Planning for the 2017 Specialty Drug Spend:

When Costs are Steep but Pockets are Not Deep

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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

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[1]

- **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

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

CV=cardiovascular

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)

T2DM=type 2 diabetes mellitus

Elafiabranor[2-3]

- **Proposed indication:** NASH
- **MOA:** Dual PPAR-α/δ 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[2]

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[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

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

Elafibranor: Clinical Impact[2]

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[4]

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

Elafibranor: Economic Impact[6-9]

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[6]

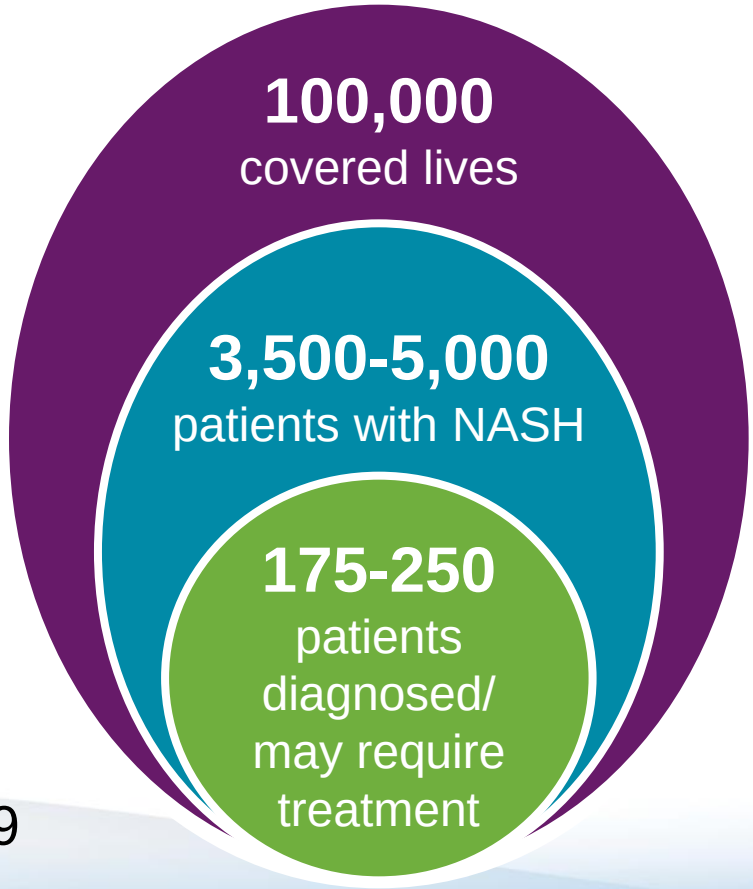
Volume

- 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

Elafibranor: Budget Impact[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[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[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

Dupilumab: Clinical Impact[13]

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[13]

Phase III LIBERTY AD CHRONOS trial: Results

Outcome	Dupilumab 300 mg QW	Dupilumab 300 mg Q2W	Placebo
Primary endpoints			
Proportion of patients with IGA 0 or 1 at 16 weeks	39% (P<0.0001)	39% (P<0.0001)	12%
Proportion of patients with EASI-75 at 16 weeks	64% (P<0.0001)	69% (P<0.0001)	23%

EASI-75=75% reduction in Eczema Activity and Severity Index score, QW=once weekly, Q2W=every two weeks

Dupilumab: Clinical Impact[13]

Phase III LIBERTY AD CHRONOS trial: Results

Outcome	Dupilumab 300 mg QW	Dupilumab 300 mg Q2W	Placebo
Secondary endpoints			
Proportion of patients with IGA 0 or 1 at 52 weeks	40% (P<0.0001)	36% (P<0.0001)	12.5%
Proportion of patients with EASI-75 at 52 weeks	64% (P<0.0001)	65% (P<0.0001)	22%

Dupilumab: Clinical Impact[14-15]

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 Disdvantages

- Current SOC is much less costly
- SC administration for a disease historically treated topically

SOC=standard of care

Dupilumab: Economic Impact[16]

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[17-20]

