



# Common Drug Review

## *Pharmacoeconomic Review Report*

July 2016

<b>Drug</b>	Aflibercept (Eylea)
<b>Indication</b>	Treatment of Visual Impairment due to Macular Edema Secondary to Branch Retinal Vein Occlusion (BRVO)
<b>Reimbursement request</b>	EYLEA (aflibercept) be reimbursed for the treatment of visual impairment due to macular edema secondary to branch retinal vein occlusion (BRVO), in a manner similar to Lucentis (ranibizumab).
<b>Dosage form(s)</b>	40 mg/mL Solution for Intravitreal Injection available as a 2 mg single-use vial
<b>NOC date</b>	December 10, 2015
<b>Manufacturer</b>	Bayer Inc.

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## **ABBREVIATIONS**

<b>BRVO</b>	branch retinal vein occlusion
<b>CDEC</b>	CADTH Canadian Drug Expert Committee
<b>CDR</b>	CADTH Common Drug Review
<b>CRVO</b>	central retinal vein occlusion
<b>NMA</b>	network meta-analysis
<b>ODB</b>	Ontario Drug Benefit
<b>PRN</b>	as needed
<b>VEGF</b>	vascular endothelial growth factor

## SUMMARY

### Background

Aflibercept (Eylea) is indicated for the treatment of visual impairment due to macular edema secondary to branch retinal vein occlusion (BRVO).<sup>1</sup> It is administered by intravitreal injection at a dose of 2 mg and available at a cost of \$1,418 per single-use vial. The manufacturer is requesting drug reimbursement similar to that of ranibizumab for BRVO.

The CADTH Common Drug Review (CDR) has previously reviewed aflibercept for wet age-related macular degeneration, diabetic macular edema, and macular edema secondary to central retinal vein occlusion (CRVO); the CADTH Canadian Drug Expert Committee (CDEC) recommended that aflibercept be listed for all three indications on the condition that aflibercept provides cost savings for the drug plans relative to ranibizumab.<sup>2-4</sup>

### Summary of the Economic Analysis Submitted by the Manufacturer

The manufacturer submitted a cost minimization analysis comparing aflibercept 2 mg to ranibizumab 0.5 mg in patients with macular edema secondary to BRVO consistent with those enrolled in the VIBRANT trial (aflibercept versus laser).<sup>5,6</sup> The analysis was conducted over a two-year time horizon from the perspective of a public health care payer. Drug acquisition costs (Ontario Drug Benefit [ODB] Formulary list prices<sup>7</sup>), as well as injection administration and monitoring costs (Ontario Schedule of Benefits for Physician Services<sup>8</sup>) were considered. A 5% discount was applied after year 1. Clinical similarity for aflibercept and ranibizumab was assumed based on the results of an unpublished network meta-analysis (NMA) that included trials of aflibercept, ranibizumab, bevacizumab, dexamethasone, triamcinolone, and laser.<sup>9</sup>

The manufacturer submitted two main analyses considering different usage of treatments: the clinical trial analysis and the equivalent injection frequency analysis. The clinical trial analysis used the mean number of injections in year 1 from the one-year VIBRANT trial<sup>5,6</sup> for aflibercept (9.0 injections), and the one-year BRAVO trial<sup>10,11</sup> for ranibizumab (8.4 injections). The mean number of injections for both drugs in year 2 were obtained from the ranibizumab HORIZON extension study<sup>12</sup> (2.1 injections). The equivalent injection frequency analysis assumed a total of 12 injections over two years for both drugs — nine in year 1 and three in year 2 — based on the CDEC recommendation that ranibizumab be reimbursed for a maximum of 12 vials over two years for the treatment of CRVO.<sup>13</sup> Both analyses assumed a total of 15 monitoring visits for aflibercept and 24 for ranibizumab. See Appendix 2 for more information on the methods used.

