AMCP Florida
Day of Education

April 22, 2023
Mission

The Florida AMCP Affiliate seeks to serve the AMCP membership in the state of Florida in three primary areas: networking, education, and advocacy.

www.amcp.org/Florida-AMCP
Mission

To improve patient health by ensuring access to high-quality, cost-effective medications and other therapies.
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Wendy Bailey, RPh, BS Pharm, MS Pharm, MBA
Vice President, Health Plan Pharmacy Strategy (Centene)
Thank you to the sponsors of the 2023 AMCP Florida Day of Education
Agenda

8:00AM-8:30AM CHECK-IN / REGISTRATION, EXHIBITS / NETWORKING & BREAKFAST

8:30AM-8:45AM WELCOME / REVIEW AGENDA / GAME

8:45AM-9:45AM Obesity (CE)
Cynthia Moreau, PharmD, CPh, BCACP, CCOES, ChemMed, Clinical Pharmacist

9:45AM-10:15AM Value Framework Assessment Overview (CE)
Cynthia Miller, MD, MPH, FACP, Precision Value, VP Medical Director-Access Experience

10:15AM-11:15AM BREAK / EXHIBITS / NETWORKING / SNACK

11:15AM-12:30PM Federal Legislative Update: Inflation Reduction Act & Panel Discussion (CE)
Moderated by Jennifer Mathieu, MA, AMCP, Vice President, Policy and Government Relations

Panel Participants:
- Cynthia Griffin, PharmD, Florida Blue, Vice President, Medicare Pharmacy Programs
- Shawn Barger, PharmD, Adena, Director of Medicare Formulary Strategy, Compliance & Operations
- Amrhy Pataniello, MHA, Arista, Medicare Pharmacy Director, Contracting & Analytics (Former Administrator, Bureau of Medicaid, Pharmacy Policy)
- Javier Gonzalez, PharmD, Abarca Health, Chief Growth & Commercial Officer
- Jonathan Hohman, PharmD, Qmerich, Medical Executive Director

12:30PM-1:30PM LUNCH / EXHIBITS / NETWORKING

1:30PM-2:30PM The Evolving Biosimilars Landscape Panel Discussion (CE)
Moderated by Wendy Bailey, RN, BSPharm, MSPharm, MBA, Centene, Vice President of Health Plan Pharmacy Strategy

Panel Participants:
- David Foss, PharmD, Florida Healthcare Plan, Clinical Pharmacy Director
- Jorge Garcia, PharmD, MS, MHA, MBA, FACHE, Baptist Health South Florida, Assistant Vice President-System Oncology Pharmacy Service Line
- Jennifer Vines, PharmD, BCACP, BCMCTMS, Jackson Health Ambulatory Care, Assistant Director of Ambulatory Clinical Pharmacy Services
- Richard Gourash, R.Ph., MBA, BoeFlus, VP Oncology

2:30PM-3:30PM Health Disparities in Healthcare (CE)
Shanesta Montemar, PharmD, BCOP, GCO2 for Lung Cancer, Director, Community Engaged Research

3:00PM-4:00PM Oncology Accelerated Drug Approvals that Lack Confirmatory Trials (CE)
Presented by Laura Roberts, PharmD, BCOP, Onco Health, Senior Vice President, Clinical Strategy & Growth

4:00PM-5:00PM EXHIBITS / NETWORKING
Kahoot Game

https://create.kahoot.it/share/amcp-day-of-education-2023-kahoot-1/797fce56-e783-4f7e-8ce6-273294e62283
Management of Obesity

Cynthia Moreau, PharmD, CPh, BCACP, CDCES
Clinical Pharmacist
ChenMed
cynthia.moreau@chenmed.com
Objectives

• Review and compare available pharmacological options for management of obesity
• Understand which patients are candidates for pharmacotherapy for weight loss
• Develop an individualized treatment plan for weight loss given based on patient characteristics
• Describe considerations in managed care for management of obesity
Adult Obesity Prevalence

https://www.cdc.gov/obesity/data/prevalence-maps.html#overall
Etiology

- Genetic
- Behavioral
- Environmental
- Cultural
- Medications
Defining Obesity

- **Body Mass Index (BMI)**
  - Measure of body weight (kilograms) adjusted for height (meters\(^2\))
  - Most useful population-level measurement of overweight and obesity

<table>
<thead>
<tr>
<th>Classification</th>
<th>BMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight</td>
<td>&lt; 18.5 kg/m(^2)</td>
</tr>
<tr>
<td>Normal weight</td>
<td>≥ 18.5 to 24.9 kg/m(^2)</td>
</tr>
<tr>
<td>Overweight</td>
<td>≥ 25.0 to 29.9 kg/m(^2)</td>
</tr>
<tr>
<td><strong>Obesity</strong></td>
<td>≥ 30 kg/m(^2)</td>
</tr>
<tr>
<td>Class I Obesity</td>
<td>30.0 – 34.9 kg/m(^2)</td>
</tr>
<tr>
<td>Class II Obesity</td>
<td>35.0 – 39.9 kg/m(^2)</td>
</tr>
<tr>
<td>Class III Obesity</td>
<td>≥ 40.0 kg/m(^2)        (extreme obesity)</td>
</tr>
</tbody>
</table>
Waist Circumference

• BMI limitations
  • Does not distinguish body fat distribution △ determinant of metabolic risk

• Waist circumference (WC)
  • Measure of excess abdominal fat
  • Most useful in BMI < 35 kg/m²
  • High-risk WC:
    Men: > 40 inches
    Women: > 35 inches
### Obesity and Disease

<table>
<thead>
<tr>
<th>Type 2 Diabetes Mellitus</th>
<th>Cancer</th>
<th>Heart Disease</th>
<th>Obstructive Sleep Apnea</th>
<th>Hepatobiliary</th>
<th>Osteoarthritis</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Central adiposity</td>
<td>• Males – colon, rectum, prostate</td>
<td>• Hypertension</td>
<td>• Males &gt; females</td>
<td>• Gallbladder disease</td>
<td>• Knees, ankles</td>
</tr>
<tr>
<td></td>
<td>• Females – breast, endometrial, gallbladder</td>
<td>• Atrial fibrillation</td>
<td>• May be life-threatening</td>
<td>• Fatty liver disease</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Heart failure</td>
<td>• Reduced nocturnal oxygen saturation</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Dyslipidemia</td>
<td>• Excess daytime sleepiness</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>• Coronary artery disease</td>
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</tbody>
</table>

Management of Patients with Obesity

1. Lifestyle interventions
2. Pharmacotherapy
3. Surgical approaches/Medical Devices
Comprehensive Lifestyle Intervention

• Initial goal: loss of 5-10% from baseline weight within 6 months
  • Clinically significant improvements in BP, lipids, glycemic control
• Calorie-reduced diet
  • Energy deficit ~500 kcal/day
    Women: 1200-1500 kcal/day
    Men: 1500-1800 kcal/day
Comprehensive Lifestyle Intervention

• No diet type superior in producing sustainable weight loss
  • Best predictor of success = adherence (patient preference)

• Physical activity:
  • Aerobic physical activity ≥ 150 minutes per week
  • 200-300 minutes per week to maintain long-term weight loss
Management of Patients with Obesity

- Lifestyle interventions
- Pharmacotherapy
- Surgical approaches/Medical Devices
Approved Medications for Weight LOSS

Long-Term Use
Orlistat (Xenical®, Alli®)
Phentermine/Topiramate ER (Qsymia®)
Naltrexone SR/Bupropion ER (Contrave®)
Liraglutide (Saxenda®)
Semaglutide (Wegovy®)

Short-Term Use
Phentermine (Adipex-P®, Lomaira®)
Diethylpropion (Tenuate®)
Benzphetamine (Regimex®)
Phendimetrazine (Bontril®)

< 12 weeks
History of Weight Loss Medications

Phentermine
• Approved: 1959

Diethylpropion
• Approved: 1959

Phendimetrazine
• Approved: 1959

Benzphetamine
• Approved: 1960

Fenfluramine
• Approved: 1973
• Withdrawn: 1997

Dexfenfluramine
• Approved: 1996
• Withdrawn: 1997

Sibutramine
• Approved: 1997
• Withdrawn: 2010

Gadde KM. *Clinical Chem.* 2018;64(1):118-129.
History of Weight Loss Medications

Phentermine
- Approved: 1959

Diethylpropion
- Approved: 1959

Phendimetrazine
- Approved: 1959

Benzphetamine
- Approved: 1960

Fenfluramine
- Approved: 1973
- Withdrawn: 1997
- Increased risk of valvular heart disease
- Fenfluramine – increased risk of pulmonary hypertension

Dexfenfluramine
- Approved: 1996
- Withdrawn: 1997

Sibutramine
- Approved: 1997
- Withdrawn: 2010
- Increased risk of nonfatal myocardial infarction and stroke

Gadde KM. Clinical Chem. 2018;64(1):118-129.
History of Weight Loss Medications

Orlistat
• Approved: 1999 (Rx); 2007 (OTC)

Lorcaserin
• Approved: 2012
• Withdrawn: 2020

Liraglutide (3 mg)
• Approved: 2014

Phentermine/Topiramate ER
• Approved: 2012

Naltrexone SR/Bupropion SR
• Approved: 2014

Semaglutide (2.4 mg)
• Approved: 2021

Gadde KM. Clinical Chem. 2018;64(1):118-129.
History of Weight Loss Medications

- **Orlistat**
  - Approved: 1999 (Rx); 2007 (OTC)

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- **Lorcaserin**
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- **Liraglutide (3 mg)**
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  - Approved: 2021

- **Potential cancer risk > benefits**
Which of the following patients is an appropriate candidate for pharmacotherapy for weight loss according to clinical guidelines?