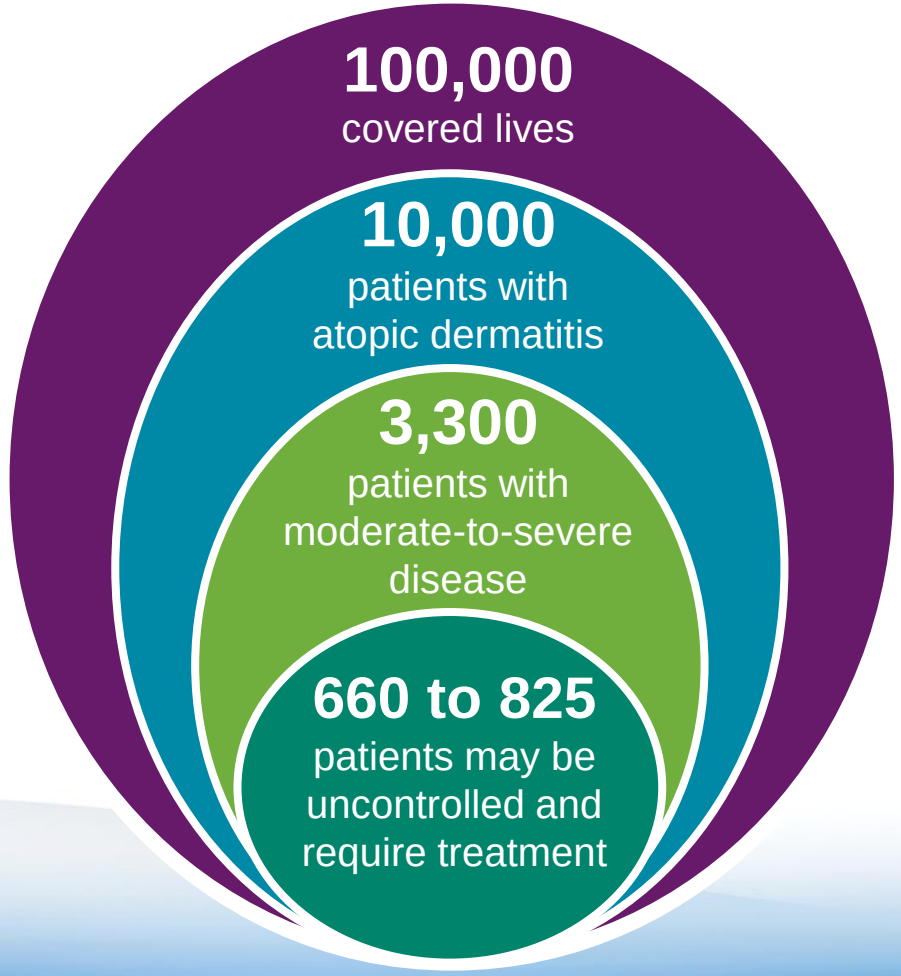
Volume

- 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[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[13]

Timeline

- Awarded Breakthrough Therapy designation
- Regulatory submission completed Q3 2016
- FDA decision may be expected in the first half of 2017

Multiple Sclerosis[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

Ocrelizumab[26]

- **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[27]

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[27]

Phase III OPERA I and II trials: Results

Outcome	IFN β-1a	Ocrelizumab	Relative reduction
ARR at 96 weeks			
OPERA I	0.292	0.156	46% (P<0.0001)
OPERA II	0.290	0.155	47% (P<0.0001)

IFN=interferon

Ocrelizumab: Clinical Impact[27]

Phase III OPERA I and II trials: Results

Outcome	Ocrelizumab	IFN β-1a	Relative reduction
T1 GdE lesions			
OPERA I	0.016	0.286	94% (P<0.0001)
OPERA II	0.021	0.416	95% (P<0.0001)

GdE=gadolinium-enhancing lesions

Ocrelizumab: Clinical Impact[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[26-27]

Phase III ORATORIO trial: Results

Outcome	Risk reduction (ocrelizumab vs. placebo)	P-value
Primary Endpoint		
Risk of progression of clinical disability sustained for ≥12 weeks (per EDSS)	24%	0.0321
Secondary Endpoint		
Risk of progression of clinical disability sustained for ≥24 weeks (per EDSS)	25%	0.0365

EDSS=Expanded Disability Status Scale

Ocrelizumab: Clinical Impact[26-27]

Phase III ORATORIO trial: Results

Outcome	Ocrelizumab	Placebo	P-value
Secondary Endpoints at 120 weeks			
Change from baseline in time to walk 25 feet	39%	55%	0.04
Change from baseline in T2 lesion volume	-3.4%	7.4%	<0.0001
Rate of brain volume loss (from baseline)	-0.9%	-1.1%	0.02

Ocrelizumab: Clinical Impact[28-31]

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[32]

MS Pipeline*

Generic Name	MOA	Proposed Indication(s)	Anticipated Approval
Laquinimod	Immuno-modulator	RRMS	2017
Siponimod	S1P receptor 1 and 5 inhibitor	RRMS, PPMS, SPMS	2017
Ponesimod	S1P receptor 1 inhibitor	RRMS	2018

*Not an all-inclusive list

Ocrelizumab: Clinical Impact[27,33-36]

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[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)

