NICE National Institute for Health and Care Excellence

NICE guidance

Dexamethasone intravitreal implant for the treatment of macular oedema secondary to retinal vein occlusion

Technology appraisal guidance
Published: 27 July 2011

www.nice.org.uk/guidance/ta229

Your responsibility

The recommendations in this guidance represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take this guidance fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this guidance is at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Commissioners and/or providers have a responsibility to provide the funding required to enable the guidance to be applied when individual health professionals and their patients wish to use it, in accordance with the NHS Constitution. They should do so in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Contents

1 Recommendations

1.1 Dexamethasone intravitreal implant is recommended as an option for the treatment of macular oedema following central retinal vein occlusion.

1.2 Dexamethasone intravitreal implant is recommended as an option for the treatment of macular oedema following branch retinal vein occlusion when:

- treatment with laser photocoagulation has not been beneficial, **or**
- treatment with laser photocoagulation is not considered suitable because of the extent of macular haemorrhage.

1.3 People currently receiving dexamethasone intravitreal implant for the treatment of macular oedema secondary to branch retinal vein occlusion who do not meet the criteria specified in 1.2 above should have the option to continue treatment until they and their clinicians consider it appropriate to stop.

2 The technology

2.1 Dexamethasone intravitreal implant (Ozurdex, Allergan) incorporates a potent corticosteroid that suppresses inflammation in the eye by inhibiting oedema, fibrin deposition, capillary leakage and phagocytic migration. Corticosteroids inhibit the expression of vascular endothelial growth factor (VEGF), a cytokine that is expressed at increased concentrations in macular oedema and is a potent promoter of vascular permeability. Corticosteroids also prevent the release of prostaglandins, some of which are mediators of cystoid macular oedema.

2.2 Dexamethasone intravitreal implant has a marketing authorisation for the treatment of adult patients with macular oedema following either branch retinal vein occlusion (BRVO) or central retinal vein occlusion (CRVO).

2.3 The most common adverse reactions are increased intraocular pressure and conjunctival haemorrhage. Conjunctival haemorrhage is related to the intravitreous injection procedure rather than the dexamethasone implant. Other common adverse events include ocular hypertension, vitreous detachment, cataract, subcapsular cataract, vitreous haemorrhage, visual disturbance, vitreous opacities, eye pain, photopsia, conjunctival oedema, and conjunctival hyperaemia. For full details of side effects and contraindications, see the summary of product characteristics.

2.4 The cost of a 700-microgram implant and applicator is £870.00 (BNF edition 61), excluding VAT. One dexamethasone intravitreal implant is administered usually every 6 months in the affected eye and up to six implants may be given. Costs may vary in different settings because of negotiated procurement discounts.

3 The manufacturer's submission

The Appraisal Committee considered evidence submitted by the manufacturer of dexamethasone and a review of this submission by the Evidence Review Group (ERG).

3.1 The manufacturer originally submitted evidence of clinical and cost effectiveness for dexamethasone versus best supportive care (observation). Following the consultation after the first Appraisal Committee meeting, the manufacturer submitted a comparison versus bevacizumab. No comparison was made with triamcinolone (Kenalog formulation), which was defined in the scope as a comparator for the treatment of macular oedema following both BRVO and CRVO. Similarly, dexamethasone was not compared with grid laser photocoagulation for non-ischaemic BRVO.

3.2 In the manufacturer's original submission, evidence of clinical effectiveness versus observation was based on two identical randomised, sham-controlled, three-arm parallel-group studies of dexamethasone intravitreal implant in people with macular oedema secondary to BRVO or CRVO. Both studies (GENEVA 008 and GENEVA 009) had an initial 6-month treatment period followed by a 6-month open-label extension in which all patients in both arms of the study who met the re-treatment criteria received a dexamethasone implant. Patients were re-treated if best corrected visual acuity (BCVA) was less than 84 letters or the retinal thickness by optical coherence tomography was more than 250 μm in the central 1 mm macular subfield and, in the investigators' opinion, the procedure would not put the patient at significant risk. All participants had macular oedema for 6 weeks to 12 months before study entry. Participants were allocated in a 1:1:1 ratio to receive a 700-microgram dexamethasone intravitreal implant (n=427), a sham implant (n=426) or a 350-microgram dexamethasone implant (n=414). This appraisal considered the 700-microgram dose which is the only dose which has a UK marketing authorisation. The sham group had a needleless applicator pressed against the conjunctiva actuated with a click. Investigators were masked to study treatment. The results were presented separately for people with retinal vein occlusion (RVO) and the subgroups of people with macular oedema secondary to CRVO, BRVO, BRVO with macular haemorrhage and BRVO with previous laser treatment. People with BRVO who are eligible for laser therapy were not included as a subgroup. The results from the two studies (GENEVA 008 and GENEVA 009)

were pooled and this formed the basis of the evidence considered by the Committee, although the data were also available separately for each study in the manufacturer's submission.

3.3 The results of the pooled analysis showed that for the total RVO population 21.3% of the 427 patients in the intention-to-treat population receiving dexamethasone had an improvement in BCVA from baseline of at least 15 letters at day 30 compared with 7.5% of 426 patients in the sham group. This rose to 29.3% at day 60 (compared with 11.3% in the sham group) but returned to 21.8% and 21.5% at day 90 and day 180 respectively (compared with 13.1% and 17.6% in the sham group). The differences were statistically significant at day 30 ($p<0.001$), 60 ($p<0.001$) and 90 ($p=0.008$) but not at day 180 ($p>0.05$). The results for patients who were re-treated at day 180 were presented as academic-in-confidence information and are therefore not presented here.

3.4 For the CRVO subgroup, 21.3% of patients in the dexamethasone group had an improvement in BCVA from baseline of at least 15 letters compared with 6.8% in the sham group at day 30 ($p<0.001$). At day 60, 28.7% in the dexamethasone group had an improvement in BCVA of at least 15 letters compared with 8.8% in the sham group ($p<0.001$). There was no statistically significant difference between the groups at days 90 and 180.