A. A 45-year-old female with a BMI of 25 and type 2 diabetes
B. A 29-year-old female with a BMI of 27 and glaucoma
C. A 30-year-old male with a BMI of 32 and no other health conditions
D. A 36-year-old male with a BMI of 28 and hypertension
Candidates for Pharmacotherapy for Weight Loss

BMI $\geq 30 \text{ kg/m}^2$

BMI $\geq 27 \text{ kg/m}^2 + \geq 1$ comorbidity

Candidates for Pharmacotherapy for Weight Loss

BMI ≥ 27 kg/m² + ≥ 1 comorbidity

• Obesity-related comorbidities:
  • Dyslipidemia
  • Hypertension
  • Type 2 diabetes
  • Obstructive sleep apnea
  • Metabolic syndrome
  • Knee osteoarthritis
  • Asthma or COPD
  • Nonalcoholic fatty liver disease
  • Polycystic ovarian syndrome
  • Coronary artery disease
History of Weight Loss Medications

- **Orlistat**
  - Approved: 1999 (Rx); 2007 (OTC)

- **Lorcaserin**
  - Approved: 2012
  - Withdrawn: 2020

- **Liraglutide (3 mg)**
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  - Approved: 2014

- **Semaglutide (2.4 mg)**
  - Approved: 2021

Gadde KM. *Clinical Chem.* 2018;64(1):118-129.
Orlistat (Xenical®, Alli®)

Mechanism of action

• Inhibits gastric and pancreatic lipase → inhibits intestinal fat absorption

Dosing

• Xenical (Rx): 120 mg three times daily before meals
• Alli (OTC): 60 mg three times daily before meals
• Take during or up to 1 hour after fat-containing meal

DEA Schedule

• Not scheduled
Orlistat (Xenical®, Alli®)

Contraindications/Warnings
- Pregnancy
- Cholestasis

Adverse Effects
- Gastrointestinal - abdominal pain, bowel urgency, steatorrhea, fecal incontinence (limit fat intake to < 30% of daily calories)
- Liver failure (rate)
- Gallbladder disease
- Increased urine oxalate (monitor renal function) (caution in hx of kidney stones)
- Decreased absorption of fat-soluble vitamins – supplement with multivitamin

Drug Interactions
- Warfarin, amiodarone, cyclosporine, levothyroxine
History of Weight Loss Medications

Orlistat
• Approved: 1999 (Rx); 2007 (OTC)

Lorcaserin
• Approved: 2012
• Withdrawn: 2020

Liraglutide (3 mg)
• Approved: 2014

Phentermine/Topiramate ER
• Approved: 2012

Naltrexone SR/Bupropion SR
• Approved: 2014

Semaglutide (2.4 mg)
• Approved: 2021

Gadde KM. Clinical Chem. 2018;64(1):118-129.
Phentermine/Topiramate ER (Qsymia®)

Mechanism of action
- Phentermine: reduces appetite through increase in norepinephrine levels in hypothalamus
- Topiramate: may reduce appetite through effect on GABA receptors

Dosing
- 3.75/23 mg once daily x 14 days ➡️ 7.5/46 mg once daily
- If weight loss < 3% after 12 weeks ➡️ 11.25/69 mg once daily x 14 days ➡️ 15/92 mg once daily

DEA Schedule
- IV
Phentermine/Topiramate ER (Qsymia®)

Contraindications/Warnings
- Pregnancy
- Glaucoma
- Hyperthyroidism
- MAO inhibitor within 14 days

Adverse Effects
- Paresthesia
- Dizziness
- Insomnia
- Altered taste
- Constipation
- Dry mouth
- Increased heart rate

Drug Interactions
- MAO inhibitors, CYP3A4/CYP1A2 inducers, Opioids/CNS depressants, diuretics (hypokalemia), estrogen contraceptives (decreased concentrations)
# Phentermine/Topiramate ER (Qsymia®)

## Contraindications/Warnings
- Pregnancy
- Glaucoma
- Hyperthyroidism
- MAO inhibitor within 14 days

## Adverse Effects
- Paresthesia
- Dizziness
- Insomnia
- Altered taste
- Constipation
- Dry mouth
- Increased heart rate

## Drug Interactions
- MAO inhibitors, CYP3A4/CYP1A2 inducers, Opioids/CNS depressants, diuretics (hypokalemia), estrogen contraceptives (decreased concentrations)

### Topiramate – increased risk of oral clefts
- Available under Risk Evaluation and Mitigation Strategy (REMS) program
- Requires negative pregnancy test before treatment and monthly during treatment.
Phentermine/Topiramate ER (Qsymia®)

Contraindications/Warnings
- Pregnancy
- Glaucoma
- Hyperthyroidism
- MAO inhibitor within 14 days

Adverse Effects
- Paresthesia
- Dizziness
- Insomnia
- Altered taste
- Constipation
- Dry mouth
- Increased heart rate

Drug Interactions
- MAO inhibitors, CYP3A4/CYP1A2 inducers, Opioids/CNS depressants, diuretics (hypokalemia), estrogen contraceptives (decreased concentrations)

Monitor heart rate; use with caution in cardiovascular disease
History of Weight Loss Medications

- **Orlistat**
  - Approved: 1999 (Rx); 2007 (OTC)

- **Phentermine/Topiramate ER**
  - Approved: 2012

- **Lorcaserin**
  - Approved: 2012
  - Withdrawn: 2020

- **Naltrexone SR/Bupropion SR**
  - Approved: 2014

- **Liraglutide (3 mg)**
  - Approved: 2014

- **Semaglutide (2.4 mg)**
  - Approved: 2021
Naltrexone SR/Bupropion SR (Contrave®)

Mechanism of action

• Bupropion: dopamine and norepinephrine reuptake inhibitor in hypothalamus
• Naltrexone: mu opioid receptor antagonist
• Effect on hypothalamus (appetite) and mesolimbic dopamine circuit (reward system) → reduced food intake

Dosing

• 8/90 mg 1 tablet once daily x 1 week → 8/90 mg 1 tablet twice daily x 1 week → 8/90 mg 2 tablets AM + 1 tablet PM x 1 week → 8/90 mg 2 tablets twice daily

DEA Schedule

• Not scheduled
# Naltrexone SR/Bupropion SR (Contrave®)

## Contraindications/Warnings

- Pregnancy
- Uncontrolled hypertension
- Seizure disorder
- Eating disorder (anorexia/bulimia)
- Chronic opioid use/acute opioid withdrawal
- MAO inhibitor within 14 days

## Adverse effects

- Gastrointestinal – nausea, vomiting, diarrhea, constipation
- Headache
- Dizziness
- Insomnia
- Dry mouth
- May increase HR

## Drug Interactions

- Opioids, bupropion-containing products, CYP2B6/CYP2D6 inhibitors
Naltrexone SR/Bupropion SR (Contrave®)

Contraindications/Warnings
- Pregnancy
- Uncontrolled hypertension
- Seizure disorder
- Eating disorder (anorexia/bulimia)
- Chronic opioid use/acute opioid withdrawal
- MAO inhibitor within 14 days

Adverse effects
- Gastrointestinal – nausea, vomiting, diarrhea, constipation
- Headache
- Dizziness
- Insomnia
- Dry mouth
- May increase HR

Drug Interactions
- Opioids, bupropion-containing products, CYP2B6/CYP2D6 inhibitors

Caution in cardiovascular disease/do not use in uncontrolled hypertension
History of Weight Loss Medications

Orlistat
- Approved: 1999 (Rx); 2007 (OTC)

Phentermine/Topiramate ER
- Approved: 2012

Lorcaserin
- Approved: 2012
- Withdrawn: 2020

Naltrexone SR/Bupropion SR
- Approved: 2014

Liraglutide (3 mg)
- Approved: 2014

Semaglutide (2.4 mg)
- Approved: 2021

Gadde KM. Clinical Chem. 2018;64(1):118-129.
Liraglutide (Saxenda®)

Mechanism of action

- Glucagon-like peptide-1 (GLP-1) receptor agonist – stimulates glucose-dependent insulin release, slows gastric emptying, reduces food intake

Dosing

- 0.6 mg SC daily x 1 week → 1.2 mg SC daily x 1 week → 1.8 mg SC daily x 1 week → 2.4 mg SC daily x 1 week → 3 mg SC daily

DEA Schedule

- Not scheduled
Liraglutide (Saxenda®)

Contraindications/Warnings
- Pregnancy
- Personal/family history medullary thyroid cancer [Boxed warning]
- Moderate/severe renal impairment
- History of pancreatitis

Adverse Effects
- Gastrointestinal – nausea, vomiting, diarrhea, constipation
- Acute pancreatitis
- Gallbladder disease
- Hypoglycemia

Drug Interactions
- Other hypoglycemic agents
Orlistat
• Approved: 1999 (Rx); 2007 (OTC)

Phentermine/Topiramate ER
• Approved: 2012

Lorcaserin
• Approved: 2012
• Withdrawn: 2020

Naltrexone SR/Bupropion SR
• Approved: 2014

Liraglutide (3 mg)
• Approved: 2014

Semaglutide (2.4 mg)
• Approved: 2021

Gadde KM. Clinical Chem. 2018;64(1):118-129.
Semaglutide (Wegovy®)

Mechanism of action

• Glucagon-like peptide-1 (GLP-1) receptor agonist – stimulates glucose-dependent insulin release, slows gastric emptying, reduces food intake

Dosing

• 0.25 mg SC once weekly x 4 weeks □ 0.5 mg SC once weekly x 4 weeks □ 1 mg SC once weekly x 4 weeks □ 1.7 mg SC once weekly x 4 weeks □ 2.4 mg SC once weekly

DEA Schedule

• Not scheduled
Semaglutide (Wegovy®)

Contraindications/Warnings

- Pregnancy
- Personal/family history medullary thyroid cancer [Boxed warning]
- Moderate/severe renal impairment
- History of pancreatitis

Adverse Effects

- Gastrointestinal – nausea, vomiting, diarrhea, constipation
- Acute pancreatitis
- Gallbladder disease
- Hypoglycemia

Drug Interactions

- Other hypoglycemic agents
History of Weight Loss Medications

- **Phentermine**
  - Approved: 1959

- **Diethylpropion**
  - Approved: 1959

- **Phendimetrazine**
  - Approved: 1959

- **Benzphetamine**
  - Approved: 1960
Phentermine (Adipex-P®, Lomaira®)

Mechanism of action

- Amphetamine analog: Stimulates release of norepinephrine in hypothalamus → reduced appetite

Dosing

- 15, 30, or 37.5 mg daily (1-2 doses daily)
  - Adipex-P = 37.5 mg; Generic = 15, 30, 37.5 mg
  - Lomaira: 8 mg three times daily before meals

DEA Schedule

- IV
Phentermine (Adipex-P®, Lomaira®)

Contraindications/Warnings

- Pregnancy
- Hyperthyroidism
- Glaucoma
- MAO inhibitor within 14 days

Adverse Effects

- Nervousness
- Dry mouth
- Insomnia
- Increased heart rate/blood pressure

Drug Interactions

- MAO inhibitors
## Phentermine (Adipex-P®, Lomaira®)

