New Drugs 2015 - Part 2
PharMEDium Lunch and Learn Series

LUNCH AND LEARN

New Drugs 2015 - Part 2

May 13, 2016

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CE Activity Information & Accreditation

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Attendance Code
Code will be provided at the end of today’s activity
Event Code not needed for On-Demand

Ask a Question

- Submit your questions to your site manager.
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Your question...?
Resources

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- Handouts
- Activity information
- Upcoming live webinar dates
- Links to receive CE credit

Mary Lynn Moody BSPharm
Clinical Associate Professor
Department of Pharmacy Practice
University of Illinois at Chicago

NEW DRUGS OF 2015 - PART 2
Learning Objectives-Pharmacists

- Describe the new drugs approved by the Food and Drug Administration in 2015
- Discuss the role of these agents in therapy
- Summarize the adverse effects and potential drug interactions of these new agents

Learning Objectives- Technicians

- Describe the new drugs approved by the Food and Drug Administration in 2015
- Discuss any unique preparation and/or dispensing requirements for these agents
- Summarize the adverse effects and potential drug interactions of these new agents that may require pharmacist intervention
Ceftazidime/avibactam

- Approved February 25, 2015
- 5th approved antibacterial drug product designated as a Qualified Infectious Disease Product (QIDP)
- 3rd generation cephalosporin beta-lactamase inhibitor
- Complicated intra-abdominal infection with metronidazole; complicated urinary tract infection including pyelonephritis
- NOT first line therapy at this time
Ceftazidime/avibactam\textsuperscript{2,3}

- Infuse over 2 hours
- Administer in 50 to 250 mL (NS or D5W)
- 10\% plasma protein bound
- Excreted unchanged (80-90\%) in the kidney
- Elimination half life: 2-3 hours

Ceftazidime/avibactam Dosing\textsuperscript{3}

- Available as 2.5 gram vial (2 gram ceftazidime and 0.5 gram avibactam)
- Dose is 2.5 grams IV every 8 hours
- Reduce the dose in patients with CrCl < 50 mL/min
- Duration of treatment
  - cIAI- 5 to 14 days
  - cUTI-7-14 days
Dosing in Renal Patients

<table>
<thead>
<tr>
<th>Est CrCl (mL/min)</th>
<th>Recommended dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater than 50</td>
<td>2.5 grams (2 grams/0.5 grams) every 8 hours</td>
</tr>
<tr>
<td>31 to 50</td>
<td>1.25 grams (1 grams/0.25 grams) every 8 hours</td>
</tr>
<tr>
<td>16 to 30</td>
<td>0.94 grams (0.75 grams/0.19 grams every 12 hours</td>
</tr>
<tr>
<td>6 to 15</td>
<td>0.94 grams (0.75 grams/0.19 grams every 24 hours</td>
</tr>
<tr>
<td>Less than or equal 5</td>
<td>0.94 grams (0.75 grams/0.19 grams) every 48 hours</td>
</tr>
</tbody>
</table>

Ceftazidime/avibactam Efficacy-cIAI

- Only Phase 1 and 2 trials required
- Ceftazidime/avibactam plus metronidazole against meropenem for 5 to 14 days in 203 patients with cIAI
  - Caucasian, 91% < 65 yrs, 69% male
  - Infection of appendix (48%), stomach/duodenum (30%) were the most common
- The primary endpoint was clinical cure 2 weeks after the last drug dose.
- Cure rates were similar between the 2 groups: 91.2% for ceftazidime/avibactam plus metronidazole versus 93.4% for meropenem (95% CI -20.4% to 12.2%).
- The incidence of adverse effects was also similar between groups.
Ceftazidime/avibactam Efficacy—cUTI

- Phase 2 trial
- Ceftazidime/avibactam with imipenem/cilastatin for 7 to 14 days in 135 patients with cUTI
- Caucasian, 75% female, 84% < 65 yrs
- Two-thirds had pyelonephritis
- The primary endpoint was clinical cure at 5 to 9 days after the last drug dose.
- Cure rates were similar between the 2 groups: 70.4% for ceftazidime/avibactam versus 71.4% for imipenem/cilastatin (95% CI -27.2% to 25.0%).
- The incidence of adverse effects was similar between groups.

