New Drug Approvals

2014

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Program Objectives

By the end of the presentation, the pharmacist will be able to:

- Identify the new molecular entities and biologic medications approved by the FDA in 2014.
- List at least three new orphan drugs and their indications.
- Describe the place in therapy of at least five new medications approved in 2014.
- List new medications with serious medication safety concerns and describe REMS programs associated with these medications.
- Discuss emerging trends in new drug approvals.
Disclosures

- Nothing to disclose
New Drug Application (NDA) Chemical Types

1. New molecular entity (NME) – new to the USA market
2. New ester, new salt, or other noncovalent derivative
3. New formulation
4. New combination
5. New manufacturer
6. New indication
7. Drug already marketed, but without an approved NDA
8. OTC (over-the-counter) switch

Review Classifications

P - Priority review drug: A drug that appears to represent an advance over available therapy

S - Standard review drug: A drug that appears to have therapeutic qualities similar to those of an already marketed drug

O - Orphan drug: A product that treats a rare disease affecting fewer than 200,000 Americans
2014 NDA Approvals (NMEs/BLAs)

- Farxiga (dapagliflozin) **P**
- Hetlioz (tasimelteon) **P O**
- Vimizim (elosulfase alfa) **O**
- Northera (droxidopa) **P O**
- Myalept (metreleptin) **O**
- Neuraceq (florbetaben)
- Impavido (miltefosine) **P O**
- Otezla (apremilast)
- Tanzeum (albiglutide)
- Cyramza (ramucirumab) **O**
- Sylvant (siltuximab) **O**
- Zykadia (ceritinib) **P O**
- Zontivity (vorapaxar sulfate)
- Entyvio (vedolizumab)
- Dalvance (dalbavancin hydrochloride) **P**
- Jublia (efinconazole)
- Sivextro (tedizolid phosphate) **P**
- Beleodaq (belinostat) **P O**
- Kerydin (tavaborole)
- Zydelig (idelalisib) **P O**
- Striverdi Respimat (olodaterol respimat)
- Jardiance (empagliflozin)
- Orbactiv (oritavancin diphosphate)
- Belsomra (surovexant)
- Plegridy (peginterferon beta-1a)
- Cerdelga (eliglustat tartrate) **P O**
- Keytruda (pembrolizumab) **O**
- Movantik (naloxegol) **P**
- Trulicity (dulaglutide)
- Lumason (sulfur hexafluoride lipid-type-A microspheres)
- Akynzeo (netupitant/palonosetron)
- Harvoni (ledipasvir/sofosbuvir) **P**
- Esbriet (pirfenidone) **O**
- Ofev (nintedanib) **O**
- Blincyto (blinatumomab) **O**
- Xtoro (finafloxacin)
- Lynparza (olaparib) **P O**
- Veikira Pak (ombitasivir, paritaprevir, ritonavir, dasabuvir)
- Zerbaxa (ceftolozane/tazobactam)
- Rapivab (peramivir)
- Opdivo (nivolumab)

**O** = Orphan; **P** = Priority Review; **Red** = BLA
Pharmaceutical Company Trends

Exhibit 4

NMEs + NBEs approved

Other companies

Historic big pharma*

*ABBV, AMGN, AZN, BAY, BMY, GSK, JNJ, LLY, MRK, NVS, PFE, ROC, SNY

NEW AGENTS FOR TYPE 2 DIABETES MELLITUS

Dapagliflozin
Empagliflozin
Albiglutide
Duraglutide
# Sodium-Glucose Co-Transporter 2 Inhibitors

## Dapagliflozin (Farziga®)
* AstraZeneca/BMS

- **Approved by FDA 1/8/2014**
- **Dose**
  - Starting dose: 5mg PO once daily in the AM (with/without food)
  - Increase dose to 10mg once daily if necessary
  - Avoid use if eGFR < 60 mL/min/1.73m²
- **ADEs**
  - Most common - female genital mycotic infections (7-8%), nasopharyngitis (6-7%), UTI (4-6%)
  - **Precautions** – volume contraction/hypotension, incre. LDL-C, bladder cancer (0.17% vs 0.03% with placebo)
- **DI**
  - Urine glucose tests, 1,5-AG assay (assessing glycemic control)
- **Cost**
  - $9.35/tablet (5mg or 10mg)
  - $280/month

## Empagliflozin (Jardiance®)
* Boehringer Ingelheim

- **Approved by FDA 8/1/2014**
- **Dose**
  - Starting dose: 10mg tablet once daily in the AM
  - Increase to 25mg once daily if necessary
  - Not for patients with eGFR < 45 mL/min/1.73m²
- **ADEs**
  - Most common – UTI (7-9%), female genital mycotic infections (5-6%)
  - **Precautions** – volume depletion/hypotension, hypoglycemia, incre. LDL-C
- **DI**
  - Diuretics, insulin or insulin secretagogues
  - Urine glucose tests, 1,5-AG assay (assessing glycemic control)
- **Cost**
  - $9.02/tablet (10mg or 25mg)
  - $270/month
# Glucagon-like Peptide 1 Receptor Agonists

<table>
<thead>
<tr>
<th><strong>Albiglutide (Tanzeum®)</strong></th>
<th><strong>Dulaglutide (Trulicity®)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GlaxoSmithKline</strong></td>
<td><strong>Eli Lilly</strong></td>
</tr>
<tr>
<td><strong>Approved by FDA 4/15/2014</strong></td>
<td><strong>Approved by FDA 9/18/2014</strong></td>
</tr>
<tr>
<td><strong>Dose</strong></td>
<td><strong>Dose</strong></td>
</tr>
<tr>
<td>▪ Start at 30mg SQ once weekly</td>
<td>▪ Start at 0.75mg SC once weekly</td>
</tr>
<tr>
<td>▪ Can titrate to 50mg once weekly</td>
<td>▪ Can titrate to 1.5mg once weekly</td>
</tr>
<tr>
<td><strong>ADEs</strong></td>
<td><strong>ADEs</strong></td>
</tr>
<tr>
<td><strong>Most common (10-15%)</strong> - URI,</td>
<td><strong>Most common (&gt;5%)</strong> – nausea,</td>
</tr>
<tr>
<td>diarrhea, nausea, injection site</td>
<td>diarrhea, vomiting, abdom pain</td>
</tr>
<tr>
<td>reaction</td>
<td><strong>BW</strong>: thyroid C-cell tumors in animals;</td>
</tr>
<tr>
<td><strong>BW</strong>: thyroid C-cell tumors in animals;</td>
<td>contraindicated in patients with</td>
</tr>
<tr>
<td>contraindicated in patients with</td>
<td>medullary thyroid CA or multiple</td>
</tr>
<tr>
<td>medullary thyroid CA or multiple</td>
<td>endocrine neoplasia syndrome type 2</td>
</tr>
<tr>
<td>endocrine neoplasia syndrome type 2</td>
<td><strong>REMS</strong>: Communications with</td>
</tr>
<tr>
<td><strong>REMS</strong>: Communications with</td>
<td>healthcare providers</td>
</tr>
<tr>
<td>healthcare providers</td>
<td><strong>DI</strong></td>
</tr>
<tr>
<td>Slows gastric emptying and can reduce rate of absorption of PO meds</td>
<td>Slows gastric emptying and can reduce rate of absorption of PO meds</td>
</tr>
<tr>
<td><strong>Cost</strong></td>
<td><strong>Cost</strong></td>
</tr>
<tr>
<td>Available as pen injectors – 30mg/0.5mL or 50mg/0.5mL $20/pen</td>
<td>Available as pen injectors – 0.75mg/0.5mL or 1.5mg/0.5mL $30/pen</td>
</tr>
</tbody>
</table>
NEW AGENTS FOR INSOMNIA