### Contraindications/Warnings
- Pregnancy
- Hyperthyroidism
- Glaucoma
- MAO inhibitor within 14 days

### Adverse Effects
- Nervousness
- Dry mouth
- Insomnia
- Increased heart rate/blood pressure

### Drug Interactions
- MAO inhibitors

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Caution in cardiovascular disease/do not use in uncontrolled hypertension
## Choosing a Medication

- No head-to-head comparison studies of approved medications
- Meta-analysis of 28 RCTs (n=29,018)

<table>
<thead>
<tr>
<th>Medication</th>
<th>Mean weight loss versus placebo</th>
<th>&gt; 5% weight loss (OR)</th>
<th>&gt; 10% weight loss (OR)</th>
<th>Discontinuation due to adverse event (OR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phentermine/topiramate</td>
<td>-8.80 kg</td>
<td>9.22</td>
<td>11.40</td>
<td>2.29</td>
</tr>
<tr>
<td>Liraglutide</td>
<td>-5.24 kg</td>
<td>5.54</td>
<td>4.99</td>
<td>2.95</td>
</tr>
<tr>
<td>Naltrexone/bupropion</td>
<td>-4.95 kg</td>
<td>3.96</td>
<td>4.19</td>
<td>2.64</td>
</tr>
<tr>
<td>Orlistat</td>
<td>-2.63 kg</td>
<td>2.70</td>
<td>2.42</td>
<td>1.84</td>
</tr>
</tbody>
</table>

*VA/DoD Clinical Practice Guideline for the Management of Adult Overweight and Obesity.*

*Meta-analysis completed in 2016; Semaglutide not yet approved for weight loss*
## Choosing a Medication

<table>
<thead>
<tr>
<th>Medication</th>
<th>Glycemic measures</th>
<th>Blood pressure</th>
<th>Lipids</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phentermine/topiramate</td>
<td>+++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Liraglutide</td>
<td>++++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Naltrexone/bupropion</td>
<td>++</td>
<td>Unfavorable</td>
<td>+</td>
</tr>
<tr>
<td>Orlistat</td>
<td>+++</td>
<td>++</td>
<td>++</td>
</tr>
</tbody>
</table>

Choosing a Medication

- **Semaglutide (Wegovy®) – STEP 1 Study**
  - n=1,961 adults (BMI > 30 or > 27 + comorbidity) WITHOUT diabetes
  - 68 weeks of treatment with once-weekly SC semaglutide 2.4 mg or placebo

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Semaglutide</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percentage mean change in body weight from baseline</td>
<td>-14.9%</td>
<td>-2.4%</td>
</tr>
<tr>
<td>Change in body weight</td>
<td>-15.3 kg</td>
<td>-2.6 kg</td>
</tr>
<tr>
<td>≥ 5% weight loss</td>
<td>86.4%</td>
<td>31.5%</td>
</tr>
<tr>
<td>≥ 10% weight loss</td>
<td>69.1%</td>
<td>12%</td>
</tr>
</tbody>
</table>

- Treatment difference: -12.4% (95% CI -13.4 to -11.5, p<0.001)

- Semaglutide – improvement in cardiometabolic risk factors
- Most common adverse events – nausea, diarrhea (more patients discontinued semaglutide vs. placebo)

Choosing a Medication

• Clinical guidelines:
  • Agents approved for long-term use preferred
  • No agent preferred over another

• Individualized approach
  • Side effects
  • Cautions/contraindications
  • Drug interactions
  • Weight-related complications and medical history

## Choosing a Medication

<table>
<thead>
<tr>
<th>Condition</th>
<th>Orlistat</th>
<th>Phentermine/Topiramate</th>
<th>Naltrexone/Bupropion</th>
<th>Liraglutide</th>
<th>Semaglutide</th>
<th>Phentermine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 2 Diabetes</td>
<td></td>
<td></td>
<td>Contraindicated in uncontrolled HTN</td>
<td>✮</td>
<td>✮</td>
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<tr>
<td>Hypertension</td>
<td></td>
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<tr>
<td>Cardiovascular disease (CAD)</td>
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</tr>
<tr>
<td>Arrhythmia</td>
<td></td>
<td>May increase HR</td>
<td>May increase HR</td>
<td>May increase HR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Seizure disorder</td>
<td></td>
<td></td>
<td>Lowers seizure threshold</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Opioid use</td>
<td></td>
<td>Caution in hx of drug abuse</td>
<td>Opioid antagonist</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperthyroidism/Glaucoma</td>
<td></td>
<td>Contraindicated</td>
<td>May trigger angle closure glaucoma</td>
<td></td>
<td></td>
<td>Contraindicated</td>
</tr>
<tr>
<td>Thyroid cancer</td>
<td></td>
<td></td>
<td></td>
<td>Contraindicated</td>
<td>Contraindicated</td>
<td></td>
</tr>
<tr>
<td>Pregnancy</td>
<td></td>
<td></td>
<td></td>
<td>REMS program</td>
<td></td>
<td>Contraindicated</td>
</tr>
</tbody>
</table>

**Key:** Green = safe to use; Yellow = use with caution; Red = contraindicated
Choosing a Medication

• Renal and hepatic impairment
  May require dosage adjustments
  Limited data in severe impairment

• Gallbladder disease
  Orlistat, liraglutide, and semaglutide

• Pancreatitis
  Avoid liraglutide and semaglutide

Monitoring of Therapy

• Medication-specific parameters
• Weight loss

Assess patients monthly x 3 months, then at least every 3 months

**Orlistat, Qsymia, Contrave, Wegovy**
- Discontinue if < 5% weight loss at 12 weeks

**Saxenda**
- Discontinue if < 4% weight loss at 16 weeks

Remember: Phentermine (Adipex-P®, Lomaira®) not recommended for use beyond 12 weeks.
Weight Regain

• STEP 1 Trial Extension
  • STEP 1 Study
    - n=1,961 adults (BMI $\geq 30$ or $\geq 27$ + comorbidity) WITHOUT diabetes
    - 68 weeks of treatment with once-weekly SC semaglutide 2.4 mg or placebo
  • Extension: 327 patients followed for additional 52 weeks off-treatment
    228 – semaglutide; 99 - placebo

New Drug Poised to Take Weight-Loss Throne

Eli Lilly's Mounjaro is outperforming Ozempic in clinical trials

By Steve Huff, Newser Staff
Posted Apr 9, 2023 2:25 PM CDT
Tirzepatide (Mounjaro®)

• GLP-1/GIP receptor agonist
• Once-weekly subcutaneous injection

SURPASS-2 trial:
  • Tirzepatide vs. semaglutide 1 mg
  • 1800 patients with type 2 diabetes
  • Primary end point: change in A1C from baseline to 40 weeks
  • A1C reduction: tirzepatide (2.3%) > semaglutide (1.86%)
  • Weight reduction: tirzepatide > semaglutide
Tirzepatide (Mounjaro®)

- **SURMOUNT-1:**
  - Tirzepatide vs. placebo
  - 2539 patients without diabetes
  - Primary end points (72 weeks):
    1. % change in weight from baseline
    2. Weight reduction of 5% or more

Tirzepatide (Mounjaro®)

Tirzepatide (Mounjaro®)

• SURMOUNT-2: *estimated completion April 2023*
  • Tirzepatide vs. placebo
  • 900 patients with type 2 diabetes
  • Primary end points (72 weeks):
    (1) % change in weight from baseline
    (2) weight reduction of 5% or more

• October 2022: FDA granted Fast Track designation for weight loss

Pharmacists’ Roles

• **Outpatient settings**
  - Patient assessment & design of individualized treatment plans (nonpharmacological and pharmacological)
  - Risk-benefit analysis for pharmacological interventions
  - Appropriate use of pharmacotherapy

• **Inpatient settings**
  - Medication reconciliation
  - Medication management for patients undergoing bariatric surgery
  - Patient education & transitions of care
Considerations in Managed Care

• Patient & provider perceptions
• Patient access
• Adherence
• Clinical burden of obesity

Considerations in Managed Care

Popularity of Ozempic, Mounjaro, similar drugs may be driving shortages for people with diabetes, obesity

Doctors say too many people are obtaining the drugs despite not being obese.

By Lisanne Robinson, Mark Muldoon, Claire Pedersen, and Ivan Pereira
February 23, 2023, 11:59 AM

Considerations in Managed Care

• Coverage of pharmacotherapy
  • Medicare
    - Medications for weight management excluded from Part D
    - Medicare Advantage plans may offer expanded coverage for weight loss treatment plans
  • Medicaid
    - Optional coverage, varies from state to state
  • Private
    - Varies
    - Requirements – prior authorization, step therapy, etc
Quality Measures in Obesity

• Centers for Medicare & Medicaid Services (CMS)
  • Preventive Care and Screening: BMI Screening and Follow-Up Plan
    Percentage of patients with BMI documented within previous 12 months AND had a follow-up plan documented (if BMI was outside normal parameters)
  • Increased screening → increasing diagnosis → increased action plans → reduced health care costs

Health Care Costs

- Retrospective analysis of 15,000 patients (2012-2018):
  - Significant health care cost savings for patients achieving clinically meaningful weight loss (lifestyle interventions and pharmacotherapy)

- Modeling studies:
  - Moderate/extensive expansion of coverage for lifestyle intervention with or without pharmacotherapy → increased treatment utilization → ~$20 billion in savings over 10 years
  - 100% uptake of pharmacotherapy by Medicare/Medicaid → ~$200 billion savings over 75 years
Summary

- Obesity can predispose patients to a number of comorbidities
- Lifestyle intervention is the foundation of effective weight management initiatives
- Several medications are FDA-approved for management of obesity
- Several barriers pose a challenge to widespread obesity treatment
Management of Obesity

Cynthia Moreau, PharmD, CPh, BCACP, CDCES
Clinical Pharmacist
ChenMed
cynthia.moreau@chenmed.com
Value Framework Assessments

How Health Care Systems and Payers Can Use Data to Inform Decision-Making
Learning Objectives

1. **Understand** the need for value framework assessments
2. **Describe** the different types of value framework assessments in the U.S.
3. **Discuss** how U.S. payers will utilize value framework assessments in the future
Faculty Disclosure

Dr. Cynthia Miller does not have any conflicts of interest associated with this presentation.
Pretest Question 1

U.S. spend drivers include all of the following except:

a. More chronic conditions
b. New therapies and technologies
c. An aging population
d. Health inequities
e. A higher number of uninsured
Pretest Question 2

All of the following are true, except:

a. ICER uses QALYs as part of its framework
b. The AHA/ACA conducts their own trials for cost-effectiveness
c. NCCN is designed to be used in shared decision making between the patient and provider
d. Real world evidence allows us to address the evidence-efficacy gap
Pretest Question 3

Which of the following are ways that the U.S. is moving towards a more value focused assessment:

a. The Inflation Reduction Act
b. FDA requirement for Patient Reported Outcomes in trials
c. FDA focus on real world evidence generation
d. Both A and C
e. A, B and C
Do we really have a spending problem?
Higher Spend ≠ Better Outcomes$^{1,2}$

**Spend and Resources**
- Higher spend percent of GDP, per person
- Lowest rate of practicing physicians and hospital beds

**Outcomes**
- Lowest life expectancy at birth
- Highest death rate for avoidable/treatable conditions
- Highest infant and infant mortality
- Highest rate chronic conditions

We are not getting the same value and the outcomes for the amount spent as other countries

---

1. We are not getting the same value and the outcomes for the amount spent as other countries.

2. The U.S. is a world outlier when it comes to health care spending.

---

**Notes:**
- 2021 data (or latest available year).
- Data points reflect share of gross domestic product. Based on Systems of Health Accounts methodology, with some differences between country methodologies. GDP = gross domestic product. OECD average reflects the average of 38 OECD member countries, including ones not shown here.