The manufacturer reported, based on administration frequencies from clinical trials (clinical trial analysis), that the use of aflibercept would result in a saving of \$1,243 per patient when compared with ranibizumab over two years (total cost per patient for aflibercept: \$17,457 versus ranibizumab: \$18,699). Alternatively, administration based on equivalent injection frequency yielded savings of \$2,376 per patient receiving aflibercept compared with ranibizumab over two years (aflibercept: \$18,749 versus ranibizumab: \$21,126); see Table 6.

### Key Limitations

- **Assumption of clinical similarity is uncertain:** The manufacturer based its assumption of clinical similarity between aflibercept and ranibizumab on the results of an unpublished NMA that included all treatments used in Canada for macular edema secondary to BRVO.<sup>9</sup> Whereas the NMA was relatively well conducted and found no statistically significant efficacy differences between aflibercept and ranibizumab, its main limitation was the weak connection between aflibercept and the rest of the network, leading to wide credible intervals, unrealistic results in the random-effect models, and an inability to assess consistency. Additionally, no indirect treatment comparisons were possible for safety outcomes.
- **Relative frequency of use:** Data from clinical trials and expert opinion suggest that aflibercept and ranibizumab are likely to be used at approximately the same average frequency for the treatment of BRVO; however, there is uncertainty in this assumption. Should the use of aflibercept lead to an increased injection frequency relative to ranibizumab, savings predicted due to the lower cost per vial of aflibercept would be reduced or eliminated.
- **Differences in monitoring protocol overestimated:** The manufacturer's assumption that aflibercept would be used on a treat-and-extend protocol (where the time between monitoring visits and injections is gradually extended after visual stability is achieved) while ranibizumab would be used on an as-needed basis (in which monitoring remains frequent but further treatment is withheld until a patient worsens after stability has been achieved) leads to the assumption of 15 monitoring visits over two years for aflibercept versus 24 for ranibizumab. This magnitude of difference is unlikely to be seen in practice, as clinicians will likely monitor all anti-vascular endothelial growth factor (anti-VEGFs) in a similar manner.

In reanalyses, CDR assumed that aflibercept and ranibizumab would be used at the same frequency, either 10 or 12 injections over two years, and that monitoring visits would be reduced to 13 for aflibercept and 14 for ranibizumab over two years (see Appendix 2).

### Issues for Consideration

- **Existence of off-label comparators:** While bevacizumab is not indicated for the treatment of BRVO or other eye disorders in Canada, it is used in clinical practice and would be of interest to jurisdictions which reimburse it for other conditions. The NMA submitted by the manufacturer also found no statistically significant efficacy differences between bevacizumab and aflibercept or ranibizumab.<sup>9</sup> Bevacizumab remains less expensive per dose than either ranibizumab or aflibercept. Of note, in requesting coverage for aflibercept in a manner similar to ranibizumab, the manufacturer surmises that patients who would receive bevacizumab instead of ranibizumab would also receive bevacizumab instead of aflibercept should aflibercept be listed (manufacturer's economic submission, page 18). An exploratory analysis was performed to assess the cost of the use of bevacizumab relative to that of aflibercept (see Appendix 2).
- **List price unlikely to reflect true cost:** For analysis, ODB list prices were used as a proxy to estimate public drug plans' confidential prices. However, the magnitude of savings (or additional cost) that could be achieved by using aflibercept instead of ranibizumab is dependent on the relative true prices of these drugs paid by public plans. See Appendix 1 for a price reduction analysis, in which the cost per vial for each comparator is varied from its current ODB list price.

**Results and Conclusions**

At the current list price of \$1,418 per dose, aflibercept is less expensive than its main indicated comparator ranibizumab (\$1,575 per dose). Assuming efficacy, safety, and injection frequency are equivalent, CDR estimated that the use of aflibercept is likely to result in savings of between \$1,600 and \$2,000 per patient over the first two years of therapy compared with ranibizumab. Treatment for BRVO is likely to continue beyond two years for most patients; however, at the current list prices, aflibercept would continue to result in savings compared with ranibizumab.