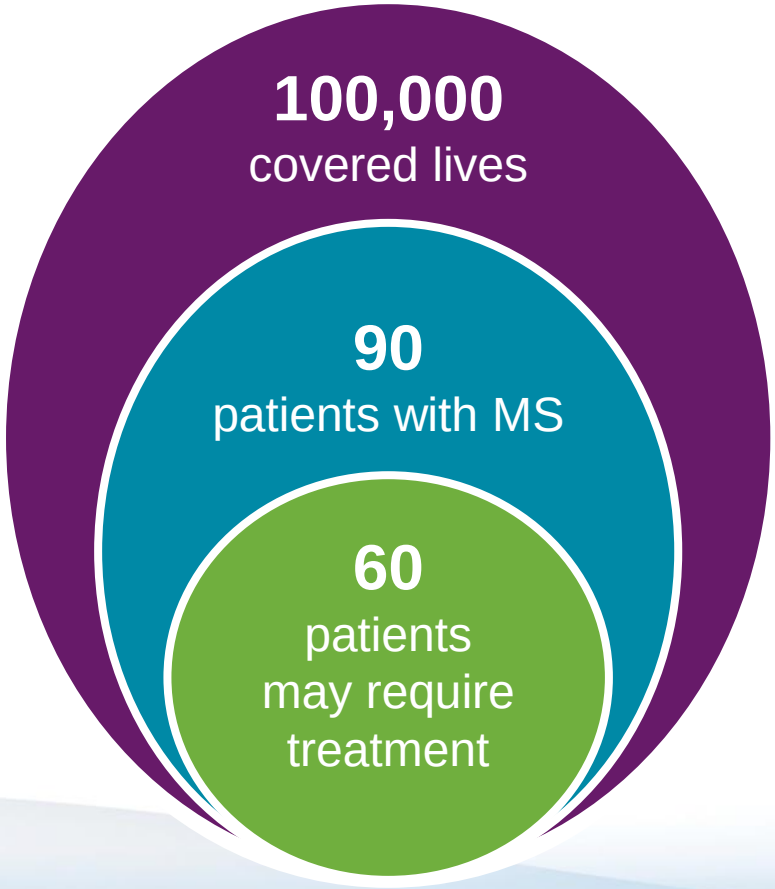
Ocrelizumab: Economic Impact[22,29,32-34]

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[37]

- **Medicaid plan**
  - Approximately $80,000/year for treatment
  - **$4.8 million/year**
- **Timeline**
  - FDA decision expected 12/28/2016



Plaque Psoriasis[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[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

mRNA=messenger ribonucleic acid, Th=T helper cell

Guselkumab: Clinical Impact[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: PASI90 response, IGA of 0 or 1 at 16 weeks vs. placebo

IGA=Investigator's Global Assessment, PASI90=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

Outcome	Guselkumab	Placebo	P-value
Primary Endpoints vs. Placebo			
Proportion of patients achieving PASI90 at 16 weeks	73.3%	2.9%	<0.001
Proportion of patients achieving IGA 0 or 1 at 16 weeks	85.1%	6.9%	<0.001

Guselkumab: Clinical Impact[41,42]

Phase III VOYAGE 1 trial: Results

Outcome	Guselkumab	Adalimumab	P-value
Primary Endpoints vs. Adalimumab			
Proportion of patients achieving PASI90 at 16 weeks	73.3%	49.7%	<0.001
Proportion of patients achieving IGA 0 or 1 at 16 weeks	85.1%	65.9%	<0.001

Guselkumab: Clinical Impact[43-47]

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

Guselkumab: Clinical Impact[48]

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[49]

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

*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[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[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
  - Crowded plaque psoriasis market, biosimilars
- Value-based contracts – achievement of PASI 75, PGA response

Guselkumab: Economic Impact[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

