interactions  
• Difficulty with complex regimen  
• Poor adherence to monitoring | • Poor adherence  
• CrCl < 30 ml/min  
• Age ≥ 75  
• CHADS₂ ≥ 3  
• Heart valve | • CrCl < 30 ml/min  
• Hepatic impairment  
• HIV  
• Heart valve  
• Bilateral THR  
• Feeding tubes | • Poor adherence  
• Heart valve  
• Dual P-gp and CYP3A4 inducers | • CrCl >95 ml/min |
| **Potential Advantages** | • Years of experience  
• Objective measurement of efficacy/safety | • Slightly better than warfarin at preventing stroke (a fib) | • VTE | • Slightly better than warfarin at preventing stroke (afib)  
• Less bleeding than warfarin | • VTE  
• Least costly of NOACs |
## NOACs Place in Therapy

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>• No monitoring</td>
<td>• No monitoring</td>
</tr>
<tr>
<td>• Fewer drug/diet interactions</td>
<td>• Cost (edoxaban is cheapest - ~$277/mo, vs $300+)</td>
</tr>
<tr>
<td>• Faster onset</td>
<td>• Adherence is critical due to short half-life</td>
</tr>
<tr>
<td>• Stroke prevention in afib</td>
<td>• Renal dosing adjustments</td>
</tr>
<tr>
<td>– Apixaban and dabigatran superior to warfarin</td>
<td>• Adverse effects</td>
</tr>
<tr>
<td>– Rivaroxaban, edoxaban similar</td>
<td>– Dabigatran: GI bleeding</td>
</tr>
<tr>
<td>• VTE <em>prevention</em> in TKA/THA</td>
<td>• Reversibility issues and hemorrhagic events</td>
</tr>
<tr>
<td>– Rivaroxaban or apixaban</td>
<td>• New agents, less clinical experience</td>
</tr>
<tr>
<td>• Treatment of DVT/PE</td>
<td></td>
</tr>
<tr>
<td>– Rivaroxaban and dabigatran</td>
<td></td>
</tr>
<tr>
<td>– Once-daily dosing (rivaroxaban or edoxaban)</td>
<td></td>
</tr>
<tr>
<td>• Decreased intracranial bleeding</td>
<td></td>
</tr>
</tbody>
</table>
Antimicrobials

• 2 new IV drugs for acute bacterial skin and skin structure infections
  – Dalbavancin (Dalvance®)
  – Oritivancin (Orbactiv®)
• Lipoglycopeptides that interfere with cell wall biosynthesis
• Long-acting!
• Indicated for treatment of acute bacterial skin and skin structure infections caused by susceptible isolates of Gram + infections
  – Staph aureus (inc. MRSA)
  – Srep. (various)
  – Enterococcus faecalis (vanco-susceptible only)
Dalbavancin (Dalvance®)

• Dosing: two-dose regimen of 1000 mg followed one week later by 500 mg (administered over 30 min IV infusion)

• DISCOVER 1 and DISCOVER 2 trials (NEJM 2014;370:2169-79)
  – Dalbavancin IV day 1 and 8 vs vancomycin (3 days min) +/- switch to linezolid
  – Treatment of acute bacterial skin and skin-structure infection
    • Abscess, surgical site infection, cellulitis
Dalbavancin (Dalvance®)

Table 6. Clinical Response Rates in ABSSSI Trials at 48-72 Hours after Initiation of Therapy

<table>
<thead>
<tr>
<th>Trial</th>
<th>Dalvance n/N (%)</th>
<th>Vancomycin/Linezolid n/N (%)</th>
<th>Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial 1</td>
<td>240/298 (83.2%)</td>
<td>233/285 (81.8%)</td>
<td>1.5% (-4.6, 7.6)</td>
</tr>
<tr>
<td>Trial 2</td>
<td>265/371 (76.8%)</td>
<td>268/368 (78.3%)</td>
<td>-1.5% (-7.4, 4.6)</td>
</tr>
</tbody>
</table>

Table 7. Patients in ABSSSI Trials with Reduction in Lesion Area of 20% or Greater at 48-72 Hours after Initiation of Therapy

