Planning for the 2017 Specialty Drug Spend: When Costs are Steep but Pockets are Not Deep

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Planning for the 2017 Specialty Drug Spend:

When Costs are Steep but Pockets are Not Deep

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November 16, 2016
Disclosure for Nicole Trask

I have no actual or potential conflict of interest in relation to this presentation.
Objectives

- Identify high-impact specialty pipeline drugs expected to reach the market in 2017-2018
- Summarize efficacy data for high-impact specialty pipeline drugs and indicate their anticipated place in therapy
- Compare specialty pipeline drugs to currently available therapeutic options
- Predict the budgetary impact of specialty pipeline drugs and discuss strategies to mitigate costs
Identifying High-Impact Drugs

Two key drivers

• Clinical impact
  – Efficacy/effectiveness
  – Therapeutic alternatives

• Economic impact
  – Cost
  – Volume
Assessing Clinical Impact

Clinical trial data
- Placebo-controlled, head-to-head studies
- Adverse events
- Potential drug-drug interactions
- Target population
- Patient willingness to use medication

Therapeutic alternatives
- Me-too drug vs. first-in-class
- Market competition
- Consensus guidelines
Assessing Economic Impact

Cost
- AWP/WAC
- Supplemental rebate
- Value-based contracts
- Value assessments (e.g., AHRQ, ICER, PCORI)

Volume
- Prevalence/incidence of disease
- Frequency of administration
- Duration of therapy

AHRQ=Agency for Healthcare Research and Quality, AWP=average wholesale price, ICER=Institute for Clinical and Economic Review, PCORI=Patient-centered Outcomes Research Institute, WAC=wholesale acquisition cost

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Assessing Budget Impact

- **Proactive pharmaceutical pipeline monitoring**
  - Focus on high-cost disease states, specialty drugs (e.g., NASH, hepatitis C, PCSK9 inhibitors, oncology, monoclonal antibodies)

- **Budget impact analysis completed for drugs with potentially high clinical *and* economic impact**
  - Medical claims data to determine prevalence
  - Estimate market share/uptake
  - Cost

NASH=non-alcoholic steatohepatitis, PCSK9=proprotein convertase subtilisin/kexin type 9
Lessons Learned

• Uptake may not be as quick as anticipated
  – Skepticism surrounding safety of new treatments
  – Consensus guideline updates take time
  – Clinical inertia
  – Patient willingness to try new medications

• Recent examples
  – PCSK9 inhibitors – uptake remains low and slow
  – HCV – 5.1% of MA Medicaid members with HCV had PA requests for sofosbuvir or simeprevir in first 1.5 years on market

HCV=hepatitis C virus, PA=prior authorization

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HIGH-IMPACT PIPELINE DRUGS
Non-alcoholic Steatohepatitis (NASH)\(^2-6\)

Sub-group of non-alcoholic fatty liver disease (NAFLD)

- Significant morbidity and mortality
  - 11% of patients progress to cirrhosis
  - 7% of patients develop hepatocellular carcinoma
  - 10-fold increased risk of liver-related death
  - Two-fold increased CV risk

- CV events are the leading cause of death
- Second most common cause of liver disease in adults awaiting liver transplant in US
Non-alcoholic Steatohepatitis (NASH)²⁻⁶

- Closely associated with obesity, T2DM, dyslipidemia
- Histologic features: hepatic steatosis, hepatic cell injury, inflammation, fibrosis
- Presence and degree of NASH measured by NAFLD activity score (NAS)
  - Steatosis (0 to 3)
  - Lobular inflammation (0 to 3)
  - Hepatocellular ballooning (0 to 2)
Elafibranor\textsuperscript{2-3}

- **Proposed indication:** NASH
- **MOA:** Dual PPAR-\(\alpha/\delta\) agonist
  - PPARs play a key role in metabolic homeostasis, immune-inflammation, and differentiation
  - May improve histology in NASH, reduce TG, increase HDL, improve glucose homeostasis
  - Reduced markers of liver inflammation in Phase IIa trials

HDL=high-density lipoprotein, MOA=mechanism of action, PPAR=peroxisome proliferator-activated receptor, TG=triglycerides
Elafibranor: Clinical Impact