Date: OECD Health Statistics 2022.

What is behind rising costs? 

Cost drivers =

Increased use of services:
- Aging population, more insured, more chronic conditions

+ Intensity of services:
- New therapies and technologies

Case Study: Accelerated approval and the FDA

44% increase in the number of adults aged 65 and older from 2020-2040

50% of American adults have at least one chronic disease

A rise in spend has highlighted potential need for reform in approval processes
Health inequities are leading to higher spend

- $320 billion annual health care spend
- In 2040, $1 trillion annual health care spend (if unaddressed; $11.8 trillion of total spend)
- $42 billion in lost productivity per year
- Late diagnosis, delayed care, poor access, income disparities, limited access to scientific advances and prevention

Addressing health inequities may mitigate rising spend

<table>
<thead>
<tr>
<th>Rate ratios compared to White, Non-Hispanic persons</th>
<th>American Indian or Alaska Native, Non-Hispanic persons</th>
<th>Asian, Non-Hispanic persons</th>
<th>Black or African American, Non-Hispanic persons</th>
<th>Hispanic or Latino persons</th>
</tr>
</thead>
</table>
| Cases
| 1.5x | 0.8x | 1.1x | 1.5x |
| Hospitalization
| 2.5x | 0.7x | 2.1x | 1.9x |
| Death
| 2.1x | 0.8x | 1.6x | 1.7x |

Race and ethnicity are risk markers for other underlying conditions that affect health, including socioeconomic status, access to health care, and exposure to the virus related to occupation, e.g., frontline, essential, and critical infrastructure workers.

Note: Adjusting by age is important because risk of infection, hospitalization, and death is different by age, and age distribution differs by racial and ethnic group. If the effect of age is not accounted for, racial and ethnic disparities can be underestimated or overestimated.
The Quintuple Aim: A Solution?^{20,21}

• Pay-for-performance (P4P) and value-based contracts are becoming more common
  – Key quality measures reported publicly
  – Emphasis and rewards (internally and externally)

• Many systems are struggling to succeed in this newly incentivized and rapidly changing environment

• Value-based programs are exposing high-cost areas in the health care system and increasing transparency

Focusing on quality, costs, and health equity through value-based arrangements may help solve the spending problem
How are we doing? Not so great \(^{23,24}\)

<table>
<thead>
<tr>
<th>Comparison</th>
<th>2017</th>
<th>2022</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fee for Service</td>
<td>41%</td>
<td>40.5%</td>
</tr>
<tr>
<td>FFS + Quality</td>
<td>25.4%</td>
<td>19.5%</td>
</tr>
<tr>
<td>APM</td>
<td>29.8%</td>
<td>32.6%</td>
</tr>
<tr>
<td>Population health</td>
<td>3.8%</td>
<td>7.4%</td>
</tr>
</tbody>
</table>

**Savings:**
- ACO* 0.4%-6.1%
- Bundled payments: $453-$1166 per episode
- Capitated: Full risk savings: $161 pmpy** or 3.6% lower than no risk

Most surveyed payers believe that the number of advanced payment models will increase and drive practice transformation efforts, resulting in better quality and more affordable care.

*ACO = Accountable Care Organization; **pmpy = per member per year
How might we translate this to drug pricing? A new model based on value rather than volume may upend the rebate-based system.
Value Assessment Frameworks

US and ex-US
What is a Value Framework Assessment?²,²⁶

Health Technology Assessment (HTA)²⁷

“Health technology assessment is a multidisciplinary process that uses explicit methods to determine the value of a health technology at different points in its lifecycle. The purpose is to inform decision-making in order to promote an equitable, efficient, and high-quality health system.” – ISPOR

Value Framework Assessment

Frameworks that inform discussions about how to define and assess value at various levels of the US health care system

Some terms:
- Opportunity cost
- Cost-benefit/cost-effectiveness
- Societal perspective
- Patient-centered outcomes
- Quality Adjusted Life Years (QALY)
- Cost-effectiveness ratio
- Incremental cost–effectiveness ratio

HTAs are commonly used in Europe to determine coverage based on pricing
What do US payers do today to assess value? Survey says:

How payers assess value (P&T* Pharmacy committee)
- Expected cost and clinical benefits
- Medical necessity
- Appropriate use
- Therapeutic alternatives
- Treatment class

How payers implement value assessments (“Value” Committee)
- Noncoverage
- Tiering
- Step therapy
- Prior authorization
- Preferred products

US payers rely on utilization management rather than a government entity to determine coverage and utilization

*P&T = Pharmacy and Therapeutics
Value-based pricing models do exist in the US\textsuperscript{30}

Image above taken from Avalere Health LLC. \textsuperscript{34}

While US payers have implemented some value-based pricing, these pricing constructs are difficult to scale, are fragmented, and remain proprietary.
## Value Framework Assessments (VFAs) in the US

### Non-oncology
- CMS (Centers for Medicare and Medicaid Services)
- ACC/AHA (American College of Cardiology/American Heart Association)
- ICER (Institute for Clinical and Economic Research)

### Oncology
- ASCO (American Society of Clinical Oncology)
- MSKCC (Memorial Sloan Kettering Cancer Center)
- NCCN (National Comprehensive Cancer Network)

Although these are the major recognized VFAs in the US, there are additional models.
CMS as a Value Framework Assessment Entity: The Inflation Reduction Act\textsuperscript{32,33}

Value Assessment Provisions

- HHS secretary negotiates maximum prices for select brand-name drugs covered under Part B and Part D
- Manufacturers submit product information (manufacturing, government support, patent) AND supporting evidence (comparative data and effectiveness, unmet need)

What is new?

- Supply side vs demand side
- Research and development costs
- Production and distribution costs

Value assessment across the life cycle

Implementation of the Inflation Reduction Act is expected to reduce innovation in the long term. The Congressional Budget Office estimates that there will be a reduction of new drugs by 1\% over 30 years\textsuperscript{33}
Institute for Clinical and Economic Review (ICER)\textsuperscript{34}

Framework
- Cost-effectiveness analysis
- QALYs
- Population level

Orientation
- Coverage
- Reimbursement
- Affordability
- Limitations
  - Not at the individual level
  - Concern about transparency

While ICER often identifies a cost-effective price, this has not led to price reductions

Image above taken from ICER\textsuperscript{35}
ICER Example: Product X for Disease A

**Disease A** affects large part of US population and does not have a cure

**Product X**
- $80,000/year treatment
- incremental cost-effectiveness ratio $20,000
- Incremental QALYs 0.6
- Delays disease progression

**Cost comparison**
- Product X TCOC $400,000
- SOC TCOC $420,000

**TERMS:** QALYs = quality-adjusted life years; SOC = standard of care; TCOC = total cost of care

QALYs incorporate both the delay of disease progression and any side effects that may detract from quality of life

Image above taken from ICER

QALYs incorporate both the delay of disease progression and any side effects that may detract from quality of life.
The ACC/AHA model has assisted in writing guidelines and pathways that are most cost-effective in the area of cardiology for not only medications but also procedures.
ACC/AHA Example\textsuperscript{36}

2022 Heart Failure Guidelines

“In patients with previous or current symptoms of chronic HFrEF, in whom ARNi is not feasible, treatment with an ACEi or ARB provides high economic value”\textsuperscript{36}

- Based on 7 cost-effectiveness trials
- Rated as “high” in the table entitled “Value Statements”

The ACC/AHA model may incorporate findings from multiple cost-effectiveness studies to create a value statement.
Oncology Frameworks $^{37,38,39,40}$

ASCO/NCCN
- Benefits and harms
- Shared decision-making
- Drug costs from provider/patient perspective

MSKCC
- DrugAbacus calculator
- Policymakers
- Willingness to pay vs innovation and development

Oncology frameworks are used to make individual-level decisions and to inform clinical pathways
**Case:**

**Drug A** is the standard of care for Disease X.

**Drug B** was testing in a clinical trial against Drug A. The two drugs showed equal overall survival and toxicity levels.

ASCO’s HTA is limited to drugs with head-to-head clinical trials.
How do they compare?

<table>
<thead>
<tr>
<th>Stakeholders</th>
<th>Methods</th>
<th>Purpose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CMS</td>
<td>Pharma, PBM</td>
<td>Price setting, negotiation</td>
</tr>
<tr>
<td>ICER</td>
<td>Payers, Pharma</td>
<td>Internal Cost-Effectiveness model</td>
</tr>
<tr>
<td>ACC/AHA</td>
<td>Physicians</td>
<td>Evaluate published cost-effectiveness trials to establish value statement</td>
</tr>
<tr>
<td>ASCO</td>
<td>Physicians, Patients</td>
<td>Evaluation Head-to-Head Trials</td>
</tr>
<tr>
<td>NCCN</td>
<td>Physicians, Patients</td>
<td>Expert Panel Literature review</td>
</tr>
<tr>
<td>MSKCC</td>
<td>Policymakers</td>
<td>Abacus calculator</td>
</tr>
</tbody>
</table>

When using VFAs, it is important to recognize their intended purpose and limitations
Ex-US Models

- France
  - Commission for Transparency
- Germany
  - Institute for Quality and Efficiency in Health Care
- Switzerland
  - Federal Office for Public Health
- England
  - National Institute for Health and Care Excellence (NICE)

Ex-US HTA evaluation can lead to pricing negotiations or coverage decisions that differ from the US

The Future of VFA: Real-World Evidence (RWE)\textsuperscript{42,43,44}

The Efficacy Evidence Gap

**Pros:** real-world treatment patterns, safety, and comparative effectiveness

**Cons:** internal validity, reporting bias, data quality, observational, transparency

Life Cycle Management

- Coverage with evidence development: studies can be expensive, costly, and lengthy
- NICE – temporary reimbursement for therapies (cancer) for 2 years

RWE allows us to understand how a medication works for the larger population and to evaluate its efficacy and safety over the long-term.
Case Study: Hereditary Angioedema

- 24-month RWE update for hereditary angioedema prophylactic therapies (post-launch)

- **Pre-launch**: attack rate 3.39, $/QALY

- **24 months post-launch**: attack rate 1.88, $/QALY

Real-world evidence can be used to validate assumptions in cost-effectiveness models to improve their accuracy.