Tasimelteon

Surovexant
**Tasimelteon (Hetlioz®) by Vanda**

| MOA & Indication | Selective melatonin receptor agonist (MT₁ and MT₂)  
Non-24-hour sleep-wake disorder |
|------------------|--------------------------------------------------|
| Dose & Administration | 20mg PO prior to bedtime, at the same time every night  
Food reduces effect – take on empty stomach |
| Adverse Effects | **Most common (>5%):** headache, increased alanine aminotransferase, nightmares or unusual dreams, URI or UTI  
6% of patients d/c therapy due to adverse effects |
| Place in Therapy | Melatonin – non Rx  
Ramelteon – for insomnia characterized by difficulty with sleep onset  
Tasimelteon – higher affinity for MT₂ (circadian rhythm regulation) |
| Cost | Approx. $60,000/year  
Avail through specialty pharmacies |

- 50-70% of blind people have non-24-hour sleep-wake disorder; longer sleep onset and daytime sleepiness is often present.

- Melatonin often used for hypnotic effects and ability to accelerate sleep onset.
**Surovexant (Belsomra®) by Merck**

| MOA & Indication | Orexin receptor antagonist – first in class  
| Treatment of insomnia due to delay in sleep onset and/or sleep maintenance |
| Dose & Administration | Usual dose: 10mg within 30 minutes of bedtime  
| | Max dose: 20mg/day  
| | With CYP3A inhibitors: 5-10 mg |
| Adverse Effects | Somnolence - 7% vs 3% with placebo  
| | Less day-time drowsiness/memory impairment expected |
| Place in Therapy | No comparison trials with available insomnia meds  
| | 2 R/DB/PC 3-month trials in adults and elderly – SS improvement in sleep onset and sleep duration vs placebo |
| Cost | Avail as 5mg, 10mg, 15mg and 20mg tablets  
| | Release expected early 2015 – DEA scheduling as CIV |
# NEW AGENTS FOR ONCOLOGY

<table>
<thead>
<tr>
<th>New Medication</th>
<th>Type of Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Belinostat</td>
<td>Peripheral T-cell Lymphoma</td>
</tr>
<tr>
<td>Blinatumomab</td>
<td>Acute Lymphoblastic Leukemia</td>
</tr>
<tr>
<td>Ceritinib</td>
<td>Lung Cancer</td>
</tr>
<tr>
<td>Idelalisib</td>
<td>CLL, NHL, Lymphocytic Lymphoma</td>
</tr>
<tr>
<td>Pembrolizumab</td>
<td>Melanoma</td>
</tr>
<tr>
<td>Nivolumab</td>
<td>Melanoma</td>
</tr>
<tr>
<td>Olaparib</td>
<td>Ovarian Cancer</td>
</tr>
<tr>
<td>Ramucirumab</td>
<td>Gastric Cancer; Lung Cancer</td>
</tr>
</tbody>
</table>
## Belinostat (Beleodaq®) by Spectrum

| MOA & Indication | Histone deacetylase inhibitor  
| Treatment of peripheral T-cell lymphoma (relapsed or refractory) |
|------------------|-------------------------------------------------------------------------------|
| **Dose & Administration** | • 1000 mg/m² IV infusion once daily over 30 minutes  
| | • Admin on days 1-5 of a 21-day cycle  
| | • Continue until disease progression or unacceptable toxicity  
| | • Decrease dose with reduced UGT1A1 activity; hematologic toxicity; severe nonhematologic toxicity |
| **Adverse Effects** | **Most common (>25%):** nausea, fatigue, pyrexia, anemia, vomiting  
| | **Warnings:** thrombocytopenia, leukopenia, anemia, serious infections, hepatotoxicity, tumor lysis syndrome, embryo-fetal toxicity |
| **Response** | 120 patients – 25.8% with Complete + Partial Response  
| | Median duration of response = 8.4 months (95% CI: 4.5-29.4) |
| **Cost** | $1500/500mg vial |
**Blinatuzumab (Blincyto®) by Onyx/Amgen**

| MOA & Indication | BiTE immunotherapy for Acute Lymphoblastic Leukemia  
|                  | • *bi*specific CD19-directed CD3 *T*-cell *engager*  
|                  | • first in class |
| Dose & Administration | • 4 weeks of continuous IV infusion  
|                    | • Inpatient management – days 1-9 (Cycle 1) and days 1-2 (Cycle 2)  
|                    | • **Cycle 1**: 9 mcg/day (days 1-7), then 28 mcg/day (days 8-28)  
|                    | • 2-weeks no treatment before Cycle 2  
|                    | • **Cycles 2+**: 28 mcg/day (days 1-28)  
|                    | • IV solution stabilizer used to coat prefilled IV bag before adding drug  
|                    | • **Premed**: dexamethasone IV prior to dose 1 and step dose on day 8 |
| Adverse Effects | **Common reactions (> 20%)**: pyrexia, headache, peripheral edema, febrile neutropenia, nausea, hypokalemia, tremor, rash, constipation  
|                  | **BW & REMS**: Life-threatening cytokine release syndrome, neurologic toxicities; prep and admin errors |
| Response | OL/MC/single-arm study in relapsed/refractory patients (n=185)  
|           | 41% complete remission with 2 cycles |
| Cost | $3178 per 35mcg kit |
## Ceritinib (Zykadia®) by Novartis