Ceftazidime/avibactam

- Use in patients with CrCl 30-50 mL/min
  - Higher incidence of mortality in trials
  - Monitor daily, adjust dose
- Adverse effects
  - Vomiting
  - Nausea
  - Constipation
  - Anxiety
Pharmacist Clinical Points

- Verify patient has resistant gram negative organism
- Review allergy history
- Confirm metronidazole co-administration in cIAI

Technician Tips

- Reconstitute with 10 mL
  - H2O, Normal Saline, Dextrose 5% in Water
- Must dilute further (50-250 mL) within 30 minutes (Normal Saline, Dextrose 5% in Water)
- Use infusion within 12 hours (room temperature) or 24 hours (refrigerated temperature)
Preparing doses

<table>
<thead>
<tr>
<th>Ceftazidime/avibactam dose</th>
<th>Volume to withdraw from vial</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.5 gram</td>
<td>12 mL (entire contents)</td>
</tr>
<tr>
<td>1.25 gram</td>
<td>6 mL</td>
</tr>
<tr>
<td>0.94 gram</td>
<td>4.5 mL</td>
</tr>
</tbody>
</table>

ISAVUCONAZONIUM (CRESEMBA®)
Isavuconazonium (Cresemba)\(^1,2\)
- Approved March 6, 2015
- Azole antifungal
- 6\(^{th}\) approved antibacterial drug product designated as a Qualified Infectious Disease Product (QIDP)
- Orphan status
- Invasive aspergillosis and invasive mucormycosis

Isavuconazonium sulfate\(^6\)
- Pro-drug
  - Hydrolyzed by esterases to isavuconazole
- Inhibits lanosterol to ergosterol
  - Ergosterol main element of fungal cell wall
- Well absorbed orally (98%)
- 99% plasma protein bound
- Excreted in the kidney (45%) and feces (46%)
- Elimination half life: 130 hours
Isavuconazonium Dosing

- Available as 186 mg capsule and 372 mg vial
- Loading dose: 372 mg every 8 hours for 6 doses. May give intravenously or orally
- Maintenance dose: 372 mg every 12 to 24 hours. May give intravenously or orally.

Isavuconazonium Efficacy

- 516 patients with invasive aspergillosis
- Compared to voriconazole
- Noninferior to voriconazole in all-cause mortality through Day 42 in the ITT population (18.6% and 20.2%, respectively, adjusted treatment difference −1.0 [95% CI: −8.0, 5.9])
Isavuconazonium Efficacy

- 42 patients with invasive mucormycosis
- Compared to voriconazole
- Noninferior to voriconazole in all-cause mortality through Day 42 in the ITT population (18.6% and 20.2%, respectively, adjusted treatment difference –1.0 [95% CI: –8.0, 5.9])

Isavuconazonium Adverse Effects

- > 15%
  - Vomiting, nausea, diarrhea, ↑ liver enzymes
- Headache
- Hypokalemia
- Dyspnea
- Peripheral edema
Isavuconazonium Interactions

- Avoid CYP3A4 inhibitors
  - Ketoconazole, ritonavir
  - Increase in isavuconazole
- Avoid CYP3A4 inducers
  - Rifampin, carbamazepine, St John’s Wort
  - Decrease in isavuconazole
- Avoid in familial short QT Syndrome

Pharmacist Clinical Points

- Verify other medications to prevent drug interactions
- Avoid vigorous shaking with the parenteral product. Do not use pneumatic transport system.
- Capsules can be taken with or without food
- No dose alteration between routes of administration
Technician Tips

- Reconstitute with 5 mL sterile water and add to 250 mL normal saline or 5% dextrose
- The infusion set should have an inline filter with pore size of 0.2 to 1.2 microns
- Infuse over at least 1 hour
- Use within 6 hours of preparation
Sugammadex (Bridion®)<sup>1,2</sup>

- Approved December 17, 2015
- NMB reversal agent
  - Reverses vecuronium and rocuronium
- Forms a complex with NMB, removes these agents from the neuromuscular junction and facilitates the return of muscle function

Sugammadex Pharmacokinetics<sup>8</sup>

- Elimination half life: 2 hours
  - Severe renal impairment- 19 hours
- 96% excreted renally (mostly unchanged)
Sugammadex Dosing