3.5 In the subgroup with BRVO, 21.3% of patients receiving dexamethasone had an improvement in BCVA from baseline of at least 15 letters at day 30 compared with 7.9% in the sham group (p0.001). The corresponding figures for the subgroup with BRVO with macular haemorrhage were 22.0 % and 8.8 % respectively ($p\leq0.001$). Both subgroups had statistically significant differences between patients treated with dexamethasone and the sham group at days 60 and 90, but not at day 180. In the subgroup with BRVO and previous laser therapy 22.2% had an improvement in BCVA from baseline of at least 15 letters at day 30 compared with 2.8% in the sham group ($p=0.028$). Differences between the dexamethasone and sham groups were also statistically significant at days 60 ($p<0.001$), 90 ($p=0.011$) and 180 ($p=0.022$).

3.6 The cumulative response rate for time to achieve an improvement in BCVA of at least 15 letters from baseline in the study eye was statistically significant for dexamethasone versus sham. The difference in mean change from baseline

BCVA, the categorical change from baseline BCVA and proportion of patients with an improvement in BCVA of at least 10 letters from baseline in the study eye were statistically significantly higher for dexamethasone versus sham at days 30, 60, 90 and 180 in the pooled analysis. For all RVO at 180 days, the most common adverse events were raised intraocular pressure, eye pain and ocular hypertension. Intraocular pressure was raised in 25.2 % of patients treated with dexamethasone compared with 1.2 % in the sham group. Of patients treated with dexamethasone, 7.4% had eye pain compared with 3.8% in the sham group. Ocular hypertension was experienced by 4% of patients in the treated group compared with 0.7% in the sham group. Presence of anterior chamber cells and retinal neovascularisation were also reported. Other reported adverse events were retinal detachment, retinal tears and cataract. Safety data for the re-treated population (receiving a second implant by day 180) were presented as academic-in-confidence information and are therefore not presented here.

3.7 Following the consultation after the first Appraisal Committee meeting, the manufacturer submitted a mixed-treatment comparison of dexamethasone versus bevacizumab. The network of evidence from a systematic review was for BRVO only and included the BRVO data from the GENEVA trials, a non-randomised study by the Branch Vein Occlusion Study group comparing laser with sham treatment (n=78) and a randomised study by Russo et al. comparing laser with bevacizumab (n=30). The outcome was improvement in BCVA using standard effect sizes and a fixed-effects model. Dexamethasone was less effective than bevacizumab with a difference in BCVA of 1.74 letters (95% confidence interval [CI] 9.57 to 6.19) when assessed at day 180. However dexamethasone was more effective than bevacizumab when assessed at day 60, with a gain of 2.55 letters (95% CI 5.28 to 10.48).

3.8 For evidence of cost effectiveness, the manufacturer submitted a de novo Markov model that compared treatment with dexamethasone with sham injection in people with macular oedema and vision loss following CRVO or BRVO. Treatment was modelled over a lifetime horizon based on the transition of people between five health states based on the Early Treatment Diabetic Retinopathy Study (EDTRS) measurement of BCVA in the affected eye and death. The worst health state represented visual acuity less than or equal to 38 letters, which equated to severe visual impairment. The best health state was visual acuity of 69 letters or over. The mean BCVA of people in the model was 54 letters, which

equates to the second best health state. The patient population was based on data from the GENEVA trials. The model assumed that 90% of people would present with macular oedema in the 'worse-seeing' eye. The model had a cycle length of 1 month for the first 3 months following presentation with RVO, followed by a 3-month cycle in months 4 to 6 and 6-monthly cycles thereafter. Patients entering the model received dexamethasone or observation. Up to 12 months, transition probabilities were based on pooled patient-level data from the GENEVA studies, including the open-label extension. Beyond 12 months, data were extrapolated from 6- to 12-month data for treatment and re-treatment and 3- to 6-month data for sham. Treatment duration was assumed to last for 2.5 years in people with BRVO and
3 years in people with CRVO; thereafter visual acuity was assumed to be stable.

3.9 The data inputs for the manufacturer's model included utility values estimated using the Visual Function Questionnaire Utility Index (VFQ-UI) and mapped onto the health states using an algorithm from a study eliciting preferences from the general population. Resource use was identified from a systematic review of the literature and input from clinical specialists. Costs included drug cost and medical resource use (hospital visits, monitoring, costs associated with blindness and the cost of treating adverse events, including raised intraocular pressure, cataracts, retinal tears/detachment). Costs associated with treating adverse events were assumed to increase with the third and fourth treatment.

3.10 Key assumptions of the economic model included:

- 90% of people treated would have macular oedema in the 'worse-seeing' eye
- the stabilisation of visual acuity for 2.5 years in people with BRVO and 3 years in people with CRVO
- re-treatment at 6-monthly intervals with a maximum of five injections for BRVO and six injections for CRVO (with assumptions over the number of treatments received)
- a risk of involvement of the other eye of 6.5% in the first year (for those with initial RVO in their 'worse-seeing' eye)
- blindness and an excess mortality hazard of 1.54 associated with a BCVA in the 'better-seeing' eye of 38 or fewer letters (measured by the EDTRS).

Sensitivity analyses included varying utility estimates, costs, stabilisation of visual acuity at day 360, extrapolation assumptions, mortality, involvement of the other eye, discounting, re-treatment, and people with a worse BCVA on entering the model. Results were presented for the entire RVO population and the subgroups of CRVO, BRVO with macular haemorrhage, BRVO with previous laser therapy, BRVO with a diagnosis of 90 days or less at the time of treatment, and BRVO with a diagnosis of more than 90 days at the time of treatment. In the original sensitivity analyses (manufacturer original submission), the factors having the largest impact on estimates of cost effectiveness for the total population were costs associated with vision loss (costs of residential care and the uptake of residential care), affected eye (proportion of people treated for macular oedema in the 'worse-seeing' eye) and rates of discount.

3.11 Following the consultation after the first Appraisal Committee meeting, the model was amended by the manufacturer, resulting in a revised base-case ICER. The revised base case used a ratio of 25% outpatient versus 75% day case procedures for administration and an adjustment to the way that the costs of vision loss were applied to the 'better-seeing' eye in patients whose BCVA in the affected eye falls below < 20/200. An adjustment of 25% plus a further 10% uplift applied every 6 months was made to the average annual costs associated with severe visual impairment. The model continued to use only the last 3 months of observation data from the GENEVA studies.

