NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

GUIDANCE EXECUTIVE (GE)

Review of 229; Dexamethasone intravitreal implant for the treatment of macular oedema secondary to retinal vein occlusion

This guidance was issued in July 2011

The review date for this guidance is 2014

1. Recommendation

The TA229 guidance should be transferred to the 'static guidance list'. That we consult on this proposal.

2. Original remit

To appraise the clinical and cost effectiveness of dexamethasone intravitreal implant within its licensed indication for the treatment of macular oedema caused by retinal vein occlusion (RVO).

3. Current guidance

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.

4. Rationale[1]

There are newly published trials that may provide data for some of the gaps in the evidence that were identified in TA229. However, the evidence gaps were not key drivers of the Committee's recommendations for dexamethasone in TA229. Further, these new data support the existing recommendations, are unlikely to change the existing recommendations and therefore do not warrant an update of TA229. The

[1] A list of the options for consideration, and the consequences of each option is provided in Appendix 1 at the end of this paper

TA229 guidance should therefore be transferred to the 'static guidance list'. The guidance will remain in place, in its current form, unless NICE becomes aware of substantive information which would make it reconsider. Literature searches are carried out every 5 years to check whether any of the Appraisals on the static list should be flagged for review. This would allow time for ongoing trials to be completed and published, providing relevant data for the review and potential review of the guidance.

5. Implications for other guidance producing programmes

There is no proposed or ongoing guidance development that overlaps with this review proposal.

6. New evidence

The search strategy from the original assessment report was re-run on the Cochrane Library, Medline, Medline In-Process and Embase. References from July 2010 onwards were reviewed. Additional searches of clinical trials registries and other sources were also carried out. The results of the literature search are discussed in the 'Summary of evidence and implications for review' section below. See Appendix 2 for further details of ongoing and unpublished studies.

7. Summary of evidence and implications for review

New marketing authorisation and changes to existing marketing authorisations

There has been no change to the marketing authorisation of dexamethasone intravitreal implant in relation to central retinal vein occlusion (CRVO) or branch retinal vein occlusion (BRVO) since the publication of TA229 in July 2011. The Kenalog formulation of triamcinolone and bevacizumab remain unlicensed for intravitreal use.

Price and patient access schemes

There has been no change to the price of dexamethasone implant since TA229.

The exact price of bevacizumab is difficult to estimate using it in the eye requires drawing small volumes of the drug into a syringe from a 4ml vial. In the Decision Support Unit's report on bevacizumab published in 2012 ("Bevacizumab in eye conditions: Issues related to quality, use, efficacy and safety", Poku et al., 2012), the price of bevacizumab for use in the eye is estimated at £50 to £100 per dose. In the health economic model presented in TA229, the manufacturer used a cost of £105.00 per dose for bevacizumab.

Kenalog was not included in the health economic model for TA229.

Comparators

Two drugs that were not included in TA229 have recently received relevant marketing authorisations. Ranibizumab received a marketing authorisation in March 2011 for "the treatment of visual impairment due to macular oedema secondary to retinal vein occlusion (branch RVO or central RVO)." Aflibercept received a

marketing authorisation in July 2013 for “the treatment of visual impairment due to macular oedema secondary to central retinal vein occlusion.”

Ranibizumab and aflibercept have been recommended in NICE Technology Appraisal guidance since the publication of TA229. Ranibizumab is recommended in TA283 (May 2013) as an option for people with visual impairment caused by macular oedema secondary to central retinal vein occlusion. In TA283, ranibizumab is also recommended as an option for treating visual impairment caused by macular oedema following branch retinal vein occlusion only if treatment with laser photocoagulation has not been beneficial, or when laser photocoagulation is not suitable because of the extent of macular haemorrhage. Aflibercept is recommended in TA305 (February 2014) as an option for people with visual impairment caused by macula oedema secondary to central retinal vein occlusion.

