Ophthalmic Vascular Endothelial Growth Factor Inhibitors: First-Year Single-Eye Therapy Cost Evaluation Using Real-World Maintenance Frequency and Claim Costs for Aflibercept, Bevacizumab and Ranibizumab

Vishwanath, S., Montalbo A., Sharma S., Eckwright D.

BACKGROUND

- Age-related macular degeneration (AMD) and diabetic macular edema (DME) are the leading causes of blindness and visual impairment, affecting 1.8 million people in the US. The National Institutes of Health predicts this number to increase to 20 million by 2050.[1]
- Ophthalmic vascular endothelial growth factor inhibitors (OVEGFi) are first-line treatments for both retinal diseases and are injected intravitreally to the affected eye to reduce leakage and growth of vessels and improve visual acuity.[2,3]
- Clinical guidelines recommend several OVEGFi drugs including compounded bevacizumab, ranibizumab and aflibercept for both AMD and DME.
- OVEGFi drugs accounted for over $4.6 billion in Medicare spend in 2020. Aflibercept is among the top 10 drugs in overall spend for both Medicare and Commercial in 2021.[4,5]
- First-year single-eye (FYSE) treatment cost can differ greatly across OVEGFi products due to pricing, loading dose, provider contracts, and varying maintenance doses, which can range from every 4 to 16 weeks depending on drug, treatment approach, and patient response.[6-8]
- Understanding real-word single-eye claim cost and real-world maintenance frequency are key factors for modeling and comparing OVEGFi FYSE treatment costs for making informed preferred product decisions.

OBJECTIVE

- Calculate the first-year single-eye treatment cost for aflibercept, bevacizumab, and ranibizumab by evaluating real-world maintenance frequency and single-eye claim cost by leveraging medical claims data.

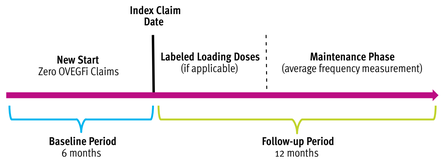
METHODS

Ophthalmic vascular endothelial growth factor inhibitor (OVEGFi) claims for aflibercept (J0178), ophthalmic bevacizumab (J9035 and C9257) and ranibizumab (J2778) were queried from 12.7 million Commercial and 600,000 Medicare members.

New Start Average Maintenance Frequency Analysis

- OVEGFi claims were queried between October 2020 and March 2021 (6-month period).
- Index claim date was defined as member's first OVEGFi medical claim with an ICD-10 code for age-related macular degeneration (AMD) or diabetic macular edema (DME).

FIGURE 1. STUDY OUTLINE



- Member inclusion criteria include:
  - Continuous enrollment 6 months prior to and 12 months after the index claim
  - New start to OVEGFi defined as having zero OVEGFi claims 6 months prior to their index claim date
  - Maintenance phase members defined as members with claims occurring after the expected number of loading doses per product's label or clinical guideline for ophthalmic bevacizumab[2,3,6,7]
  - Resulting members' maintenance claims were included in the average maintenance frequency (i.e., days between claims) calculation

Single-Eye Claim Cost Analysis

- Single-eye claim cost equaled the number of Healthcare Common Procedure Coding System (HCPCS) units required to treat a single eye multiplied by the average allowed amount per unit found between April 2021 through March 2022 (12-month period).

First-Year Single-Eye Treatment Cost Calculation

- First-year single-eye (FYSE) treatment cost equaled the number of expected first-year doses (labeled loading doses plus remaining first-year maintenance doses calculated from the average maintenance frequency) multiplied by the single-eye claim cost.
- Reference FYSE treatment cost was defined as the number of first-year doses informed by label or guideline multiplied by the average sales price (ASP) to treat a single eye plus 6%.

Real-world metrics reveal **considerable cost differences** among ophthalmic vascular endothelial growth factor inhibitors for Commercial and Medicare members providing insight into preferred product strategies.