<table>
<thead>
<tr>
<th>Trial</th>
<th>Dalvance n/N (%)</th>
<th>Vancomycin/Linezolid n/N (%)</th>
<th>Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial 1</td>
<td>259/288 (89.9%)</td>
<td>259/285 (90.0%)</td>
<td>-0.1% (-5.7, 4.0)</td>
</tr>
<tr>
<td>Trial 2</td>
<td>325/371 (87.6%)</td>
<td>316/368 (85.9%)</td>
<td>1.7% (-3.2, 6.7)</td>
</tr>
</tbody>
</table>

Table 3. Additional Secondary Analyses of Treatment Success.†

<table>
<thead>
<tr>
<th>Variable</th>
<th>Dalbavancin (N=652)</th>
<th>Vancomycin–Linezolid (N=651)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>number/total number</td>
<td>percent</td>
</tr>
<tr>
<td>Clinical response according to infection type</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cellulitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>At 48–72 hr</td>
<td>281/354 (79.4)</td>
<td>269/349 (77.1)</td>
</tr>
<tr>
<td>At end of therapy</td>
<td>294/324 (90.7)</td>
<td>276/301 (91.7)</td>
</tr>
<tr>
<td>Major abscess</td>
<td></td>
<td></td>
</tr>
<tr>
<td>At 48–72 hr</td>
<td>133/163 (81.6)</td>
<td>149/173 (86.1)</td>
</tr>
<tr>
<td>At end of therapy</td>
<td>125/133 (94.0)</td>
<td>133/139 (95.7)</td>
</tr>
<tr>
<td>Traumatic wound or surgical-site infection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>At 48–72 hr</td>
<td>111/142 (78.2)</td>
<td>103/131 (78.6)</td>
</tr>
<tr>
<td>At end of therapy</td>
<td>98/113 (86.7)</td>
<td>93/105 (88.6)</td>
</tr>
<tr>
<td>Investigator-assessed clinical response at end of therapy according to baseline pathogen†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>187/191 (97.9)</td>
<td>171/177 (96.6)</td>
</tr>
<tr>
<td>Methicillin-resistant S. aureus</td>
<td>72/74 (97.3)</td>
<td>49/50 (98.0)</td>
</tr>
<tr>
<td>Streptococcus pyogenes</td>
<td>19/19 (100.0)</td>
<td>12/13 (92.3)</td>
</tr>
<tr>
<td>Clinical response at end of therapy according to diabetes mellitus status at baseline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>60/71 (84.5)</td>
<td>67/76 (88.2)</td>
</tr>
<tr>
<td>No diabetes mellitus</td>
<td>457/499 (91.6)</td>
<td>435/469 (92.7)</td>
</tr>
<tr>
<td>Clinical response at end of therapy according to SIRS status at baseline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SIRS</td>
<td>257/296 (86.8)</td>
<td>263/290 (90.7)</td>
</tr>
<tr>
<td>No SIRS</td>
<td>260/274 (94.9)</td>
<td>239/255 (93.7)</td>
</tr>
</tbody>
</table>

* The success rates at 48 to 72 hours were assessed in the intention-to-treat population, and the success rates at the end of therapy were assessed in the clinical per-protocol population of patients.
† The success rates at the end of therapy were assessed in the subgroup of patients with monomicrobial infection in the microbiologic per-protocol population.

(NEJM 2014;370:2169-79)
Oritavancin (Orbactiv®)

• Dosing: single 1200 mg IV dose (administered over 3 hrs)

• SOLO I trial (NEJM 2014;370:2180-90)
  – Oritavancin 1200 mg IV x 1 vs vancomycin 7-10 days in acute bacterial skin/skin-structure infections (wound infection, cellulitis, major cutaneous abscess)
  – Primary efficacy outcome: composite of assessment of clinical cure post-therapy and decrease in lesion area by 20%+ from baseline to early clinical eval
Oritavancin (Orbactiv®)

Table 5: Clinical Response Rates in ABSSSI Trials using Responders$^{1,2}$ at 48-72 Hours after Initiation of Therapy

<table>
<thead>
<tr>
<th></th>
<th>ORBACTIV n/N (%)</th>
<th>Vancomycin n/N (%)</th>
<th>Difference (95% CI)$^{3}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial 1</td>
<td>391/475 (82.8)</td>
<td>378/479 (78.9)</td>
<td>3.4 (-1.6, 8.4)</td>
</tr>
<tr>
<td>Trial 2</td>
<td>403/503 (80.1)</td>
<td>416/503 (82.9)</td>
<td>-2.7 (-7.5, 2.0)</td>
</tr>
</tbody>
</table>