- Administer as single injection over 10 seconds
- 2-4 mg/kg based on actual body weight
- For rapid reversal of rocuronium (SD 1.2 mg/kg): Give 16 mg/kg

- Available as 200 mg/2 mL (100 mg/mL) and 500 mg/5 mL (100 mg/mL)

Neostigmine Comparison

- Anticholinesterase antagonist
- Workhorse in the OR
- Not as effective in deep level of blockade
- Use may be limited to modest blockade
Sugammadex Efficacy\textsuperscript{8}

- 157 patients receiving NMB then randomized to neostigmine or sugammadex
- Measures recovery of Train of Four ratio (>0.9 then recovery from neuromuscular blockade)
- Neostigmine not expected to work
- 2.7 minutes (R) and 3.3 minutes (V)

Sugammadex Warnings\textsuperscript{2,8}

- Anaphylaxis (0.3%)
  - Occurred at all doses
  - Urticaria, flushing, skin eruption
  - Hypotension requiring vasopressors
  - Extended hospitalization
- Recurrence of Neuromuscular blockade
- Respiratory function must be monitored
- Severe bradycardia leading to cardiac arrest
- Changes in INR
Sugammadex Adverse Effects

- Common ADEs (> 10%)
  - Vomiting
  - Pain
  - Nausea
  - Hypotension
  - Headache

- Do not use in severe renal impairment

Sugammadex Interactions

- Reduces effectiveness of oral birth control
- Use another from of contraception for 7 days
- Recovery can be delayed in patients using toremifene (Fareston)
Pharmacist Clinical Points

- Avoid use if allergic reaction in the past
- Monitor airway until fully recovered from NMB
- May inject into running IV line of dextrose, saline, Ringers
- Flush line with NS after administration
- Do not mix with other drugs
- Warning regarding oral contraceptive use

Technician Tips

- Do not mix with other drugs
- Visually incompatible with verapamil, ondansetron and ranitidine
- Compatible with Saline, 5% dextrose, Ringers
- Protect vial from light
Statins have been the mainstay of treatment since 1980’s
- 2 PCSK9 inhibitor antibodies approved
- Proprotein convertase subtilisin kexin 9
- Must be used with maximally tolerated statins
Evolocumab

- Regulates the lifespan of the receptor on the liver that clears cholesterol
- By binding the protein, paradoxically, you lower cholesterol
- Protein causes the liver receptor that clears cholesterol to be destroyed and recycled
- Binding the protein, the receptor stays on the liver longer and clears more cholesterol from the body.

Evolocumab Pharmacokinetics

- Absolute bioavailability is 72%
- Mean peak concentrations reached in 3-4 days
- Vd=3.3L
- T1/2= 11-17 days
- Metabolized through PCSK9 or proteolytic pathway
- No adjustment needed in organ failure
Evolocumab Dosing

- Heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic heart disease requiring additional lowering of LDL: 140 mg subcutaneously every 2 weeks or 420 mg once a month
- Homozygous familial hypercholesterolemia (HoFH): 420 mg subcutaneously once a month

Evolocumab dosing (cont)

- Available as 140 mg/mL syringe
- Must administer multiple doses at the same time
- If miss a dose (2 weeks) give if there are more than 7 days until next dose
Evolocumab Efficacy

- 2 open label randomized trials
- Following 12 phase 2 or 3 trials
- 2:1 ratio of evolocumab or standard therapy
- Reduced LDL-C 61% (median of 120-48 mg/dL)
- CV events at 1 yr: 2.18% to 0.95%
- Neurocognitive effects in evolocumab group

Evolocumab Contraindications

- Contraindicated if allergic to drug
- Warning: Rash and urticaria
Evolocumab Adverse Effects

- Nasopharyngitis
- Upper respiratory tract infection
- Back pain
- Injection site reaction
- Flu like symptoms

Pharmacist Clinical Points

- Administer in abdomen, thigh, upper arm
- 140 mg/mL syringe - may need 3 syringes
- Rotate the injection site
- Discuss the importance of compliance
- Verify patient understands how and when to get refills
- Consider automatic refills and delivery
Technician Tips$^{2,9}$

