AMCP Format for Formulary Submission

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Presented by:

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Outline

- What is it?
- What are the elements to this format?
- Why is it important? Why do we want to use it?
- What are the manufacturers and health plan's opinions on a standardized format?
- What do we look at to evaluate formulary status and how does this standard format help us with it?
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History of Formulary Submissions

- Pharmacy and therapeutics committees (P&T)
  - Request drug information from manufactures to assist in formulary review process

- Drug Information
  - Marketing materials and clinical trial reprints
  - Primary focus on safety and efficacy with secondary focus on cost effectiveness
    - *What is its **value**? – Is this adequately addressed?*
  - Concerns for comprehensiveness and accuracy (bias)

Background

- Who is this for?
  - Manufacturers of pharmaceuticals and P&T Committees/Formulary Decision Makers
    - Formulary Submission
- What is it?
  - Evidence Dossier Template
    - Centerpiece of formulary submission – standardized set of clinical and economic evidence
- Why do we have it?
  - Standardizing product information requirement
  - Projections of product impact on organization and patient population
  - Value of the product
  - Transparency of evidence and rational supporting use

Key Questions in Formulary Additions

- **Do we *need*** to add the drug to formulary?
- What is the **evidence to support** this drug?
- Are there any **safety issues** to be considered?
- Is there any potential for **misuse or overuse**?
- **All else being equal**, can we **justify the cost** of this drug?

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Key Terms in Formulary Additions

- Effectiveness vs. Efficacy
  - **Actual** effect (real life situation) vs. **potentia**l effect (under optimal circumstances)
- Pharmacodynamics Curve
  - Max Therapeutic Benefit → How effective is it on the population?
  - Eg: Claritin (Loratidine)
    - *Recommended dose works on 50% of the population – is this effective?*
- Comparative Effectiveness Research (CER)
  - *Treatment heterogeneity*
  - Placebo control vs. Active control trials
  - Real world effectiveness
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Example: Pharmacodynamic Curve

