Managing High Cost (Specialty) Pharmacy Spend
[Why we should be worried?]

E. Paul Amundson, MD FAAFP
Chief Medical Officer, DAKOTACARE

Presentation Objectives

- Understand Specialty Medication principles; i.e., definitions, coding/billing practices, evolving role of PBM and/or Specialty Pharmacies, and benefit placement strategy.
- Explain opportunities for payer oversight management of cost and utilization associated with select specialty medications and/or conditions.
- Understand future cost driver(s) in the area of specialty medications which are projected to have significant cost implications to payers.

Annual US Healthcare Spending

Medical Bills
By 2021, health care is expected to account for about a fifth of the U.S. economy, as health spending growth picks up.
National health expenditures, change from previous year

Health spending as share of GDP

Source: Centers for Medicare and Medicaid Services, THE WALL STREET JOURNAL
Specialty Continues to Grow: By 2018, It Will Represent 50% of all Drug Spend¹

Total Industry Specialty Spend¹

Key Factors driving trend
- Increasing utilization
- Aging population
- Robust pipeline
- Expanding indications
- Increasing prices
  - Brand-name drug price inflation
  - Higher cost for innovative drugs

² Half of spend under medical benefit with increased visibility

¹ NHE, Artemetrx, CVS Health Internal Analysis, 2013.

Specialty Rx 101
What is a Specialty Medication?

• No current consensus on an "industry standard" definition
• Thus term is not consistently defined by health plans and PBMs
• CMS categorizes a specialty drug as one with a minimum monthly cost of $600 with respect to the Part D drug benefit.
• A medication considered a specialty pharmaceutical may have some or all of the following key characteristics:
  • Treatment of complex, chronic, and/or rare conditions
  • High cost, often exceeding $10,000 per drug
  • Availability through exclusive, restricted, or limited distribution
  • Special storage, handling, and/or administration requirements
  • Ongoing monitoring for safety and/or efficacy
  • Risk Evaluation Mitigation Strategy (REMS) program

Specialty Rx 101
What is a Specialty Pharmacy?

• The Academy of Managed Care Pharmacy and the Specialty Pharmacy Association of America both recently published definitions of specialty pharmacy.
• Commonalities seen within the definitions:
  • distribution of specialty pharmaceuticals
  • high-touch, patient-centered management
• Ideally, this translates into improved care with measurable, positive clinical outcomes.
Specialty Rx 101
What is a Specialty Pharmacy?

• As part of their patient-focused model, specialty pharmacies offer services above and beyond those typically offered at the retail level as part of their standard of care. Examples:
  • 24/7 access to pharmacists
  • Benefits investigation
  • Prior authorization assistance
  • Communication and follow-up with the prescribing provider
  • Dispensing of specialty pharmaceuticals and shipping coordination
  • Financial assistance and enrollment in patient assistance programs
  • Patient education and medication adverse effect counseling
  • Patient monitoring for adherence management, safety and efficacy
  • Payer and/or manufacturer reporting

Specialty Rx 101
Billing Codes

• NDC: National Drug Code
  – A unique, 11-digit number that refers to the drug or product, strength, and package size produced by a certain drug manufacturer.
  – NDC pricing is normally updated on a monthly basis to reflect changes in drug cost.
  – Using NDCs on medical claims helps facilitate more accurate payment to providers (reimbursement based on what was used)
• J-code: permanent codes used to report injectable drugs that ordinarily cannot be self-administered
  – J-codes are specific for one medication and strength, but could represent dozens of manufacturers with variations in cost: J1956 = levofloxacin 250mg per unit
  – J-codes do not differentiate between package sizes (20mL vial used vs 30mL vial used)

Specialty Rx 101: Billing Codes

NDC v J-code: which is preferred?