Phase II GOLDEN-505 trial: Design

• Randomized, placebo-controlled
• Population: N=274; histologic diagnosis of non-cirrhotic NASH
• Intervention: elafibranor 80 mg or 120 mg by mouth once daily or placebo for 52 weeks
• Primary outcome: reversal of NASH without worsening of fibrosis
  – Absence of ≥1 of 3 components of NASH (i.e., steatosis, ballooning, inflammation)
Elafibranor: Clinical Impact\textsuperscript{2}

Phase II GOLDEN-505 trial: Results

- Resolution of NASH without worsening fibrosis: Protocol-defined definition
  - No difference in response rate overall
    - 23%, 21%, and 17% for elafibranor 80 mg, 120 mg, and placebo, respectively; P=0.280
  - Post-hoc analysis of patients with NAS ≥4: significant difference in response rate
    - 20%, 20%, and 11% for elafibranor 80 mg, 120 mg, and placebo, respectively; P=0.018

NAS=NAFLD activity score

November 16, 2016
Planning for the 2017 Specialty Drug Spend
Elafibranor: Clinical Impact \(^2\)

Phase II GOLDEN-505 trial: Results

- Resolution of NASH without worsening fibrosis: Modified* definition
  - Significant improvement in response rate with elafibranor 120 mg vs. placebo
    - All patients: 19% vs. 12% for elafibranor 120 mg and placebo, respectively (P=0.045)
    - Baseline NAS ≥4: 19% vs. 9% for elafibranor 120 mg and placebo, respectively (P=0.013)

*Modified definition of resolution of NASH: disappearance of ballooning together with either disappearance of lobular inflammation or persistence of mild lobular inflammation

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Elafibranor: Clinical Impact²

Phase II GOLDEN-505 trial: Results

• Patients with NASH resolution on elafibranor 120 mg
  – Improvement in liver fibrosis: -0.65±0.61 in responders vs. 0.10±0.98 in non-responders (P<0.001)
  – Significant improvements in steatosis, ballooning, and inflammation vs. non-responders (P<0.05, P<0.001, and P<0.05, respectively)
Elafibranor: Clinical Impact

Therapeutic alternatives

• No FDA-approved treatments indicated for NASH
• Weight loss
• Treatment of risk factors for CVD
  – Diabetes, dyslipidemia
• Vitamin E is first-line pharmacotherapy*
  – Improves liver histology
• Pioglitazone may be used
  – Lack of long-term safety/efficacy data, potential AEs

*In the absence of diabetes
AE=adverse events, CVD=cardiovascular disease
Elafibranor: Clinical Impact*^2,5-6

NASH Pipeline*

• Obetacholic acid (OCA)
  – FXR ligand FDA-approved for primary biliary cholangitis (PBC)
  – ICER evidence rating of “insufficient” based on clinical trial data and unanswered questions
    • Phase IIb FLINT study achieved primary endpoint
    • Unpublished Phase II study in Japanese patients missed primary endpoint

*Not an all-inclusive list
FXR=farnesoid X nuclear receptor

Planning for the 2017 Specialty Drug Spend
Elafibranor: Economic Impact

Cost

- Cost data not available for elafibranor
- OCA recently approved for PBC
  - ~$18,000/month* for off-label treatment of NASH
- Supplemental rebate – preferred NASH product
- Value-based contracts – low response rates

*WAC
Elafibranor: Economic Impact

Volume

• Prevalence 3.5% to 5% with ~5% diagnosed
  – ICER estimates 567,000 individuals eligible for treatment
  – ICER estimates low uptake of ~10%

• Duration of treatment indefinite
  – Treatment continues until progression to cirrhosis (liver transplant) or until resolution (F0)

F0=fibrosis stage 0

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Elafibranor: Budget Impact\textsuperscript{6-9}

- **Medicaid plan**
  - $72,000/year for treatment
  - Scenarios
    - 10% uptake: $1.3 to $1.8 million per year
    - All diagnosed patients treated: $12.6 to $18 million per year

- **Timeline**
  - Awarded Fast Track designation
  - Approval anticipated ~2018-2019
Atopic Dermatitis\textsuperscript{10-12}

Clinical features
- Chronic, inflammatory skin condition
- Characterized by rash, scaly patches on skin, intense itching
- May lead to skin infection

Prevalence
- Affects 7% to 30% of children and 1% to 10% of adults with 95% of cases starting before age 5
- 50% of patients with atopic dermatitis in childhood continue to have milder symptoms as an adult
Dupilumab\textsuperscript{10-12}