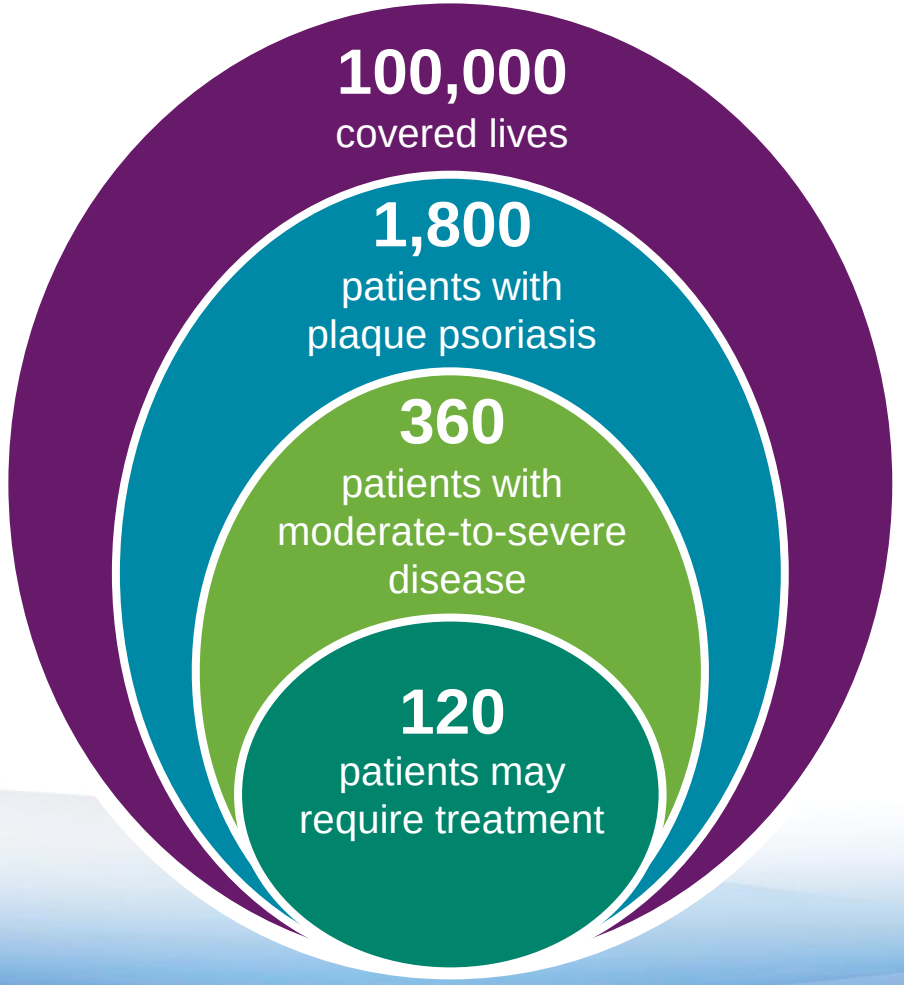
Guselkumab: Budget Impact[38,40,43-47]

Medicaid plan

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

Timeline

- Regulatory submission anticipated Q4 2016



Migraine[50-52]

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[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

Erenumab: Clinical Impact[56]

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[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[56]

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[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

NSAID=non-steroidal antiinflammatory drug

Erenumab: Clinical Impact[61-64]

CGRP Pipeline*

Generic/ Investigational Name	Stage of Development	Other Key Facts
ALD403	Phase III	IV infusion Q3M; also being studied as SC, IM injection
Galcanezumab	Phase III	SC injection monthly
TEV-48125	Phase III	SC injection monthly

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

Erenumab: Clinical Impact[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[66]

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

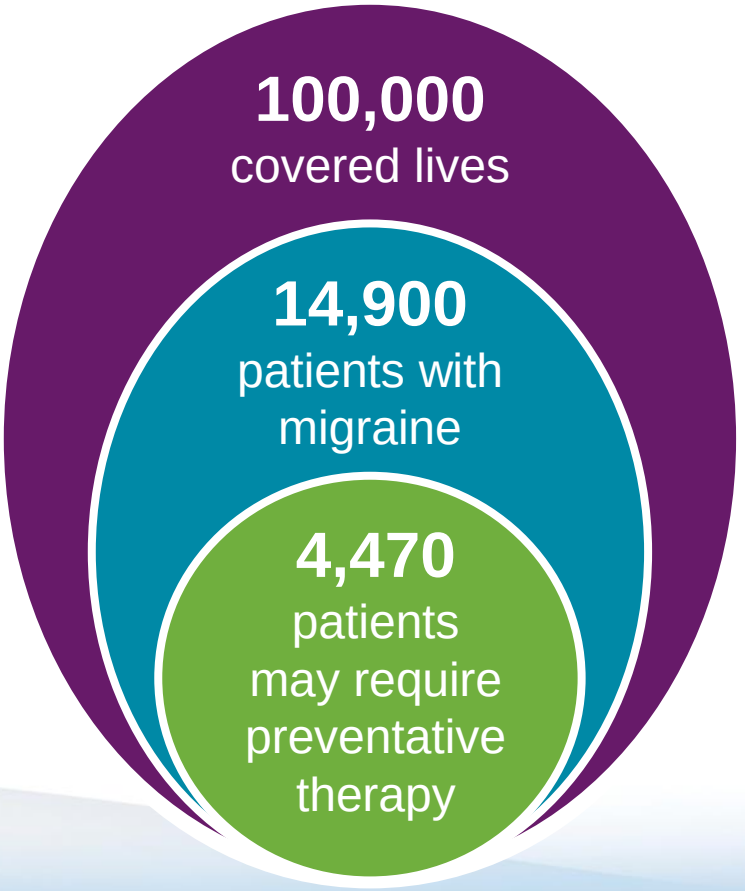
Erenumab: Economic Impact[65,67,68]

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[65,67-69]

- **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
- Speciality 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?