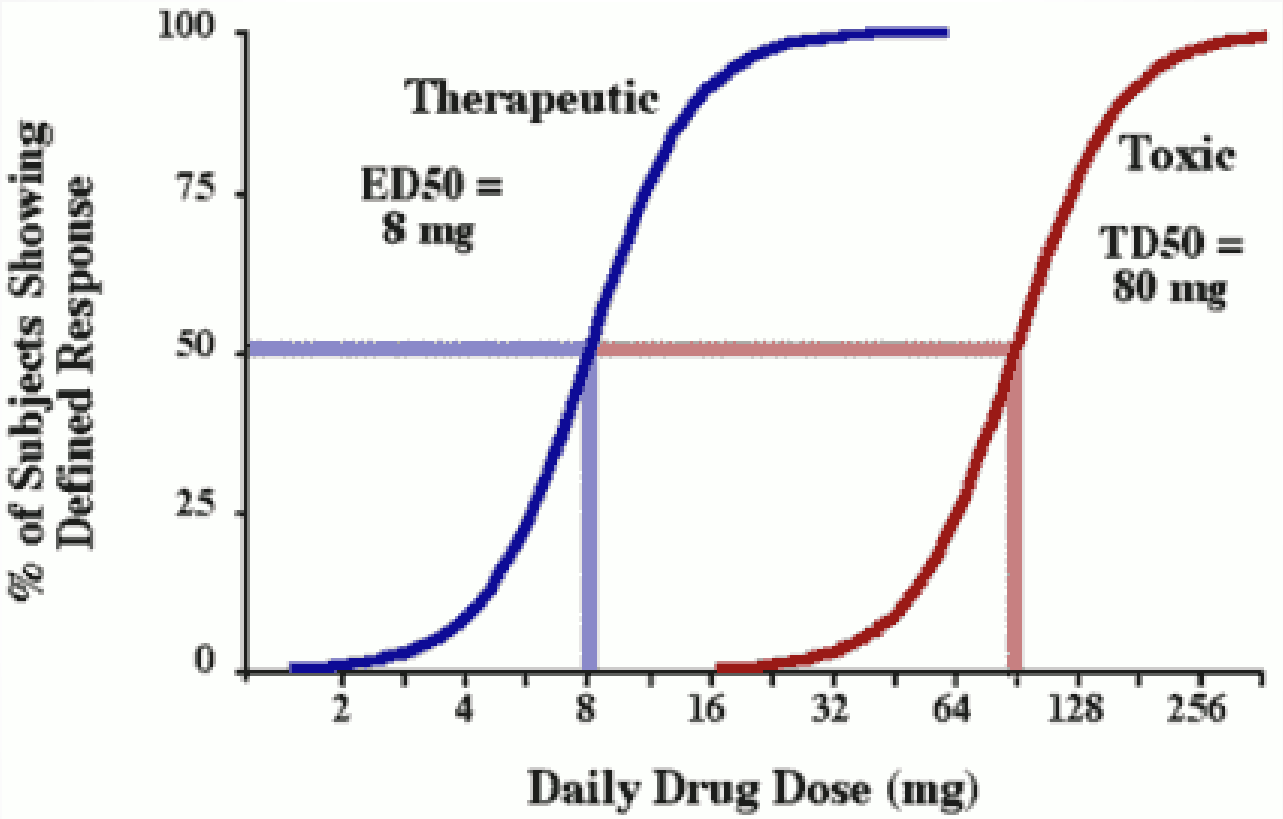


Figure 5. *The quantal dose-response relation describes the percentage of the population of subjects (experimental animals or patients) that show a predefined response as the dose or concentration of drug is incrementally increased. The curves are cumulative and are determined for both the therapeutic as well as undesired effects.*

General Format

- **Evidence dossier:**
  - **1.0**: Executive Summary - Clinical and Economic Value of Product
  - **2.0**: Product Information and Disease Description
  - **3.0**: Supporting Clinical Evidence
  - **4.0**: Economic Value and Modeling Report
  - **5.0**: Other Supporting Evidence
  - **6.0**: Supporting Information

What does the dossier give us?

Dossier:

1. Clinical Efficacy
2. Safety
3. Economic Value

- Paves way for healthcare professionals to produce individual drug monographs for P&T Submission
  - 5 Issues present in AMCP's recommended template for drug monographs
    1. What is the evidence of efficacy from clinical trials?
    2. Is there sufficient evidence to assess real world comparative effectiveness?
    3. What is the evidence of safety?
    4. What is the value proposition for this product?
    5. Are there identifiable patient subgroups in which this treatment will be most cost-effective?