- Proposed indication: atopic dermatitis
- MOA: MoAB targeting IL-4/IL-13
  - IL-4/IL-13 signaling pathway implicated in inflammatory response
  - SC injection
- If approved, dupilumab would be the first biologic indicated for atopic dermatitis

IL=interleukin, MoAB=monoclonal antibody, SC=subcutaneous
Phase III LIBERTY AD CHRONOS trial: Design

- Randomized, placebo-controlled
- Population: N=740; adults with moderate-to-severe atopic dermatitis
- Intervention: dupilumab 300 mg SC QW, 300 mg SC Q2W, or placebo
  - All patients received medium potency TCS*
- Primary outcome: proportion of patients achieving IGA 0 or 1 at 16 weeks

* Low potency TCS used for areas where medium potency TCS were deemed unsafe
IGA=Investigator’s Global Assessment Scale, QW=once weekly, Q2W=every two weeks, TCS=topical corticosteroids
Dupilumab: Clinical Impact

Phase III LIBERTY AD CHRONOS trial: Results

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Dupilumab 300 mg QW</th>
<th>Dupilumab 300 mg Q2W</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary endpoints</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proportion of patients with IGA 0 or 1 at 16 weeks</td>
<td>39% (P&lt;0.0001)</td>
<td>39% (P&lt;0.0001)</td>
<td>12%</td>
</tr>
<tr>
<td>Proportion of patients with EASI-75 at 16 weeks</td>
<td>64% (P&lt;0.0001)</td>
<td>69% (P&lt;0.0001)</td>
<td>23%</td>
</tr>
</tbody>
</table>
### Phase III LIBERTY AD CHRONOS trial: Results

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Dupilumab 300 mg QW</th>
<th>Dupilumab 300 mg Q2W</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Secondary endpoints</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proportion of patients with IGA 0 or 1 at 52 weeks</td>
<td>40% (P&lt;0.0001)</td>
<td>36% (P&lt;0.0001)</td>
<td>12.5%</td>
</tr>
<tr>
<td>Proportion of patients with EASI-75 at 52 weeks</td>
<td>64% (P&lt;0.0001)</td>
<td>65% (P&lt;0.0001)</td>
<td>22%</td>
</tr>
</tbody>
</table>
Therapeutic alternatives

- TCS, emollients
- Topical calcineurin inhibitors
  - e.g., tacrolimus, pimecrolimus
- Phototherapy
- Systemic immunosuppressant therapy
  - e.g., cyclosporine
- First generation antihistamines may help improve sleep
**Dupilumab: Clinical Impact**\(^{11,13-15}\)

### Potential Advantages
- Significant improvements in outcomes vs. SOC
- Potential for Q2W dosing
- May be the first targeted therapy for underlying cause of disease
- Well-tolerated safety profile

### Potential Disadvantages
- Current SOC is much less costly
- SC administration for a disease historically treated topically
Cost

- Cost data not available
- Industry news blasts suggest $30,000/year
- Supplemental rebate – limited market competition
- Value-based contracts – some subjectivity in treatment outcomes, monitoring issues
Dupilumab: Economic Impact\textsuperscript{17-20}

Volume

- Prevalence 10.7\% of children, 10.2\% of adults
  - Estimated that 33\% of children with atopic dermatitis have moderate-to-severe disease
  - 7 to 8 million adults in the US; approximately 1.6 million with uncontrolled disease per physician survey

- Duration of treatment is indefinite

- Other key facts
  - Also being studied in asthma, nasal polyposis
Dupilumab: Budget Impact\textsuperscript{13,16,21}

Medicaid plan
- Up to $30,000/year for treatment
- Scenarios
  - 10% uptake: $2 to $2.5 million/year
  - All uncontrolled patients treated: $19.8 to $24.8 million/year
Dupilumab: Budget Impact\textsuperscript{13}

Timeline

- Awarded Breakthrough Therapy designation
- Regulatory submission completed Q3 2016
- FDA decision may be expected in the first half of 2017
Multiple Sclerosis\textsuperscript{22-25}

Clinical features

- Chronic, immune-mediated disease
- Immune system attacks myelin, nerve fibers
- Characterized by sensory disturbances: numbness/weakness, vision loss, pain, tremor, fatigue, etc.
- Four subtypes: RRMS, PPMS, SPMS, PRMS

Prevalence

- Affects 400,000 people in the US
- More common in women than men

MS=multiple sclerosis, PPMS=primary-progressive MS, PRMS=progressive-relapsing MS, RRMS=relapsing-remitting MS, SPMS=secondary-progressive MS