### Table 3.3. Comparison of 2018 and Observational RWE Update Base-Case Results for HAE Prophylaxis versus no Prophylaxis

<table>
<thead>
<tr>
<th>Treatment</th>
<th>2018 Report Cost per QALY gained</th>
<th>Observational RWE Update Cost per QALY gained</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cinryze</td>
<td>$5,950,000</td>
<td>$30,070,000</td>
</tr>
<tr>
<td>Haegarda</td>
<td>$328,000</td>
<td>$13,430,000</td>
</tr>
<tr>
<td>Takhzyro</td>
<td>$1,110,000</td>
<td>$12,370,000</td>
</tr>
</tbody>
</table>

QALY: quality-adjusted life year
How do we elevate value in the US health care system?
Payers and use of VFA: What’s the core problem?²,²⁸,³⁵

Policy

• CMS does not allow for cost-per-QALY thresholds in decision-making
• QALYs are controversial

US Customer Expectations

• Tension between innovation, access, and cost

Implementation

• Outcomes-based pricing is resource intensive and lacks proven savings

Significant conflicts of interest and incentive misalignment lead to difficulties implementing value framework assessments in the US
What is the future of payers and VFA?  

Government policy

- Intermediary solutions (IRA, Biden new budget proposal)
- Segmented strategic approach

Increased use of real-world evidence

- FDA focus on evaluating RWE

Incorporation of patient-reported/patient-centered outcomes (PROs)

- FDA requiring PROs in trials to understand impact on the patient

A government/policy approach will likely encourage use of HTAs for pricing discussions
Will VFAs help us get more for our money?
Post-test Question 1

U.S. spend drivers include all of the following except:

a. More chronic conditions
b. New therapies and technologies
c. An aging population
d. Health inequities
e. A higher number of uninsured
All of the following are true, except:

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Post-test Question 3

Which of the following are ways that the U.S. is moving towards a more value focused assessment

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d. Both A and C
e. A, B and C
References


References


References


References


Value Framework Assessments

How Health Care Systems and Payers Can Use Data to Inform Decision-Making
Break Networking Exhibits
Federal Legislative Update:
Inflation Reduction Act

Moderated by
Jennifer L. Mathieu, MA
Senior Vice President, Professional & Government Affairs, AMCP
Learning Objectives

1. Explain the basic timeline for Medicare drug price provisions
2. Describe how the IRA will impact drug affordability
3. Identify potential unintended consequences of IRA requirements
Panelists

Shawn Barger, PharmD
Director, Medicare Formulary Strategy
Aetna

Javier Gonzalez, PharmD
Chief Growth & Commercial Officer
Abarca Health

Cynthia Griffin, PharmD
Vice President, Medicare
Pharmacy Programs
Florida Blue
Panelists

Jonathan Hickman, PharmD
Medical Executive Director
Genentech

Ashley Peterson, MHA
Medicaid Pharmacy Director,
Contracting & Analytics
Artia
Inflation Reduction Act Overview
Political Outlook

- Narrow majorities in both House and Senate
- No looming “must pass” health care-related legislation
- Debt ceiling, inflation, military aid to Ukraine crowding out other issues
Inflation Reduction Act (H.R. 5376)

- Originally introduced as the Build Back Better Act by Congressman John Yarmuth (D-KY-03)
- Signed into law by President Biden on August 16, 2022
- Drug pricing provisions include:
  - Drug price negotiation program
  - Inflationary rebates
  - Part D redesign
- Enhances payments for biosimilars, extends expanded Affordable Care Act (ACA) tax credits, and delays the Trump-era Rebate Rule

• Drug Price Negotiation Program
  • Requires government negotiation of the prices of certain prescription drugs under Medicare beginning in 2026

• Inflationary Rebates
  • Requires manufacturers to pay rebates for certain drugs paid under Medicare Parts B or D if their average price increases faster than the rate of inflation

• Part D Redesign

• Enhanced Payments for Biosimilars
  • Temporarily increases the Part B add-on payment for qualifying biosimilars from 6% to 8% of the reference product’s Average Sales Price for a 5-year period

• Extension of Expanded ACA Premium Tax Credit
  • Extends the temporary ACA premium tax credit expansions that were included in the American Rescue Plan Act through 2025

• Rebate Rule Delay
  • Prevents implementation or enforcement of the Trump-era Rebate Rule until January 1, 2032
Key Concerns

- Cost-shifting to commercial sector
- Additional instability for generic and biosimilar market
- Higher launch prices resulting from inflation penalty rebates

Slide designed by Melissa Andel, MPP, Principal, CommonHealth Solutions LLC.
Inflation Reduction Act – Regulatory Implementation

• January 11 - HHS issued a timeline for implementation of IRA:
  • CMS will seek feedback on implementation through a series of 3 information collection requests (ICRs) and will issue draft guidance to solicit comments on key elements of the Medicare Drug Price Negotiation Program.
  • Among the key dates:
    • By Sept. 1, 2023, CMS will publish the first 10 Medicare Part D drugs selected for the Medicare Drug Price Negotiation Program.
    • The negotiated maximum fair prices for these drugs will be announced by Sept. 1, 2024 and prices will be effective starting Jan. 1, 2026.
    • CMS will select 15 additional Part D drugs for 2027, 15 more Part B or Part D drugs for 2028, and 20 more Part B or Part D drugs for each subsequent year.
Center for Medicare and Medicaid Innovation (CMMI) announced the selection of three new healthcare payment and delivery models that will test relating to the prescription drug provisions of the Inflation Reduction Act (IRA), with the intent of lowering drug costs and promoting access to innovative drug therapies.

Medicare Part D manufacturer discount program (MDP) beginning Jan. 1, 2025

Participating manufacturers must enter into agreements with CMS by Mar. 1, 2024 to participate in the MDP in 2025.
On Feb. 7, 2023, CMS issued an information collection request under the Paperwork Reduction Act of 1995 (PRA). Information in this collection is needed to set up agreements between manufacturers and CMS. Note that this is a notice about CMS’ intention to collect this information and comments can be submitted until April 10, 2023.

Information will be collected from respondents electronically, through HPMS.
Key Dates

- **Sept. 2023:** Initial 10 Part D drugs selected for negotiation identified
- **Sept. 2024:** Negotiated price for initial Part D drugs published
- **Sept. 2025:** Selection of 15 Part D drugs for negotiation for CY 2027
- **Jan. 2025:** Full Part D redesign takes effect
- **Jan. 2027:** Second 15 negotiated prices effective
- **Oct. 2022:** Inflation penalty rebates for Part D drugs begin
- **Late 2025:** CMS begins sending inflation penalty rebate invoices to manufacturers
- **Jan. 2026:** First 10 negotiated prices effective

How does a potential change in Presidential administration impact implementation?

Source: Congress.gov. H.R. 5376, Inflation Reduction Act of 2022. Slide designed by Melissa Andel, MPP, Principal, CommonHealth Solutions LLC.
Commercial Takeaways

Understand relationship between and commercial market exposure of drugs selected for negotiation

Consider how increased uncertainty in generic/biosimilar market could have ripple effects

Consider Medicare market exposure for new drugs and how inflation penalty rebates may influence launch prices
Manufacturer Takeaways

Are IRA reforms “enough”?

Consider how government price negotiation could change standard approach for end of drug’s lifecycle or generic/biosimilar industry

Impact of delayed rebate invoices
Panel Discussion
Lunch Networking Exhibits
Kahoot Game

https://create.kahoot.it/share/amcp-day-education-2023-kahoot-2/e325b175-b2a0-4335-9e4a-62b457e8f002
Learning Objectives

1. Discuss the current level of understanding of biosimilars in the marketplace
2. Describe the scientific evidence that supports the use of biosimilars, interchangeability, and the adoption of biosimilars in the healthcare community
3. Identify nuances between medical and pharmacy billing/dispensing for biosimilars
Panelists

Jorge Garcia, PharmD, MS, MHA, MBA, FACHE
Assistant Vice President – System Oncology Pharmacy Service Line
Baptist Health South Florida

Jennifer Miles, PharmD, BCACP, BCMTMS
Assistant Director of Ambulatory Clinical Pharmacy Services
Jackson Health Ambulatory Care

Richard Gourash, RPh, MBA
Vice President of Oncology
BioPlus Specialty Pharmacy

David Fox, PharmD
Administrator of Clinical Pharmacy Services
Florida Healthcare Plan
Biosimilar Overview
**Biosimilar History**

**EU**
- The European Medicines Agency (EMA) developed guidelines for the approval of biosimilars in 2005.
- Omnitrope (somatropin) was the first biosimilar approved in the EU in 2006.

**USA**
- The Biologics Price Competition and Innovation Act was signed into law in 2010, paving the way for biosimilars in the US.
- Filgrastim-sndz (Zarxio) was the first biosimilar approved in the US on March 6, 2015.

**USA**
- Adoption of biosimilars was slow due to negative messaging from innovator/originator companies.
- Both the Ensuring Innovation Act and the Advancing Education on Biosimilars Act were signed into law on April 23, 2021.
Biosimilars launched to date account for 24% of competitive molecule volume

Exhibit 4: Percentage of biologics sales accessible to approved and launched biosimilars and biosimilar efficiency. Q1 2015–Q3 2022

Since 2007, 30 biosimilars have launched in the U.S. with 10 more approved and set to launch by the end of 2023.

Exhibit 5: Biosimilars approved and launched in the U.S.