Summary of new evidence

Dexamethasone vs. sham

There were 2 new publications identified that compared dexamethasone with sham treatment (Haller et al., 2010 and Sadda et al., 2013) and an associated open label study (Haller et al., 2011):

- The Haller (2010) publication included 2 identical RCTs of people with CRVO or BRVO that compared dexamethasone with sham treatment in 1267 eyes. At 6 months, there were statistically significantly more eyes with an improvement of 15 or more letters and statistically significantly fewer eyes with a 15 or more letter loss in the dexamethasone group (both $p<0.001$). The time needed to achieve an improvement in BCVA of 15 letters or greater was statistically significantly less with dexamethasone than sham ($p<0.001$). At day 180 there was no significant difference in the percentage of patients with intraocular pressure or cataracts, or needing cataract surgery.

- The Haller (2011) open label extension study of the trials reported in Haller (2010) concluded that single and repeated dexamethasone treatment had a favourable safety profile over 12 months. The Haller (2011) study provides longer-term treatment data than the GENEVA study used in TA229 and may help to provide additional safety evidence. However, it does not provide any additional efficacy evidence than was included in the TA229 appraisal. The Sadda publication was a post hoc analysis of data from 2 phase 3 clinical trials that compared dexamethasone with sham treatment in 329 eyes with CRVO or BRVO. There were statistically significantly fewer unreadable assessments because of haemorrhage at day 180 with dexamethasone compared to sham ($p=0.029$). There was a statistically significant difference in rate of neovascularisation between the groups by day 180 ($p=0.026$). There was no statistically significant difference in overall non-perfusion or mean area of macular capillary non-perfusion.

There is an ongoing study of dexamethasone versus sham in 265 people with RVO (NCT01660802). It was expected to complete in August 2014 but the online record of the trial details has not been updated since March 2014.

Non-comparative studies of dexamethasone

There were 4 new studies that presented results for dexamethasone from non-

comparative studies (Bezatis et al., 2013, Meyer et al., 2013, OCTOME, and SHASTA):

- The Bezatis study was a retrospective chart review of 102 eyes included in the SOLO study. It reported a statistically significant improvement in BCVA and statistically significant maintenance of mean central retinal thickness in patients with BRVO or CRVO.

- The Meyer study was a prospective study of 16 patients with CRVO or BRVO. It reported that BCVA improved to a peak after 2 months then declined at 12 months. It also reported that central retinal thickness initially decreased but increased with recurring macular oedema. The study reported that 69% of patients had an increase in intraocular pressure of at least 5 mmHg and 50% had an increase greater than 10 mmHg. The increase in intraocular pressure was statistically significant at 1, 2, 3 and 8 months. The study concluded that secondary glaucoma may have been underestimated in the GENEVA studies. The Meyer study had a longer follow up than the GENEVA studies and may help to fill the gap in the evidence surrounding long-term treatment that was identified in TA229.

- OCTOME was a prospective open label study of 30 people with RVO. The study reported a significant change in central subfoveal field thickness up to 32 weeks. It also reported a significant improvement in all visual functions except contrast sensitivity by 24 weeks.

- SHASTA was a retrospective chart review of 289 patients with BRVO or CRVO with follow-up for up to 6 months after each patient's last implant. It reported improved central retinal thickness and visual acuity with each injection of dexamethasone and no safety concerns with multiple implants. The safety of multiple re-treatments was identified as a gap in the evidence in TA229 and the SHASTA study may provide data to fill this gap.

There are 2 ongoing studies of dexamethasone in patients with CRVO or BRVO (EudraCT Number 2012-000800-13 and 2011-000425-72). 1 study (2012-00080013) will look at 40 patients and the other (2011-000425-72) will look at 15 patients. The completion date for either study is unknown.

Dexamethasone vs. other treatments
There were 2 systematic reviews (Edwards et al. 2012 and Ford JA, Clar D, et al. 2014) and 1 network meta-analysis (Ford JA, Shyangdan C, et al. 2014) published since TA229 that include dexamethasone as an intervention:

- The Edwards systematic review compared ranibizumab with standard care, dexamethasone, and bevacizumab in patients with CRVO or BRVO. It concluded that whilst the direction of effect favoured ranibizumab over dexamethasone, there was insufficient evidence available to draw any firm conclusions.