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Ocrelizumab

- Proposed indication: Relapsing MS, PPMS
- MOA: MoAB that selectively targets CD20-positive B cells
  - CD20-positive B cells are key contributors to myelin and axonal damage
  - Ocrelizumab binds to CD20 cell surface proteins expressed on B cells (not stem or plasma cells), preserving key functions of the immune system
Ocrelizumab: Clinical Impact

Phase III OPERA I and II trials: Design

- Randomized, active-controlled
- Population: N=828; patients with RRMS
- Intervention: ocrelizumab 600 mg IV infusion every six months or interferon β-1a 44 mcg SC thrice weekly for two years
- Primary outcomes: ARR at 96 weeks

ARR=annualized relapse rate, IV=intravenous
**Ocrelizumab: Clinical Impact**

**Phase III OPERA I and II trials: Results**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>IFN β-1a</th>
<th>Ocrelizumab</th>
<th>Relative reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARR at 96 weeks</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OPERA I</td>
<td>0.292</td>
<td>0.156</td>
<td>46% (P&lt;0.0001)</td>
</tr>
<tr>
<td>OPERA II</td>
<td>0.290</td>
<td>0.155</td>
<td>47% (P&lt;0.0001)</td>
</tr>
</tbody>
</table>

IFN=interferon

November 16, 2016  Planning for the 2017 Specialty Drug Spend
# Ocrelizumab: Clinical Impact

## Phase III OPERA I and II trials: Results

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Ocrelizumab</th>
<th>IFN β-1a</th>
<th>Relative reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1 GdE lesions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OPERA I</td>
<td>0.016</td>
<td>0.286</td>
<td>94% (P&lt;0.0001)</td>
</tr>
<tr>
<td>OPERA II</td>
<td>0.021</td>
<td>0.416</td>
<td>95% (P&lt;0.0001)</td>
</tr>
</tbody>
</table>

GdE=gadolinium-enhancing lesions
Ocrelizumab: Clinical Impact\textsuperscript{26-27}

Phase III ORATORIO trial: Design

- Randomized, placebo-controlled
- Population: N=732; patients with PPMS
- Intervention: ocrelizumab 600 mg IV infusion every six months or placebo (minimum of 5 doses)
  - All patients pre-medicated with methylprednisolone
- Primary outcomes: progression of clinical disability
# Ocrelizumab: Clinical Impact

## Phase III ORATORIO trial: Results

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Risk reduction (ocrelizumab vs. placebo)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary Endpoint</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risk of progression of clinical disability sustained for ≥12 weeks (per EDSS)</td>
<td>24%</td>
<td>0.0321</td>
</tr>
<tr>
<td><strong>Secondary Endpoint</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risk of progression of clinical disability sustained for ≥24 weeks (per EDSS)</td>
<td>25%</td>
<td>0.0365</td>
</tr>
</tbody>
</table>

EDSS = Expanded Disability Status Scale
Ocrelizumab: Clinical Impact\textsuperscript{26-27}

Phase III ORATORIO trial: Results

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Ocrelizumab</th>
<th>Placebo</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Secondary Endpoints at 120 weeks</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change from baseline in time to walk 25 feet</td>
<td>39%</td>
<td>55%</td>
<td>0.04</td>
</tr>
<tr>
<td>Change from baseline in T2 lesion volume</td>
<td>-3.4%</td>
<td>7.4%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Rate of brain volume loss (from baseline)</td>
<td>-0.9%</td>
<td>-1.1%</td>
<td>0.02</td>
</tr>
</tbody>
</table>

November 16, 2016 Planning for the 2017 Specialty Drug Spend
Therapeutic alternatives

**Injectable**
- IFN β-1a
- IFN β-1b
- Daclizumab
- Glatiramer acetate
- Natalizumab
- Alemtuzumab
- Mitoxantrone

**Oral**
- Fingolimod
- Teriflunomide
- Dimethyl fumarate
Ocrelizumab: Clinical Impact\(^{22-25}\)

**MS Pipeline**

- **Ozanimod**
  - Oral, S1P receptor 1 and 5 modulator
  - Selectivity may avoid AEs associated with fingolimod
  - RRMS: ↓MRI brain lesions by 86% and ↓ARR* by 53% vs. placebo
  - Regulatory submission for MS anticipated 2017-2018