3.12 In the revised base case for all RVO, the total incremental cost was £3,698 for dexamethasone compared with observation and the incremental QALYs were 0.21. The incremental cost-effectiveness ratio (ICER) was £17,558 per QALY gained for dexamethasone intravitreal implant compared with observation in all RVO. In the revised base case for CRVO, the total incremental cost was £4,732 and the incremental QALYs were 0.29. The cost per QALY gained was £16,522 for dexamethasone compared with observation. In the revised base case for BRVO with macular haemorrhage, the total incremental cost was £3,119 and the incremental QALYs were 0.18. The incremental cost per QALY gained was £17,741. In the revised base case for BRVO with previous laser therapy, the total incremental cost was £1,857 and the incremental QALYs were 0.29. The incremental cost per QALY was £6,361 for dexamethasone compared with

observation for BRVO with previous laser treatment.

3.13 In addition, the manufacturer also provided additional scenario analyses in response to requests in the appraisal consultation document. Alternative scenario analyses for the re-treatment rate included scenarios in which proportions re-treated were as at day 180 for the five injections after the first injection in people with CRVO, proportions re-treated were as at day 180 for the four injections after the first injection in people with BRVO and proportions re-treated were varied between the two extremes of the base case and the GENEVA studies. When proportions re-treated were as at day 180, the ICERs for CRVO, BRVO with macular haemorrhage and BRVO with previous laser treatment increased from £16,522, £17,741 and £6,361 to £22,083, £45,878 and £16,548 per QALY gained respectively. When the mid-point was used, the ICERs for CRVO, BRVO with macular haemorrhage and BRVO with previous laser treatment increased from £16,522, £17,741 and £6,361 to £20,257, £31,123 and £10,876 per QALY gained respectively.

3.14 Following the consultation after the first Appraisal Committee meeting, the manufacturer submitted an additional cost–utility analysis versus bevacizumab for BRVO. This used the mixed-treatment analysis to obtain treatment effects for bevacizumab compared with dexamethasone (a non-significant mean gain of 1.74 letters for bevacizumab compared with dexamethasone at 6 months). Compared with bevacizumab, in the base case for all RVO, the net marginal benefit for dexamethasone (where net marginal benefit is larger than zero and treatment with dexamethasone considered cost effective) was £1,927 at £30,000 per QALY gained. The manufacturer submitted a cost-minimisation analysis for dexamethasone versus bevacizumab in CRVO assuming equivalent efficacy for bevacizumab and dexamethasone in CRVO. This was associated with a cost saving of £4,463 with dexamethasone which was mainly a result of a lower frequency of injections with dexamethasone compared with bevacizumab and fewer subsequent follow-up visits.

3.15 The manufacturer also submitted a second exploratory cost-minimisation analysis for BRVO and a comparison using ranibizumab as a substitute for bevacizumab. This analysis was submitted as commercial in confidence because of its exploratory nature and so is not presented here.

3.16 The manufacturer also provided more information about the location and extent of macular haemorrhage in the subgroup of patients for whom laser treatment was not considered appropriate because of macular haemorrhage. In the GENEVA trials, the location and extent was assessed by standardised fundus photographs evaluated by trained graders using a standardised grading protocol (the ETDRS macular oedema grading protocol) and masked to patient group. Retinal haemorrhage in the macula was defined when the grader was at least 90% certain that the retinal haemorrhage was present in the grid (macular area).

3.17 The ERG considered the GENEVA trials to be of high quality. Although there was a statistically significant increase in the BCVA based on the mean letter score with the dexamethasone implant, the ERG did not consider this to be clinically significant because most patients did not achieve a 15-letter improvement from baseline. However, a higher proportion had an improvement of at least 10 letters. The effectiveness of the dexamethasone implant appeared to peak at around 60 days. The ERG highlighted that the trial protocol did not allow for early re-treatment and during the trial and open-label follow-on patients received only two injections of dexamethasone. The ERG noted that the main benefit from re-treatment was in patients whose condition had responded during the initial 180-day trial period. The ERG also commented that the number of treatments needed in practice is not known and that clinical opinion estimated a maximum of six.

3.18 The ERG also highlighted that because the trial included a maximum of two dexamethasone treatments, the impact of up to six treatments on the incidence of adverse events was not known. The ERG also expressed concern over the size of the needle which is larger for dexamethasone intravitreal implant than for other treatments. The ERG stated that the main weaknesses in the evidence were lack of long-term follow-up data and data on earlier re-treatment before 180 days.

3.19 The ERG considered the robustness of the manufacturer's original model. It highlighted cost inputs (particularly the cost of dexamethasone administration and the cost of severe visual impairment), structural assumptions in the model (such as the duration of trial data on which to base extrapolation of health states in the treatment and observation arms, assumptions related to the stability of visual acuity in 'resolved' patients, the proportion of people who will present with RVO in their 'worse-seeing' eye and the modelling of fellow eye involvement).

3.20 The ERG considered that a number of the unit costs applied in the model had been overestimated. For example, the cost of administering the dexamethasone intravitreal implant might have been overestimated because the implant could be given on an outpatient basis (£150) but costs were based on day-case (£648) care in the manufacturer's submission. The ERG also estimated that the cost of residential care was £16,999 instead of £23,972 as used in the base case, and the cost of cataract extraction was £789 rather than £965 as in the base-case model.

3.21 The ERG conducted a sensitivity analysis on the unit costs applied in the manufacturer's model and other assumptions related to the extrapolation of effectiveness data beyond the trial. According to the ERG, key uncertainties related to the extrapolation of data remain in the evaluation of cost effectiveness. The likely maximum number of dexamethasone administrations and frequency of re-treatment, the likelihood of resolution, the likelihood of cataract development and extraction, the likelihood of involvement of the other eye and the likelihood of the RVO leading to macular oedema are all important aspects of this uncertainty.

3.22 The ERG highlighted factors in the manufacturer's original sensitivity analyses that appeared to have a particular impact on cost effectiveness. When visual acuity was assumed to be stable after a year with no further dexamethasone treatments (rather than at 2.5 years with BRVO and 3 years with CRVO) the base-case ICER increased from £7,368 to £10,764 per QALY gained for the RVO population. When those not treated were all assumed to have the observation transition probabilities applied up to 2.5 years for BRVO and 3 years for CRVO (rather than transition probabilities weighted by proportion of people who were not treated who resolved at day 180 and those who discontinued treatment for other reasons), the base-case ICER increased from £7,368 to £24,924 per QALY gained for the RVO population. When the proportions re-treated were based on the re-treatment rate in the trial (day 180) for the five injections after the first in CRVO (85.7%) and the four injections after the first in BRVO (78.8%), this increased the base-case ICER from £7,368 to £19,100 per QALY gained for the RVO population. When there was a decline in vision in 1.5% of patients in each health state, worsening by one health state every 6 months was assumed (compared with visual stability from 2.5 years for BRVO and 3 years for CRVO in the base case). This had a small effect on the base-case ICER, which increased from £7,368 to £7,685 per QALY gained for the RVO population.