Source: IQVIA Institute, Dec 2022.
Expected launches and uptake are likely to increase overall spending on biosimilars significantly to $20–49Bn in 2027


Source: IQVIA MIDAS, Jun 2022; IQVIA Institute, Nov 2022.
Savings over the next five years as a result of biosimilars are projected to exceed $180Bn, though uncertainties remain.

Exhibit 22: Biologic estimated savings from biosimilars at invoice prices

Source: IQVIA MIDAS, Jun 2022. IQVIA Institute, Nov 2022.
Entry of new immunology biosimilars in 2023 will increase competition in a rapidly growing market

Exhibit 23: Historic and future immunology volume in defined daily doses (DDDs) by biosimilar competition, 2013–2027

Source: IQVIA MIDAS, Jun 2022; IQVIA Institute, Dec 2022.
Figure 4. Adoption of biosimilars typically accelerates quickly after market introduction.

Source: IQVIA; Accessed via IQVIA National Sales Perspective (NSP) SMART Data, 3October 2021.
Payer/PBM Formulary Considerations

- Will Biosimilar Partners Commit Long Term and Deliver Value

- Patient Support- Copay/Device Replacement

- Rebate Strategy can be a Defensive Maneuver to Preserve Brand Market Share
  Payer/PBM Execution Risk in Removing/Disadvantaging Brand

- Brand Company Lowers Price/Offeres Non-Branded Products
  Will This Discourage Pharma-Companies to Invest in Biosimilars

- Can Biosimilars Bring Value Outside of the Initial Innovator Product?
  Biosimilar Humira Vs Other TNFs or Interleukins (ie. IL 17, IL 23, IL 12-23)
Figure 5. Downward Trend in ASP for Biosimilars and Reference Products Over Time

Source: Amgen 2022 Biosimilar Trend Report
The Evolving Biosimilars Landscape: Panel Discussion

Moderated by
Wendy Bailey, RPh, BS Pharm, MS Pharm, MBA
Vice President, Health Plan Pharmacy Strategy, Centene Corporation
Disclosures

• Research is supported by
  • Bristol Myers Squibb
  • Merck Corporation
  • Sanofi
  • Mirati Therapeutics
Learning Objectives

- Discuss local/national health care performance and historical factors that result in health inequities
- Describe the social and structural factors that contribute to different health outcomes in marginalized populations
- Understand the interconnections and relationships between individual outcomes, socioeconomic context, and systemic barriers contributing to health inequalities
- Summarize how various stakeholders can advance health equity in their practice or organization
Health Care Spending as a Percentage of GDP, 1980–2019

Notes: Current expenditures on health. Based on System of Health Accounts methodology, with some differences between country methodologies. GDP refers to gross domestic product.

* 2019 data are provisional or estimated for Australia, Canada, and New Zealand.

Data: OECD Health Data, July 2021.


https://doi.org/10.26099/01DV-H208
Health Care System Performance Compared to Spending

Note: Health care spending as a percent of GDP. Performance scores are based on standard deviation calculated from the 10-country average that excludes the US. See How We Conducted This Study for more detail.

Data: Spending data are from OECD for the year 2019 (updated in July 2021).

https://doi.org/10.25099/0D4V-120B
### EXHIBIT 1

Health Care System Performance Rankings

<table>
<thead>
<tr>
<th></th>
<th>AUS</th>
<th>CAN</th>
<th>FRA</th>
<th>GER</th>
<th>NETH</th>
<th>NZ</th>
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<th>SWE</th>
<th>SWIZ</th>
<th>UK</th>
<th>US</th>
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<tr>
<td><strong>OVERALL RANKING</strong></td>
<td>3</td>
<td>10</td>
<td>8</td>
<td>5</td>
<td>2</td>
<td>6</td>
<td>1</td>
<td>7</td>
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<td>4</td>
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<tr>
<td>Access to Care</td>
<td>8</td>
<td>9</td>
<td>7</td>
<td>3</td>
<td>1</td>
<td>5</td>
<td>2</td>
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<td>4</td>
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<tr>
<td>Care Process</td>
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<td>4</td>
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<td>9</td>
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<td>1</td>
<td>8</td>
<td>11</td>
<td>7</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Administrative Efficiency</td>
<td>2</td>
<td>7</td>
<td>6</td>
<td>9</td>
<td>8</td>
<td>3</td>
<td>1</td>
<td>5</td>
<td>10</td>
<td>4</td>
<td>11</td>
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<td>Equity</td>
<td>1</td>
<td>10</td>
<td>7</td>
<td>2</td>
<td>5</td>
<td>9</td>
<td>8</td>
<td>6</td>
<td>3</td>
<td>4</td>
<td>11</td>
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<tr>
<td>Health Care Outcomes</td>
<td>1</td>
<td>10</td>
<td>6</td>
<td>7</td>
<td>4</td>
<td>8</td>
<td>2</td>
<td>5</td>
<td>3</td>
<td>9</td>
<td>11</td>
</tr>
</tbody>
</table>

Data: Commonwealth Fund analysis.


https://doi.org/10.25099/01DV-H208
What is Health Equity?

• Health equity provides everyone with a fair and just opportunity to be as healthy as possible

• Avoidable differences in health outcomes

• Removing obstacles to health such as poverty, discrimination, and their consequences, including powerlessness and lack of access to good jobs with fair pay, quality education and housing, safe environments, and health care
Profound racial and ethnic inequities in health and health care exist across and within states.

Health system performance scores, by state and race/ethnicity

Notes: Scores are based on the percentile distribution of each group's final composite score across all indicators/dimensions; rank-ordered by score of state's highest group. The 50th percentile represents the median health performance score among all the groups measured. Summary performance scores not available for all racial and ethnic groups in all states; missing dots for a particular group indicate that there are insufficient data for that state. AANHPI = Asian American, Native Hawaiian, and Pacific Islander; AIMN = American Indian/Alaska Native.

Data: Commonwealth Fund 2021 Health System Performance Scores.

“Of all the forms of inequality, injustice in health care is the most shocking and inhuman.”
Why Health Equity Matters?

- Delayed care and inadequate health care coverage may increase the cost of care exponentially
- Longer-term reliance on the health care system for preventable chronic diseases
- Lost productivity from illness-related employee absenteeism (costs employers $530 billion per year)

$93b
Estimated total annual cost of racial and ethnic health disparities in the US in excess medical care costs.¹

$230b
Direct medical care expenses from health disparities from 2003-2006, in which 1 trillion dollars could have been reduced in indirect cost by eliminating health disparities.²

2 People, Same Zip Code, Different Outcomes

Factors of Health Outcome

- Occupation
- Education
- Race
- Ethnicity
- Veteran status
- Religion
- Language
- Heritage/History
- Immigration Status
- Age
- Ability
- Income
- Gender
- Family Status
- Geographic Location
- Aboriginality
Social Determinants of Health

• Conditions in which people are born, grow, live, work and age

• These circumstances are shaped by the distribution of money, power and resources at global, national and local levels
Structural Racism

• Laws and policies that allocate resources in ways that disempower and devalue members of racial and ethnic minority groups, resulting in inequitable access to high-quality care\(^1\)

• Residential segregation
  - Redlining
  - Jim crow era

Residential Segregation

- Home Owner Loan Corporation (HOLC) was established in 1933 for the purpose of stabilizing the mortgage lending system in the nation.

- HOLC residential security maps neighborhoods classification:
  - A – “Best” areas, colored green
  - B – “Desirable” areas, colored blue
  - C – “Declining” areas, colored yellow
  - D – “Hazardous” areas, colored red

Impact of Residential Segregation$^{1,2}$

- Substandard housing
- Underfunded public schools
- Employment disadvantages
- Exposure to crime
- Environmental hazards
- Physician shortages
- Food deserts
- Health inequities/hospital closures
- Economic stress may induce “maladaptive” coping behaviors, such as smoking and alcohol use

Physical Environment¹

• Communities of color are often disproportionately exposed to fine particles in the air called PM$_{2.5}$

• In counties where Black people were highly segregated from White people, total PM$_{2.5}$ levels were twice as high as in well-integrated counties

• Populations living in racially segregated communities breathe a form of pollution that is much more concentrated in toxic, cancer-causing compounds

Health Care Access: Safety Net Providers

• Safety-net providers play a valuable role in reducing health inequities because of their commitment to and experiences with underserved communities.

• Tend to score lower on patient satisfaction surveys, underperform on evidence-based metrics, and report higher rates of adverse safety events and complications.

Safety Net Challenges

• Influx of patients with complex biopsychosocial challenges
• Patients with low levels of health literacy require more time to explain treatment
• Posttraumatic stress management among refugees requires working across differences in language and cultural beliefs
• Specialty services are often not easily available for the uninsured
• Preventive care services may be neglected in the face of multiple and competing providers’ demands

Health Care Access: Reimbursement

• Federal laws require reimbursement to be sufficient to ensure equitable access to high-quality health care for Medicaid beneficiaries

• Medicaid payments are notoriously low and have been cited as a reason for low provider participation

• Numerous lawsuits have challenged low rates as violations of federal Medicaid requirements

  In 2017, Medicaid beneficiaries and providers in California challenged rates on antidiscrimination grounds, alleging that the low Medicaid rates were discriminatory against the growing Latino population, creating “a separate and unequal system of health care”
Private Payment Rates Are Higher Than Medicare Rates for Hospital and Physician Services

- Average Private Insurance Rates as a Percentage of Medicare Rates, Across Studies Using 2010-2017 Data

<table>
<thead>
<tr>
<th>Service Type</th>
<th>Average Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Hospital Services</td>
<td>259%</td>
</tr>
<tr>
<td>Inpatient Hospital Services</td>
<td>222%</td>
</tr>
<tr>
<td>Outpatient Hospital Services</td>
<td>358%</td>
</tr>
<tr>
<td>Physician Services</td>
<td>179%</td>
</tr>
</tbody>
</table>

SOURCE: KFF analysis of 19 published studies comparing private insurance and Medicare payments to providers. Because some studies analyze payments to providers in multiple service categories, the number of studies across all categories is greater than 19.
Health Care Access: Reimbursement

• Value-based payment reform is a Medicare pay-for-performance program to improve health care quality and reduce costs
• Programs do not account for social determinants of health when determining provider performance, ranking, and payment
• Safety-net providers serving low-income minorities are more likely to be penalized and receive lower Medicare reimbursement

Health Care Access: Insurance Coverage

• Inadequate health insurance coverage is one of the largest barriers to health care access
• The unequal distribution of coverage contributes to disparities in health
• Many low-income employees fall into the Medicaid coverage gap—unable to afford private insurance, not eligible for Medicaid or subsidies through the Affordable Care Act
Health Care Access: Insurance Coverage

• Medicaid expansion allows for more low-income individuals to qualify for Medicaid, without additional stipulations of pregnancy, children, elderly or having a disability

• Many states have not expanded Medicaid, which leaves high-risk patients who are in the low SES to go without insurance coverage, leaving significant coverage gaps
Coverage: Medicaid Expansion

- Reinforces racial hierarchy and results in inequities in coverage
- Evident in southern states with large numbers of Black and Latino residents

Figure: Status of State Action on the Medicaid Expansion Decision. 2023. Available from: https://www.kff.org/health-reform/state-indicator/state-activity-around-expanding-medicaid-under-the-affordable-care-act/?currentTimeframe=0&selectedDistributions=status-of-medicaid-expansion-decision&sortModel=%7B%22colId%22:%22Location%22,%22sort%22:%22asc%22%7D
Health Care Access: Individual Barriers

• Unfortunately, Americans too often do not receive the care they need, or they receive care that causes harm\(^1\)
  • Provider Bias/Stigma\(^2,3\)
  • Poor provider-patient communication\(^4\)
  • Lack of cultural awareness\(^5\)

• Care can be delivered too late or without full consideration of a patient’s preferences and values\(^1\)

Outcomes of Health Inequities\textsuperscript{1,2}

• Ample evidence suggests that Black and Latino people receive lower-quality care compared with White people, even after insurance coverage and income are adjusted for.