*Not statistically powered to detect significance
S1P=sphingosine 1-phosphate
# Ocrelizumab: Clinical Impact

## MS Pipeline*

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>MOA</th>
<th>Proposed Indication(s)</th>
<th>Anticipated Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laquinimod</td>
<td>Immuno-modulator</td>
<td>RRMS</td>
<td>2017</td>
</tr>
<tr>
<td>Siponimod</td>
<td>S1P receptor 1 and 5 inhibitor</td>
<td>RRMS, PPMS, SPMS</td>
<td>2017</td>
</tr>
<tr>
<td>Ponesimod</td>
<td>S1P receptor 1 inhibitor</td>
<td>RRMS</td>
<td>2018</td>
</tr>
</tbody>
</table>

*Not an all-inclusive list

November 16, 2016 Planning for the 2017 Specialty Drug Spend
Ocrelizumab: Clinical Impact

Potential Advantages

• May be the first FDA-approved treatment for PPMS
• Significantly reduced risk of disease progression in difficult-to-treat PPMS
• Dosed every six months vs. every month with natalizumab

Potential Disadvantages

• Higher doses in Phase III RA trial were associated with serious, opportunistic infections
• Development in RA, LE halted due to incidence of opportunistic infection and death in clinical trials
• Lacking long-term safety data

LE=lupus erythematosus, RA=rheumatoid arthritis
Ocrelizumab: Economic Impact\textsuperscript{32,36}

Cost

• Cost data not available
  – Currently available injectable agents range in cost from $1,000 to $106,000 per year (most ~$80,000)
• Supplemental rebate – limited market competition for PPMS; may select preferred RRMS agent
• Value-based contracts – reduction in risk of progression (PPMS), reduction in ARR (RRMS)
Ocrelizumab: Economic Impact \(^{22,29,32-34}\)

**Volume**

- Prevalence 90 per 100,000 individuals in US
- Duration: chronic condition; treatment is indefinite
- Other key facts
  - May be the first approved treatment for PPMS
  - Several injectable, oral options on the market for RRMS
  - Injectable agents ~70% of the RRMS market
Ocrelizumab: Budget Impact

- **Medicaid plan**
  - Approximately $80,000/year for treatment
  - $4.8 million/year

- **Timeline**
  - FDA decision expected 12/28/2016
Plaque Psoriasis\textsuperscript{38,39}

**Clinical features**
- Chronic, immune-mediated disease
- Characterized by infiltration of inflammatory cells into the skin, excessive keratinocyte proliferation, and development of raised, scaly skin (plaques)
- ↑ incidence of lymphoma, heart disease, obesity, T2DM, metabolic syndrome

**Prevalence**
- Affects ~6 million people in the US
- Most common form of psoriasis
Guselkumab\textsuperscript{40}

- Proposed indication: plaque psoriasis
- MOA: fully-human MoAB that inhibits IL-23
  - Specifically targets the p19 subunit of IL-23
    (p19 mRNA elevated in psoriatic lesions)
  - Th17/IL-23 pathway key in amplification phase of psoriasis
  - SC injection

\textit{mRNA}=messenger ribonucleic acid, \textit{Th}=T helper cell
Guselkumab: Clinical Impact\textsuperscript{41,42}

Phase III VOYAGE 1 trial: Design

- Randomized, placebo- and active-controlled
- Population: N=837; adults with moderate-to-severe plaque psoriasis
- Intervention:
  - Placebo at weeks 0, 4, 12 then guselkumab at weeks 16 and 20 and Q8W thereafter
  - Guselkumab 100 mg SC at weeks 0, 4, 12 then Q8W
  - Adalimumab 80 mg SC at week 0, 40 mg at week 1, then Q2W thereafter
- Primary outcomes: PASI\textsuperscript{90} response, IGA of 0 or 1 at 16 weeks vs. placebo

\textsuperscript{IGA=Investigator’s Global Assessment, PASI\textsuperscript{90}=90\% improvement in Psoriasis Area Sensitivity Index, Q2W=every two weeks, Q8W=every eight weeks}
## Guselkumab: Clinical Impact\(^{41,42}\)

### Phase III VOYAGE 1 trial: Results

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Guselkumab</th>
<th>Placebo</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary Endpoints vs. Placebo</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proportion of patients achieving PASI90 at 16 weeks</td>
<td>73.3%</td>
<td>2.9%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Proportion of patients achieving IGA 0 or 1 at 16 weeks</td>
<td>85.1%</td>
<td>6.9%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
# Guselkumab: Clinical Impact\textsuperscript{41,42}

## Phase III VOYAGE 1 trial: Results

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Guselkumab</th>
<th>Adalimumab</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary Endpoints vs. Adalimumab</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proportion of patients achieving PASI90 at 16 weeks</td>
<td>73.3%</td>
<td>49.7%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Proportion of patients achieving IGA 0 or 1 at 16 weeks</td>
<td>85.1%</td>
<td>65.9%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Therapeutic alternatives

- **Topical**
  - Emollients, keratolytics, corticosteroids, etc.