<table>
<thead>
<tr>
<th>MOA &amp; Indication</th>
<th>Tyrosine kinase inhibitor ALK+ metastatic non-small cell lung cancer resist/intolerant to crizotinib</th>
</tr>
</thead>
</table>
| Dose & Administration | - 750mg orally once daily  
- Admin at least 2 hours before/after meals  
- Reduce dose/DC if persistent GI symptoms, other toxicities |
| Adverse Effects | **Common (>25%):** D/C/N/V, increased transaminases, abdominal pain, fatigue, anorexia  
**Warnings:** GI toxicity, hepatotoxicity, lung-disease, QT prolongation, hyperglycemia, bradycardia, embryofetal toxicity |
| Response | OL/MC/single-arm study in pts intolerant/progressed on crizotinib (n=163)  
Complete Response = 2.5%  
Partial Response = 41%  
Median Response = 7.1 months |
| Cost | $90 per 150mg capsule  
$13,500/month |
**Idelalisib (Zydelig®) by Gilead Sciences**

<table>
<thead>
<tr>
<th>MOA &amp; Indication</th>
<th>Kinase inhibitor – phosphoinositide 3 kinase (PI3k) Treatment of relapsed chronic lymphocytic leukemia, follicular B-cell non-Hodgkin lymphoma or small lymphocytic lymphoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose &amp; Administration</td>
<td>Starting dose - 150mg PO twice daily Modify dose based on adverse reactions (50% of patients)</td>
</tr>
</tbody>
</table>
| Adverse Effects | **Common (≥20%):** D/N. pyrexia, fatigue, cough, pneumonia, abdominal pain, chills, rash  
**Lab Abnormalities (≥30%):** neutropenia, hypertriglyceridemia, hyperglycemia, ALT and AST elevations  
**BW:** Fatal and/or serious hepatotoxicity (14%); diarrhea or colitis (14%); pneumonitis, or intestinal perforation  
**REMS:** communication with healthcare providers, patient fact sheet |
| Response | Relapsed CLL (n=220): PFS 10.7+ vs 5.5 months (placebo)  
Relapsed B-cell NHL (n=72): Overall Response 54%; median duration 14.8 months  
Relapsed SLL (n=26): Overall Response 58%; med dur 12 mon |
| Cost | $120 per tab (100mg or 150mg); $7200/month |
# Human Programmed Death Receptor-1 (PD-1) Blocking Antibodies for Melanoma

## Pembrolizumab (Keytruda®)
*Merck*

- **Approved by FDA**: 9/4/2014
- **Dose**: 2mg/kg IV infusion over 30 min, Every 3 weeks
- **ADEs**: Most common (>20%): fatigue, cough, N/C/D, pruritis, rash, loss of appetite, arthralgia
  - Immune-mediated rxns: pneumonitis, colitis, hepatitis, hypophysitis, nephritis, hypo/hyperthyroidism
- **Clinical Trials**: 173 pts in MC/OL/R dose-comp trial: ORR 24%; ongoing response in 18 pts (1.4-8.5+ months)
  - Both doses with similar response
- **Cost**: $2158/50mg vial, Approx $6500/dose in 70kg pt

## Nivolumab (Opdivo®)
*Bristol Myers Squibb*

- **Approved by FDA**: 12/22/2014
- **Dose**: 3mg/kg IV infusion over 60 min, Every 2 weeks
- **ADEs**: Most common (>20%): Rash
  - Immune-mediated rxns: pneumonitis, colitis, hepatitis, hypophysitis, nephritis, hypo/hyperthyroidism
- **Clinical Trials**: 120 pts in MC/OL trial: ORR 32%
  - with ongoing response in 33 pts (2.6-10+ months)
- **Cost**: $959 for 40mg (4mL) vial, $2398 for 100mg (10mL) vial
  - Approx $5800/dose in 70kg pt
**Olaparib (Lynparza®) by AstraZeneca**

| MOA & Indication | PARP inhibitor for advanced ovarian cancer (BRCA+)  
First in class |
|------------------|---------------------------------------------------|
| Dose & Administration | 400mg (8 x 50mg capsules) twice daily  
Continue until disease progression or toxicity |
| Adverse Effects | **Common (>20%):** anemia, N/V/D, fatigue, headache, dyspepsia  
**Labs:** increased creatinine, MCV elevation, decreased Hg, decreased lymphocytes/ANC/platelets  
**Warnings:** myelodysplastic syndrome/acute myeloid leukemia; pneumonitis, embryofetal toxicity |
| Response | Monotherapy in patients with BRCA+ advanced ovarian cancer after failed treatment with ≥ 3 lines of chemo  
137 patients in OL trial: 34% ORR; median duration of response 7.9 months |
| Cost | $25 per 50mg capsule  
$12,000/month |
# Ramucirumab (Cyramza®) by Eli Lilly

| MOA & Indication | Human vascular endothelial growth factor (VEGF) receptor 2 antagonist  
|                  | Treatment of gastric cancer (single-agent or with paclitaxel)  
|                  | Treatment of metastatic non-small cell lung cancer (with docetaxel) |
| Dose & Administration | Gastric CA: 8mg/kg IV infusion every 2 weeks  
|                      | Lung CA: 10mg/kg IV infusion on day 1 of a 21-day cycle  
|                      | • 60 minute infusion |
| Adverse Effects | Most common: hypertension, diarrhea; in combination with paclitaxel – fatigue, neutropenia, diarrhea, epistaxis; in combination with docetaxel – neutropenia, fatigue/asthenia, stomatitis/mucosal inflammation  
|                  | BW: risk of hemorrhage |
| Response | **Gastric CA/monotherapy (n=355):** Overall Survival 5.2 (drug) vs 3.8 months (placebo); PFS 2.1 (drug) vs 1.3 months (placebo)  
|          | **Gastric CA/with paclitaxel (n=665):** Overall survival 9.6 (drug+P) vs 7.4 months (placebo+P); PFS 4.4 vs 2.9 months  
|          | **NSCLC/with docetaxel (n=1253):** OS 10.5 (drug +D) vs 9.1 months (placebo+D); PFS 4.5 vs. 3.0 months |
| Cost | $1020 per 100mg/10mL vial; $5100 per 500mg/50mL vial |
NEW ANTIBIOTICS, ANTIFUNGALS AND ANTIVIRALS