**Cost Comparison Table**

Clinical experts have deemed the treatments presented in Table 1 for the treatment of BRVO to be appropriate. Options may be recommended (appropriate) practice versus actual practice. Options are not restricted to drugs but may be devices or procedures. Existing Product Listing Agreements are not reflected in the table and as such may not represent the actual costs to public drug plans.

**TABLE 1: COST COMPARISON TABLE — BRANCH RETINAL VEIN OCCLUSION TREATMENTS**

Drug/ Comparator	Strength	Dosage Form	Unit Price (\$)	Recommended Treatment Dose	Annual Cost (\$)
Aflibercept (Eylea)	40 mg/mL (0.278 mL vial)	Intravitreal injection	1,418.00 <sup>a</sup>	2 mg monthly; interval may be extended up to 3 months based on visual and anatomic outcomes	\$17,016 (12 injections)  \$12,762 <sup>b</sup> (9 injections)  \$4,254 <sup>b</sup> (3 injections)
Ranibizumab (Lucentis)	10 mg/mL (0.23 mL vial)	Intravitreal injection	1,575.00	0.5 mg monthly  Treatment is continued until VA is achieved (stable VA for 3 consecutive months)	18,900 (12 injections)  14,175 (9 injections) <sup>b</sup>  4,725 (3 injections) <sup>b</sup>
Laser photocoagulation (one eye)	NA	Procedure	182.75 <sup>c</sup>	Operator-dependent	183 (per treatment per eye)
<b>Other treatments used that are not currently indicated</b>					
Bevacizumab (Avastin)	100 mg/4 mL 400 mg/16 mL	Intravitreal injection	600.00 <sup>d</sup> 2,400.00 <sup>d</sup>	1.25 mg per dose <sup>d</sup>  Likely to be used similarly to aflibercept and ranibizumab	7,200 <sup>e</sup> (12 injections)  5,400 (9 injections) <sup>b,d</sup>  1,800 (3 injections) <sup>b,d</sup>

## CDR PHARMACOECONOMIC REVIEW REPORT FOR EYLEA BRVO

Drug/ Comparator	Strength	Dosage Form	Unit Price (\$)	Recommended Treatment Dose	Annual Cost (\$)
Dexamethasone intraocular implant (Ozurdex)	0.7 mg	Implant device	1,295.00 <sup>e</sup>	0.7 mg not more than every 6 months <sup>f</sup>	1,295 (1 treatment)  2,590 (2 treatments)
Triamcinolone (Triesence)	40 mg/1 mL	Intraocular injection	43.40	1 mg to 4 mg every 3 months	174

BRVO = branch retinal vein occlusion; NA = not applicable; VA = visual acuity.

<sup>a</sup> Manufacturer's submission, as well as the Ontario Drug Benefit list price.

<sup>b</sup> Based on the CADTH Canadian Drug Expert Committee recommendation for ranibizumab of maximum 12 injections over 2 years for retinal vein occlusion, assumed to be 9 in year 1 with remainder in year 2.

<sup>c</sup> Ontario Schedule of Benefits for Physician Services, effective December 21, 2015.

<sup>d</sup> PPS® Buyer's Guide, July 2015.<sup>14</sup> Annual costs assume that vials are not split between patients. Actual cost per dose is likely to range between \$15 and \$50, depending on dose preparation costs.<sup>15</sup>

<sup>e</sup> Quebec formulary price (January 2016).

<sup>f</sup> Monograph recommends limit of 2 doses per patient; however, clinical practice may differ.

Source: Ontario Drug Benefit (January 2016) unless otherwise stated. Annual cost of all comparators assumes wastage of unused portions of vials.

## APPENDIX 1: PRICE REDUCTION ANALYSIS

To explore the impact of variations in current or future prices for aflibercept and ranibizumab, the CADTH Common Drug Review ran a price reduction analysis varying the cost of each comparator from its current Ontario Drug Benefit list price down to a 50% reduction. Markups, dispensing fees, administration fees, and monitoring costs are not included.