Recommended Strategy: Allow J-code billing, but negotiate maximum allowed based on current NDC pricing – pay all claims to the lowest cost option (This occurs in retail pharmacies – MAC pricing)
Specialty Rx 101
Medical vs Pharmacy Benefit

- Medical: medications that cannot be self-administered (IV, IM, provider administered SQ (Prolia®))
- Pharmacy: medications that should be self-administered: SQ, oral, etc (Enbrel® or Humira® SQ)
- Plans can modify coverage to access more aggressive contracts
  - Oncology – difficult to outsource (chemotherapy is Hazmat)

Specialty Rx 101
Medical vs Pharmacy Contracting

- Pharmacy contracts:
  - Tend to be more aggressive = higher savings (uses PBM contracts)
  - Ability to require members to receive specialty services from one provider (leverage volume discounts)
- Medical contracts:
  - More variety (percent off billed $$$ - fee schedule $)
  - Opportunities to tier medical providers to encourage selection of lower cost providers (home health vs outpatient infusion vs hospital)

More than Medication: Specialty Patient Care
Accounts for 25% of Total Health Care Costs


<table>
<thead>
<tr>
<th>Specialty Portion of Total Health Care Spend</th>
<th>All-other medical costs</th>
<th>Specialty drugs are Nearly One Third of the Total Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specialty Drugs</td>
<td>25%</td>
<td>8%</td>
</tr>
<tr>
<td>Specialty Patient Care</td>
<td>21%</td>
<td>1%</td>
</tr>
<tr>
<td>Other medical costs</td>
<td>3%</td>
<td>1%</td>
</tr>
<tr>
<td>Other costs</td>
<td>5%</td>
<td>1%</td>
</tr>
<tr>
<td>Total Health Care Spend</td>
<td>11%</td>
<td>1%</td>
</tr>
</tbody>
</table>
Increasing Utilization of Specialty Drugs

**THREE KEY DRIVERS 2011-2014**

- **New Drugs**
- **New Indications**
- **Aging Population**

\[
\text{New Drugs} + \text{New Indications} + \text{Aging Population} = \text{Increasing Utilization}
\]

<table>
<thead>
<tr>
<th>Year</th>
<th>New Drugs</th>
<th>New Indications</th>
<th>Aging Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2012</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2013</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2014</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Utilization Trend**

Radians per million members per month

<table>
<thead>
<tr>
<th>Year</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>6,622</td>
<td>6,973</td>
<td>7,457</td>
<td>8,099</td>
</tr>
</tbody>
</table>

Increasing Specialty Drug Prices:

**Annual Inflation and Higher Launch Prices**

<table>
<thead>
<tr>
<th>Brand</th>
<th>2010 Price</th>
<th>2014 Price</th>
<th>CAGR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Copaxone</td>
<td>$2.8B</td>
<td>$3.3B</td>
<td>9.8%</td>
</tr>
<tr>
<td>Enbrel</td>
<td>$3.0B</td>
<td>$3.3B</td>
<td>9.8%</td>
</tr>
<tr>
<td>Humira</td>
<td>$3.5B</td>
<td>$3.6B</td>
<td>9.8%</td>
</tr>
<tr>
<td>Tysabri</td>
<td>$2.7B</td>
<td>$3.0B</td>
<td>9.8%</td>
</tr>
<tr>
<td>Revlimid</td>
<td>$3.5B</td>
<td>$3.6B</td>
<td>9.8%</td>
</tr>
<tr>
<td>Tasigna</td>
<td>$1.7B</td>
<td>$2.1B</td>
<td>9.8%</td>
</tr>
<tr>
<td>Cimzia</td>
<td>$2.7B</td>
<td>$3.0B</td>
<td>9.8%</td>
</tr>
<tr>
<td>Incivek</td>
<td>$3.0B</td>
<td>$3.3B</td>
<td>9.8%</td>
</tr>
<tr>
<td>Sovaldi</td>
<td>$1.7B</td>
<td>$2.1B</td>
<td>9.8%</td>
</tr>
<tr>
<td>Harvoni</td>
<td>$1.7B</td>
<td>$2.1B</td>
<td>9.8%</td>
</tr>
<tr>
<td>Tecfidera</td>
<td>$2.0B</td>
<td>$2.5B</td>
<td>9.8%</td>
</tr>
</tbody>
</table>

**Biosimilars That May Significantly Affect the Treatment Paradigm**

- Source: CVS/caremark internal data, 2014.
Infusion Therapy for Specialty Conditions:
Selecting Optimal Site of Care is Imperative

INFUSED DRUGS... are estimated to account for $35 billion of the specialty market.