RESULTS

TABLE 1. ATTRITION & MAINTENANCE FREQUENCY

Identification Criteria	Commercial				Medicare			
	N				N			
OVEGFi for AMD or DME	9,730				8,253			
Continuous Enrollment	5,520				4,384			
New Starts	2,065				963			
Maintenance Phase	1,488				782			
Maintenance Phase members	AMD		DME		AMD		DME	
	N	MNTF	N	MNTF	N	MNTF	N	MNTF
Aflibercept	68	46	187	37	77	55	15	47
Bevacizumab	152	48	925	51	464	49	189	46
Ranibizumab	23	43	133	49	18	51	19	51
Total N	243	-	1,245	-	559	-	223	-

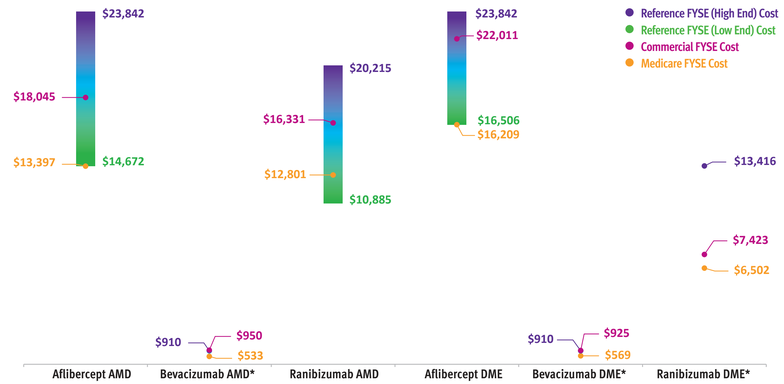
AMD=Age-related macular degeneration; MNTF=average maintenance frequency in days; DME=Diabetic macular edema; N=number of unique members; OVEGFi= Ophthalmic vascular endothelial growth factor inhibitor. Commercial population was 12.7 million and Medicare population was 600,000 members.

TABLE 2. EXPECTED FIRST-YEAR DOSES & SINGLE-EYE CLAIM COST

	Drug (dose)	Loading		Maintenance				First-Year Doses (Loading + Maintenance)			Single-Eye Claim Cost		
		Duration (Days)	Label Doses	Duration (Days)	Label/ GL Doses	COM Doses*	MED Doses*	Label/ GL	COM	MED	ASP‡	COM	MED
AMD	Aflibercept (2mg)	84	3	281	5 to 10	6.1	5.1	8 to 13	9.1	8.1	$1,834	$1,983	$1,654
	Bevacizumab (1.25mg)	0	0	365	13	7.6	7.4	13	7.6	7.4	$70^	$129^	$72^
	Ranibizumab^ (0.5mg)	84	3	281	4 to 10	6.5	5.5	7 to 13	9.5	8.5	$1,555	$1,719	$ 1,506
DME	Aflibercept (2mg)	140	5	225	4 to 8	6.1	4.8	9 to 13	11.1	9.8	$1,834	$1,983	$1,654
	Bevacizumab (1.25mg)	0	0	365	13	7.4	7.9	13	7.4	7.9	$70^	$129^	$72^
	Ranibizumab (0.3mg)	0	0	365	13	7.2	7.2	13	7.2	7.2	$1,032	$1,031	$903

AMD=Age-related macular degeneration; ASP=average sales price; COM=Commercial; DME=Diabetic macular edema; GL=guideline; MED=Medicare
First-year was defined as 365 days
*Number of doses were calculated by dividing the maintenance duration (days) by the average real-world frequency (Table 1)
^Label allows 3 initial doses (loading dose) every 28 days and 4 doses (maintenance doses) in the remaining 9 months
†Bevacizumab single-eye claim cost is the blended cost between J9035 (10 mg) and C9257 (0.25 mg)
‡The average ASP from April 2021 through March 2022 plus 6%
#represents J9035

FIGURE 2. FIRST-YEAR SINGLE-EYE TREATMENT COST



Reference FYSE (High End): defined as the highest number of label informed first-year doses multiplied by the ASP + 6%.
Reference FYSE (Low End): defined as the lowest number of label informed first-year doses multiplied by the ASP + 6%.
*Label/guideline's recommended maintenance dosing does not vary
ASP=average sales price

DISCUSSION

Attrition & Maintenance Frequency (Table 1)

- Of the members identified as newly initiating maintenance phase ophthalmic vascular endothelial growth factor inhibitors (OVEGFi) therapy:
  - 84% (1,245 of 1,488) and 16% (243 of 1,488) of Commercial (COM) members had diabetic macular edema (DME) and age-related macular degeneration (AMD), respectively.
  - 29% (223 of 782) and 71% (559 or 782) of Medicare (MED) members had DME and AMD, respectively.
- Average maintenance frequency differed by less than 7 days among drugs within the same indication and line of business apart from DME for COM where the average frequency differed by 12 to 14 days (i.e., aflibercept 37 days compared to bevacizumab 51 days and ranibizumab 49 days).