- Keep in refrigerator, Do not shake
- Instruct patient to bring to room temperature by removing from refrigerator 30 minutes before injecting
- May store at room temperature, but only stable for 30 days
- Work with pharmacist to develop call out to ensure refills of this medication
- Alert pharmacist if not refilled on time

MEPOLIZUMAB  
(NUCALA®)
Mepolizumab (Nucala)$^{1,11}$

- Interferon-5 antagonist monoclonal antibody
- Add-on maintenance of severe asthma
- Must have eosinophilic phenotype
- Not for acute bronchospasm or status asthmaticus

Mepolizumab$^{11}$

- Interleukin-5-growth and differentiation and survival of eosinophils
- IL-5 is one of the cells involved in inflammation
- Inhibits IL-5, reduces production and survival of eosinophils.
- Less inflammatory cells
Mepolizumab Pharmacokinetics

- Absolute bioavailability is 80%
- Mean peak concentrations reached in 3-4 days
- Vd=3.6 L
- T1/2= 16-25 days
- Metabolized by proteolytic enzymes

Mepolizumab Dosing

- Approved for use in children (over 12 years) and adults
- 100 mg administered subcutaneously once every 4 weeks
- Administer in upper arm, thigh, abdomen
- Administered by healthcare professional
Mepolizumab Efficacy

- 3 randomized trials
- 24-52 weeks duration
- 1,327 patients with moderate to severe asthma
- Fewer exacerbations requiring hospitalization and/or emergency department visits, and a longer time to the first exacerbation

Mepolizumab Contraindications\textsuperscript{11}

- Contraindicated if allergic to drug
- Warning: Angioedema, bronchospasm, hypotension, rash and urticaria have been reported
- Usually within hours of administration
Mepolizumab Warnings

- Do not use for acute asthma symptoms
- Herpes zoster reported, consider vaccine before starting Nucala
- Do not abruptly stop corticosteroids
- Parasitic infections—eosinophils are involved in response to parasite infections

Mepolizumab Adverse Effects

- Hypersensitivity reactions
  - Angioedema
  - Bronchospasm
  - Hypotension
  - Urticaria and rash
- Opportunistic infections
  - Herpes zoster
  - Parasites
Pharmacist Clinical Points

- Confirm presence of eosinophilic phenotype
- Not for acute symptoms
- Administered in abdomen, thigh, upper arm
- Assess need for Herpes Zoster Vaccine
- Do not abruptly stop corticosteroids
- $32,500 per year

Technician Tips

- Do not shake, leads to foaming or precipitation
- Direct diluent onto the center of the lyophilized cake. Gently swirl until dissolved
- 100 mg vial (latex free)
- Discard if not used within 8 hours of reconstitution
References