- **Systemic**
  - Traditional DMARDs
    - MTX, sulfasalazine, cyclosporine, tacrolimus, azathioprine, hydroxyurea, leflunomide, etc.
  - Biologic DMARDs
    - Adalimumab*, etanercept*, infliximab, ixekizumab, secukinumab, ustekinumab*

- **Phototherapy**

---

*Recommended as first-line treatment option per consensus guidelines
DMARD=disease-modifying antirheumatic drug, MTX=methotrexate
Plaque Psoriasis Pipeline*

- Brodalumab
  - Investigational fully-human IL-17 receptor MoAB
  - SC injection
  - FDA AdComm voted 18-0 in favor of approval with conditions related to product labeling, post-marketing/risk management requirements
  - Safety concerns: increased risk of suicidal ideation and behavior, serious infections
  - FDA decision expected 11/16/2016

*Not an all-inclusive list
AdComm=Advisory Committee
**Guselkumab: Clinical Impact**

**Plaque Psoriasis Pipeline**

- **Tildrakizumab**
  - Investigational fully-human IL-23 receptor antibody targeting p19 subunit
  - SC injection
  - Demonstrated superiority vs. placebo and etanercept in Phase III trials†
    - PASI75 response at week 12
    - PGA response (score of 0 or 1 with ≥2 point reduction)
  - BLA anticipated late 2016

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*Not an all-inclusive list
†Tildrakizumab 100 mg was superior to etanercept for PASI75, only PASI75=75% improvement in Psoriasis Area Sensitivity Index*
Guselkumab: Clinical Impact\textsuperscript{27,33-36}

**Potential Advantages**
- Demonstrated superior efficacy vs. adalimumab, current market leader
- Similar safety profile compared to adalimumab in clinical trials
- Ongoing clinical trial comparing guselkumab to ustekinumab

**Potential Disadvantages**
- Biosimilars for market leaders, including adalimumab
- Crowded plaque psoriasis market
- Brodalumab may reach market first
Guselkumab: Economic Impact\textsuperscript{40,43-47}

Cost

- Cost data not available
  - Adalimumab, etanercept, and ustekinumab cost
    \$37,000 to \$57,000 per year
- Supplemental rebate – identify preferred IL-23 agent
  - Crowd plaque psoriasis market, biosimilars
- Value-based contracts – achievement of PASI 75, PGA response
Guselkumab: Economic Impact\textsuperscript{38,39}

**Volume**

- Prevalence: 2\% of the US population has psoriasis; 90\% of patients with psoriasis have plaque psoriasis
  - Approximately 20\% have moderate-to-severe disease
- Duration: chronic condition; duration of treatment is indefinite
- Other key facts
  - Given superior efficacy vs. adalimumab, may become a first-line treatment option
  - Also being studied in psoriatic arthritis
Guselkumab: Budget Impact

Medicaid plan
- Approximately $50,000/year for treatment
- $6 million/year

Timeline
- Regulatory submission anticipated Q4 2016

100,000 covered lives
1,800 patients with plaque psoriasis
360 patients with moderate-to-severe disease
120 patients may require treatment

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Migraine

Clinical features
- May be episodic (0 to 14 headache days/month) or chronic (≥15 headache days/month)
- Characterized by incapacitating head pain, physical impairment; commonly associated with nausea, vomiting, and sound/sensory disturbances

Prevalence
- Affects ~3 to 7 million people in the US
- Health care and lost productivity costs associated with migraine ~$36 billion/year in the US
Erenumab$^{53-55}$

- **Proposed indication:** prevention of episodic migraine, chronic migraine
- **MOA:** fully-human MoAB targeting CGRP receptor
  - CGRP receptors are thought to transmit signals that can cause incapacitating pain
  - Blocking CGRP reduces vasodilation and neurogenic inflammation associated with migraine