Expected First-Year Doses and Single-Eye Claim Cost (Table 2)

- The number of expected first-year doses was similar to guideline and label recommendations except for bevacizumab for AMD and DME and ranibizumab for DME (7 to 8 expected first-year doses vs. 13 guideline/label first-year doses).
- Ranibizumab had the highest number of expected first-year doses for AMD with 0.4 more doses than aflibercept (COM and MED) and 1.1 (MED) and 1.9 (COM) more doses than bevacizumab.
- Aflibercept had the highest number of expected first-year doses for DME with 3.9 more doses than ranibizumab and 3.7 more doses than bevacizumab for COM. Similarly, aflibercept had 2.6 more doses than ranibizumab and 1.9 more doses than bevacizumab for MED.
- The lowest to highest single-eye claim cost drug was bevacizumab, ranibizumab and aflibercept across COM and MED for DME and AMD.

First-Year Single-Eye (FYSE) Treatment Cost (Figure 2)

- Aflibercept had the highest FYSE treatment cost ranging between $14,672 to $22,011 across COM and MED for both AMD and DME.
- Ranibizumab had the second highest FYSE treatment cost but was only slightly less than aflibercept for AMD ($596 less for MED and $1,714 less for COM) but was considerably less than aflibercept for DME ($9,707 less for MED and $14,588 less for COM) due to lower dose for DME and lower expected first-year doses.
- Bevacizumab had the lowest FYSE treatment cost for COM and MED which ranged from $12,268 to $17,095 less for AMD and $5,933 to $21,086 for DME depending on comparator drug (i.e., aflibercept or ranibizumab) and payor type (i.e., COM or MED).

LIMITATIONS

- Differences among groups in terms of disease severity, age, gender, drug efficacy (e.g., improvement in visual acuity), and reasons for varying dosing frequencies (e.g., treat to extend, non-adherence, etc.) were not evaluated.
- Single-eye treatment cost was not adjusted for the site of service or fee-schedule strategies.
- Claims data did not capture drug rebates or cash paid claims.

CONCLUSIONS

- Of the members newly initiating ophthalmic vascular endothelial growth factor inhibitors (OVEGFi) in maintenance phase, most Commercial members had diabetic macular edema (DME) while most Medicare members had age-related macular degeneration (AMD).
- Bevacizumab had the lowest first-year single-eye cost which was ~$6,000 to ~$21,000 less than aflibercept and ranibizumab.
- Additional cost differences exist between aflibercept and ranibizumab across both indications for Commercial and Medicare members; however, the largest difference in cost was seen in DME (~$10,000 to ~$15,000) which may be more applicable for Commercial payers due to higher prevalence.
- Due to variations among multiple factors (e.g., manufacturer pricing, maintenance dosing ranges, provider contracting, etc.), it is essential for payers to evaluate real-world maintenance frequencies and single-eye claim costs to accurately model first-year single-eye costs to inform effective formulary strategies.
- Further research is needed to investigate new and upcoming OVEGFi drugs and biosimilars for real-world maintenance frequencies and therapy cost.

REFERENCES

1. National Institutes of Health. National Eye Institutes Eye Health and Data Statistics. Accessed Jan 11, 2023. https://www.nei.nih.gov/learn-about-eye-health/eye-health-data-and-statistics
2. American Academy of Ophthalmology. What Is Macular Degeneration? Accessed Jan 11, 2023. https://www.aao.org/eye-health/diseases/amd-macular-degeneration#treatment
3. American Academy of Ophthalmology. Diabetic Macular Edema: Diagnosis and Management. Accessed Jan 11, 2023. https://www.aao.org/eyenet/article/diabetic-macular-edema-diagnosis-and-management
4. Centers for Medicare & Medicaid Services. Medicare Part B Spending by Drug. CMS.gov. Accessed Jan 11, 2023. https://data.cms.gov/summary-statistics-on-use-and-payments/medicare-medicaid-spending-by-drug/medicare-part-b-spending-by-drug
5. Magellan Rx Management Medical Pharmacy Trend Report, 2022, 12th Edition
6. Regeneron Pharmaceuticals, Inc. Eylea Package Insert. Date: 8/30/2022.
7. Genentech, Inc. Lucentis Package Insert. Date: 10/20/2022.
8. Genentech, Inc. Vabysmo Package Insert. Date: 2/2/2022.

DISCLOSURES

- This research was conducted by Magellan Rx Management, a Prime Therapeutics LLC company, Eagan MN, without external funding.