Table 6: Clinical Response Rates$^{1}$ in ABSSSI Trials using Reduction in Lesion Area of 20% or Greater at 48-72 Hours after Initiation of Therapy

<table>
<thead>
<tr>
<th></th>
<th>ORBACTIV n/N (%)</th>
<th>Vancomycin n/N (%)</th>
<th>Difference (95% CI)$^{2}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial 1</td>
<td>413/475 (85.9)</td>
<td>397/479 (82.9)</td>
<td>4.1 (-0.5, 8.6)</td>
</tr>
<tr>
<td>Trial 2</td>
<td>432/503 (85.9)</td>
<td>426/503 (85.3)</td>
<td>0.6 (-3.7, 5.0)</td>
</tr>
</tbody>
</table>

Table 8: Outcomes by Baseline Pathogen (microFF)

<table>
<thead>
<tr>
<th>Pathogen$^{4}$</th>
<th>Early Clinical Response$^{5}$</th>
<th>≥ 50% reduction in lesion size$^{6}$</th>
<th>Clinical Success$^{7}$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ORBACTIV n/N (%)</td>
<td>Vancomycin n/N (%)</td>
<td>ORBACTIV n/N (%)</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>38/475 (80.3)</td>
<td>39/475 (82.5)</td>
<td>41/475 (86.2)</td>
</tr>
<tr>
<td>Methicillin-resistant Staphylococcus aureus</td>
<td>22/246 (89.1)</td>
<td>23/272 (85.3)</td>
<td>21/246 (86.6)</td>
</tr>
<tr>
<td>Methicillin-susceptible Staphylococcus aureus</td>
<td>18/198 (94.4)</td>
<td>19/204 (93.3)</td>
<td>17/198 (90.3)</td>
</tr>
<tr>
<td>Streptococcus pyogenes</td>
<td>21/31 (67.7)</td>
<td>20/32 (62.5)</td>
<td>24/31 (77.4)</td>
</tr>
<tr>
<td>Streptococcus agalactiae</td>
<td>7/10 (70.0)</td>
<td>6/10 (60.0)</td>
<td>12/10 (100.0)</td>
</tr>
<tr>
<td>Streptococcus dysgalactiae</td>
<td>7/9 (77.8)</td>
<td>6/9 (66.7)</td>
<td>6/9 (66.7)</td>
</tr>
<tr>
<td>Streptococcus anginosus group</td>
<td>28/35 (80.0)</td>
<td>30/35 (85.7)</td>
<td>28/35 (80.0)</td>
</tr>
</tbody>
</table>

Orbactiv package insert
Dalbavancin and Oritavancin

Table 1: Incidence of Selected Adverse Reactions Occurring in ≥ 1.5% of Patients Receiving ORBACTIV in the Pooled ABSSSI Clinical Trials

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>ORBACTIV N=976 (%)</th>
<th>Vancomycin N=983 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>36 (3.7)</td>
<td>32 (3.4)</td>
</tr>
<tr>
<td>Nausea</td>
<td>97 (9.9)</td>
<td>103 (10.5)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>45 (4.6)</td>
<td>46 (4.7)</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dizziness</td>
<td>26 (2.7)</td>
<td>26 (2.6)</td>
</tr>
<tr>
<td>Headache</td>
<td>69 (7.1)</td>
<td>66 (6.7)</td>
</tr>
<tr>
<td>General disorders and administration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infusion site phlebitis</td>
<td>24 (2.5)</td>
<td>15 (1.5)</td>
</tr>
<tr>
<td>Infusion site reaction</td>
<td>19 (1.9)</td>
<td>34 (3.5)</td>
</tr>
<tr>
<td>Infections and infestations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abscess (limb and subcutaneous)</td>
<td>37 (3.8)</td>
<td>23 (2.3)</td>
</tr>
<tr>
<td>Investigations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alkaline aminotransferase increased</td>
<td>27 (2.8)</td>
<td>15 (1.5)</td>
</tr>
<tr>
<td>Aspartate aminotransferase increased</td>
<td>18 (1.8)</td>
<td>15 (1.5)</td>
</tr>
<tr>
<td>Cardiac disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tachycardia</td>
<td>24 (2.5)</td>
<td>11 (1.1)</td>
</tr>
</tbody>
</table>