Table 1 – New drugs of 2015

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
<th>Manufacturer</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Edoxaban</td>
<td>Savaysa</td>
<td>Daiichi Sankyo</td>
<td>Reduce the risk of stroke and blood clots in patients with atrial fibrillation not caused by a heart valve problem</td>
</tr>
<tr>
<td>2. Secukinumab</td>
<td>Cosentyx</td>
<td>Novartis</td>
<td>Treatment of moderate to severe plaque psoriasis</td>
</tr>
<tr>
<td>3. Parathyroid hormone</td>
<td>Natpara</td>
<td>NPS Pharm</td>
<td>To control hypocalcemia in patients with hypoparathyroidism</td>
</tr>
<tr>
<td>4. Palbociclib*</td>
<td>Ibrance</td>
<td>Pfizer</td>
<td>Treatment of advanced breast cancer</td>
</tr>
<tr>
<td>5. Lenvatinib</td>
<td>Lenvima</td>
<td>Eisai</td>
<td>Treatment of progressive, differentiated thyroid cancer</td>
</tr>
<tr>
<td>6. Panobinostat</td>
<td>Fardyak</td>
<td>Novartis</td>
<td>Treatment of multiple myeloma</td>
</tr>
<tr>
<td>7. Ceftazidime-avibactam</td>
<td>Avycaz</td>
<td>Forest Labs</td>
<td>Treatment of complicated, intra-abdominal infections or complicated urinary tract infections including kidney infections</td>
</tr>
<tr>
<td>8. Isavuconazonium</td>
<td>Cremba</td>
<td>Astellas Pharma</td>
<td>Treatment of invasive aspergillosis and invasive mucormycosis</td>
</tr>
<tr>
<td>9. Dinutuximab</td>
<td>Unituxin</td>
<td>United Therapeutics</td>
<td>Treatment of high-risk neuroblastoma in children</td>
</tr>
<tr>
<td>10. Cholic acid</td>
<td>Cholbam</td>
<td>Asklepiion Pharm</td>
<td>Treatment of bile acid synthesis disorders and for patients with peroxisomal disorders</td>
</tr>
<tr>
<td>11. Ivabradine</td>
<td>Corlanor</td>
<td>Amgen</td>
<td>Reduce hospitalization from worsening heart failure</td>
</tr>
<tr>
<td>12. Deoxycholic acid</td>
<td>Kybella</td>
<td>Kythera Biopharm</td>
<td>Treatment of moderate to severe fat below the chin</td>
</tr>
<tr>
<td>13. Eluxadoline</td>
<td>Viberzi</td>
<td>Forest Pharm</td>
<td>Treatment of irritable bowel syndrome with diarrhea</td>
</tr>
<tr>
<td>14. Canagrelor</td>
<td>Kengreal</td>
<td>The Medicines Co</td>
<td>To prevent the formation of harmful blood clots in the coronary arteries for adult patients undergoing percutaneous coronary intervention</td>
</tr>
<tr>
<td>15. Lumacaftor/ivacaftor*</td>
<td>Orkambi</td>
<td>Vertex Pharm</td>
<td>Treatment of cystic fibrosis</td>
</tr>
<tr>
<td>16. Sacubitril/valsartan</td>
<td>Entresto</td>
<td>Novartis</td>
<td>Treatment of heart failure</td>
</tr>
<tr>
<td>17. Brexpiprazole</td>
<td>Rexulti</td>
<td>Otsuka America</td>
<td>Treatment of schizophrenia and as add-on therapy for major depressive disorder</td>
</tr>
<tr>
<td>18. Alirocumab</td>
<td>Praluent</td>
<td>Sanofi-Aventis</td>
<td>Treatment of high cholesterol in certain patients</td>
</tr>
<tr>
<td>19. Sonidegib</td>
<td>Odomzo</td>
<td>Novartis</td>
<td>Treatment of locally advanced basal cell carcinoma</td>
</tr>
<tr>
<td>20. Daclatasvir</td>
<td>Daklinza</td>
<td>BMS</td>
<td>Treatment of Hepatitis C (genotype 3)</td>
</tr>
<tr>
<td>21. Fibanserin</td>
<td>Addyi</td>
<td>Sprout Pharm</td>
<td>Treatment of acquired, generalized hypoactive sexual desire disorder (HSDD) in premenopausal women</td>
</tr>
<tr>
<td>22. Evolocumab</td>
<td>Repatha</td>
<td>Amgen</td>
<td>Treatment of high cholesterol in certain patients</td>
</tr>
<tr>
<td>23. Rolapitant</td>
<td>Varubi</td>
<td>Tesaro</td>
<td>Prevention of delayed phase chemotherapy-induced nausea and vomiting</td>
</tr>
<tr>
<td>24. Uridine triacetate*</td>
<td>Xuriden</td>
<td>Wellstat Therapeutics</td>
<td>Treatment of hereditary orotic aciduria</td>
</tr>
<tr>
<td>Generic Name</td>
<td>Brand Name</td>
<td>Manufacturer</td>
<td>Indication</td>
</tr>
<tr>
<td>-----------------------</td>
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<td>---------------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>25. Cariprazine</td>
<td>Vraylar</td>
<td>Actavis</td>
<td>Treatment of schizophrenia and bipolar disorder</td>