- The Ford and Clar (2014) systematic review included 8 randomised controlled trials but a meta-analysis was not undertaken due to a lack of comparable studies. The included dexamethasone study (GENEVA) was included in

TA229 and so the review does not provide any new evidence for the efficacy of dexamethasone.

- The Ford and Shyangdan (2014) network meta-analysis included 7 randomised controlled trials of 1140 eyes with CRVO. It included the GENEVA study for dexamethasone and concluded that triamcinolone, ranibizumab, bevacizumab and aflibercept have a higher probability of gaining greater than 3 lines than dexamethasone.

There are several ongoing or unpublished studies comparing dexamethasone monotherapy with other relevant treatments:

- There are 2 complete but unpublished randomised controlled trials comparing ranibizumab with dexamethasone (NCT01396057/COMRADE-B and NCT01396083). The COMRADE-B study is looking at 244 patients with BRVO and the NCT01396083 trial is looking at 243 patients with CRVO.

- There is an additional ongoing randomised controlled trial (NCT01427751) comparing ranibizumab with dexamethasone in 307 patients with BRVO. The estimated completion date is October 2014.

- There is also 1 unpublished non-comparative study of dexamethasone in 10 people with RVO following treatment with anti-VEGF injections (NCT01449682). The study was due to complete in September 2013 but the online record of the trial details has not been updated since January 2013.

The searches identified 3 new comparative studies that included dexamethasone as part of a sequence or combination of treatments (Iu et al., 2014, Maturi et al., 2014, and Pichi et al., 2014):

- The Iu study compared ranibizumab followed by dexamethasone with dexamethasone monotherapy in a retrospective study of 33 eyes with RVO. Statistically significantly more patients in the sequential treatment group had a visual acuity gain of at least 0.5 (p=0.044) and the speed of visual acuity gain was statistically significantly faster (p=0.020) compared with the monotherapy group. Macular oedema was also statistically significantly better controlled in the sequential group at 3 and 4 months.

- The Maturi randomised controlled trial compared bevacizumab and dexamethasone combination therapy with bevacizumab monotherapy in 31 eyes with BRVO or CRVO. Combined therapy resulted in fewer bevacizumab injections (p=0.02), greater mean reductions in central subfoveal thickness (p=0.01) and was more likely to lead to resolution of all oedema (p=0.02) compared with bevacizumab monotherapy. There was no statistically significant difference in the mean visual acuity changes in the two groups (p=0.75). In TA229 the Committee acknowledged that there was a gap in the evidence for the comparative effectiveness of dexamethasone compared with bevacizumab. The Maturi study is unlikely to provide relevant data for this comparison, as bevacizumab is present in both arms.

- The Pichi randomised controlled trial compared dexamethasone in combination with macular grid laser to dexamethasone monotherapy in BRVO patients. The study authors concluded that the combination treatment increased BCVA and lengthened time between injections. TA229 highlighted that the efficacy and safety of laser photocoagulation for people with BRVO was unclear. The Pichi study may help fill this gap in the evidence.

There are 2 ongoing studies of dexamethasone as part of a sequence or combination of treatments:

- There is an ongoing randomised controlled trial (NCT01827722, ORION) comparing dexamethasone, ranibizumab, and a combination treatment of dexamethasone and ranibizumab in 45 patients with CRVO. The estimated primary completion date was May 2014, but the online record for the clinical trial has not been updated since July 2013.

- There is an ongoing study of dexamethasone and bevacizumab combination therapy compared with bevacizumab monotherapy in 68 people with CRVO (NCT01295112). It is due to complete in June 2015. This study may provide data for the efficacy of dexamethasone compared with bevacizumab that was missing in TA229.

Health economic evaluations
One recently published economic evaluation was identified (Kowalski et al., 2012). It compared dexamethasone with observation based on the GENEVA data and was specific to the Italian national healthcare system. In the base case, the cost per QALY was €31,148. Extensive sensitivity analyses showed that the price remained under €45,000. The study concluded that dexamethasone was a cost effective use of resources.

Other relevant evidence
Since the publication of TA229, a report from the Decision Support Unit (Poku et al., 2012) has been published that discussed the effectiveness of bevacizumab in people with RVO.