- Up to 33% of pipeline
- Make up as much as 33% of specialty drugs in the pipeline

INFLIXIMAB (REMICADE), STANDARD DOSING OF 100 KG PATIENT

<table>
<thead>
<tr>
<th>Drug Cost by Site of Service</th>
<th>Average Cost of Admin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Home</td>
<td>Hospital Outpatient</td>
</tr>
<tr>
<td>$4,215</td>
<td>$7,457</td>
</tr>
<tr>
<td>$171</td>
<td>$933</td>
</tr>
</tbody>
</table>

Cost Driver #1

Doctors Object to High Cancer-Drug Prices

“More than 100 oncologists call for new regulations to control soaring patient costs in U.S.”

Wall Street Journal

In Support of a Patient-Driven Initiative and Petition to Lower the High Price of Cancer Drugs

Mayo Clinic Proceedings

Published Online: July 23, 2015
During the past 15 years, the average price of cancer drugs has increased five- to 10-fold to more than $120,000 as of 2014.

Total Cost of Care Analysis

Oncology Rx Management Challenges

- Practice variation contributes to the high cost of healthcare and wasteful spending
- Published reports indicate that 30%-40% of oncology treatments deviate from evidence-based standards
- Reducing unwarranted variation is a necessary step to improving quality and reducing cost

1Wu X-C et al. JCO 2012; Harlan LC et al. JCO
Oncology Rx Management Strategies

- Individual medication utilization management
- Decision support tools
- Treatment pathways
  +/- Oncologist reimbursement incentives
- Patient-Centered Medical Home

DAKOTACARE Turns to Oncology Management Program

- Implemented 2011
- Proprietary web-based oncology decision-support platform
- Independent, third-party expert with nearly a decade of experience
- Members benefit from appropriate treatment for their cancer
- Physicians gain systematic access to the latest, most comprehensive evidence-based treatment standards and clinical decision-support tools, as well as streamlined reimbursement
- Assurance that members are receiving care within the scope of their plan benefits.
- Capability to perform evidence-based oncology & radiation therapy treatment plan UM while ensuring proper claims adjudication

Cost Driver #2
Treating patients with HCV is expensive and complex.

3M U.S. Adults Are Infected with the Hepatitis C Virus (HCV)¹

- Baby boomers are 5X more likely to have HCV²; CDC recommends testing³
- Genotype 1 (GT1) accounts for ~76% of all infections in the U.S.³
- Chronic Hepatitis C (CHC) is the leading cause of liver transplants⁴
- 99% of HCV patients have a related comorbid condition⁴
- 1 in 4 people with HIV also have HCV⁵
- HCV prevalence varies widely from state to state: 1.3% to 0.4%⁶

Chronic Hepatitis C

- Contagious liver disease
- Resulting from infection with the hepatitis C virus
- Spreads primarily through exposure with infected blood (e.g., IV drug use, sexual contact)
- Develops very slowly, sometimes over decades
- Frequently asymptomatic until liver damage occurs
- Can lead to the development of cirrhosis, liver failure or liver cancer known as hepatocellular carcinoma (HCC)

The Varying Regional Prevalence of HCV

MAP OF THE 2013 STATE PREVALENCE OF DIAGNOSED AND UNDIAGNOSED HCV IN THE UNITED STATES — U.S. HCV PREVALENCE: 0.86% (2,642,520)
### 2013 HCV Prevalence By Health Insurance Type