**Intravenous**
- Dalbavancin hydrochloride
- Oritavancin diphosphate
- Ceftolozane/tazobactam
- Peramivir

**Otic**
- Finafloxacin

**Intravenous or Oral**
- Tedizolid phosphate

**Topical**
- Tavaborole
- Ivermectin
Scientists discover a new superbug.

You're right - it's wearing a red cape and blue tights!
# Lipoglycopeptides for Gram^+^ Acute Bacterial Skin and Skin Structure infections

<table>
<thead>
<tr>
<th>Dalbavancin (Dalvance®)</th>
<th>Oritavancin (Orbactiv®)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Approved by FDA 5/23/2014</strong></td>
<td><strong>Approved by FDA 8/16/2014</strong></td>
</tr>
<tr>
<td><strong>Dose</strong></td>
<td><strong>Dose</strong></td>
</tr>
<tr>
<td>Two doses – 1000mg IV x1 then 500mg IV one week later</td>
<td>1200mg x1 via IV infusion over 3 hours</td>
</tr>
<tr>
<td>CrCl &lt; 30 mL/min: 750mg x1 then 375mg one week later</td>
<td>No dosage adjustment with CrCl &gt; 30mL/min</td>
</tr>
<tr>
<td>Administer IV infusion over 30 minutes</td>
<td></td>
</tr>
<tr>
<td><strong>ADEs</strong></td>
<td><strong>ADEs</strong></td>
</tr>
<tr>
<td>Most common: nausea (5.5%), headache (4.7%), diarrhea (4.4%)</td>
<td>Most Common (&gt;5%): headache, nausea</td>
</tr>
<tr>
<td><strong>Warnings:</strong> Red man syndrome with rapid IV infusion; ALT elevations; anaphylaxis; CDAD</td>
<td><strong>Warnings:</strong> Prolongs aPTT (artificially) up to 48 hours (UFH contraindicated); Prolongs PT and INR up to 24 hours (incre. risk of bleeding with coumadin); Infusion-related reactions; CDAD; osteomyelitis</td>
</tr>
<tr>
<td><strong>Clinical Trials</strong></td>
<td><strong>Clinical Trials</strong></td>
</tr>
<tr>
<td>Two Phase 3, R/DB/DD trials (n=1312): 2 weeks with dalbavancin vs vancomycin/linezolid PO Non-inferior to vanco/linezolid</td>
<td>Two Phase 3, R/DB/MC trials (n=1987): 7-10 days with oritavancin vs vancomycin Non-inferior to vanco/linezolid</td>
</tr>
<tr>
<td><strong>Cost</strong></td>
<td></td>
</tr>
<tr>
<td>$1490/500mg vial</td>
<td>$966/400mg vial</td>
</tr>
<tr>
<td>Total cost of therapy = $4470</td>
<td>$2898 per 1200mg dose</td>
</tr>
</tbody>
</table>
**Tedizolid phosphate (Sivextro®) by Cubist**

| MOA & Indication | Oxazolidinone antibacterial agent  
| Pro-drug of tedizolid  
| Acute bacterial skin and skin structure infections |
| Dose & Administration | • 200mg once daily for six days  
| • Oral tablet or IV infusion over 1 hour; same dose PO & IV  
| • Consider alternatives in patients with neutropenia |
| Adverse Effects | **Most common (>2%)**: nausea, headache, diarrhea, vomiting, dizziness  
| **Warnings**: not studied in patient with neutropenia; CDAD |
| Clinical Trials | 2 R/MC/DB international (n=1315) tediz 200mg once daily x 6 days vs linezolid 600mg q12h x 10 days  
| Non-inferior to linezolid |
| Cost | $1770 per course of PO therapy ($295/200mg tablet)  
| $235/200mg vial |
Cetolozane/tazobactam (Zerbaxa®) by Cubist

| MOA & Indication | 5th generation cephalosporin + beta-lactamase inhibitor  
Complicated intra-abdom infections (with metronidazole)  
Complicated UTI, including pyelonephritis |
|------------------|--------------------------------------------------------------------------------------------------|
| Dose & Administration | 1.5 g IV every 8 hours – 1 hour infusion  
CrCl 30-50 mL/min: 750mg IV every 8 hours  
CrCl 15-29 mL/min: 374mg IV every 8 hours  
ESRD: 750mg LD, then 150mg IV every 8 hours |
| Adverse Effects | Most Common (>5%): nausea, diarrhe, headache, pyrexia  
Warnings: monitor CrCl, anaphylaxis, CDAD |
| Clinical Trials | Intra-abdom trial (n=979): C/T+ metro non-inferior to meropenem  
Complicated UTI trial (n=1068): C/T non-inferior to levofloxacin |
| Cost | $83/1.5gm vial |
## Peramivir (Rapivab®) by Biocryst Pharma

| MOA & Indication | Neuraminidase inhibitor for acute uncomplicated influenza  
|                  | - Only for age > 18 years  
|                  | - Symptoms for no more than 2 days |
| Dose & Administration | 600mg IV over at least 15 min  
|                     | Reduce dose for renal impairment: 200mg (30-49mL/min), 100mg (10-29 mL/min) |
| Adverse Effects | Diarrhea is most common (2%)  
|                 | **Warnings:** serious hypersensitivity; neuropsychiatric events |
| Clinical Trials | Acute uncomplicated influenza R/MC/B trial in Japan (n=98): symptom alleviation 21hrs sooner than with placebo.  
|                 | Serious influenza R/DB/MC/PC trial (n=398) – no improvement in time to clinical resolution vs. standard of care alone |
| Cost | NA |
# Finafloxacin (Xtoro®) by Alcon

<table>
<thead>
<tr>
<th>MOA &amp; Indication</th>
<th>Quinolone for acute otitis externa due to <em>P. aeruginosa</em> and <em>S. aureus</em></th>
</tr>
</thead>
</table>
| Dose & Administration | 0.3% Otic suspension  
4 drops in affected ear twice daily for seven days |
| Adverse Effects | Ear pruritus and nausea in 1% of patients  
Warning: allergic reactions; overgrowth of resistant bacteria |
| Clinical Trials | 71% clinical cure on Day 11 vs 33% for vehicle alone |
| Cost | 5 mL bottle  
Price NA |
# Topical Antifungal Agents for Toenail Infections

<table>
<thead>
<tr>
<th><strong>Efinconazole (Jublia®)</strong></th>
<th><strong>Tavabarole (Kerydin®)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Valeant/Dow</strong></td>
<td><strong>Anacor Pharm</strong></td>
</tr>
<tr>
<td>Approved by FDA 6/6/2014</td>
<td>Approved by FDA 7/7/2014</td>
</tr>
</tbody>
</table>

