Response to NICE consultation on pegaptanin and ranibizimab for ARMD on behalf of **Derbyshire County PCT (DCPCT)**
(ACD December 2007)

1 It is noted that many of the points raised in the initial response from Derbyshire County PCT have been specifically addressed in the December 2007 ACD. That is gratifying to see.

2 The PCT remains concerned that the quality of life estimates are based on the effects immediately after loss of vision, either using data obtained from clinic patients or by means of simulated ARMD in volunteers. This over-estimates the consequences compared to when patients have accommodated to their central visual loss. The average loss of QoL seems high given how great are the achievements of many totally blind people.

3 The drug cost cap.

3.1 Data would suggest that, given the slow rate of deterioration once on treatment (as per PrONTO), treatment is likely to be lifelong for the vast majority of patients (90%?). The major determinant of cost is actually clinic costs which exceed drug costs. Thus the suggested cap of 14 injections would only reduce costs by a small amount as clinic charges will continue to fall to the NHS.

3.2 A financial model has been attached. Assuming an average 10 years on treatment and 39 injections over that period, the cap reduces the lifetime costs of ranibizumab by 2/3rds but overall costs by only 1/3rd. Yellow cells permit variations in cost estimates to be made. Indeed such is the burden of clinic costs, even using bevacizumab is very costly.

4 Thresholds

4.1 The low end visual acuity threshold of 6/60 is supported but should also be recommended as a cessation threshold, beyond which treatment will cease.

4.2 There is no recommended upper end commencement visual acuity threshold. PCTs have commonly been using 6/12

5 One or two eyes?

5.1 It is unclear whether this is a first eye policy or a both eyes policy. If the former, guidance should be given as to what to do if the second eye becomes affected: should treatment be switched to the second eye if the vision is better in that eye at that time? What if, having started treatment on the better eye, sight deteriorates faster than the other eye despite treatment?

5.2 If this is a two eye policy the cost implications are significantly higher. If the second eye is treated, it may be that only a single clinic cost is charged to test both eyes but it may not be possible to inject both eyes at the same time (so incurring just one 'daycase' charge) if treatment is triggered by deterioration in vision. If deterioration is random (ie rate is not the same in

both eyes) then an additional 2 injection visits would be required further increasing costs. A two eye policy is included in the financial model, though zero costs for clinics is assumed, and clinic usage is set as per first eye. The model could be altered to cover more complexity but a simple estimate could be made of the effect of an extra two injection clinics by changing the formula in cells D23-L23 to =2*(B10-B9).

5.3 Any second eye 'insurance policy' designed to prevent blindness in two eyes should be subject to a proper actuarial analysis of likelihood vs cost of avoidance to calculate its value for money. The DH has encouraged PCTs to use actuarial techniques!

6 Financial implications

6.1 As will be seen from the model the financial consequences of the ACD are very considerable indeed. The model includes information on all PCTs concerning the proportion of the population over 50 whom this disease affects. The DH has announced a flat increase in resource allocation of just under 5.5%. After taking off general inflation at 2.1%, the real uplift is 3.4%. For the whole of England the ARMD ACD proposal if for 2 eyes would account for 10.9% of this real uplift. However the burden will fall inequitably amongst PCTs because of the differences in the proportion of their population over 50. For Dorset, with 45% over 50, the figure is 15.1% but only 4.2% in Tower Hamlets (where population over 50 is 17.4%). The consequences are therefore very different until the allocation formula is adjusted to give greater age specific allocations for those over 50. **

6.2 Such a large proportion of the uplift appears disproportionate. The financial consequences continue to rise for 10 years, by which time it is estimated that this treatment might consume between 0.5 and 0.8% of total NHS financial resources even allowing for a continued rise in NHS funding at 5.5%. The PCT requests that the Committee is made aware of these estimated costs with demonstrations of the effects of the variables using the model. The opportunity costs are very considerable and unequal amongst PCTs as allocations currently stand.

6.3 Such is the burden of clinic costs, even using bevacizumab is very costly but about half the costs for 2 eyes and 1/3rd cheaper for first eye only.

6.4 If the second eye clinic costs were £0 and bevacizumab used, the marginal costs are quite small (£5m vs £175m for ranibizumab in the first year). Indeed, under a zero cost for clinics for second eye scenario, using bevacizumab in the second eye would probably have a better ICER than first eye treatment, despite the smaller benefits of binocular vision.

** NICE may wish to consider this issue of differing consequences for PCTs in future Guidance.

7 Implications for ophthalmology services

7.1 The implications for ophthalmology are also considerable. We have looked at ophthalmology activity and costs for 06/07 for DCPCT. Outpatient activity (just for eye tests) will need to rise by 5% each year for the next 10 years. Day case (if that's where injections are to be done) increase by 18% in year one for first eye only, reaching a 190% increase by year 10. If 2 eye injections are not simultaneous, then the figure will be larger. Our TOTAL ophthalmology costs were £8.8m. ARMD first eye only policy would cost DCPCT £2.67m year 1, £10.8m year 10. This would represent an interesting challenge for Programme Budgeting.