<table>
<thead>
<tr>
<th>Health Insurance Type</th>
<th>Total U.S. Population (thousands)</th>
<th>Estimated Prevalence of HCV RNA+</th>
<th>Estimated Number of HCV RNA+ (thousands)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uninsured</td>
<td>49,600</td>
<td>2.08%</td>
<td>1,012</td>
</tr>
<tr>
<td>Veteran Affairs</td>
<td>5,600</td>
<td>5.40%</td>
<td>302</td>
</tr>
<tr>
<td>Commercial</td>
<td>164,200</td>
<td>0.47%</td>
<td>779</td>
</tr>
<tr>
<td>Dual Medicare and Medicaid</td>
<td>6,000</td>
<td>2.51%</td>
<td>201</td>
</tr>
<tr>
<td>Medicare (non-dual)</td>
<td>37,600</td>
<td>0.31%</td>
<td>117</td>
</tr>
<tr>
<td>Medicaid</td>
<td>41,300</td>
<td>0.87%</td>
<td>377</td>
</tr>
<tr>
<td>Other Military</td>
<td>2,200</td>
<td>0.47%</td>
<td>10</td>
</tr>
<tr>
<td>Prison</td>
<td>1,000</td>
<td>30.0%</td>
<td>450</td>
</tr>
<tr>
<td>Total</td>
<td>310,000</td>
<td>1.05%</td>
<td>3,249</td>
</tr>
<tr>
<td>Total without Prison</td>
<td>308,500</td>
<td>0.91%</td>
<td>2,799</td>
</tr>
</tbody>
</table>

**Notes:**
- Source: Authors' analysis of NHANES. Variable: LBXHCR - Hepatitis C RNA (HCV RNA) in NHANES.

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### HCV Treatment Can Mitigate Disease Progression and Total Costs

- **ANNUAL COSTS PER PATIENT BY CONDITION:**
  - HCV infection is a leading cause of cirrhosis, liver cancer and liver transplant.
  - 10% to 20% of CHC patients will develop cirrhosis; up to 5% will progress to liver cancer.
  - HCV is associated with nearly 50% of all liver transplants.

- **SUSTAINED Virologic Response (SVR) CAN REDUCE RISK OF LIVER CANCER, END-STAGE LIVER DISEASE, LIVER TRANSPLANT, DIABETES AND MORTALITY.**
  - $62,000
  - $160,000
  - $577,000

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### The Evolving Landscape of HCV Treatment

<table>
<thead>
<tr>
<th>Year</th>
<th>Treatments Available</th>
</tr>
</thead>
<tbody>
<tr>
<td>2001</td>
<td>Pegylated interferons with or without ribavirin (PEG/RBV)*</td>
</tr>
</tbody>
</table>
| 2011 | Incivek with PEG/RBV*  
Incitaxel with PEG/RBV* |
| 2013 | Olysio with PEG/RBV*  
Voxilap with PEG/RBV* with/without PEG** |
| 2014 | Harvoni*  
Viekira Pak with or without PEG* |

- New drugs offer additional options and improved outcomes.

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### Notes:
- For genotype 1.
- **For genotypes 1, 2, 3, 4.
- ***For certain treatment naïve patients.
- Olysio prescribing information.
- Sovaldi prescribing information.
- Sovaldi Prescribing Information.
- Viekira Pak prescribing information.
Effective HCV Therapy by Genotype

AASLD/IDSA/IAS–USA HCV GUIDANCE

<table>
<thead>
<tr>
<th>HCV Genotype</th>
<th>% of HCV population with Genotype</th>
<th>Sovaldi</th>
<th>Harvoni</th>
<th>Viekira Pak</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>76%</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>2</td>
<td>12%</td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>10%</td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>1%</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>5</td>
<td>&lt;1%</td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>&lt;1%</td>
<td>x</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

• ~25% of the HCV population requires a Sovaldi based regimen and cannot be treated with Harvoni or Viekira Pak.