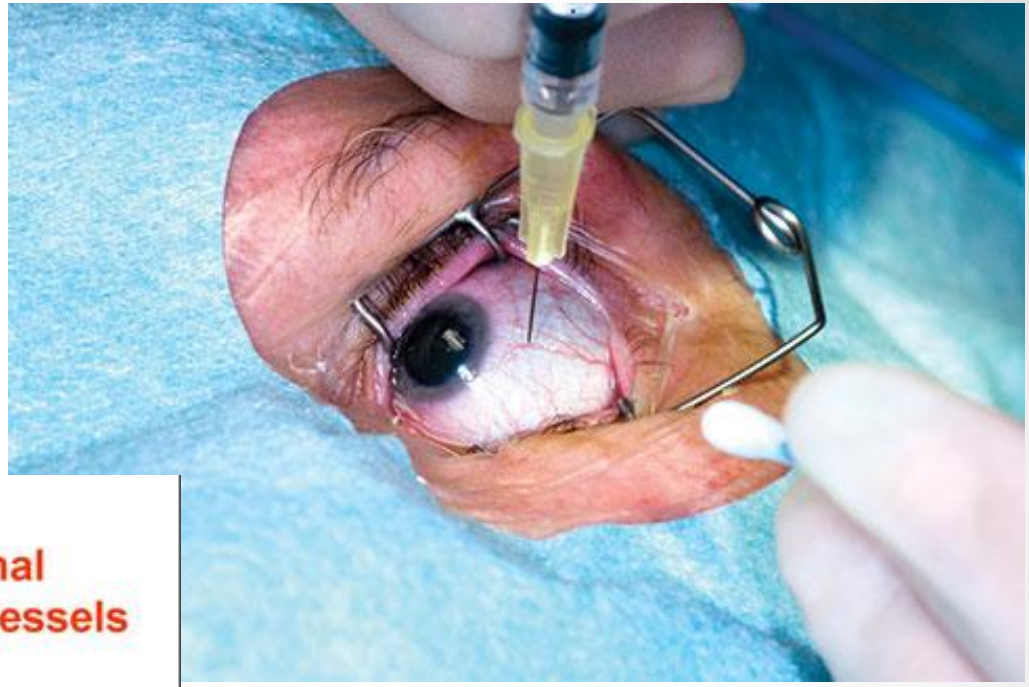
Example

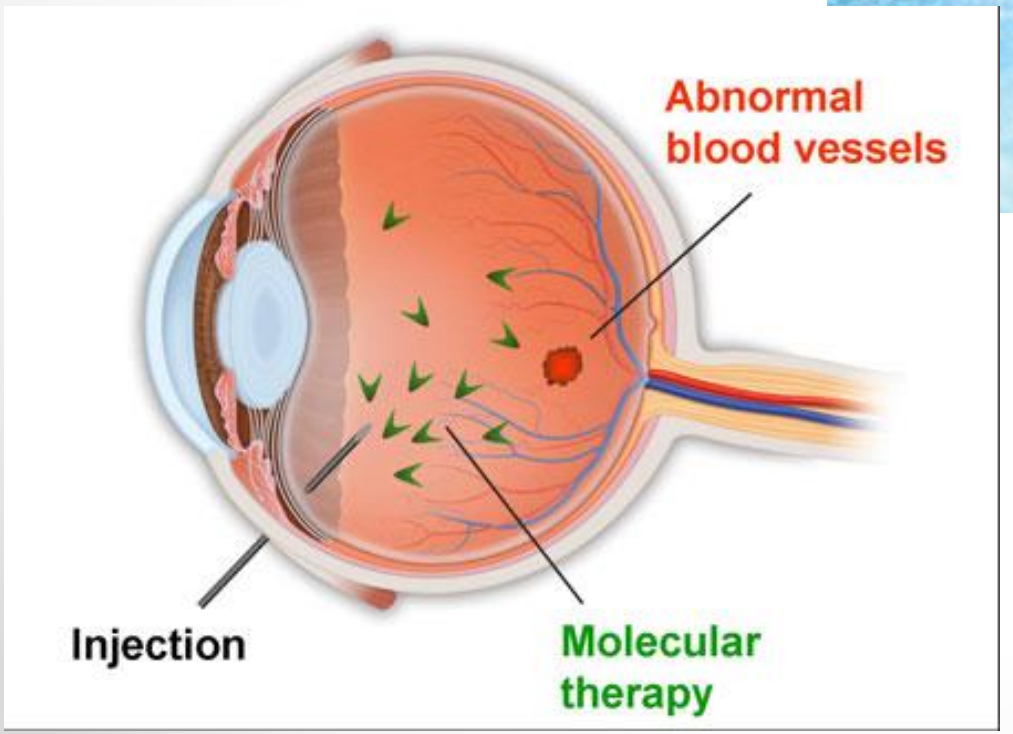
Drug of Interest:

- Aflibercept (Eylea) Intravitreal Injection (IAI)
  - For the treatment of Neovascular (Wet) Age-Related Macular Degeneration (AMD)
  - Vascular Endothelial Growth Factor Inhibitor (VEGF-I)

- Comparators:
  - Ranibizumab (Lucentis) – "Gold Standard"
    - 2 mg IAI every 4 weeks
    - Also a VEGF-I