3.23 The ERG also conducted its own additional exploratory analyses on the manufacturer's original economic model which updated the modelling of fellow eye involvement. The ERG compared the manufacturer's model, which included the Weibull function for fellow eye involvement, with the same model with no fellow eye involvement. At the same time, the ERG also varied the proportion of people entering the model with macular oedema in the 'worse-seeing' eye from 90% (as in the manufacturer's model) to 97% (based on the proportion treated in the 'worse-seeing' eye in the trials). The alternative assumption of no fellow eye involvement changed the base-case ICERs for CRVO, BRVO with macular haemorrhage and BRVO with previous laser from £6,041, £7,987 and dominant to £17,279, £34,277 and £11,905 per QALY gained respectively. The alternative assumption of 97% with macular oedema in the 'worse-seeing' eye changed the base-case ICER for CRVO, BRVO with macular haemorrhage and BRVO with previous laser from £6,041, £7,987 and dominant to £15,800, £10,206 and dominant per QALY gained respectively.

3.24 In addition, the ERG questioned the way in which 6-month data from the open-label phase were used for the extrapolation of results with dexamethasone treatment and the use of 3- to 6-month data from the trial phase for extrapolation in the observation arm of the original model. After the first Committee meeting the Committee had requested that all data be included in a revised model. When extrapolation was based on 6- to 12-month data from the open-label phase of the trial for dexamethasone treatment and 0- to 6-month data for the observation arm (with 90% of people being treated in the 'worse-seeing' eye) the base-case ICER increased from £6,041 to £15,395 per QALY gained for the RVO population.

3.25 The manufacturer submitted two additional original base-case models: one involving structural changes in the modelling of fellow eye involvement, and another which also included lower costs of dexamethasone administration. The revised modelling of fellow eye involvement took account of age with differential survival by collapsing the model into two health states. Without inclusion of lower costs for dexamethasone administration, the revised model was associated with higher ICERs for dexamethasone versus observation of £10,271 per QALY gained for all RVO, £8,165 for CRVO, £11,403 for BRVO with macular haemorrhage, and dominance for dexamethasone over observation for BRVO with previous laser treatment. With revised cost assumptions (outpatient appointments rather than

day-case costs, reduced costs of residential care and reduced costs of cataract removal), ICERs were reduced to £7,616 per QALY gained for all RVO, £6,221 for CRVO, £8,848 for all BRVO, £8,313 for BRVO with macular haemorrhage, and dominance for dexamethasone over observation for BRVO with previous laser treatment.

3.26 The ERG noted that the manufacturer's model applied the cost associated with severe visual impairment to people with visual acuity less than or equal to 38 letters in the 'worse-seeing' eye. The ERG noted that the cost of severe visual impairment should only be applied when both eyes have visual acuity less than 38 letters. The ERG conducted a sensitivity analysis in which the cost of severe visual impairment was applied when both eyes entered the worse state (visual acuity less than 38 letters) and assumed perfect correlation in the BCVA of both eyes and no correlation between the eyes. This increased the base-case ICER for CRVO from £6,221 to £15,956 per QALY gained when there was perfect correlation and to £18,091 per QALY gained when there was no correlation between eyes. The corresponding base-case ICERs for BRVO with macular haemorrhage increased from £8,313 to £9,674 and £21,443 per QALY gained respectively.

3.27 Following the consultation after the first Appraisal Committee meeting, the ERG noted that the manufacturer's revised analysis of cost effectiveness included several deviations from the analysis requested by the Committee at its first meeting. The manufacturer included administration costs for 75:25 day-case to outpatient procedures whereas the Committee had requested day-case costs for all patients. No bevacizumab vial sharing was included in the base case. Extrapolation from data for the last 3 months of observation in the GENEVA studies was used although the Committee requested that all 6 months of data be used. In addition, severe visual impairment was not modelled as requiring bilateral involvement. Cost of reduction of severe visual impairment was reduced by 25% as a proxy with 10% applied every 6 months. The ERG noted that the 10% was not applied annually and it was unclear from where the 10% figure was derived. When the ERG removed this 10% uplift per cycle, the manufacturer's estimated ICERs for CRVO, BRVO with macular haemorrhage and BRVO with previous laser treatment increased from £16,522, £17,741 and £6,361 to £22,831, £23,847 and £12,857 per QALY gained respectively. When the ERG included all 6 months of observational data from the GENEVA studies, the manufacturer's estimated ICERs

for CRVO, BRVO with macular haemorrhage and BRVO with previous laser treatment increased from £16,522, £17,741 and £6,361 to £25,336, £38,489 and £11,650 per QALY gained respectively.

3.28 The ERG considered that a number of the unit costs applied in the revised model had been overestimated for bevacizumab and the costs used favoured dexamethasone. For example, administration costs were used for 25% outpatient and 75% day-case procedures, there was uncertainty over the calculation of the administration costs for outpatients, a high bevacizumab cost was used and a large number of bevacizumab administrations included. Also, the ERG stated that the frequency of cataracts with steroids was underestimated. When the ERG made adjustments for these costs (a cost of bevacizumab of £50, less frequent bevacizumab administration and follow-up based on the Pan American Collaborative Retina Study group data, and 100% outpatient procedures), the base-case cost minimisation for CRVO, which estimated a cost saving of £4,463 with dexamethasone versus bevacizumab, became a cost saving for bevacizumab of £2,127 versus dexamethasone.

3.29 The ERG highlighted that there was a considerable amount of data on bevacizumab treatment from trials including bevacizumab, laser therapy and triamcinolone in RVO (992 observed patient-years) and agreed that this type of observational and uncontrolled data generates uncertainty. The ERG concluded that more data could have been included in the network model by using data on triamcinolone treatment.

3.30 Full details of all the evidence are in the manufacturer's submission and the ERG report.

4 Consideration of the evidence

4.1 The Appraisal Committee reviewed the data available on the clinical and cost effectiveness of dexamethasone, having considered evidence on the nature of macular oedema secondary to RVO and the value placed on the benefits of dexamethasone by people with the condition, those who represent them, and clinical specialists. It also took into account the effective use of NHS resources.