**TABLE 2: ESTIMATED ADDITIONAL COST (SAVINGS) PER VIAL FOR AFLIBERCEPT VERSUS RANIBIZUMAB AT VARIOUS PRICE REDUCTIONS**

% Reduction, Price Per Vial		Ranibizumab					
		0%, \$1,575	10% \$1,418	20%, \$1,260	30%, \$1,103	40%, \$945	50%, \$788
Aflibercept	0%, \$1,418	(\$157)	\$1	\$158	\$316	\$473	\$631
	10%, \$1,279	(\$299)	(\$141)	\$16	\$174	\$331	\$489
	20%, \$1,134	(\$441)	(\$283)	(\$126)	\$32	\$189	\$347
	30%, \$993	(\$582)	(\$425)	(\$267)	(\$110)	\$48	\$205
	40%, \$851	(\$724)	(\$567)	(\$409)	(\$252)	(\$94)	\$63
	50%, \$709	(\$866)	(\$709)	(\$551)	(\$394)	(\$236)	(\$79)

## APPENDIX 2: REVIEWER WORKSHEETS

TABLE 3: SUMMARY OF MANUFACTURER'S SUBMISSION

Drug Product	Aflibercept (Eylea)
Treatment	Aflibercept 2 mg intravitreal injection
Comparator(s)	Ranibizumab 0.5 mg intravitreal injection
Study Question	"What is the incremental cost (or savings), from the perspective of a provincial government payer, over a two-year time horizon, for aflibercept compared to ranibizumab for the treatment of visual impairment due to macular edema secondary to BRVO"
Type of Economic Evaluation	Cost minimization analysis
Target Population	Patients with visual impairment due to macular edema secondary to BRVO
Perspective	Public health care payers
Outcome(s) Considered	Direct costs (drug, administration, and monitoring costs)
Key Data Sources	
Cost	Ontario Drug Benefit Formulary list prices, Ontario Schedule of Benefits for Physician Services
Clinical Efficacy	Network meta-analysis comparing aflibercept and ranibizumab using data from the VIBRANT and BRAVO trials
Harms	Equivalent safety assumed based on individual trials and evidence from trials in other indications
Time Horizon	2 years, sensitivity analyses up to 4 years
Results for Base Case	Aflibercept was cost-saving when compared with ranibizumab <b>Clinical trial analysis:</b> \$1,243 savings with aflibercept over 2 years  <b>Equal injection frequency analysis:</b> \$2,376 savings with aflibercept over 2 years

BRVO = branch retinal vein occlusion.

### Manufacturer's Results

The manufacturer's analyses<sup>16</sup> contain four main inputs: drug costs, taken from ODB Formulary list prices;<sup>7</sup> frequency of injections, derived from the VIBRANT,<sup>5,6,17</sup> BRAVO,<sup>10,11</sup> and HORIZON<sup>12</sup> trials in the clinical trial analysis (described below) and assumed based on a previous CADTH Canadian Drug Expert Committee (CDEC) recommendation in the equivalent injection analysis (described below); frequency of monitoring, based on an interpretation of the respective product monographs;<sup>1,18</sup> and the cost per injection and monitoring visit, taken from the Ontario Schedule of Benefits for Physician Services<sup>8</sup> (see Table 4).

**TABLE 4: MANUFACTURER’S DRUG, ADMINISTRATION, AND MONITORING COSTS**

Item	Cost	Source
<b>Drug acquisition costs</b>		
Aflibercept 2 mg	<b>\$1,418 per vial</b>	Bayer, ODB list price (Feb. 2016)
Ranibizumab 0.5 mg	<b>\$1,575 per vial</b>	ODB List Price (Feb. 2016)
<b>Administration cost (injection fee)</b>		
Intravitreal injection	<b>\$90.00</b>	ON SOB 2015: Code E149
<b>Monitoring visit costs</b>		
Partial ophthalmology assessment	\$28.95	ON SOB: Code A234
Optical coherence tomography	\$25.00	ON SOB: CodeG822
Tonometry	\$5.10	ON SOB: Code G435
<b>TOTAL monitoring visit costs</b>	<b>\$59.05</b>	