Intravitreal Injection





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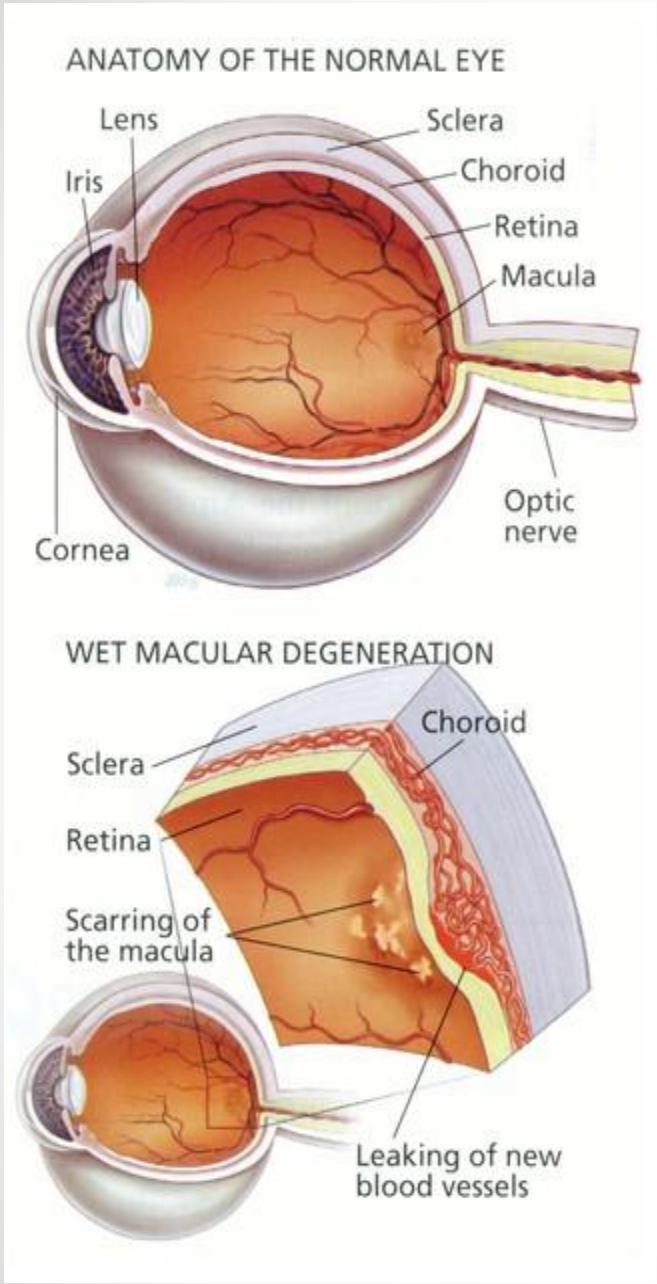
Disease Burden: Wet-AMD



- Degenerative eye disease that leads to progressive loss of central vision. Leading cause of vision loss in Americans >60 y.o.
- Affects the macula, located in central area of retina
- Total financial burden for many visual disorders aged 40+ is ~$35.4 billion in 2004

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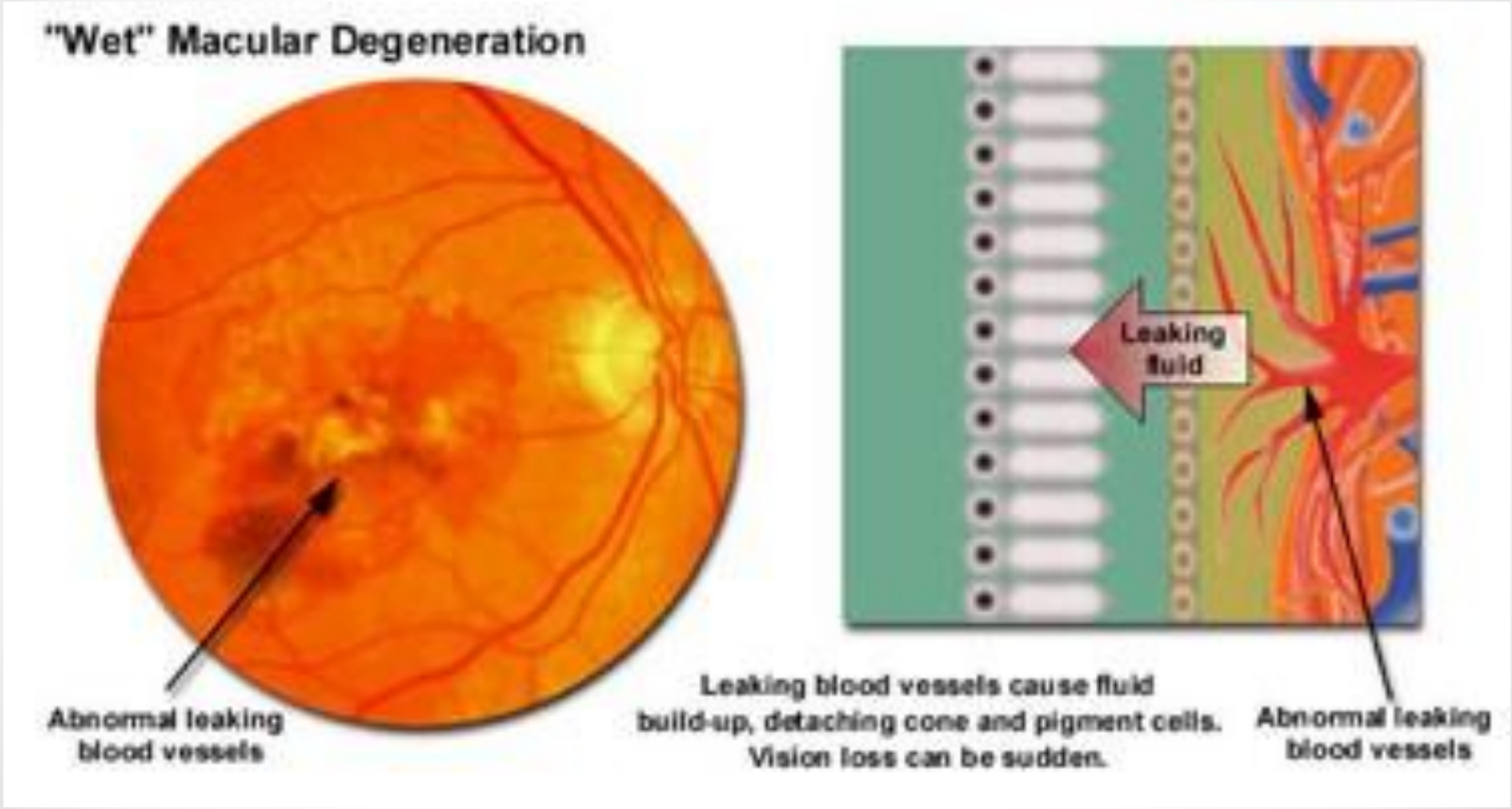
Wet-AMD