4.2 The Committee considered the impact of macular oedema on the everyday life of patients. It heard from patient experts about the problems associated with macular oedema and related vision loss, including difficulties with driving in the dark, taking part in hobbies such as craftwork, picking up small things, reading, using computers and distinguishing objects in crowded places. The patient experts also noted the negative impact of macular oedema on social activities. The patient experts acknowledged that although people may be worried about having an injection in the eye, this is preferable to loss of vision. They also noted that the injections were administered from the side and so could not be seen. The Committee concluded that loss of vision caused by macular oedema secondary to RVO had a negative impact on health-related quality of life and that there was a need for appropriate treatment.

4.3 The Committee considered the decision problem submitted by the manufacturer. It noted that the manufacturer's initial submission compared dexamethasone with best supportive care (observation) alone. This was not consistent with the scope, which defined the comparators for both BRVO and CRVO as triamcinolone acetonide (IVTA; Kenalog formulation or equivalent), bevacizumab and best supportive care, and for non-ischaemic BRVO as grid pattern photocoagulation.

4.4 The Committee considered the use of triamcinolone to treat RVO in UK clinical practice. It heard from clinical specialists that the triamcinolone formulation available in the UK is contraindicated for ocular use (Kenalog formulation); it also heard from the manufacturer of the intraocular formulation of triamcinolone (Trivaris) that it is not available in the UK and would not be marketed anywhere in the world. The Committee concluded that triamcinolone is not available and would not be a relevant comparator for dexamethasone.

4.5 The Committee considered the use of bevacizumab to treat RVO in UK clinical practice. It noted that bevacizumab does not have a UK marketing authorisation for the treatment of RVO and heard from patient experts that they were concerned about the use of any unlicensed treatments for which there was no formal post-marketing surveillance, particularly if there were alternatives that had a UK marketing authorisation. The Committee understood that licensing is not a prerequisite for consideration of a comparator in a NICE appraisal as long as it is in routine use or best practice. It heard from clinical specialists that bevacizumab is currently reasonably widely used in the NHS, being routinely used in some centres, for some RVO cases only in others, and not at all in other centres. It heard from the experts that some clinicians and patients want more information about its long-term efficacy and safety. It also noted consultee comments following consultation confirming the use of bevacizumab by many ophthalmologists in the UK The Committee considered the results of the independent survey supplied by the manufacturer which indicated that a proportion of consultant ophthalmologists use bevacizumab for RVO either regularly or occasionally. It acknowledged that the sample size for the survey was small and could be subject to some selection bias. The Committee concluded that bevacizumab is in routine use to treat RVO in some parts of the UK; and it is therefore relevant for consideration as a comparator to dexamethasone.

4.6 The Committee considered laser photocoagulation as a treatment for BRVO. It noted that the manufacturer restricted the analysed population to those people with BRVO who cannot receive or have already tried and not benefited from laser photocoagulation. The Committee noted that the manufacturer defined those who cannot receive laser photocoagulation as people with macular haemorrhage. It noted comments from clinical specialists and consultees that all cases of RVO have a degree of macular haemorrhage and the decision to treat using laser photocoagulation is relatively subjective. Therefore, the Committee recognised that for a subgroup of people with BRVO with a lesser extent of macular haemorrhage, laser photocoagulation would be a treatment option and that this subgroup is within the licensed indication for dexamethasone. The Committee concluded that because no evidence had been provided for this subgroup, any recommendation for dexamethasone would be optimised to those subgroups of people with BRVO who cannot receive or have already tried and not benefited from laser photocoagulation.

Clinical effectiveness

4.7 The Committee considered the potential of dexamethasone to offer additional health-related benefits compared with currently available treatment options. It heard from the patient experts about the impact of dexamethasone on their quality of life. Patients advised that after the administration of dexamethasone their sight improved and they were able to resume normal daily activities.

4.8 The Committee considered the evidence for the efficacy of dexamethasone intravitreal implant compared with best supportive care from the GENEVA trials. It noted that the primary outcome was the percentage of patients with an improvement of BCVA of 15 letters or more, which represented a gain of three lines on the EDTRS chart (this enables patients to see letters half the height of those they could see before). The Committee heard from clinical specialists that this represented the gold standard for assessing the effect of treatment on visual acuity, although a gain of 10 letters is also considered to be clinically significant.

4.9 The Committee considered the results from the trials. It first considered the pooled primary outcome data from the GENEVA trials for the entire population with macular oedema following RVO. The Committee noted that dexamethasone is associated with a statistically significant improvement in visual acuity (based on percentage of patients with an improvement of BCVA of 15 letters or more) compared with sham treatment at day 30, 60 and 90, but there was no statistically significant improvement at day 180. The Committee also noted that dexamethasone was associated with a statistically significant improvement in mean change in BCVA at day 30, 60, 90 and 180 for all people with macular oedema following RVO. The Committee also considered the pooled primary outcome data from the GENEVA trials for the CRVO and BRVO subgroups. It noted that dexamethasone was associated with a statistically significantly higher proportion of people gaining BCVA of 15 letters or more compared with sham treatment for CRVO (day 30 and 60), BRVO (day 30, 60 and 90), BRVO with macular haemorrhage (day 30, 60 and 90) and at all time points for BRVO with previous laser treatment. These results for the subgroups were similar to those obtained for the combined population with RVO. The Committee concluded that treatment with dexamethasone is clinically effective when compared with best supportive care.

4.10 The Committee considered the evidence for adverse events associated with dexamethasone. These included cataracts, raised intraocular pressure and infection. The Committee noted that evidence was limited by trial duration to adverse events after two treatments with data collected up to 360 days. The Committee discussed the impact of dexamethasone in causing cataracts and the potential issues for people with diabetes, who have a higher risk of developing glaucoma and cataracts. The Committee heard from the clinical specialist that a similar infection risk to that of its comparators would be expected. It also heard that the incidence of raised intraocular pressure was 25% with dexamethasone but that this is usually well managed with eye drops and that 1% of people required laser or surgical procedures for management of elevated intraocular pressure. A higher percentage was likely to need surgery for cataracts according to the number of dexamethasone injections given. The Committee concluded that there were some concerns about the long term safety of dexamethasone treatment because the marketing authorisation is based on a evidence base trial with two re-treatments over 360 days and the manufacturer assumed that up to six treatments would be given and there are limited data on long-term treatment and multiple re-treatment (see section 3.6).