ODB = Ontario Drug Benefit;<sup>7</sup> ON = Ontario; SOB = Schedule of Benefits for Physician Services.<sup>8</sup>  
 Source: Manufacturer’s Pharmacoeconomic submission, Tables 9 and 13.<sup>16</sup>

The manufacturer presented two main analyses: the clinical trial analysis and the equivalent injection analysis. The clinical trial analysis used the mean number of injections in year 1 from the one-year VIBRANT trial<sup>5,6,17</sup> for aflibercept (9.0 injections), and the one-year BRAVO trial<sup>10,11</sup> for ranibizumab (8.4 injections). Both drugs were assumed to use the mean number of injections from the ranibizumab HORIZON extension study<sup>12</sup> in year 2 (2.1 injections). The equivalent injection frequency analysis assumed a total of 12 injections over two years for both drugs — nine in year 1 and three in year 2 (see Table 5).

The manufacturer assumed that patients receiving Eylea would be monitored at each injection visit in year 1 (nine in total) and bimonthly in year 2 (six visits), whereas ranibizumab patients would receive monthly monitoring visits (12 in each year) based on their interpretation of the Lucentis product monograph’s as-needed (PRN) dosing and the *Optimal Treatment of Retinal Vein Occlusion: Canadian Expert Consensus*<sup>19</sup> recommendation that patients receiving anti-vascular endothelial growth factor (VEGF) therapy PRN would be frequently monitored, ideally monthly.

**TABLE 5: MANUFACTURER’S ADMINISTRATION AND MONITORING FREQUENCIES**

Comparator	Year 1	Year 2	Source
<b>Clinical trial analysis —number of vials</b>			
Aflibercept 2 mg	9.0	2.1	VIBRANT, <sup>5,6</sup> HORIZON <sup>12</sup>
Ranibizumab 0.5 mg	8.4	2.1	BRAVO, <sup>10,11</sup> HORIZON <sup>12</sup>
<b>Equivalent injection frequency analysis — number of vials</b>			
Aflibercept 2 mg	9	3	Assumption based on CDEC CRVO recommendation for ranibizumab <sup>13</sup>
Ranibizumab 0.5 mg	9	3	
<b>Both analyses —number of monitoring visits</b>			
Aflibercept 2 mg	9	6	Product monograph, <sup>1</sup> assumption
Ranibizumab 0.5 mg	12	12	Product monograph, <sup>18</sup> assumption

CDEC = Canadian Drug Expert Committee; CRVO = central retinal vein occlusion.  
 Source: Manufacturer’s Pharmacoeconomic submission, Tables 10, 11, and 12.

Over two years, in the clinical trial analysis, the manufacturer’s results indicate that aflibercept (\$17,457) would save \$1,243 per patient when compared with ranibizumab (\$18,699). In the equivalent injection frequency analysis, the use of aflibercept (\$18,749) was associated with a savings of \$2,376 per patient when compared with ranibizumab (\$21,126) over two years (see Table 6).

**TABLE 6: MANUFACTURER’S CLINICAL TRIAL AND REIMBURSEMENT REQUEST ANALYSES RESULTS**

Comparator	Year 1 Drug Costs	Year 2 Drug Costs	Total Drug Costs	Administration and Monitoring Costs	Total Costs
<b>Clinical trial analysis</b>					
Aflibercept 2 mg	\$12,762	\$2,836	\$15,598	\$1,859	\$17,457
Ranibizumab 0.5 mg	\$13,230	\$3,150	\$16,380	\$2,319	\$18,699
<b>Difference (aflibercept minus ranibizumab)</b>			<b>-\$782</b>	<b>-\$461</b>	<b>-\$1,243</b>
<b>Equivalent injection frequency analysis</b>					
Aflibercept 2 mg	\$12,762	\$4,051	\$16,813	\$1,936	\$18,749
Ranibizumab 0.5 mg	\$14,175	\$4,500	\$18,675	\$2,451	\$21,126
<b>Difference (aflibercept minus ranibizumab)</b>			<b>-\$1,862</b>	<b>-\$515</b>	<b>-\$2,376</b>

Note: Costs are discounted 5% in the second year.