Table 1. Selected Adverse Reactions in Phase 2/3 Trials (Number (% of Patients)

<table>
<thead>
<tr>
<th></th>
<th>Dalbavancin (N = 1778)</th>
<th>Comparator* (N = 1224)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>98 (5.5)</td>
<td>78 (6.4)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>50 (2.8)</td>
<td>37 (3.0)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>79 (4.4)</td>
<td>72 (5.9)</td>
</tr>
<tr>
<td>Headache</td>
<td>83 (4.7)</td>
<td>59 (4.8)</td>
</tr>
<tr>
<td>Rash</td>
<td>48 (2.7)</td>
<td>30 (2.4)</td>
</tr>
<tr>
<td>Pruritus</td>
<td>38 (2.1)</td>
<td>41 (3.3)</td>
</tr>
</tbody>
</table>

*Comparators included linezolid, ceftazolin, cephalexin, and vancomycin.
# Late Stage 2015 Drugs to Watch

<table>
<thead>
<tr>
<th>Drug name</th>
<th>Sponsors</th>
<th>Properties</th>
<th>Indication</th>
<th>Event due in 2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>Secukinumab</td>
<td>Novartis</td>
<td>IL-17-specific antibody</td>
<td>Psoriasis</td>
<td>PDUFA decision in January</td>
</tr>
<tr>
<td>Palbociclib</td>
<td>Pfizer</td>
<td>CDK inhibitor</td>
<td>Breast cancer</td>
<td>PDUFA decision in April</td>
</tr>
<tr>
<td>Toujeo</td>
<td>Sanofi</td>
<td>Insulin glargine</td>
<td>Diabetes</td>
<td>PDUFA decision in May</td>
</tr>
<tr>
<td>Talimogene laherparevec</td>
<td>Amgen</td>
<td>Oncolytic virus</td>
<td>Melanoma</td>
<td>PDUFA decision in July</td>
</tr>
<tr>
<td>Evolocumab</td>
<td>Amgen</td>
<td>PCSK9-specific antibody</td>
<td>Hypercholesterolaemia</td>
<td>PDUFA decision by September</td>
</tr>
<tr>
<td>Lumacaftor plus ivacaftor</td>
<td>Vertex</td>
<td>CFTR corrector and CFTR potentiator</td>
<td>Cystic fibrosis</td>
<td>PDUFA decision in November</td>
</tr>
<tr>
<td>Alirocumab</td>
<td>Sanofi/Regeneron</td>
<td>PCSK9-specific antibody</td>
<td>Hypercholesterolaemia</td>
<td>PDUFA decision</td>
</tr>
<tr>
<td>LCZ696</td>
<td>Novartis</td>
<td>Angiotensin-receptor inhibitor and neutral endopeptidase inhibitor</td>
<td>Congestive heart failure</td>
<td>PDUFA decision</td>
</tr>
<tr>
<td>Ryzodeg</td>
<td>Novo Nordisk</td>
<td>Co-formulation of insulin degludec and insulin aspart</td>
<td>Diabetes</td>
<td>Cardiovascular outcomes data, to address 2012 complete response letter</td>
</tr>
<tr>
<td>Anacetrapib</td>
<td>Merck &amp; Co.</td>
<td>CETP inhibitor</td>
<td>Hypercholesterolaemia</td>
<td>Interim efficacy analysis of Phase III trial</td>
</tr>
<tr>
<td>Ocrelizumab</td>
<td>Roche</td>
<td>CD20-specific antibody</td>
<td>Multiple sclerosis</td>
<td>Top-line Phase III data</td>
</tr>
<tr>
<td>Baricitinib</td>
<td>Eli Lilly</td>
<td>JAK1- and JAK2- inhibitor</td>
<td>Rheumatoid arthritis</td>
<td>Top-line Phase III data</td>
</tr>
</tbody>
</table>

Event data are from BioMedTracker. CDK, cyclin-dependent kinase; CETP, cholesteryl ester transfer protein; CFTR, cystic fibrosis transmembrane conductance regulator; IL-17, interleukin-17; JAK, Janus kinase; PCSK9, proprotein convertase subtilisin kexin type 9; PDUFA, Prescription Drug User Fee Act.