## Dose
- **Efinconazole (Jublia®)**: Topical application once daily for 48 weeks • 10% topical solution
- **Tavabarole (Kerydin®)**: Topical application once daily for 48 weeks • 5% topical solution

## ADEs
- **Efinconazole (Jublia®)**: Redness, itching, swelling, irritation of the toes
- **Tavabarole (Kerydin®)**: Redness, itching, swelling, irritation of the toes

## Clinical Trials
- **Efinconazole (Jublia®)**: 15-18% cure rate in 48 week study
- **Tavabarole (Kerydin®)**: 6.5-9% cure rate in 48 week trials

## Cost
- **Efinconazole (Jublia®)**: $449/4mL bottle
- **Tavabarole (Kerydin®)**: NA
NEW RESPIRATORY MEDICATIONS

Idiopathic Pulmonary Fibrosis
- Pirfenidone
- Nintedanib

Inhaler for COPD
- Olodaterol
# Olodaterol (Striverdi Respimat®) by Boehringer Ingelheim

<table>
<thead>
<tr>
<th>MOA &amp; Indication</th>
<th>Long-acting beta2-adrenergic agonist COPD, including chronic bronchitis and/or emphysema</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose &amp; Administration</td>
<td>Two inhalations once daily at the same time each day</td>
</tr>
</tbody>
</table>
| Adverse Effects           | **Common reactions (>2%)**: nasopharyngitis, URI, bronchitis, UTI, cough, dizziness, rash, diarrhea, back pain, arthralgia  
**Warnings**: asthma; do not exceed dose; life-threatening bronchospasm; caution in patients with sensitivity to sympathomimetic drugs  
**BW**: LABA class effects: increased risk of asthma-related deaths |
| Place in Therapy          | 4th LABA available  
Phase 3 studies - signif better than placebo |
| Cost                      | $72/2.5mcg (4mL) mist inhaler (28 inhalations)  
$155.70 per mist inhaler (60 inhalations) |
## Agents for Idiopathic Pulmonary Fibrosis

<table>
<thead>
<tr>
<th><strong>Pirfenidone (Esbriet®)</strong></th>
<th><strong>Nintedanib (Ofev®)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intermune/Roche</strong></td>
<td><strong>Boehringer Ingelheim</strong></td>
</tr>
<tr>
<td>Approved by FDA 10/15/2014</td>
<td>Approved by FDA 10/15/2014</td>
</tr>
</tbody>
</table>

### Dose
- **Pirfenidone**: 801 mg (3 capsules) TID with food; Titrate to full dose over 15 days; begin with 1 cap TID; Obtain baseline LFTs
- **Nintedanib**: 150mg every 12 hours, with food; Obtain baseline liver function tests

### ADEs
- **Pirfenidone**: Most common (>20%): N/D, rash, abdom pain, URI, fatigue, headache
  
  **Warnings**: incre. liver enzymes; photosensitivity/rash; GI disorders

- **Nintedanib**: Most common (>20%): D/N
  
  **Warnings**: incre. liver enzymes; GI disorders; embryofetal toxicity; arteriothrombotic events

### Clinical Trials
- **Pirfenidone**: 3 trials (n=1247) vs placebo
  2 of 3 trials – SS change in % FVC from baseline; no change in all-cause mortality

- **Nintedanib**: 3 trials (n=1231)
  
  SS change in % FVC from baseline over 52 weeks in all trials
  
  No change in all-cause mortality

### Cost
- **Pirfenidone**: Expected cost approx. $100,000/year

- **Nintedanib**: $133/capsule (100mg or 150mg $8000/month)
# Medications for Rare Diseases

<table>
<thead>
<tr>
<th>New Medication</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elosulfase alfa</td>
<td>Morquio A Syndrome</td>
</tr>
<tr>
<td>Metroleptin</td>
<td>Leptin Deficiency</td>
</tr>
<tr>
<td>Siltuximab</td>
<td>Castleman’s Disease</td>
</tr>
<tr>
<td>Miltefosine</td>
<td>Leishmaniasis</td>
</tr>
<tr>
<td>Eliglustat tartrate</td>
<td>Gaucher Disease</td>
</tr>
</tbody>
</table>
Morquio A Syndrome

1) **Cause:**
   - Autosomal recessive inherited disease – 1 in 200,000
   - Low levels of N-acetylglactosamine-6 sulfatase (GALNS) to break down glycosaminoglycans (GAGs)
   - GAGs build-up and result in heart disease, skeletal abnormalities, vision/hearing loss, difficulty breathing, early death
   - Diagnosis in infancy/childhood

2) **Treatment:**
   - Guided by symptom severity – surgery vs non-surgical treatments
   - Enzyme replacement
## Elosulfase alfa (Vimizim®) by BioMarin

<table>
<thead>
<tr>
<th><strong>MOA &amp; Indication</strong></th>
<th>Human enzyme replacement in patients with Morquio A syndrome - first in class</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dose &amp; Administration</strong></td>
<td>2mg/kg once weekly IV infusion over at least 3.5-4.5 hours</td>
</tr>
</tbody>
</table>
| **Adverse Effects** | **Most common (>10%):** pyrexia, vomiting, headache, nausea, abdominal pain, chills, fatigue  
**BW:** life-threatening anaphylaxis during infusions (anti-drug antibodies are seen in all patients)  
**Warnings:** anaphylaxis/hypersensitivity reactions; acute respiratory complications |
| **Clinical Trials** | 24-week R/DB/PC trial (n=176); patient ages 5-57 years.  
Efficacy endpoint = change in 6-minute walk test; 22.5 m increase with elosulfase alfa  
Extension trial (+48 weeks) – no additional improvement |
| **Cost** | $1068 per 5mg (5mL) vial |
Congenital or Acquired Leptin Deficiency