</tr>
<tr>
<td>26. Trifluridine and tipiracil</td>
<td>Lonsurf</td>
<td>Taiho Oncology</td>
<td>Treatment of advanced colorectal cancer unresponsive to other therapy</td>
</tr>
<tr>
<td>27. Insulin degludec</td>
<td>Tresiba</td>
<td>Novo Nordisk</td>
<td>Treatment of diabetes</td>
</tr>
<tr>
<td>28. Aripiprazole lauroxol</td>
<td>Aristada</td>
<td>Alkermes</td>
<td>Treatment of schizophrenia</td>
</tr>
<tr>
<td>29. Idarucizumab*</td>
<td>Praxbind</td>
<td>Boehringer Ingelheim</td>
<td>Reversal agent for dabigatran (Pradaxa)</td>
</tr>
<tr>
<td>30. Patiromer</td>
<td>Veltassa</td>
<td>Relypsa</td>
<td>Treatment of hyperkalemia</td>
</tr>
<tr>
<td>31. Trabectedin</td>
<td>Yondelis</td>
<td>Janssen Biotech</td>
<td>Treatment of specific soft-tissue sarcomas (liposarcoma, leiomyosarcoma)</td>
</tr>
<tr>
<td>32. Asfotase alfa*</td>
<td>Strensiq</td>
<td>Alexion</td>
<td>Treatment of hypophosphatasia</td>
</tr>
<tr>
<td>33. Mepolizumab</td>
<td>Nucala</td>
<td>GSK</td>
<td>Maintenance treatment of asthma</td>
</tr>
<tr>
<td>34. Combination tablet of elvitegravir, cobicistat, emtricitabine, and tenofovir alafenamide</td>
<td>Genvoya</td>
<td>Gilead Sciences</td>
<td>Treatment of HIV-1 infection</td>
</tr>
<tr>
<td>35. Cobimetinib</td>
<td>Cotelic</td>
<td>Genentech</td>
<td>Treatment of advanced melanoma in patients with abnormal gene (BRAF, V600E, V600K)</td>
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<tr>
<td>36. Osimertinib*</td>
<td>Tagrisso</td>
<td>AstraZeneca</td>
<td>Treatment of non-small cell lung cancer</td>
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<tr>
<td>37. Daratumumab*</td>
<td>Darzalex</td>
<td>Janssen Biotech</td>
<td>Treatment of multiple myeloma</td>
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<tr>
<td>38. Ixazomib</td>
<td>Ninlaro</td>
<td>Takeda</td>
<td>Treatment of multiple myeloma</td>
</tr>
<tr>
<td>40. Elotuzumab*</td>
<td>Empliciti</td>
<td>BMS</td>
<td>Treatment of multiple myeloma</td>
</tr>
<tr>
<td>41. Sebelipase alfa*</td>
<td>Kanuma</td>
<td>Alexion</td>
<td>Treatment of lysosomal acid lipase deficiency</td>
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<tr>
<td>42. Alectinib*</td>
<td>Alecensa</td>
<td>Genentech</td>
<td>Treatment of ALK-positive lung cancer</td>
</tr>
<tr>
<td>43. Sugammadex</td>
<td>Bridion</td>
<td>Merck Sharp and Dohme Corp</td>
<td>To reverse effects of neuromuscular blocking drugs used during surgery</td>
</tr>
<tr>
<td>44. Selexipag</td>
<td>Uptravi</td>
<td>Actelion Pharmaceuticals</td>
<td>Treatment of pulmonary arterial hypertension</td>
</tr>
<tr>
<td>45. Lesinurad</td>
<td>Zurampic</td>
<td>AstraZeneca</td>
<td>Treatment of gout</td>
</tr>
</tbody>
</table>

*Breakthrough status
Table 2 – 2015 Approved Orphan Drug List¹

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alectinib</td>
<td>Alecensa</td>
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<tr>
<td>Cholic acid</td>
<td>Cholbam</td>
</tr>
<tr>
<td>Cobimetinib</td>
<td>Cotellic</td>
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<tr>
<td>Isavuconazonium</td>
<td>Cresemba</td>
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<td>Daratumumab</td>
<td>Darzalex</td>
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<td>Elotuzumab</td>
<td>Empliciti</td>
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<td>Panobinostat</td>
<td>Farydak</td>
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<td>Sebelipase alfa</td>
<td>Kanuma</td>
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<td>Lenvatinib</td>
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<td>Parathyroid hormone</td>
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<td>Ixazomib</td>
<td>Ninlaro</td>
</tr>
<tr>
<td>Lumacaftor/ivacaftor</td>
<td>Orkambi</td>
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<td>Yondelis</td>
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* Repatha was submitted with two indications. One indication received Orphan designation while the other did not.