Summary
The results of trials published since TA229 support the safety and efficacy data for dexamethasone compared with sham in the existing guidance. The results of the non-comparative dexamethasone studies published since TA229 also broadly support the efficacy and safety data presented in the existing guidance.

The trials published since TA229 comparing dexamethasone with other treatments provide new data for laser photocoagulation for people with BRVO, indirect evidence of the efficacy of dexamethasone compared to bevacizumab, and evidence for the number of bevacizumab injections used in eye conditions. There is a published indirect comparison that compares dexamethasone with ranibizumab as well as unpublished and ongoing trials that will provide a direct comparison of the 2 treatments.

There are several ongoing and unpublished trials of the efficacy and safety of dexamethasone for RVO.

Implications for review

There are newly published trials that may provide data for some of the gaps in the evidence that were identified in TA229. However, the evidence gaps were not key drivers of the Committee's recommendations for dexamethasone in TA229. Further, these new data support the existing recommendations and do not warrant an update of TA229. There are several ongoing and unpublished trials of the efficacy and safety of dexamethasone in people with RVO. The timing of these trials to be completed and published may provide more data for the review and potential update of the guidance, several years ahead.

Taking into account that the published data for dexamethasone is unlikely to change the existing recommendations and that there are ongoing and unpublished trials, which will not publish for several years, the most appropriate course of action would be to transfer TA229 to the 'static guidance list'. The guidance will remain in place, in its current form, unless NICE becomes aware of substantive information which would make it reconsider. Literature searches are carried out every 5 years to check whether any of the Appraisals on the static list should be flagged for review.

Implementation

A submission from Implementation is included in Appendix 3.

After the publication of TA229 in July 2011, the volume of dexamethasone being prescribed in hospitals and dispensed in the community in England initially increased. In Q1 of 2012/2013, the volume being prescribed started decreasing, and the most recent data available (Q4 2013/2014) showed that the volume being prescribed in hospitals and dispensed in the community was less than before the publication of TA229.

The volume of dexamethasone prescribed and dispensed in the community was increasing prior to TA229 and increased further after its publication in July 2011. Since then, the volume of dexamethasone being prescribed and dispensed in the community has stayed fairly constant with only slight fluctuations. The most recent data available (Q4 2013/2014) showed that the volume of dexamethasone being prescribed and dispensed in the community was about the same as when TA229 was published.

The field team reported 1 commissioning PCT that was reluctant to agree to the use of dexamethasone. The field team also reported local concern about the clinical effectiveness of the drug.

It is not reported whether clinical practice has changed since the publication of TA229.

8. Equality issues

No equality issues were raised in the original guidance.

GE paper sign off: Frances Sutcliffe 28 October 2014

Contributors to this paper:

Information Specialist:	Sadia Mughal
Technical Lead:	Ella Fields
Implementation Analyst:	Liesl Millar
Project Manager:	Andrew Kenyon

Appendix 1 – explanation of options

When considering whether to review one of its Technology Appraisals NICE must select one of the options in the table below:

Options	**Consequence**	**Selected – 'Yes/No'**
A review of the guidance should be planned into the appraisal work programme. The review will be conducted through the [specify STA or MTA] process.	A review of the appraisal will be planned into the NICE's work programme.	No
The decision to review the guidance should be deferred to [specify date or trial].	NICE will reconsider whether a review is necessary at the specified date.	No
A review of the guidance should be combined with a review of a related technology appraisal. The review will be conducted through the MTA process.	A review of the appraisal will be planned into NICE's work programme as a Multiple Technology Appraisal, alongside the specified related technology.	No
A review of the guidance should be combined with a new technology appraisal that has recently been referred to NICE. The review will be conducted through the MTA process.	A review of the appraisal(s) will be planned into NICE's work programme as a Multiple Technology Appraisal, alongside the newly referred technology.	No
The guidance should be incorporated into an on-going clinical guideline.	The on-going guideline will include the recommendations of the technology appraisal. The technology appraisal will remain extant alongside the guideline. Normally it will also be recommended that the technology appraisal guidance is moved to the static list until such time as the clinical guideline is considered for review. This option has the effect of preserving the funding direction associated with a positive recommendation in a NICE technology appraisal.	No