1) Leptin - a hormone made by fat tissue; regulates food intake and other hormones (e.g. insulin)
2) Leptin deficiency
   - Congenital – autosomal recessive; results from gene mutations
   - Acquired
     - E.g. associated with highly active antiretroviral therapy for HIV
     - Severe insulin resistance also present
     - Hypertriglyceridemia
3) Treatment:
   - hormone replacement
| MOA & Indication | Leptin analog – first in class  
For leptin deficient patients with congenital or acquired generalized lipodystrophy |
|------------------|-----------------------------------------------------------------------------------------------------------------------------------|
| Dose & Administration | • Males > 40kg: 2.5mg/day SQ, titrate to max 10mg/day  
• Females > 40kg: 5mg/day SQ, titrate to max 10mg/day  
• Patients ≤ 40kg: 0.06mg/kg/day SQ, titrate to max 0.13 mg/kg/day |
| Adverse Effects | **Common (≥10%):** headache, hypoglycemia, decreased weight, abdominal pain  
**BW:** anti-metreleptin antibodies (84% of patients); T-cell lymphoma  
**REMS/ETASU** – restricted access; prescriber training and enrollment; prescription authorization form; med guide; monitoring requirements |
| Clinical Trials | Open-label, single-arm trial (n=48;32 congenital, 16 acquired)  
Med duration 2.7 years; signif reductions in HbA1c, fasting glucose and triglycerides; results at 4 months similar to 1 year |
| Cost | $1472/5mg (5mL) vial  
$44,160/month @ 5mg dose |
Castleman’s Disease

1) Lymphoproliferative disorder

2) Patient characteristics
   - Age at diagnosis: 50-60 years old
   - High levels of IL-6

3) Presentation and Treatment
   - Unicentric/localized
     - Affecting one group of lymph nodes
     - Symptoms – lumps/swellings, difficulty breathing, abdominal fullness, cough
     - Treat with surgery and/or radiation
   - Multi-centric/widespread
     - Symptoms – lumps/swelling, fever, fatigue, night sweats, weight loss, anorexia, nausea/vomiting, numbness, leg swelling, rashes
     - Treat symptoms – corticosteroids, chemotherapy, immunotherapy
**Siltuximab (Sylvant®) by Janssen Biotech**

| MOA & Indication | Interleukin-6 (IL-6) antagonist – monoclonal antibody  
| Treatment of Castleman’s disease in patients who are negative for HIV and human herpesvirus-8 |
| Dose & Administration | • 11mg/kg admin by IV infusion over 60 minutes  
| | • Admin every 3 weeks in setting with resuscitation access  
| | • Avoid use in patients with severe infections |
| Adverse Effects | **Common (>10%)**: pruritus, increase in weight, rash,  
| | hyperuricemia, URI  
| | **Warnings**: avoid use in patients with infections; avoid live vaccines; GI perforation risk |
| Clinical Trials | Phase 2 MN/R/DB/PC trial (n=79) treatment until failure  
| | 34% durable tumor response vs 0% with placebo  
| | 1 year survival 100% vs 92% with placebo |
| Cost | $833/100mg vial  
| | $3332/400mg vial |
Leishmaniasis

1) **Etiology**
   - Protozoan parasite *Leishmania major* and *L. tropica* affecting macrophages and dendritic cells of host’s immune system
   - Vector – female sand flies
   - Reservoirs – gerbils, birds, dogs
   - Geography – Northern Africa, Middle East, India, Latin America

2) **Disease**
   - Presentation – lesions at site of sand fly bite
   - Resolution after 3-6 months
   - Cutaneous, mucosal and visceral disease

3) **Treatment**
   - Fluconazole PO x 6 weeks
   - Topical or intralesional injections with antimony etc.
## Miltefosine (Impavido®) by Paladin Therapeutics

| MOA & Indication | Phospholipid anti-parasitic medication  
Visceral, cutaneous and mucosal leishmaniasis |
<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Dose &amp; Administration</td>
<td></td>
</tr>
</tbody>
</table>
• For adults and adolescents ≥ 12 years old  
• 30-44 kg: 50mg PO twice daily for 28 days  
• > 45 kg: 50mg PO three times a day for 28 days  
• Administer with food |
| Adverse Effects | Common (>10%): motion sickness, abdominal pain, N/D/V, headache, dizziness, decrease in appetite  
BW: embryo-fetal toxicity  
Warnings: reproductive/renal/hepatic/GI effects, thrombocytopenia, Stevens-Johnson syndrome |
| Clinical Trials | **Visceral Disease/India** (n=398) 3:1 drug:amphoB; equivalent cure rates (98%); 3% treatment failure with drug vs 0% with amphoB  
**Cutaneous Disease/Colombia & Guatemala** (n=133) 2:1 drug:placebo 66% definite cure vs 30% with placebo at 2 weeks after end of treatment  
**Mucosal Disease/Bolivia** (n=79) 62% complete resolution at 1 year |
| Cost | NA |
1) Etiology

- Lysosomal Storage Disorder – 1 in 20,000 live births
- Deficiency of lysosomal enzyme acid beta-glucosidase
  - Beta-glucosidase catalyzes glucocerebroside into glucose and ceramide
  - Glucosylceramide builds up in macrophages – leading to foam cells or “Gaucher cells” in liver, spleen, bone marrow, etc

2) Treatment – enzyme replacement

- 1994 – imiglucerase (Cerezyme®) – 60 units/kg IV infusion 3 times a week, every 2 weeks
- 2010 - velalglucerase alfa (Vpriv®) – 60 units/kg IV infusion over 60 minutes every 2 weeks
- 2012 – taliglucerase alfa (Elelyso®) – plant-based medication – 60 units/kg IV once every 2 weeks
## Eliglustat tartrate (Cerdelga®) by Genzyme

| MOA & Indication | Glucosylceramide synthase inhibitor  
| Gaucher disease type 1 – can be used as first-line agent |
|------------------|--------------------------------------------------|
| Dose & Administration | 84mg PO twice daily (CYP2D6 EM or IM)  
| | 84mg PO once daily (CYP2D6 PM)  
| | DI: eliglustat is a CYP2D6 and CYP3A substrate |
| Adverse Effects | Common (≥10%): fatigue, headache, N/D, back pain, pain in extremities, abdominal pain |
| Clinical Trials | Trial 1: R/DB/PC/MC (n=40 treatment naïve) SS reduction in spleen volume, Hgb levels, liver volume, platelet count  
| | Trial 2: R/OL/AC/MC (n=159) eliglustat non-inferior to imiglucerase |
| Cost | $425/84mg capsule |
NEW CARDIOVASCULAR MEDICATIONS