• Racial and ethnic minority patients are less likely to receive:
  - Evidence-based cardiovascular care
  - Kidney transplants when indicated
  - Age-appropriate diagnostic screening for breast and colon cancer
  - Timely treatment related to cancer and stroke
  - Appropriate mental health treatment
  - Adequate treatment when presenting suffering from pain

Comparative Health Care System Performance Scores

Note: To normalize performance scores across countries, each score is the calculated standard deviation from a 10-country average that excludes the US. See How We Conducted This Study for more detail.

Data: Commonwealth Fund analysis.

https://doi.org/10.26099/01DV-VZ2B
High Performing Countries Solutions

1. Provide for universal coverage and remove cost barriers so people can get care when they need it and in a manner that works for them
2. Invest in primary care systems to ensure that high-value services are equitably available locally in all communities to all people, reducing the risk of discrimination and unequal treatment
3. Reduce the administrative burdens on patients and clinicians that cost them time and effort and can discourage access to care, especially for marginalized groups
4. Invest in social services that increase equitable access to nutrition, education, child care, community safety, housing, transportation, and worker benefits that lead to a healthier population and fewer avoidable demands on health care

Clinicians

- Offer treatment and screening to eligible patients
- Follow the “no”
- Inclusive support groups to support several marginalized patient needs
Health Care Systems

- Representation in healthcare
- Establishing coordinated care models (i.e., navigators/telehealth services/social workers) through more systematic engagement
- Disaggregating data
- Recognize that biases may be unintentionally built into current algorithms and artificial intelligence platforms
- Reviewing formulary restrictions and exclusion policies
Researchers/Academicians

• Develop and test culturally appropriate educational materials for patients within your catchment area to improve health and health insurance literacy

• Implementation of community partnered/based participatory research
Insurance Companies

- Acknowledge and consider that racial disparities may exist in initial benefit design process
- Consider variable cost-sharing and premiums, such as on a sliding scale based on income
- Offer a preventive medication benefit with a low or $0 copay
- Use automated tools such as real-time benefit checks and electronic prior authorization to assist those with less time or fewer resources to navigate benefits and utilization management
- Identify opportunities for new or revised programs around payment incentives or disincentives for health care providers who participate in equity efforts

It Takes a Village

- Awareness
- Grant Funding/Research
- Revising/Designing Frameworks
- Building DEI Strategy/Organizational Rebranding
- Program Department Expansion
- Collaboration
Thank you

Shanada Monestime
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650-226-5492
Oncology Accelerated Drug Approvals that Lack Confirmatory Trials

Laura R. Bobolts, PharmD, BCOP
SVP, Clinical Strategy and Growth
OncoHealth
lbobolts@oncohealth.us
Learning Objectives

1. Explain the FDA Accelerated Approval Program process and how it applies to medications used for oncology treatment.
2. Discuss indication withdrawals and failed confirmatory trials for oncology agents.
3. Review key clinical and financial implications when reviewing oncology medications approved via the Accelerated Approval Program pathway.
What is the Accelerate Approval Pathway?

Expedites authorization of new therapies that:

- Treat serious conditions, like cancer
- Fill an unmet medical need
- Based on surrogate endpoints, likely to predict clinical benefit (e.g., ORR, DOR)

Subject to post-marketing research, confirmatory trial(s), to confirm clinical benefit outweighs risks.

- Did the confirmatory trial use another surrogate endpoint?
- Was the confirmatory trial done timely?
- Has a confirmatory trial been done at all?

ORR = Overall Response Rate; DOR = Duration of Response; FDA. https://www.fda.gov/drugs/information-health-care-professionals-drugs/accelerated-approval-program
Background

• Accelerated Approval Pathway developed by the FDA in 1992 in response to the HIV/AIDS crisis

• Codified into law under the Food and Drug Safety and Innovation Act (FDASIA) in 2012

• Majority Accelerated Approvals granted for oncology
  • Due to the serious & life-threatening nature of cancer
  • Can improve access to life-saving or life-prolonging therapy a median of 3.1 years before available otherwise
  • Availability of surrogate clinical endpoints in oncology

Oncology Surrogate Endpoints

Measure thought to predict clinical benefit but is not itself a measure of clinical benefit

**ORR**
Objective Response Rate
% with partial response (PR) or complete response (CR); ≥ 30% decrease in size

**DOR**
Duration of Response
Time to disease progression or death in patients with a PR or CR

**pCR**
Pathological Complete Response
Absence of cancer in tissue removed during surgery after treatment

**PFS**
Progression Free Survival
Time to disease progression or death

**DFS**
Disease Free Survival
Time to disease recurrence or death

**Expedited FDA Approval Programs**

- **Accelerated Approval**: Approval based on surrogate endpoint (e.g. ORR) in an unmet need.
- **Fast Track Designation**: Facilitates expedited review in an unmet need.
- **Priority Review**: 6 Month application decision goal.
- **Breakthrough Therapy**: Substantial improvement over available therapies in preliminary data.
- **Regenerative Medicine Advanced Therapy Designation**: Cellular therapy addresses unmet need (e.g. CAR-T).


How Do You Know it’s an Accelerated Approval?

FDA states therapy is “granted accelerated approval” in indication announcement on FDA’s website.

Accelerated approval status listed in the “Indications and Usage” Section (section1) of prescribing information.

On November 14, 2022, the Food and Drug Administration granted accelerated approval to mirvetuximab soravtansine-gynx (Elahere, Immunogen, Inc.) for adult patients with folate receptor alpha (FRα) positive, platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer, who have received one to three prior systemic treatment regimens. Mirvetuximab soravtansine-gynx is a folate receptor alpha directed antibody and microtubule inhibitor conjugate. Patients are selected for therapy based on an FDA-approved test.

ELAHERE is a folate receptor alpha (FRα)-directed antibody and microtubule inhibitor conjugate indicated for the treatment of adult patients with FRα positive, platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer, who have received one to three prior systemic treatment regimens. Select patients for therapy based on an FDA-approved test. 

This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.
FDA Draft Guidance on Oncology Accelerated Approvals

• FDA recommendations (not legally enforceable) to sponsors for designing, conducting, and analyzing data for oncology accelerated approval trials

• FDA considers a randomized controlled trial (RCT) the preferred approach over single-arm studies

• Single-arm trials have been commonly used to support accelerated approval
  • Lack direct comparisons to available therapy
  • Add uncertainty to the assessment of a drug’s safety/efficacy

• RCT can address limitations of single-arm trials

• Guidance goal: increase RCTs

FDA Draft Guidance on Oncology Accelerated Approvals

FDA suggests 2 clinical trial approaches:

- **Single randomized controlled trial**
  - Supports accelerated approval & verifies clinical benefit (the “one-trial” approach)
  - Sample size should be adequately powered to detect clinically meaningful & significant improvement in endpoints for accelerated approval (e.g., ORR), plus verify clinical benefit (e.g., PFS or OS) for full approval

- **2 separate trials**
  - One for accelerated approval & another confirmatory trial
  - FDA *strongly recommends* the confirmatory trial be well underway, if not fully enrolled, by the time of the accelerated approval

• Confirmatory trial may be acceptable to evaluate the drug in the same cancer type but in another line of therapy
• Timely completion of the trial(s) intended to verify clinical benefit is critical
• Evidence *should* be provided to support the individual contribution of components to the claimed effect(s)
• Control arm *should* represent the current appropriate available therapy
Confirmatory Trials

• Postmarketing requirements agreed to by the company & FDA, including projected date by which confirmatory trial will be completed & projected date by which the final report of these studies will be submitted to FDA

• Full approval is granted based on results of confirmatory trial

• Often conducted in earlier lines of therapy and in different combinations of drugs than original trial
  • Patients may not want to enroll in a trial with a control arm if an effective therapy is already available on the market

Hard to identify what is the confirmatory trial for an accelerated approval indication

Top of Mind Questions

• Is the confirmatory trial underway?
• Are patients fully enrolled?
• When are the results of the confirmatory trial expected?
• What is the primary endpoint of the confirmatory trial?
  • Same surrogate endpoint as the primary study? Is it overall survival?
• What is the design of the confirmatory trial?
  • Inclusion/exclusion criteria may adjust your coverage criteria
**Example: Mirvetuximab soravtansine**

- Accelerated approval (AA) November 14, 2022
- Indication: Folate receptor alpha (FRα) positive, platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer patients after 1-3 prior systemic treatments

<table>
<thead>
<tr>
<th>SORAYA: single-arm trial supported AA</th>
<th>MIRASOL: confirmatory trial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample size: 104 patients</td>
<td>RCT MIRV vs. chemo in similar patient population but no bevacizumab required</td>
</tr>
<tr>
<td>Prior bevacizumab required</td>
<td>Enrollment: ~ 453 patients</td>
</tr>
<tr>
<td>ORR 31.7%, median DOR 6.9 months</td>
<td>Underway, results expected H2 2023</td>
</tr>
<tr>
<td>Trial fully published January 30, 2023</td>
<td>Primary endpoint: PFS</td>
</tr>
<tr>
<td>Median OS 15 months available March 25, 2023</td>
<td></td>
</tr>
</tbody>
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- **Cost ~ $24,880 - $39,808/month**

**SORAYA**: single-arm trial supported AA
- Sample size: 104 patients
- Prior bevacizumab required
- ORR 31.7%, median DOR 6.9 months
- Trial fully published January 30, 2023
- Median OS 15 months available March 25, 2023

**MIRASOL**: confirmatory trial
- RCT MIRV vs. chemo in similar patient population but no bevacizumab required
- Enrollment: ~453 patients
- Underway, results expected H2 2023
- Primary endpoint: PFS

If step therapy was added requiring prior bevacizumab, that may need to be revisited if MIRASOL results are positive

Need More Info?