Options	Consequence	Selected – 'Yes/No'
The guidance should be updated in an on-going clinical guideline.	Responsibility for the updating the technology appraisal passes to the NICE Clinical Guidelines programme. Once the guideline is published the technology appraisal will be withdrawn. Note that this option does not preserve the funding direction associated with a positive recommendation in a NICE Technology Appraisal. However, if the recommendations are unchanged from the technology appraisal, the technology appraisal can be left in place (effectively the same as incorporation).	No
The guidance should be transferred to the 'static guidance list'.	The guidance will remain in place, in its current form, unless NICE becomes aware of substantive information which would make it reconsider. Literature searches are carried out every 5 years to check whether any of the Appraisals on the static list should be flagged for review.	Yes

NICE would typically consider updating a technology appraisal in an ongoing guideline if the following criteria were met:

i. The technology falls within the scope of a clinical guideline (or public health guidance)

ii. There is no proposed change to an existing Patient Access Scheme or Flexible Pricing arrangement for the technology, or no new proposal(s) for such a scheme or arrangement

iii. There is no new evidence that is likely to lead to a significant change in the clinical and cost effectiveness of a treatment

iv. The treatment is well established and embedded in the NHS. Evidence that a treatment is not well established or embedded may include;

- Spending on a treatment for the indication which was the subject of the appraisal continues to rise
- There is evidence of unjustified variation across the country in access to a treatment
- There is plausible and verifiable information to suggest that the availability of the treatment is likely to suffer if the funding direction were removed

- The treatment is excluded from the Payment by Results tariff

v. Stakeholder opinion, expressed in response to review consultation, is broadly supportive of the proposal.

Appendix 2 – supporting information

Relevant Institute work

Published

Ranibizumab for treating visual impairment caused by macular oedema secondary to retinal vein occlusion. Technology Appraisal TA283, issued May 2013. Review date: TBC

Aflibercept for treating visual impairment caused by macular oedema secondary to central retinal vein occlusion. Technology Appraisal TA305, issued February 2014. Review date: TBC

Arteriovenous crossing sheathotomy for branch retinal vein occlusion. Interventional Procedure IPG334, issued March 2010. Review date: TBC

In progress

Dexamethasone intravitreal implant for treating diabetic macular oedema [ID 653]. Technology Appraisal, due April 2015.

Details of changes to the indications of the technology

Indication considered in original appraisal	Proposed indication (for this appraisal)
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).	Unchanged

Details of new products

Drug (manufacturer)	Details (phase of development, expected launch date,)
Aflibercept (Bayer)	Macular oedema secondary to branch retinal vein occlusion (BRVO). Intravitreal route Pre-registration (filed) UK Launch plans: [redacted]

Drug (manufacturer)	Details (phase of development, expected launch date,)
Aflibercept (Bayer)	Macular oedema secondary to central retinal vein occlusion (CRVO). Intravitreal route Launched in UK

Registered and unpublished trials

Trial name and registration number	Details
Safety and Efficacy Study of Ozurdex® Compared to Lucentis® in Patients With Branch Retinal Vein Occlusion NCT01427751 Phase 4	This study is ongoing, but not recruiting participants Enrollment: 307 Estimated study completion date: October 2014
Efficacy and Safety of Ranibizumab Intravitreal Injections Versus Dexamethasone Intravitreal Implant in Patients With Central Retinal Vein Occlusion (CRVO) NCT01396083 Phase 3	Study was recently completed Enrollment: 243 Study completion date: January 2014
Effect of Ozurdex® 0.7 mg on Improvement of Efficacy of Bevacizumab for Central Retinal Vein Occlusion NCT01295112 Phase 2/ Phase 3	This study is currently recruiting participants. Enrollment: 68 Estimated study completion date: June 2015
Ozurdex Versus Ranibizumab Versus Combination for Central Retinal Vein Occlusion NCT01827722 Phase 4	This study is currently recruiting participants. Enrollment: 45 Estimated primary completion date: May 2014
Safety and Efficacy Study of Dexamethasone in the Treatment of Patients With Macular Edema Following Retinal Vein Occlusion (RVO) NCT01660802 Phase 3	This study is ongoing, but not recruiting participants Enrollment: 265 Estimated study completion date: August 2014