AASLD/IDSA/IAS–USA HCV Guidance: Treatment is Recommended for all Patients with CHC Infection

• Advanced fibrosis (F3 or compensated cirrhosis (F4))
• Organ transplant
• Type 2 or 3 essential mixed cryoglobulinemia with end-organ manifestations (e.g., renal)
• Progressive, nephrotic syndrome, or membranoproliferative glomerulonephritis

Visit the HCV Guidance website, www.hcvguidelines.org, to access the most up-to-date version.

Adherence to Medication is Critical for Treatment Success

• Therapy milestones are measured by virologic response
• SVR is the best predictor of long-term response to treatment; SVR at 12 weeks post therapy determines treatment success

Virologic Response Milestones

<table>
<thead>
<tr>
<th>Week 4</th>
<th>Week 12</th>
<th>End of Therapy*</th>
<th>12 Weeks Post Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid virologic response (SVR)</td>
<td>Early virologic response (SVR)</td>
<td>End of treatment response (SVR)</td>
<td>Sustained virologic response (SVR)</td>
</tr>
</tbody>
</table>

Therapy Start

• Undetectable viral load
• Undetectable or ≥2 log drop viral load

Sustainable project funded by the National Institute on Aging under Grant 5R01AG16515-09A2.
HCV Spending Projections Through 2022

Selected HCV Treatment Regimens in Development

<table>
<thead>
<tr>
<th>DRUG NAME/ MANUFACTURER</th>
<th>DRUG CLASS</th>
<th>INDICATION</th>
<th>ROUTE OF ADMINISTRATION</th>
<th>PROJECTIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daklinza (daclatasvir)</td>
<td>NS5A inhibitor</td>
<td>Treatment of chronic HCV genotype 3 infection in combination with sofosbuvir</td>
<td>Oral. Once daily</td>
<td>8/26/15</td>
</tr>
<tr>
<td>asunaprevir/daclatasvir/beclabuvir</td>
<td>Protease inhibitor/NS5A inhibitor/Non-nucleoside polymerase inhibitor</td>
<td>Treatment of chronic HCV genotype 1 infection with or without ribavirin</td>
<td>Oral. Twice daily</td>
<td>2Q 2016</td>
</tr>
<tr>
<td>ledipasvir/sofosbuvir</td>
<td>DNA polymerase inhibitor/NS5A inhibitor</td>
<td>Treatment of chronic HCV infection in treatment-naive and treatment-experienced patients with genotype 1, 2, 3, 4, 5 or 6</td>
<td>Oral. Once daily</td>
<td>2Q 2017</td>
</tr>
</tbody>
</table>

Selected HCV Treatment Regimens in Development (cont.)

<table>
<thead>
<tr>
<th>DRUG NAME/ MANUFACTURER</th>
<th>DRUG CLASS</th>
<th>INDICATION</th>
<th>ROUTE OF ADMINISTRATION</th>
<th>PROJECTED LAUNCH</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACH3102</td>
<td>NS5A inhibitor</td>
<td>Treatment of chronic HCV genotype 1 infection in combination with ribavirin</td>
<td>Oral</td>
<td>N/A</td>
</tr>
<tr>
<td>sovaprevir</td>
<td>HCV protease inhibitor</td>
<td>Treatment of chronic HCV infection in combination with other antiviral agents</td>
<td>Oral</td>
<td>N/A</td>
</tr>
</tbody>
</table>
**High Cholesterol Puts Individuals at Risk of Developing Heart Disease**

- 71 million American adults (33.5%) have high LDL or "bad" cholesterol.
- Only 1 out of every 3 adults with high cholesterol has the condition under control; less than half get treatment.
- People with high total cholesterol have ~2X the risk of heart disease as people with optimal levels.

- A comprehensive approach consisting of diet, exercise and pharmacological management is recommended to help lower cholesterol.

**FDA Approves New LDL-Lowering Agent Alirocumab (Praluent)**

BETHESDA, MD

July 24, 2015

As widely expected, the US Food and Drug Administration (FDA) today approved alirocumab (Praluent, Sanofi/Regeneron) for lowering LDL-cholesterol (LDL-C).