"Wet" Macular Degeneration
Abnormal leaking blood vessels
Leaking fluid
Leaking blood vessels cause fluid build-up, detaching cone and pigment cells. Vision loss can be sudden.
Abnormal leaking blood vessels

Product Disease Description

- Primary symptoms are 1) Object distortion 2) Blurred vision 3) Central scotoma (black or gray patch)
- VEGF-I are primary target for Wet-AMD. VEGF-A is an important regular of angiogenic process.
- Ranibizumab (Lucentis) is current standard of care which is dosed every 4 weeks (monthly) IAI and must be performed under care of retinal specialist.

Product Disease Description

- **Aflibercept (Eylea)** is an IAI injection
- **Mechanism**: VEGF-I
- **Dose**: 2 mg (IAI) every 4 weeks for 12 weeks, then every 8 weeks
- **Pharmacokinetics**:
  - Route: Ophthalmic intravitreal injection
  - Bioavailability: 15 – 30% free aflibercept
  - Time to Peak: 0.02 mcg/mg 1 – 3 days after 2 mg IAI
  - Clearance: Saturable high affinity binding to VEGF and proteolytic catabolism processes
-

Product Disease Description

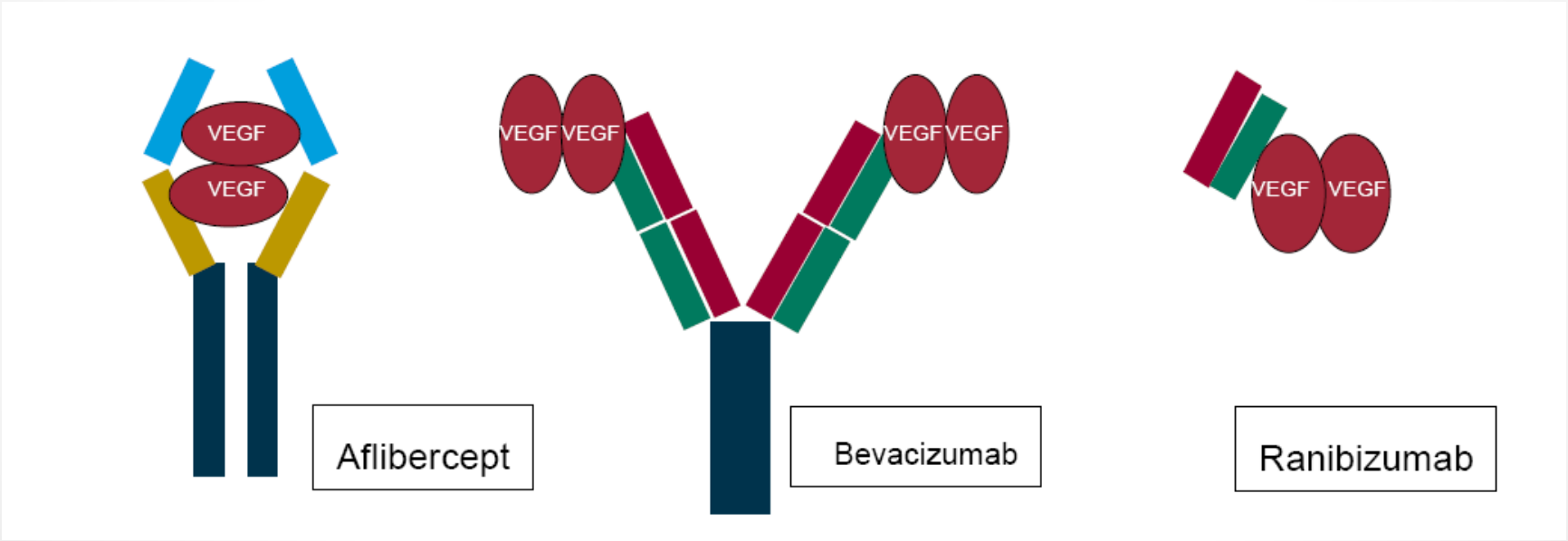
- **Adverse Effects:**
  - Conjunctival hemorrhage (28%)
  - Eye pain (9%)
  - Conjunctival hyperemia (8%)
  - Intraocular pressure increase (7%)