Trial name and registration number	Details
Influence of sustained-release dexamethasone on intraocular cytokines and growth factors and retinal blood vessels in retinal vein occlusion EudraCT Number: 2012-000800-13	Ongoing
Treatment of macular edema secondary to central or branch vein occlusion by dexamethazone intravitreal injection EudraCT Number: 2011-000425-72	Ongoing

References

Bezatis A, Spital G, Höhn F et al. (2013) Functional and anatomical results after a single intravitreal Ozurdex injection in retinal vein occlusion: a 6-month follow-up -- the SOLO study. *Acta ophthalmologica.* 91 (5): e340-e347.

Capone A, Jr., Singer MA, Dodwell DG et al. (Feb. 2014) Efficacy and safety of two or more dexamethasone intravitreal implant injections for treatment of macular edema related to retinal vein occlusion (Shasta study). *Retina.* 34 (2): 342-351.

Edwards SJ, Barton S, Trevor N et al. (2012) Comparisons of the clinical effectiveness of treatments for macular oedema (MO) caused by retinal vein occlusion (RVO). *Value in Health.Conference: ISPOR 15th Annual European Congress Berlin Germany.Conference Start: 20121103 Conference End: 20121107.Conference Publication: (var.pagings).15 (7) (pp A568), 2012.Date of Publication: November 2012.* (var.pagings): A568-.

Ford JA, Shyangdan D, Uthman OA et al. (2014) Drug treatment of macular oedema secondary to central retinal vein occlusion: A network meta-analysis. *BMJ Open.4 (7) , 2014.Article Number: e005292.Date of Publication: 2014.* (7).

Ford JA, Clar C, Lois N et al. (2014) Treatments for macular oedema following central retinal vein occlusion: Systematic review. *BMJ Open.4 (2) , 2014.Article Number: e004120.Date of Publication: 2014.* (2).

Haller JA, Bandello F, Belfort R et al. (2010) Randomized, sham-controlled trial of dexamethasone intravitreal implant in patients with macular edema due to retinal vein occlusion. *Ophthalmology.* 117 (6): 1134-1146.

Haller JA, Bandello F, Belfort R, Jr. et al. (Dec. 2011) Dexamethasone intravitreal implant in patients with macular edema related to branch or central retinal vein occlusion twelve-month study results. *Ophthalmology.* 118 (12): 2453-2460.Iu LP, Zhao P, Yeung IY et al. (Aug. 2014) Sequential therapy with ranibizumab and dexamethasone intravitreal implant is better than dexamethasone monotherapy for macular oedema due to retinal vein occlusion. *Br J Ophthalmol.*

Iu LP, Zhao P, Yeung IY et al. (Aug. 2014) Sequential therapy with ranibizumab and dexamethasone intravitreal implant is better than dexamethasone monotherapy for macular oedema due to retinal vein occlusion. *Br J Ophthalmol.*

Kowalski JW, Hayward E, Mazzi S et al. (2012) Economic evaluation with dexamethasone biodegradable intravitreal implant for the treatment of patients with macular edema following retinal

vein occlusion in Italy
OT - Valutazione economica del trattamento con impianto intravitreale biodegradabile di desametasone di pazienti affetti da edema maculare secondario a occlusione della vena retinica, in Italia. *PharmacoEconomics - Italian Research Articles.14 (1) (pp 29-38), 2012.Date of Publication: 2012.* (1): 29-38.

Mathew R, Pearce E, Muniraju R et al. (2014) Monthly OCT monitoring of Ozurdex for macular oedema related to retinal vascular diseases: Re-treatment strategy (OCTOME Report 1). *Eye (Basingstoke).28 (3) (pp 318-326), 2014.Date of Publication: March 2014.* (Basingstoke): 318-326.

Maturi RK, Chen V, Raghinaru D et al. (2014) A 6-month, subject-masked, randomized controlled study to assess efficacy of dexamethasone as an adjunct to bevacizumab compared with bevacizumab alone in the treatment of patients with macular edema due to central or branch retinal vein occlusion. *Clinical Ophthalmology.* 8: 1057-1064.