The indication is for patients with heterozygous familial hypercholesterolemia or those at high CV risk who cannot lower their LDL-C with statins.
PCSK9 Inhibitors: Next-Generation Therapy

**PCSK9 INHIBITORS**

- Increase the number of LDL-C receptors in the liver and increase the liver’s ability to remove LDL-C from the blood
- Represent a new potential treatment class for the management of severe hyperlipidemia, including FH
- Require self injection every 2 to 4 weeks (subcutaneous)

**PRALUENT (ALIROCUMAB) [REGENERON/SANOFI]**

- Potential Indication: Hyperlipidemia and HeFH
- PDUFA Date: 7/24/2015

**REPATHA (EVOLOCUMAB) [AMGEN]**

- Potential Indication: Hyperlipidemia, HeFH and HoFH
- PDUFA Date: 8/27/2015

* Estimated average cost of therapy is $471 to $850 per patient per month.*

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Populations Where Statins May Not be Enough

- A high-risk population with severe LDL-C elevation (LDL-C ≥ 190 mg/dL) due to genetic defect
- Increased risk of cardiac events, including premature cardiovascular disease
- Require aggressive management and substantial LDL-C reductions to reduce risk of premature CVD

- Muscular and hepatic symptoms are the most common side effects for statins
- Majority of patients with statin intolerance are able to tolerate statin rechallenge

- May require additional cholesterol-lowering therapy

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Familial Hypercholesterolemia

**INCLUDES ~620,000 PEOPLE IN THE U.S. WHO HAVE FH**

<table>
<thead>
<tr>
<th>Trait/Condition</th>
<th>Heterozygous FH (HeFH)</th>
<th>Homozygous FH (HoFH)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inheritance</td>
<td>Inherited from one parent</td>
<td>Inherited from both parents</td>
</tr>
<tr>
<td>Incidence</td>
<td>1 in 300 to 500 people worldwide</td>
<td>1 out of every 1,000,000</td>
</tr>
<tr>
<td>Typical levels of LDL-C</td>
<td>190 to 350 mg/dL</td>
<td>400 to 1,000 mg/dL</td>
</tr>
<tr>
<td>Mean age at onset or diagnosis of CVD</td>
<td>Men—42 to 46 years, Women—51 to 52 years</td>
<td>20 years of age</td>
</tr>
</tbody>
</table>

* People with FH are at increased risk for cardiac events, including premature CVD.
Current Management of FH

**GUIDELINES: ACC/AHA AND NATIONAL LIPID ASSOCIATION EXPERT PANEL RECOMMENDATIONS**

- FH requires aggressive management and substantial LDL-C reductions to reduce premature CVD risk.
- Goal of therapy is to achieve at least a 50% reduction in LDL-C with statin therapy.
- For individuals not meeting treatment goals or with statin intolerance, nonstatin cholesterol-lowering therapies should be initiated.
- Patients with severe HoFH and HoFH may require additional therapies, such as lipid apheresis.

**JUPAPID (LOMIPAPID)**

Oral therapy for adjunct treatment of HoFH
- Adjust therapy reduced LDL-C by about 35%.
- IMEPA ~ $346,000/year (as high as $1M/year).
- REMS.
- Black box warning for liver toxicity.

**KYNAMRO (MIPOMESEN)**

Subcutaneous injection for adjunct treatment of HoFH
- Adjust therapy reduced LDL-C by about 24%.
- IMEPA ~ $200,000/year.
- REMS.
- Black box warning for liver toxicity.

**Guidelines may change in response to the recent IMPROVE-IT trial and as new therapies come to market.**

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**Statin Intolerance**

**TRUE STATIN INTOLERANCE**

- Requires at least one of the following muscle symptoms:
  - Intolerable muscle symptoms persisting ≥ 2 weeks with CK ≥ 10 times upper limit of normal and recurrent symptoms with a statin re-challenge with a high intensity statin.
  - CK ≥ 10 times the upper limit of normal.
  - Rhabdomyolysis — severe muscle injury that can lead to kidney failure.