4.11 The Committee considered the evidence for re-treatment from the open-label extension of the GENEVA trials (which was submitted as academic-in-confidence information, as described in section 3.6, and is therefore not presented here). The Committee noted that for the whole population the proportion of patients with an improvement in BCVA of at least 15 letters was higher in the group that received dexamethasone at day 0 and day 180 compared with those who received sham at day 0 and dexamethasone at day 180. The Committee also considered the expected frequency of treatment with dexamethasone at day 180. The Committee heard from the clinical specialist that the criteria for re-treatment were based on the patient's experience with previous treatment (whether their vision had initially improved with treatment but had started to deteriorate), deterioration in visual acuity as assessed by BCVA and the persistence of macular oedema. The Committee was further advised that it is difficult to use a cut-off value for visual acuity that would indicate re-treatment, but that with a loss of five letters it would be appropriate to consider re-treatment. The Committee agreed with the clinical specialist that although the safety data relate to 6-monthly treatment, it is expected that clinicians may re-treat at 4 months in clinical practice, but may not treat more frequently because of the risk of adverse

events from the accumulation of dexamethasone in the eye.

4.12 The Committee then considered the clinical effectiveness of dexamethasone compared with bevacizumab. It heard from the clinical specialist that bevacizumab is generally considered by ophthalmologists to be efficacious and safe, although there is some uncertainty as to the optimal dosing schedule, relative effectiveness versus dexamethasone and frequency of treatments. The Committee considered the results of the mixed-treatment comparison provided by the manufacturer in response to requests made at the first Appraisal Committee meeting. It noted that the difference in BCVA was marginally favourable for dexamethasone over bevacizumab at day 60, but that at day 180 the difference in BCVA was marginally favourable for bevacizumab over dexamethasone. However, at both time points the confidence intervals were wide and therefore little certainty could be placed in either of the findings. The Committee noted the ERG's misgivings about the lack of completeness of the mixed-treatment comparison and also that the two cost–utility analyses provided by the manufacturer favoured bevacizumab in terms of efficacy. Nevertheless the Committee considered that a clinical efficacy advantage for dexamethasone over bevacizumab could not be concluded with certainty based on current evidence.

4.13 The Committee considered the mode of delivery and adverse events associated with dexamethasone and bevacizumab, including infection and needle phobia. The clinical specialist informed the Committee that dexamethasone was administered with a larger needle than existing treatments and that dexamethasone was associated with increased intraocular pressure and cataracts. However, more injections of bevacizumab were needed and this presented a greater infection risk. The clinical specialist also informed the Committee that with bevacizumab, which had no agreed protocol for use, sterile endophthalmitis had been reported, but was rare. The Committee concluded that the adverse events associated with dexamethasone were expected to be more severe and more difficult to treat than those associated with bevacizumab.

Cost effectiveness

4.14 The Committee considered the cost effectiveness of dexamethasone relative to best supportive care. It noted the manufacturer's revised base-case estimate of

the ICER for all people with RVO of £17,600 per QALY gained. It understood that this estimate incorporated an assumption that 90% of people would be treated for macular oedema in their 'worst-seeing eye'. It heard from clinical specialists that in practice this proportion would be between 90% and 97%. It further heard from clinical specialists that the manufacturer's estimate of the percentage (6.5%) of people who require treatment for the other eye (fellow eye involvement) was plausible. Patient experts had highlighted the importance of treating the first eye affected, even though overall acuity depends mostly on the 'better-seeing' eye, because RVO and other eye conditions may later affect the critical second eye. The Committee concluded that in this instance it was appropriate to treat the first eye affected.

4.15 The Committee considered the manufacturer's response to requests made at the first Appraisal Committee meeting. It understood that the revised base-case estimate of the ICER incorporated revised assumptions for the setting for the administration of dexamethasone and the cost of care for people with blindness. It further understood that the manufacturer had provided scenario analyses to demonstrate the effect of different re-treatment rates. The Committee noted that the revised base-case ICER did not incorporate the Committee's request that the extrapolation of data for the observation arm should be based on those trial data between 0 and 6 months rather than 3 to 6 months. The Committee discussed each of these assumptions, and the results of the sensitivity analyses for re-treatment rates, in turn.

4.16 The Committee considered the setting for the administration of dexamethasone. It noted that the revised base case was based on an assumption of 75% of procedures being performed in a day-case unit and 25% in an outpatient clinic, instead of 100% in an outpatient clinic as requested by the Committee at the first Appraisal Committee meeting. The Committee noted comments from consultees that it was reasonable to expect a higher proportion to be performed in a day-case unit while ophthalmologists are gaining familiarity with dexamethasone administration, but that in time it would be expected that most would be performed in an outpatient clinic. The Committee therefore accepted the proportions used by the manufacturer in the revised base case for the setting for the administration of dexamethasone.

4.17 The Committee considered the revised assumption for the cost associated with

blindness in the revised base case. It understood that the manufacturer had accepted the rationale for applying this cost to only those people who have both eyes in the worst health state. However, the Committee noted that in the revised base-case estimate, the cost associated with blindness was reduced as a proxy for adjusting the proportion of people who fall into this health state of severe visual impairment in both eyes. The manufacturer adjusted the cost associated with blindness to 25% of the full cost (that is, £1,490 instead of £5,963), and increased this every 6 months by 10% of the reduced cost (that is, an increase of £149 for each cycle). The Committee accepted this to be a reasonable reduction and concluded that although it would have been preferable to have adjusted the assumptions around the number of people with severe visual impairment in both eyes, the manufacturer's adjustment went some way towards meeting the Committee's request and was considered acceptable.

4.18 The Committee considered the extrapolation of health-state data beyond the trial for the observation arm. It noted the manufacturer's assertion that it was inappropriate to include 0- to 3-month data for BRVO because spontaneous resolution occurs in approximately a quarter of people during that period. The Committee also heard from the manufacturer that although it may be appropriate to include 0- to 3-month data for CRVO, the ERG's exploratory analysis used aggregate data rather than transition probabilities based on individual patient data. The manufacturer stated that this had led to an overestimation of the ICER for CRVO by the ERG. The Committee accepted that spontaneous resolution occurs in BRVO and therefore it was not appropriate to include the first 3 months of data for this subgroup. It further concluded that using individual patient data for the first 6 months may have been relevant for CRVO, but that the increased ICER for CRVO from the ERG's analysis (from £16,500 to £25,300 per QALY gained including a decrease from 0.29 to 0.22 of net total QALYs and an increase in total cost from £4,732 to £5,469) may be an overestimate. The Committee concluded that 0- to 3-month data for the observation arm of the GENEVA trials for people with CRVO would not have a substantial impact on the overall ICER and therefore accepted the manufacturer's use of 0- to 3-month data in the revised base case.