DROXIDOPA

VORAPAXAR SULFATE
## Droxidopa (Northera®) by Lundbeck/Chelsea

| MOA & Indication | Synthetic norepinephrine precursor  
For neurogenic orthostatic hypotension |
|------------------|--------------------------------------|
| Dose & Administration | 100mg capsule three times a day  
Titrate to max dose of 600mg three times daily  
Take last dose at least 3 hours prior to bedtime/elevate head of bed |
| Adverse Effects | **Common (>5%)**: headache, dizziness, nausea, hypertension, fatigue  
**BW**: Supine hypertension  
**Warnings**: hyperpyrexia, confusion, may exacerbate heart disease, allergic reactions |
| Clinical Trials | 3 MC/DB/R/PC trials: efficacy at week 1 was not sustained beyond 2 weeks |
| Cost | $1409/month (100mg capsules)  
$2818/month (200mg capsules)  
$4227/month (300mg capsules) |
# Vorapaxar sulfate (Zontivity®) by Merck

## MOA & Indication
<table>
<thead>
<tr>
<th>Antiplatelet agent - protease-activated receptor-1 (PAR-1) antagonist – <strong>First in Class</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>For reducing thrombotic CV events in pts with h/o MI or PAD</td>
</tr>
</tbody>
</table>

## Dose & Administration
<table>
<thead>
<tr>
<th>One tablet once daily (2.08 mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contraindicated with h/o stroke, TIA, ICH, active pathologic bleeding</td>
</tr>
<tr>
<td><strong>DI:</strong> avoid with strong CYP3A inhibitors/inducers, warfarin</td>
</tr>
<tr>
<td>No dose adj for renal or hepatic impairment</td>
</tr>
</tbody>
</table>

## Adverse Effects
<table>
<thead>
<tr>
<th><strong>Bleeding</strong> is the most common ADE – GUSTO bleeding 25% vs 19.8% with placebo (55% increase with vorapaxar)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BW:</strong> not for pts with h/o stroke, TIA, ICH or active bleeding; antiplatelet agents incre. risk of bleeding, ICH and fatal bleeding</td>
</tr>
</tbody>
</table>

## Clinical Trials
<table>
<thead>
<tr>
<th>Irreversible; effective t ½ = 3-4 days; terminal t ½ = 8 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase 3 study (n=13,186) over 3 years vs placebo and standard of care with median f/u 2.5 years – 0.88 hazard ratio ss for composite endpoint (11.2% vs 12.4% with placebo)</td>
</tr>
</tbody>
</table>

## Cost
<table>
<thead>
<tr>
<th>$8.91/2.08mg tablet</th>
</tr>
</thead>
<tbody>
<tr>
<td>$267/month</td>
</tr>
</tbody>
</table>
NEW GASTROINTESTINAL MEDICATIONS

NALOXEGOL

NETUPITANT/PALONOSETRON

VEDOLIZUMAB
### Naloxegol (Movantik®) by AstraZeneca

| MOA & Indication | Opioid antagonist C-II  
| Treatment of opioid-induced constipation in patients with chronic non-cancer pain |
|------------------|---------------------------------------------------------------|
| Dose & Administration | 25mg tablet once daily  
| Can reduce to 12.5 mg once daily if ADRs or CrCl < 60mL/min  
| Take on empty stomach; avoid grapefruit juice  
| **Avoid**: laxatives during first 3 days; CYP3A inhibitors/inducers; |
| Adverse Effects | **Most common (>5%)**: abdom pain, diarrhea, nausea, flatulence, vomiting  
| **Warnings**: GI perforation, opioid withdrawal |
| Clinical Trials | Primary endpoint (>3 spontaneous BMs per week and change from baseline of ≥1 SBM per week) superior to placebo: patient response 35-41% (12.5mg) and 40-44% (25mg) vs. 29% (placebo) |
| Cost | Will be available in first half of 2015 |
## Netupitant/palonosetron (Akynzeo®) by Helsinn Healthcare

| MOA & Indication | Substance P/neurokinin 1 (NK1) receptor antagonist + serotonin-3 (5-HT3) receptor antagonist  
Prevention of nausea (acute/delayed) and vomiting with chemotherapy; given with dexamethasone |
|------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Dose & Administration | One capsule PO 1 hour prior to start of chemotherapy  
300 mg netupitant/0.5 mg palonosetron  
**Avoid use** with CYP3A4 inducers and CYP3A4 substrates; severe hepatic or renal impairment |
| Adverse Effects | **Most common** (≥3% and greater than palonosetron): Headache, asthenia, dyspepsia, fatigue, constipation, erythema  
**Warnings:** Serotonin syndrome possible |
| Clinical Trials | SS better than palonosetron alone in preventing emesis and use of rescue meds in acute phase (0-24hrs) and overall (0-120hrs) in 2 studies; 1 study also with SS CR in delayed phase (25-120hrs) |
| Cost | $476/tablet |
Vedolizumab (Entyvio®) by Millennium/Takeda

| MOA & Indication | Integrin receptor antagonist (α<sub>4</sub>β<sub>7</sub> integrins)  
Second or third-line agent for ulcerative colitis and adult Crohn’s Disease |
|------------------|---------------------------------------------------------------------|
| Dose & Administration | • 300mg IV over 30 min  
• Admin at weeks 0, 2 and 6; then every 8 weeks  
• D/C if no therapeutic benefit evidence by week 14 |
| Adverse Effects | Common (>10%): nasopharyngitis, headache, arthralgia  
Warnings: Infusion-related reactions; Incre. risk of infection (pre-screen for TB); PML with other integrin receptor antagonists |
| Clinical Trials | Natalizumab – less specific integrin inhibitor  
UC Study 1 (n=374): 47% clin response at week 6 vs 26% w pbo  
UC Study 2 (n=373): 42% clin remission at week 52 vs 16% pbo  
CD Trial 1 & 2 (n=368 and 416): clin remission 15% at week 6 vs 7% and 12% with pbo  
CD Trial 3 (n=460): 39% clin remission at week 52 vs 22% pbo |
| Cost | $4819/300mg vial |
# New Medications for Chronic Conditions

<table>
<thead>
<tr>
<th>New Medication</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apremilast</td>
<td>Psoriatic Arthritis or Plaque Psoriasis</td>
</tr>
<tr>
<td>Peginterferon beta-1A</td>
<td>Relapsing Multiple Sclerosis</td>
</tr>
<tr>
<td>Ledipasvir/sofosbuvir</td>
<td>Hepatitis C</td>
</tr>
<tr>
<td>Ombitasivir/paritaprevir/ritonavir/dasabuvir</td>
<td>Hepatitis C</td>
</tr>
</tbody>
</table>
# Apremilast (Otezla®) by Celgene

## MOA & Indication
Phosphodiesterase 4 inhibitor – immunomodulator of inflammatory mediators from immune cells

Treatment of active psoriatic arthritis or mod/sev plaque psoriasis when not a candidate for phototherapy or systemic therapy

## Dose & Administration
30 mg PO twice daily

Titrate to full dose over 6 days – start at 10 mg in AM, then BID, etc.