**CONTRAINDICATIONS**

- Contraindication to statin use:
  - Active liver disease; persistent ALT elevations ≥ 2 times upper limit of normal.
  - Women who are pregnant or may become pregnant.
  - Nursing mothers.

**MANAGEMENT STRATEGIES**

- Management strategies to overcome perceived intolerance:
  - Rechallenge with the same or different statin with observation of symptoms.
  - Lower initial dosage with titration.
  - Less than daily dosing.

- There is only a very small proportion of patients who are truly statin intolerant.

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**PCSK9 Inhibitor Efficacy and Safety**

- LDL-C reductions of up to 75% above what had been possible with previous therapy.
- Studies involved various treatment regimens and patient populations.
- Recent preliminary analysis suggests a reduction in cardiovascular events.
- To date, adverse events similar to placebo or control arm (other than injection site reactions) with no safety signals published.

- Average LDL-C reductions with statins and PCSK9 inhibitors:
  - Low intensity statin.
  - Moderate intensity statin.
  - High intensity statin.
  - PCSK9 inhibitors.

- Ongoing studies are needed to assess neurocognitive function and other adverse events. Additional benefits, including a decrease in mortality, require clinical trials.
PCSK9 Inhibitors Can Potentially Have a Significant Impact on the Health Care System

Up to 7M potential eligible patients; 400,000 in the first year¹

Estimated at $5K to $10K per patient per year²

Up to $70B potential annual spend; $4B in the first year³

Careful utilization supported by guidelines will be paramount to help control health care costs once these drugs are approved.

PCSK9 Inhibitors Can Potentially Have a Significant Impact on the Health Care System

POPULATIONS WITH HIGH CHOLESTEROL¹

- HoFH: 1,400
- Statin intolerance: 4.4 million
- Uncontrolled LDL: 3.3 million
- CVD: 14 million
- Risk factors: 24 million
- Primary prevention: 60 million

¹. CVS Health Internal data. ². Estimated at $5K to $10K per patient per year. ³. Estimated at $5K to $10K per patient per year.

Four Groups of Individuals Most Likely to Benefit from Cholesterol-Lowering Therapy

ACC/AHA 2013 TREATMENT GUIDELINES

<table>
<thead>
<tr>
<th>Patient Population</th>
<th>Treatment Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical ASCVD (CHD, peripheral arterial disease or revascularization, stroke or transient ischemic attack, or atherosclerotic coronary artery disease)</td>
<td>Moderate-intensity to high-intensity statin (varies by age)</td>
</tr>
<tr>
<td>• Age ≤ 75 years (high*)</td>
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</tr>
<tr>
<td>• Age &gt;75 years OR not candidate for high-intensity statin (moderate)</td>
<td></td>
</tr>
<tr>
<td>Primary elevations of LDL-C ≥ 190 mg/dL</td>
<td>High-intensity statin*</td>
</tr>
<tr>
<td>40 to 75 years of age with diabetes and LDL-C 70 to 189 mg/dL without clinical ASCVD</td>
<td>Moderate-intensity to high-intensity statin (varies by risk)</td>
</tr>
<tr>
<td>• Estimated 10-year ASCVD risk ≥ 7.5% (high*)</td>
<td></td>
</tr>
<tr>
<td>40 to 75 years of age with LDL-C 70 to 189 mg/dL and estimated 10-year ASCVD risk ≥ 7.5%</td>
<td>Moderate-intensity to high-intensity statin (varies by risk)</td>
</tr>
<tr>
<td>Risk scoring: Guidelines recommend the Pooled Cohort Equations (<a href="http://tools.cardiosource.org/ASCVD-Risk-Estimator/">http://tools.cardiosource.org/ASCVD-Risk-Estimator/</a>)</td>
<td></td>
</tr>
</tbody>
</table>

*Moderate-intensity statin recommended if not a candidate for high-intensity statin.

QUESTIONS?
THANK YOU!

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