CGRP = calcitonin-gene related peptide
Erenumab: Clinical Impact\textsuperscript{53,54}

Phase III ARISE trial: Design

- Randomized, placebo-controlled
- Population: N=577; patients with episodic migraine
  - Average of 8 migraines/month at baseline
- Intervention: erenumab 70 mg SC monthly vs. placebo
- Primary outcome: change in monthly migraine days from baseline to the last four weeks of the 12-week treatment phase
Phase III ARISE trial: Results

• Statistically significant reduction in monthly migraine days from baseline
  – 2.9-day reduction in the erenumab treatment arm vs.
    1.8-day reduction in the placebo arm
Erenumab: Clinical Impact\textsuperscript{53,54}

Phase II 20120295 study: Design

- Randomized, placebo-controlled
- Population: N=667; patients with chronic migraine
  - Average of 18 migraines/month at baseline
- Intervention: erenumab 140 mg SC or 70 mg SC monthly vs. placebo
- Primary outcome: change in monthly migraine days from baseline to the last four weeks of the 12-week treatment phase
Erenumab: Clinical Impact

Phase II 20120295 study: Results

- Statistically significant reduction in monthly migraine days from baseline
  - 6.6-day reduction in the erenumab treatment arms vs. 4.2-day reduction in the placebo arm
Erenumab: Clinical Impact\textsuperscript{57-60}

Therapeutic alternatives

- **Acute treatment**
  - NSAIDs
  - Combination analgesics (e.g., acetaminophen/aspirin/caffeine)
  - Triptans

- **Prophylactic treatment**
  - Amitriptyline
  - Calcium channel blockers
  - Beta blockers
  - Antiepileptics
  - Onabotulinum toxin A

\textsuperscript{NSAID=non-steroidal antiinflammatory drug

\textsuperscript{November 16, 2016 Planning for the 2017 Specialty Drug Spend

\textsuperscript{Erenumab: Clinical Impact\textsuperscript{57-60}}
**Erenumab: Clinical Impact**[^61-64]

### CGRP Pipeline*

<table>
<thead>
<tr>
<th>Generic/Investigational Name</th>
<th>Stage of Development</th>
<th>Other Key Facts</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALD403</td>
<td>Phase III</td>
<td>IV infusion Q3M; also being studied as SC, IM injection</td>
</tr>
<tr>
<td>Galcanezumab</td>
<td>Phase III</td>
<td>SC injection monthly</td>
</tr>
<tr>
<td>TEV-48125</td>
<td>Phase III</td>
<td>SC injection monthly</td>
</tr>
</tbody>
</table>

*Not an all-inclusive list
IM=intramuscular, Q3M=every three months

[^61-64]: Planning for the 2017 Specialty Drug Spend

November 16, 2016
Erenumab: Clinical Impact\textsuperscript{53-57,60-65}

Potential Advantages

- May be the first targeted therapy for prevention of migraine
- Similar safety profile vs. placebo in clinical trials
- CGRP agents may have similar efficacy but improved safety vs. standard oral preventative therapies

Potential Disadvantages

- Lacking long-term safety data to understand impact of blocking CGRP receptor
- SC administration for a condition typically treated with oral medications
Erenumab: Economic Impact

Cost

• Cost data not available
• Industry news blasts suggest ~$14,000/year
• Supplemental rebate – select preferred CGRP agent
• Value-based contracts – reduction in headache days/month, patient adherence measures
Erenumab: Economic Impact\textsuperscript{65,67,68}

Volume

- Prevalence 14.9% of individuals in US
  - Approximately 30% of patients with migraine have used preventative therapies
- Duration: chronic condition; treatment is indefinite
  - Preventative therapies historically associated with poor adherence
    - Non-adherence after six months ~65% to 75%
Erenumab: Budget Impact

- Medicaid plan
  - $14,000/year for treatment
  - Scenarios
    - 10% uptake: $6.3 million/year
    - All candidates for preventative therapy treated: $62.6 million/year
- Timeline
  - Approval anticipated ~2018-2019
Conclusions

- Biologics in development may offer first FDA-approved targeted treatments for NASH, atopic dermatitis
- Specialty pipeline agents may offer important therapeutic, safety advantages
- Specialty pipeline agents in existing therapeutic classes represent opportunities for supplemental rebate, value-based contracts
- Proactive pipeline monitoring and a solid understanding of plan membership are key to anticipating budget impact of new drugs
QUESTIONS?