4.19 The Committee considered the sensitivity analyses around re-treatment rates provided by the manufacturer in response to requests made by the Committee at the first meeting. The Committee understood that the manufacturer had

combined the revised assumptions relating to the setting for administering dexamethasone (see section 4.16) and the costs associated with blindness (see section 4.17) with three scenario analyses for different re-treatment rates. The Committee noted that the re-treatment scenarios covered the extreme positions of both the base-case estimates (in which re-treatment rates were based on clinical opinion) and those re-treated at day 180 in the GENEVA trials. The Committee noted that for all people with RVO, the ICER varied between £17,600 (including incremental costs of £3,698 and incremental QALYs of 0.40) and £34,700 (including incremental costs of £8,041 and incremental QALYs of 0.44) per QALY gained for these scenarios respectively. The Committee further noted the manufacturer's scenario analysis in which the re-treatment rates were at the mid-points between the two extremes. With this assumption the ICER for all people with RVO was £26,300 per QALY gained. The Committee accepted the assumption of mid-point re-treatment rates.

4.20 On the basis of previous discussions (see sections 4.17 to 4.21), the Committee accepted the revised manufacturer's base-case estimate using the mid-point re-treatment rates from the manufacturer's scenario analysis as the most appropriate estimate of the ICER for its consideration. It therefore concluded that the decision regarding the cost effectiveness of dexamethasone compared with best supportive care should be based on the manufacturer's ICER of £26,300 per QALY gained for all people with RVO. The Committee further concluded that this represented an acceptable level of cost effectiveness in this case and that dexamethasone intravitreal implant for the treatment of RVO represents a cost-effective use of NHS resources when compared with best supportive care.

4.21 The Committee considered the cost effectiveness of dexamethasone relative to bevacizumab. It understood that the manufacturer had presented a cost-minimisation approach for CRVO and that the cost assumptions from this approach had been used in both cost–utility analyses (that is, the mixed-treatment comparison, and the indirect comparison using a different anti-VEGF treatment as a proxy for bevacizumab; see sections 3.14 and 3.15). The Committee therefore considered that its discussion on the relative cost effectiveness of dexamethasone compared with bevacizumab should focus on the assumptions within the manufacturer's cost-minimisation analysis.

4.22 The Committee considered the assumptions in the manufacturer's cost-

minimisation analysis between dexamethasone and bevacizumab. It noted comments from the ERG that the cost of bevacizumab had been modelled on the higher of the two estimates from the two suppliers of bevacizumab for eye treatment (that is, £150 per vial rather than £50 per vial). The ERG further highlighted that the manufacturer's estimate of the average number of doses of bevacizumab was 13.75 in the first 2 years, but that the Pan American Collaborative Retina Study Group had found an average of 7 doses over this time period. The Committee heard from the manufacturer that this study was a small cohort follow-up study and may not be representative of UK clinical practice. In addition the manufacturer highlighted to the Committee that the recently reported HORIZON study found that 3.8 injections per year of ranibizumab were insufficient to maintain the clinical effects seen in the first year (ranibizumab, another anti-VEGF, was given monthly in the CRUISE study). Therefore the manufacturer considered 7 doses of bevacizumab over 2 years to be lower than UK clinical practice. The Committee understood that the cost-minimisation analysis also assumed that the setting for the administration of both bevacizumab and dexamethasone would be the same (that is, 75% of procedures would be carried out in a day-case unit and 25% would be carried out in an outpatient clinic). The Committee noted the ERG's view that all anti-VEGF injections are currently administered in an outpatient clinic. The Committee concluded, on the one hand, that the cost of bevacizumab may have been overestimated, and on the other, that there was uncertainty around the number of injections of bevacizumab. The Committee concluded that the assumptions used in the manufacturer's cost-minimisation analysis between dexamethasone and bevacizumab may overestimate the cost of bevacizumab, but considered the cost may not be as low as suggested by the ERG.

4.23 The Committee considered the results of the cost-minimisation analysis. It noted that the manufacturer estimated the cost of dexamethasone treatment to be approximately £4,500 less per patient than bevacizumab, but that with the ERG's amendments, dexamethasone could cost up to £2,100 more per patient than bevacizumab. On the basis of previous discussion (see section 4.22) the Committee accepted that there was some uncertainty around the assumptions used to calculate the cost of bevacizumab and concluded that it was as likely that dexamethasone might cost more than bevacizumab as it was that dexamethasone might cost less. The Committee therefore concluded that a cost advantage of dexamethasone compared with bevacizumab had not been

conclusively demonstrated.

4.24 In summary, the Committee considered the costs and clinical effectiveness of dexamethasone. It considered that comparisons with best supportive care and bevacizumab were both relevant to the NHS. It acknowledged that an incremental analysis in which dexamethasone, bevacizumab and best supportive care were simultaneously assessed was not available. The Committee recognised the difficulties within the evidence base for bevacizumab and commended the manufacturer's attempts to provide a comparison of the relative clinical and cost effectiveness of bevacizumab and dexamethasone. It considered that a clinical efficacy advantage for dexamethasone over bevacizumab could not be concluded with certainty based on presently available evidence and that the adverse events associated with dexamethasone were expected to be more severe and more difficult to treat than those associated with bevacizumab. It also accepted that there was uncertainty around the assumptions used in the cost minimisation comparing dexamethasone with bevacizumab. Based on the manufacturer's revised ICER of £26,300 per QALY gained compared with best supportive care for all people with RVO, the Committee concluded that dexamethasone intravitreal implant represents a cost-effective use of NHS resources and should be offered as an option for the treatment of macular oedema secondary to RVO.

4.25 The Committee considered whether there were any equalities considerations affecting population groups protected by equality legislation and concluded that there were no equality issues relating to this appraisal that required addressing in the guidance.

5 Implementation

5.1 Section 7(6) of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires clinical commissioning groups, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this appraisal within 3 months of its date of publication.