    ***Most adverse effects were related to injection process*

- **Contraindications/Drug Interactions**
  - None drug interactions known
  - Contraindicated with ocular infections, intraocular inflammation, or hypersensitivity

- **Packaging:**
  - Single use 0.278 mL vial of 40 mg/mL.
  - CPT code 67028 pays $109.07 for injection when performed in office setting
  - Cost is reimbursed separately at $980.50 per 1 mg injection
  - Aflibercept AWP = $1850/injection

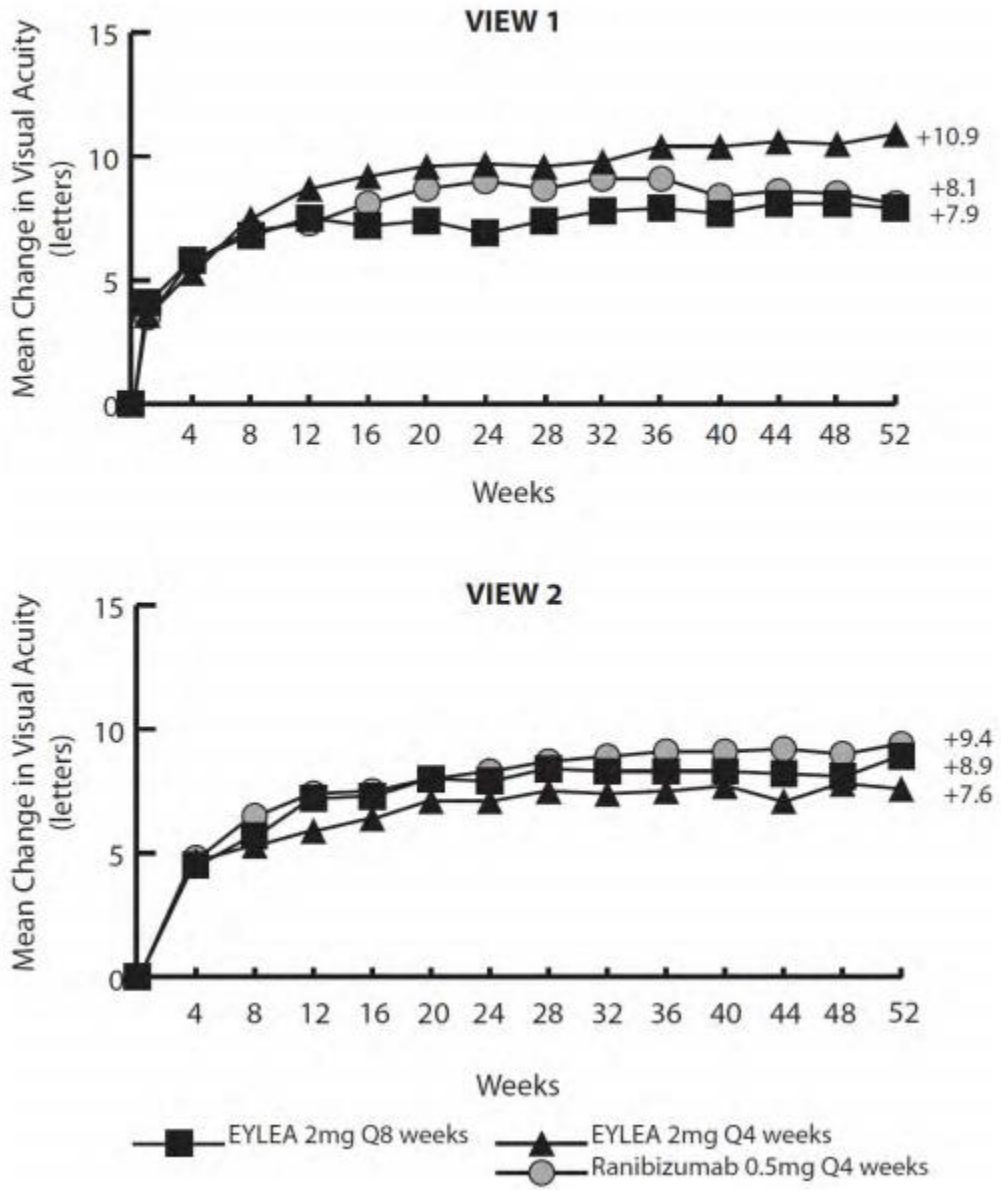
Binding Comparisons



Supporting Clinical Evidence

- VIEW 1 and VIEW 2 trials (**V**EGF Trap Eye: **I**nvestigation of **E**fficacy and Safety in **W**et AMD)
  - Sample Size = 2419, Duration = 52 weeks
  - Demographics