Severe renal impairment: 30 mg once daily

Avoid use with strong CYP450 inducers

## Adverse Effects
**Common (>5%)**: Diarrhea, nausea and headache

Can cause depression, weight loss

## Clinical Trials
**Psoriatic arthritis**: 3 clin trials (n=1493) demonstrated 32%-41% ACR 20 at week 16 vs 18%-18% with placebo

**Psoriasis**: 2 clin trials (n=1257) demon. 29%-33% Psoriasis Area and Severity Index 75% vs 5.3% and 5.8% with placebo at wk 16

## Cost
$31/30mg tablet

$1875/month
# Peginterferon beta-1a (Plegridy®) by Biogen Idec

| MOA & Indication | Interferon beta  
| Treatment of relapsing multiple sclerosis |
|------------------|------------------|
| **Dose & Administration** | Usual dose: 125 mcg SC every 14 days  
| | Day 1 – 63mcg injection  
| | Day 15 – 94mcg injection  
| | Day 29 – 125mcg injection and continue every 14 days |
| **Adverse Effects** | **Common (>20%):** inj site erythema, flu-like illness (take analgesics, antipyretics), pyrexia, headache  
| | **Warnings:** liver impairment, depression, seizures, anaphylaxis, CHF, autoimmune disorders |
| **Clinical Trials** | R/DB/PC trial (n=1012) patients with 2 or more relapses in past 3 years; excluded progressive MS  
| | 36% relative risk reduction (RRR) in annualized relapse rate  
| | 38% RRR in proportion of patients with relapses |
| **Cost** | $2386/125mcg pen injector or syringe  
| | $4772/63 & 94mcg pen injector or syringe starter pack |
Ledipasvir/sofosbuvir (Harvoni®) by Gilead Sciences

<table>
<thead>
<tr>
<th>MOA &amp; Indication</th>
<th>Hep C virus NS5A inhibitor (ledipasvir) + HCV nucleotide analog NS5B polymerase inhibitor (sofosbuvir) Treatment of chronic hepatitis C genotype 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose &amp; Administration</td>
<td>One tablet once daily <strong>x 12 weeks</strong> (treatment naïve or experienced but without cirrhosis); or, <strong>x 24 weeks</strong> (treatment experienced with cirrhosis) 90 mg ledipasvir/400 mg sofosbuvir Not recommended with P-gp inducers, severe renal impairment/failure</td>
</tr>
<tr>
<td>Adverse Effects</td>
<td>Fatigue (18%) and headache (17%)</td>
</tr>
<tr>
<td>Place in Therapy</td>
<td>First once-daily, single tablet regimen for patients with advanced liver disease Does not require interferon or ribavirin co-administration</td>
</tr>
<tr>
<td>Cost</td>
<td>$1125/tablet $94,500 for a 12 week course of therapy</td>
</tr>
</tbody>
</table>
**Ombitasvir, paritaprevir, ritonavir, dasabuvir (Veikira Pak®) by Abbvie**

<table>
<thead>
<tr>
<th>MOA &amp; Indication</th>
<th>HCV NS5A inibitor (ombitasvir), HCV NS3/4A protease inhibitor (paritaprevir), CYP3A inhibitor (ritonavir), and an HCV non-nucleoside NS5B palm polymerase inhibitor (dasabuvir) Genotype 1 hepatitis C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose &amp; Administration</td>
<td>2 tabs of ombitavir/paritaprevir/ritonavir once in the morning 1 tab of dasabuvir twice daily (AM and PM) with a meal Not for use with decompensated liver disease 12 or 24 weeks duration – depending on genotype and presence of cirrhosis; regimen with ribavirin except genotype 1B without cirrhosis</td>
</tr>
<tr>
<td>Adverse Effects</td>
<td><strong>Most common (&gt;10%):</strong> fatigue, nausea, pruritis, skin reactions, insomnia, asthenia</td>
</tr>
<tr>
<td>Place in Therapy</td>
<td>91% - 100% cure rate in trials Take with ribavirin unless Genotype 1b, without cirrhosis</td>
</tr>
<tr>
<td>Cost</td>
<td>$83,319 for 12 week course of therapy</td>
</tr>
</tbody>
</table>
NEW RADIOACTIVE DIAGNOSTIC AGENTS

Florbetaben F 18

Sulfur Hexafluoride Lipid-Type A Microspheres
## Radioactive Diagnostic Agents

<table>
<thead>
<tr>
<th>Florbetaben F18 (Neuraceq®)</th>
<th>Sulfur Hexafluoride Lipid-Type A Microspheres (Lumason®)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Piramal</strong></td>
<td><strong>Bracco</strong></td>
</tr>
<tr>
<td>Approved by FDA 3/19/2014</td>
<td>Approved by FDA 10/10/2014</td>
</tr>
<tr>
<td><strong>Indication</strong></td>
<td>Ultrasound contrast agent</td>
</tr>
<tr>
<td>Radioactive diagnostic agent for PET imaging of brain For evaluation of Alzheimer’s Disease</td>
<td>For opacification of left ventricle and better delineation of the left ventricular endocardial border in patients with suboptimal echocardiogram</td>
</tr>
<tr>
<td><strong>Dose</strong></td>
<td></td>
</tr>
<tr>
<td>• 300 MBq (8.1 mCi) slow IV bolus (6 sec/mL)</td>
<td>• 2mL IV bolus during echo</td>
</tr>
<tr>
<td>• PET imaging 45 – 130 minutes after admin</td>
<td>• Second dose of 2mL may be used</td>
</tr>
<tr>
<td>• Flush with 5mL NS after each dose</td>
<td>• Flush with 5mL NS after each dose</td>
</tr>
<tr>
<td><strong>ADEs</strong></td>
<td></td>
</tr>
<tr>
<td>IV site erythema (1.7%), irritation (1.2%), pain (3.9%)</td>
<td>Headache (0.9%), nausea (0.6%)</td>
</tr>
<tr>
<td>Contributes to patient’s radiation exposure False positives possible</td>
<td><strong>BW</strong>: serious reactions including cardiopulmonary reactions may occur within 30 min of admin</td>
</tr>
<tr>
<td><strong>Sensitivity</strong>: 96-98%</td>
<td></td>
</tr>
<tr>
<td><strong>Specificity</strong>: 77-80%</td>
<td></td>
</tr>
</tbody>
</table>
Questions?