Source: Adapted from manufacturer’s Pharmacoeconomic submission, Tables 15 and 16.

The manufacturer ran several sensitivity analyses: varying the treatment time horizon from one to four years in both the clinical trial analysis and equivalent injection frequency analyses, as well as assuming that patients receiving aflibercept would also be monitored monthly. Aflibercept remained cost-saving in all scenarios due to its lower cost per vial.

**CADTH Common Drug Review Results**

Whereas the *Optimal Treatment of Retinal Vein Occlusion: Canadian Expert Consensus*<sup>19</sup> does recommend that monitoring should initially be monthly for retinal vein occlusion patients using anti-VEGFs, it neither strongly recommends this (Level III recommendation based on expert consensus) nor differentiates between anti-VEGF drugs as implied in the manufacturer’s submission. Additionally, the consensus paper states several times that central retinal vein occlusion (CRVO) patients should be monitored more frequently than branch retinal vein occlusion (BRVO) patients, suggesting that long-term monthly monitoring is not expected in the BRVO population. The clinical expert consulted by the CADTH Common Drug Review (CDR) did not believe there would be significant differences in how anti-VEGFs were monitored and administered after patients achieved stable visual acuity; physicians preferring treat-and-extend regimens (where the time between monitoring visits and injections is gradually extended after visual stability is achieved) would do so for all anti-VEGFs, as would physicians following PRN regimens (where monitoring remains frequent but further treatment is withheld until a patient worsens after stability has been achieved). The expert did consider it possible that ranibizumab patients might receive one extra monitoring session in the first year, as clinicians may be more likely to immediately extend aflibercept monitoring to two months after attaining visual stability based on experience with bimonthly dosing in other indications, while ranibizumab patients might initially receive their first scheduled monitoring visit six weeks after attaining visual stability. The expert also considered it likely that both drugs would be monitored approximately every three months in year 2 rather than bimonthly or monthly in patients who had achieved visual stability. CDR therefore assumed that patients receiving aflibercept would be monitored nine times in year 1, as assumed by the manufacturer, while patients receiving ranibizumab would be monitored 10 times, with all patients assumed to be monitored four times in year 2 (see Table 7).

Of note, whereas CDEC did recommend that usage not typically exceed 12 vials over two years for patients using ranibizumab for CRVO, the recommendation for BRVO patients was that usage not typically exceed 10 vials over two years.<sup>13</sup> CDR thus conducted analyses including both 12- and 10-vial assumptions (see Table 7).

**TABLE 7: THE CADTH COMMON DRUG REVIEW’S ADMINISTRATION AND MONITORING FREQUENCIES**

Comparator	Year 1	Year 2	Source
<b>Equivalent injection frequency analysis — 12 vials over 2 years</b>			
Aflibercept 2 mg	9	3	Assumption based on CDEC CRVO recommendation for ranibizumab
Ranibizumab 0.5 mg	9	3	
<b>Equivalent injection frequency analysis — 10 vials over 2 years</b>			
Aflibercept 2 mg	8	2	Assumption based on CDEC BRVO recommendation for ranibizumab
Ranibizumab 0.5 mg	8	2	
<b>Both analyses — number of monitoring visits</b>			
Aflibercept 2 mg	9	4	Assumption
Ranibizumab 0.5 mg	10	4	Assumption

BRVO = branch retinal vein occlusion; CDEC = Canadian Drug Expert Committee; CRVO = central retinal vein occlusion.

Over two years, assuming patients receive 12 anti-VEGF treatments, aflibercept (\$17,457) would save \$1,921 per patient when compared with ranibizumab (\$18,699). When patients are assumed to receive 10 anti-VEGF treatments over two years, the use of aflibercept (\$15,693) would save \$1,614 when compared with ranibizumab (\$17,307) per patient (see Table 8).