    - Mean age of **78** for VIEW 1 and **74** for VIEW 2
    - **96.6%** White for VIEW 1 and **72.8%** for VIEW 2
  - Eylea 2 mg every 4 weeks for first 12 weeks followed by 2 mg once **every 8 weeks**
    - **Non-inferior** to ranibizumab 0.5 mg **every 4 weeks**
    - Primary endpoint of proportion of patients who maintained vision (less than 15 letters loss) at week 52
  - Similar rates of adverse effects in active and control groups. Injection was generally well tolerated.

Figure 9: Mean Change in Visual Acuity from Baseline to Week 52 in VIEW1 and VIEW2 Studies



VIEW 1 + 2 Comparisons*

***For Primary Endpoint**

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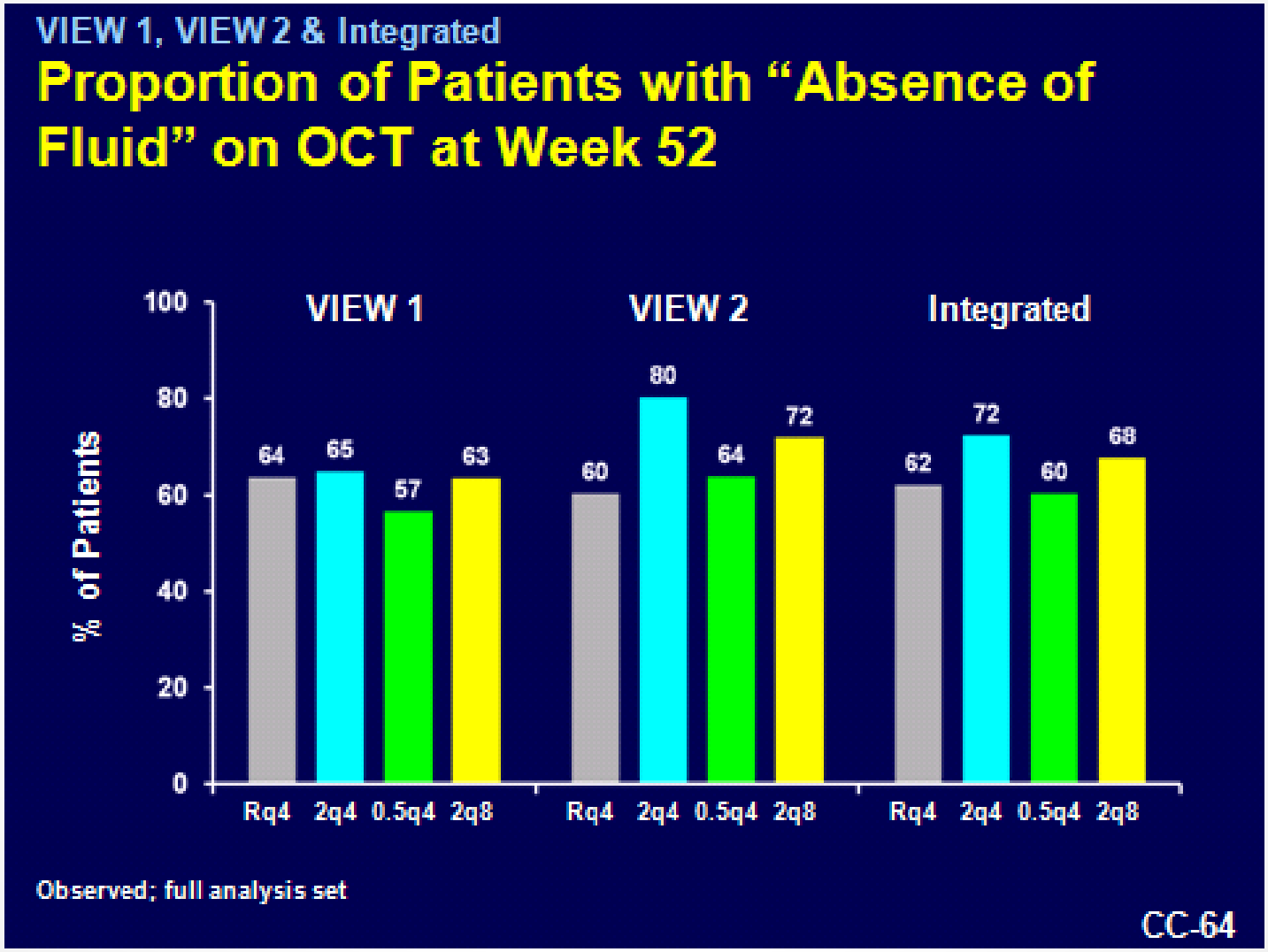
VIEW 1 + 2 Comparisons