8 Research

8.1 NICE has recommended research to compare ranibizumab with bevacizumab. However once a ranibizumab based policy is issued such research is unlikely to happen: this was a problem in the case of Alzheimers disease when research recommended by NICE became impossible after the Guidance was issued and AD2000 had to be curtailed.

8.2 The second eye might represent an ethical research opportunity, though from the evidence as bevacizumab is likely to be as effective and safe, there seems to be no ethical bar to a head-to-head trial.

8.3 Urgent research is needed on whether there are early predictors of rate of progression that could determine the intervals for testing in an individual in a modified PrONTO 'test and treat' regimen.

8.4 The previous suggestion that research into early detection/screening should be recommended, is repeated.

[redacted]

10 January 2008

		YEAR	1	2
Unit costs				
FIRST EYE				
drugs				
ranibizumab		894	5175	3322
bevacizumab		50	336	186
test/treatment				
Ophth op (test)		100	621	829
injection		400	2314	1486
total clinic costs			2936	2314
cost per patient LUCENTIS			8111	5636
cost per patient AVASTIN			3271	2500
SECOND EYE				
drugs				
ranibizumab		894	5175	3322
bevacizumab		50	336	186
test/treatment				
Ophth op (test)		0	0	0
injection		0	0	0
total clinic costs			0	0
cost per patient LUCENTIS			5175	3322
cost per patient AVASTIN			336	186
numbers				
initial 'induction'		3		
number of maintenance injections pa (as per PrONTO, in which average lifetime TOTAL injections, including first 3 would be 39)		3.714285714		
non-treatment eye tests pa		8.285714286		
no of ranibizumab injections funded by NHS		14		
years of NHS drug funding		3.211538462		
treatment expectancy (assumed initially as life expectancy)		10		
population 50+		**16956241**		
rate of ARMD amongst 50+		0.1277819%		
first eye incidence cases		21667		
cumulative first eye numbers (prevalence)			21667	43334
proportion presenting with 2 eyes affected		0.7		
second eye incidence rate after single eye presentation		0.1		
cumulative second eye numbers			15817	32219
No of patients with ARMD = monthly clinic atendances			**21667**	**43334**

Daily clinic attendances	**1028**	**2055**
Total eyes to be treated	**37484**	**75553**
Total cost first eye LUCENTIS	**175,730,529**	**297,853,974**
Total cost first eye AVASTIN	**70,882,043**	**125,049,543**
Total cost second eye LUCENTIS	**81,849,357**	**134,394,623**
Total cost second eye AVASTIN	**5,309,963**	**8,247,389**
Total cost LUCENTIS	**257,579,886**	**432,248,597**
Total cost AVASTIN	**76,192,006**	**133,296,932**
LUCENTIS-AVASTIN	**181,387,880**	**298,951,666**

3	4	5	6	7	8	9
703	0	0	0	0	0	0
186	186	186	186	186	186	186
829	829	829	829	829	829	829
1486	1486	1486	1486	1486	1486	1486
2314	2314	2314	2314	2314	2314	2314
3017	2314	2314	2314	2314	2314	2314
2500	2500	2500	2500	2500	2500	2500
703	0	0	0	0	0	0
186	186	186	186	186	186	186
0	0	0	0	0	0	0
0	0	0	0	0	0	0
0	0	0	0	0	0	0
703	0	0	0	0	0	0
186	186	186	186	186	186	186

65001	86668	108335	130002	151669	173336	195003
49147	66550	84378	102591	121149	140018	159167
65001	**86668**	**108335**	**130002**	**151669**	**173336**	**195003**

3083	4111	5138	6166	7194	8221	9249
114148	153218	192713	232593	272818	313354	354170
363,224,102	413,367,731	463,511,359	513,654,988	563,798,617	613,942,245	664,085,874
179,217,043	233,384,543	287,552,043	341,719,543	395,887,043	450,054,543	504,222,043
145,509,968	145,509,968	145,509,968	145,509,968	145,509,968	145,509,968	145,509,968
11,184,815	14,122,241	17,059,667	19,997,093	22,934,520	25,871,946	28,809,372
508,734,071	558,877,699	609,021,328	659,164,956	709,308,585	759,452,213	809,595,842
190,401,858	247,506,784	304,611,710	361,716,636	418,821,562	475,926,489	533,031,415
318,332,213	311,370,915	304,409,618	297,448,320	290,487,022	283,525,725	276,564,427

10

10 yr total

0	9200
186	2007
829	8079
1486	15686
2314	23764
2314	32964
2500	25771

0	9200
186	2007
0	0
0	0
0	0
0	9200
186	2007

216670

178567

216670

10277	
395237	
714,229,502	4,783,398,921
558,389,543	3,146,357,929
145,509,968	1,380,323,727
31,746,798	185,283,803
859,739,471	6,163,722,648
590,136,341	3,331,641,731
269,603,130	2,832,080,916