**TABLE 8: CADTH COMMON DRUG REVIEW 10- AND 12-VIAL EQUIVALENT INJECTION ANALYSES RESULTS**

Comparator	Year 1 Drug Costs	Year 2 Drug Costs	Total Drug Costs	Administration and Monitoring Costs	Total Costs
<b>Equivalent injection frequency analysis — 12 vials</b>					
Aflibercept 2 mg	\$12,762	\$4,051	\$16,813	\$1,824	\$17,457
Ranibizumab 0.5 mg	\$14,175	\$4,500	\$18,675	\$1,883	\$18,699
<b>Difference (aflibercept minus ranibizumab)</b>			<b>-\$1,862</b>	<b>-\$59</b>	<b>-\$1,921</b>
<b>Equivalent injection frequency analysis — 10 vials</b>					
Aflibercept 2 mg	\$11,344	\$2,701	\$14,045	\$1,648	\$15,693
Ranibizumab 0.5 mg	\$12,600	\$3,000	\$15,600	\$1,707	\$17,307
<b>Difference (aflibercept minus ranibizumab)</b>			<b>-\$1,555</b>	<b>-\$59</b>	<b>-\$1,614</b>

Note: Costs are discounted 5% in the second year.

The main driver in these analyses — those of the manufacturer, as well as those of CDR — is the cost per dose for each comparator. Thus, the savings that could be achieved with aflibercept when compared with ranibizumab are highly dependent on the true prices paid by public plans per dose for each drug; the ODB list prices are merely a proxy for these unknown confidential prices. See Appendix 1 for a price reduction analysis, in which the cost per vial for each comparator is varied from its current ODB list price down to a 50% reduction.

As an exploratory analysis, CDR compared the cost of aflibercept therapy to that of bevacizumab, a third anti-VEGF drug. Bevacizumab is not indicated for retinal conditions in Canada or elsewhere, but is used

in clinical practice and reimbursed by some Canadian jurisdictions. Whereas the cost per dose of bevacizumab can range from approximately \$13 to \$50, depending on the preparation costs incurred by payers for the labour and supplies needed to split 100 mg vials into individual doses of 1.25 mg in a sterile environment, CDR assumed a cost of \$40 in order to be conservative and to align with the recent economic analysis in the CADTH therapeutic review of anti-VEGF drugs for the treatment of retinal conditions.<sup>15</sup>

For the purposes of this analysis, CDR assumed that bevacizumab would be administered at the same frequency as aflibercept and ranibizumab (eight or nine times in year 1; two or three times in year 2), and monitored at the same frequency as ranibizumab was in the previous analysis (10 times in year 1, four times in year 2).

Over two years, assuming patients receive 12 anti-VEGF treatments, aflibercept (\$17,457) would cost \$16,280 more per patient than bevacizumab (\$2,357). When patients are assumed to receive 10 anti-VEGF treatments over two years, the use of aflibercept (\$15,693) would cost \$13,590 more than bevacizumab (\$2,103) per patient (see Table 9).

**TABLE 9: CADTH COMMON DRUG REVIEW BEVACIZUMAB EXPLORATORY ANALYSIS RESULTS**

Comparator	Year 1 Drug Costs	Year 2 Drug Costs	Total Drug Costs	Administration and Monitoring Costs	Total Costs
<b>Equivalent injection frequency analysis — 12 vials</b>					
Aflibercept 2 mg	\$12,762	\$4,051	\$16,813	\$1,824	\$17,457
Bevacizumab 1.25 mg	\$360	\$114	\$474	\$1,883	\$2,357
<b>Difference (aflibercept minus bevacizumab)</b>			<b>\$16,339</b>	<b>-\$59</b>	<b>\$16,280</b>
<b>Equivalent injection frequency analysis — 10 vials</b>					
Aflibercept 2 mg	\$11,344	\$2,701	\$14,045	\$1,648	\$15,693
Bevacizumab 1.25 mg	\$320	\$76	\$396	\$1,707	\$2,103
<b>Difference (aflibercept minus bevacizumab)</b>			<b>\$13,649</b>	<b>-\$59</b>	<b>\$13,590</b>

Note: Costs are discounted 5% in the second year.

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