Economic Value

Established from previous slides: Non-inferiority

Aflibercept AWP = $1850/injection

Ranibizumab AWP = $1950/injection

* *AWP = Average Wholesale Price*

- Ranibizumab is effectively double the cost of Aflibercept (2x frequency)

Treatment	Cost	QALYs	ICER (Cost/QALY)
Aflibercept 2Q8	$30,459	1.314	Reference
Aflibercept 2Q4	$55,882	1.317	$9,852,953
Ranibizumab 0.5Q4	$58,069	1.312	Dominated

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Economic Value

- Eylea 2 mg every 8 weeks following initial doses every 4 weeks
  - For 1 million patients >65 years old
  - Save ~$17.3 million in first year to $55.8 million in 5th year

Budgetary Impact*	Year 1	Year 2	Year 3	Year 4	Year 5
Total	$-17,277,634	-$24,679,859	-$36,315,577	-$47,454,923	-$55,759,640
PMPM**	-$1.44	-$2.06	-$3.03	-$3.95	-$4.64

*Budget Impact Supplied by Manufacturer

**PMPM = Per Member Per Month

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Importance

- Why do we need a standard format?
  - Reduces chances for bias – "cherry picking trials"
  - Streamlines process for formulary review – easy to compare data among all comparators
- Why would P&T Committees want this?
  - Standardized format – Much easier to streamline meetings and to compare data among comparators
  - Gives members all the available data on the product. Tells them the **value** and **impact** on their population
- Why would manufacturers want to do this?
  - Helps present overall impact and value of the product for a population in a real world setting
    - *Why do we need it?*
    - 95% of manufacturers responding to a survey reported that an economic model played a role in improving product positioning on formularies at least once in their experience

Limitations

- Not everyone submits a dossier and not everyone follows the format
  - **Guideline, not a mandate**
  - In a 2007 survey, 58% manufacturers supplied a dossier in response to a unsolicited request
    - 84% followed the AMCP Format, 16% did not
      - Of the 16%: 3 dossiers were missing large number of trials, 2 dossier only included the most favorable data for the product

- Can it impact formulary decisions?
  - 2 articles published in 2007 evaluating the AMCP Format
    - In one health plan – 54% of products with submitted dossiers received preferred formulary status
    - Another health plan – 16% of products with submitted dossiers received preferred formulary status (compared to 33% for those who did not)
  - Conclusion:
    - *By itself, receipt of dossier did not influence formulary decision*

Conclusion

- The AMCP Format provides a clean and efficient way for formulary decision makers to evaluate all the criterion necessary for a specific product
  - Provides information on effectiveness/efficacy, the safety, the value, and the overall impact of a specific product for their specific population of interest

References

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