5.2 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 2 months of the first publication of the final appraisal document.

5.3 When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a patient has macular oedema secondary to retinal vein occlusion and the healthcare professional responsible for their care thinks that a dexamethasone intravitreal implant is the right treatment, it should be available for use, in line with NICE's recommendations.

6 Appraisal Committee members, and NICE project team

Appraisal Committee members

The Appraisal Committees are standing advisory committees of NICE. Members are appointed for a 3-year term. A list of the Committee members who took part in the discussions for this appraisal appears below. There are four Appraisal Committees, each with a chair and vice chair. Each Appraisal Committee meets once a month, except in December when there are no meetings. Each Committee considers its own list of technologies, and ongoing topics are not moved between Committees.

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

The minutes of each Appraisal Committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

Dr Kathryn Abel Reader and Consultant Psychiatrist; and Director of Centre for Women's Mental Health, University of Manchester

Dr David Black Director of Public Health, Derbyshire County Primary Care Trust

Dr Daniele Bryden Consultant in Intensive Care Medicine and Anaesthesia, Sheffield Teaching Hospitals NHS Trust

Dr Andrew Burnett Director for Health Improvement and Medical Director, NHS Barnet, London

David Chandler Lay member

Dr Mary Cooke Lecturer, School of Nursing, Midwifery and Social Work, University of Manchester

Dr Chris Cooper GP, London

Professor Peter Crome Consultant Geriatrician and Professor of Geriatric Medicine, Keele University

Dr Christine Davey Research Adviser, North and East Yorkshire Alliance Research and Development Unit, York

Richard Devereaux-Phillips Public Affairs and Reimbursement Manager UK and Ireland, Medtronic

Professor Rachel A Elliott Lord Trent Professor of Medicines and Health, University of Nottingham

Dr Wasim Hanif Consultant Physician and Honorary Senior Lecturer, University Hospital Birmingham

Dr Alan Haycox Reader in Health Economics, University of Liverpool Management School

Professor Cathy Jackson Professor of Primary Care Medicine, University of St Andrews

Dr Peter Jackson Clinical Pharmacologist, University of Sheffield

Henry Marsh Consultant Neurosurgeon, St George's Hospital, London

Professor Gary McVeigh Professor of Cardiovascular Medicine, Queens University Belfast and Consultant Physician, Belfast City Hospital

Dr Eugene Milne Deputy Regional Director of Public Health, North East Strategic Health Authority, Newcastle upon Tyne

Dr Neil Myers GP, Glasgow

Dr Richard Nakielny Consultant Radiologist, Sheffield Teaching Hospitals Foundation Trust

Dr Danielle Preedy Lay member

Dr Martin Price Head of Outcomes Research, Janssen-Cilag

Ellen Rule Programme Director, NHS Bristol

Dr Peter Selby Consultant Physician, Central Manchester University Hospitals NHS Foundation Trust

Dr Surinder Sethi Consultant in Public Health Medicine, North West Specialised Services Commissioning Team, Warrington

Professor Andrew Stevens Chair of Appraisal Committee C; Professor of Public Health, University of Birmingham

Dr John Stevens Lecturer in Bayesian Statistics in Health Economics, School of Health and Related Research, Sheffield

Dr Matt Stevenson Technical Director, School of Health and Related Research, University of Sheffield

Professor Paul Trueman Professor of Health Economics, Brunel University, London

Dr Judith Wardle Lay member

NICE project team

Each technology appraisal is assigned to a team consisting of one or more health technology analysts (who act as technical leads for the appraisal), a technical adviser and a project manager.

Jennifer Priaulx Technical Lead

Joanne Holden Technical Adviser

Lori Farrar Project Manager

7 Sources of evidence considered by the Committee

The Evidence Review Group (ERG) report for this appraisal was prepared by Aberdeen Health Technology Assessment Group (AbHTAG):

- Shyangdan D, Cummins E, Lois N, et al. Dexamethasone implants in the treatment of macular oedema due to retinal vein occlusion: a single technology appraisal. December 2010

The following organisations accepted the invitation to participate in this appraisal as consultees and commentators. They were invited to comment on the draft scope, the ERG report and the appraisal consultation document (ACD). Manufacturers or sponsors were also invited to make written submissions. Professional or specialist and patient or carer groups, and other consultees, had the opportunity to give their expert views. Manufacturers or sponsors, professional or specialist and patient or carer groups, and other consultees, also have the opportunity to appeal against the final appraisal determination.

Manufacturer or sponsor:

- Allergan Ltd UK

Professional or specialist and patient or carer groups:

- Royal National Institute of Blind People (RNIB)
- Royal College of Nursing
- Royal College of Ophthalmologists
- Royal College of Physicians

Other consultees:

- Department of Health
- Welsh Assembly Government

- Waltham Forest PCT

Commentator organisations (did not provide written evidence and without the right of appeal):

- BNF
- Commissioning Support Appraisals Service
- Department of Health, Social Services and Public Safety for Northern Ireland
- NHS Quality Improvement Scotland
- Bristol Myers Squibb (triamcinolone)
- Roche Products (bevacizumab)
- Aberdeen HTA Group
- National Institute for Health Research Health Technology Assessment Programme

The following individuals were selected from clinical specialist and patient expert nominations from the non-manufacturer or sponsor consultees and commentators. They gave their expert personal view on Dexamethasone intravitreal implant for the treatment of macular oedema caused by retinal vein occlusion by attending the initial Committee discussion and providing written evidence to the Committee. They are invited to comment on the ACD.

- Ian Pearce, Consultant Ophthalmologist, nominated by The Royal College of Ophthalmologists – clinical specialist
- Lady Sandra Taylor, Lead Ophthalmologist research Nurse Manager, nominated by Royal College of Nurses Ophthalmic Nurse Forum – clinical specialist
- Barbara McLaughlan, Campaigns Manager, nominated by Royal National Institute of Blind people – patient expert
- Carol Read, nominated by Royal National Institute of Blind people – patient expert

Representatives from the following manufacturer or sponsor attended Committee meetings. They contributed only when asked by the Committee chair to clarify specific issues and comment on factual accuracy.

- Allergan Ltd UK

Update information

February 2014: Implementation section updated to clarify that dexamethasone intravitreal implant is recommended as an option for treating macular oedema secondary to retinal vein occlusion.

ISBN: 978-1-4731-7095-7