- Find the NCT# and look up the study on clinicaltrials.gov
- Helpful estimated study completion dates
- More detailed inclusion/exclusion criteria

Status of Accelerated Approvals

Total Accelerated Approvals in Oncology Since 1995

190

Increases or Decreases

Accelerated Approval Status*

- Traditional Approval
- Withdrawn
- Ongoing, Awaiting
- Final Decision

Lack of Confirmatory Trials

- Over $\frac{1}{3}$rd of oncology accelerated approvals are “ongoing” – without confirmatory results supporting full approval
- From 2009-2022, average 2.8 years (range: 0.05 - 13.56 years) on market without obtaining full approval
- Creates uncertainty around long-term safety & effectiveness of these drugs

Sept 2009
Pralatrexate in peripheral T-cell lymphoma

April 2023
Pembrolizumab + enfortumab vedotin in urothelial cancer

Oncology (Cancer) / Hematologic Malignancies Approval Notifications.
https://www.fda.gov/drugs/resources-information-approved-drugs/oncology-cancer-hematologic-malignancies-approval-notifications. Accessed April 1, 2023
Oncology Accelerated Approvals Past 5 Years

- Only 23% of accelerated approvals from 2018-2022 are now fully approved.
- FDA approved the most accelerated approvals in 2020 during the pandemic.
- 42% of 2018-2019 accelerated approvals are ongoing, lacking confirmatory trials supporting full approval.
- Concerns confirmatory trials are not always conducted & some drugs later prove to be ineffective.

*Based on approval date; Oncology (Cancer) / Hematologic Malignancies Approval Notifications. https://www.fda.gov/drugs/resources-information-approved-drugs/oncology-cancer-hematologic-malignancies-approval-notifications. Accessed April 1, 2023
Ongoing Therapies Lacking Confirmatory Trials

FDA “Project Confirm”

• FDA Oncology Center of Excellence initiative to promote the transparency of outcomes related to accelerated approval in oncology
• Goal: Enhance the balance of access and verification of oncology drug benefit
• FDA provides a searchable database with information on the status of all oncology accelerated approvals, although data is as current as the humans that maintain it!

Ongoing Therapy Example: Lurbinectedin

• Accelerated approval
  June 15, 2020

• Indication: metastatic small cell lung cancer (SCLC) with disease progression on/after platinum-based chemo

• Efficacy (Study B-005; NCT02454972)
  Among the 105 patients, the ORR was 35%, median DOR 5.3 months

Confirmatory trial, ATLANTIS due 2/28/21 per FDA

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  June 15, 2020

- **Indication:** metastatic small cell lung cancer (SCLC) with disease progression on/after platinum-based chemo

- **Efficacy (Study B-005; NCT02454972)**
  Among the 105 patients, the ORR was 35%, median DOR 5.3 months

**Cost ~ $20,085/month**

Confirmatory trial, ATLANTIS due 2/28/21 per FDA

Lurbinectedin Lacks Confirmation of Benefit

**ATLANTIS Confirmatory trial:**
- Phase III RCT in relapsed SCLC, randomized to lurbinectedin + doxorubicin (n=307) vs chemo (topotecan (n=127) or CAV (n=179))
- Lurbinectedin + doxorubicin did not improve overall survival vs control
- mOS 8.6 months L+D vs 7.6 months control (HR, 0.97, p=0.70)

Lurbinectedin was given at a lower dose in combo therapy, remains on market due to perceived unmet need

---

Dec 2, 2020
ATLANTIS failure press release

Sept 13, 2021
ATLANTIS OS numbers presented

Dec 2021
Company initiated LAGOON, another confirmatory trial

Oct 14, 2022
ATLANTIS Published

Oct 24, 2022
Citizens petition to withdraw lurbinectedin denied by FDA

June 2025
LAGOON results anticipated

When Confirmatory Trials Fail

- Company may voluntarily withdraw drug or indication
- FDA may withdraw after public hearing
- Status Quo – NO action taken
- Cancer patient’s life is in the hands of these drugs
When Confirmatory Trials Fail

- **FDA may withdraw after public hearing**
- **Status Quo – NO action taken**
- **Company may voluntarily withdraw drug or indication**
- **Cancer patient’s life is in the hands of these drugs**

"Dangling" Accelerated Approval

- Negative confirmatory trial that did not verify clinical benefit yet the therapy is still on the market
- FDA may wait for another confirmatory trial to result
## Therapy Failure or Withdrawal: What’s Next?

<table>
<thead>
<tr>
<th>Evaluate each subsequent authorization request carefully</th>
<th>Review NCCN Compendium Language</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Reauthorizations</strong></td>
<td>• Coverage may still be required</td>
</tr>
<tr>
<td>• May consider continuing auth if no disease progression</td>
<td>• Lag in NCCN removal</td>
</tr>
<tr>
<td><strong>New starts</strong></td>
<td>• Lag in NCCN Category 3 (deems therapy not medically necessary)</td>
</tr>
<tr>
<td>• Evaluate if other coverage sources continue to support the therapy, which may require coverage</td>
<td>• NCCN may continue to support therapy as Category 1 or 2A</td>
</tr>
</tbody>
</table>

### What can WE do?

- Learn about negative clinical trials or withdrawals
- Educate providers and offer more efficacious alternatives
Withdrawn but Still in NCCN: Pembrolizumab in SCLC

- **Accelerated approval June 17, 2019**
  - Indication: Metastatic small cell lung cancer (SCLC) with disease progression on/after platinum-based chemo & ≥ 1 other prior line of therapy
- **Company voluntarily withdrew use March 30, 2021**
  - Confirmatory KEYNOTE-604 trial met one of its dual primary endpoints of PFS but did not reach statistical significance for OS (announced Jan 2020)
- **Today:** Remains supported NCCN Category 2A for SCLC
  - As subsequent single agent therapy for either relapse following response or stable disease w/ primary treatment (*discouraged* if progression on maintenance atezolizumab or durvalumab), or primary progressive disease

### PARP Inhibitors Withdrawn: Ovarian Cancer Treatment

3 PARP inhibitors were withdrawn in 2022 for later line treatment of advanced ovarian cancer after data found a 31 - 33% increased risk of death vs chemo.

<table>
<thead>
<tr>
<th>FDA Approval</th>
<th>Withdrawal</th>
<th>Years to Withdrawal</th>
</tr>
</thead>
<tbody>
<tr>
<td>12/19/2014*</td>
<td>Olaparib</td>
<td>2022</td>
</tr>
<tr>
<td>12/19/2016*</td>
<td>Rucaparib</td>
<td>2022</td>
</tr>
<tr>
<td>10/23/2019</td>
<td>Niraparib</td>
<td>2022</td>
</tr>
</tbody>
</table>

- Today these agents are used as maintenance therapy in earlier lines, limiting the impact of these withdrawals.
- What about the thousands of patients that received these agents for treatment?
- How many millions in healthcare dollars were spent on suboptimal care?

Cost ~ $19,064 - $31,121/month

Practical Tips: Learning About Failures/Withdrawals

- Browse biotech websites (e.g., FiercePharma.com)
- Browse oncology-specific websites (e.g., OncLive.com)
- Sign up for email alerts (FDA, ASCO Post)
- Read press releases
- Talk with the colleagues you work with, educate each other
- Communicate openly with pharmaceutical colleagues
## Accelerated Approvals: Take the Good with the Bad

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Faster time to market for lifesaving or life prolonging therapies</td>
<td>• Questionable value</td>
</tr>
<tr>
<td>• Shorter clinical trials</td>
<td>• Small sample sizes</td>
</tr>
<tr>
<td>• Accelerated scientific advances</td>
<td>• Response rates may not predict long-term outcomes</td>
</tr>
<tr>
<td>• Nearly half of accelerated approvals have gone on to full approval</td>
<td>• Multiple agents may obtain similar accelerated approval indication</td>
</tr>
<tr>
<td></td>
<td>• Risk of withdrawal</td>
</tr>
<tr>
<td></td>
<td>• Risk of financial toxicity for potentially suboptimal therapy</td>
</tr>
</tbody>
</table>
Managed Care Strategies for Accelerated Approvals

**KEEP UP WITH LATEST DATA**
Monitor data as it constantly evolves in oncology with positive and negative results.

**EDUCATE**
Communicate latest data with internal clinical teams and educate providers of negative data/withdrawals.

**DRAFT DETAILED CRITERIA**
Consider drafting more detailed coverage criteria as the value of the therapy may not be fully understood.

**MAINTAIN CRITERIA**
May need to remove indication or adjust criteria based on withdrawal or full approval.

**INTERVENE IF BETTER OPTION**
Engage providers to discuss patient-tailored alternatives in lieu of therapy with low value.
Managed Care Strategies for Accelerated Approvals

• Consider drafting prior authorization criteria closer to clinical trial inclusion/exclusion criteria

  - Consider adding ECOG performance status
  - Evaluate WHAT data can be readily collected during PA
  - Add drugs to criteria if included or excluded in trial

• Accelerated approval indications may not be added to clinical oncology pathways or value-based care provider incentives

• ?Outcomes-based contracting?
Conclusion

• The FDA’s accelerated approval process in oncology can help bring drugs to market faster that meet an unmet clinical need.

• The accelerated approval pathway is widely used in oncology, many times with limited data available at the time of approval and unknown long-term outcomes.

• Managed care pharmacists must diligently access the value of an oncology therapy that has obtained accelerated approval and monitor data releases for confirmatory trial results.
Oncology Accelerated Drug Approvals that Lack Confirmatory Trials

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SVP, Clinical Strategy and Growth
OncoHealth
Thank you for attending the AMCP Florida 2nd Annual Day of Education!