Meyer LM, Schonfeld C-L (2013) Secondary Glaucoma after Intravitreal Dexamethasone 0.7 mg Implant in Patients with Retinal Vein Occlusion: A One-Year Follow-Up. *Journal of Ocular Pharmacology and Therapeutics.29 (6) (pp 560-565), 2013.Date of Publication: 01 Jul 2013.* (6): 560-565.

Pichi F, Specchia C, Vitale L et al. (Mar. 2014) Combination therapy with dexamethasone intravitreal implant and macular grid laser in patients with branch retinal vein occlusion. *American Journal of Ophthalmology.* 157 (3): 607-615.

Poku Em Rathbone J, Everson-Hock E et al. (Aug. 2012) Bevacizumab in eye conditions: Issues related to quality, use, efficacy and safety. Report by the Decision Support Unit.

Appendix 3 – Implementation submission

Review of NICE technology appraisal guidance No.229; Dexamethasone intravitreal implant for the treatment of macular oedema secondary to retinal vein occlusion

Please contact Liesl Millar regarding any queries Liesl.Millar@nice.org.uk

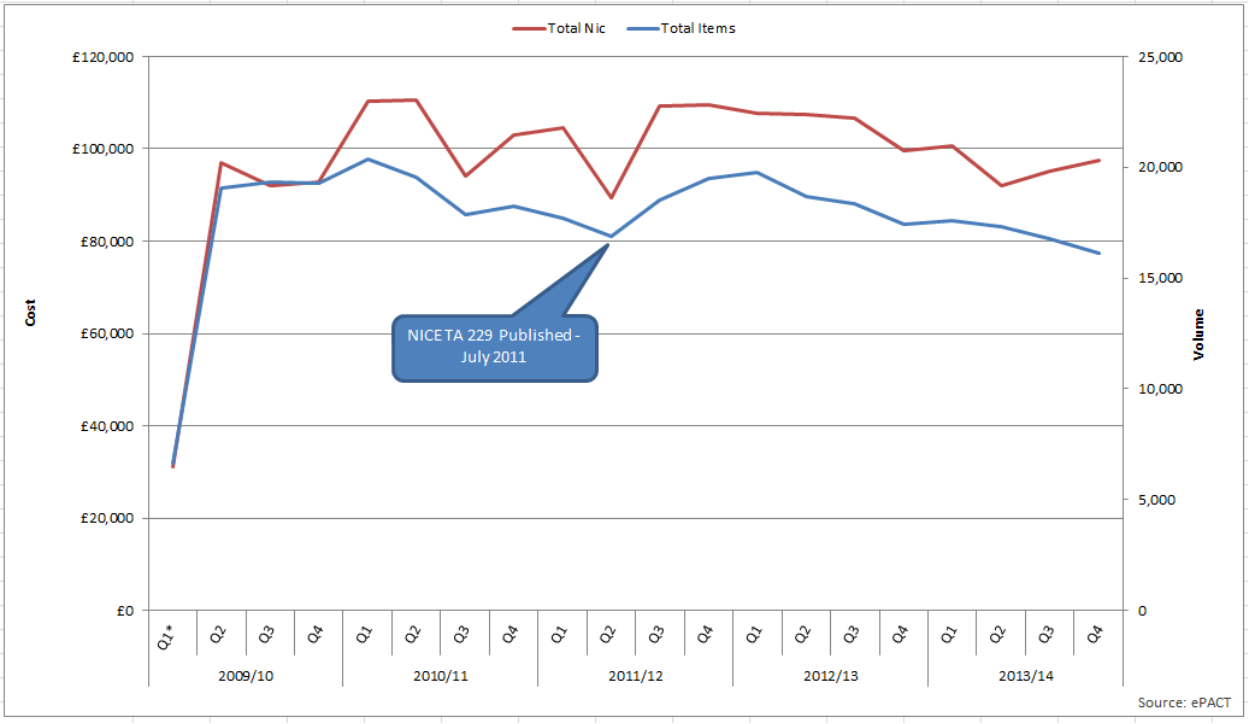
Contents

1. Routine healthcare activity data

ePACT data

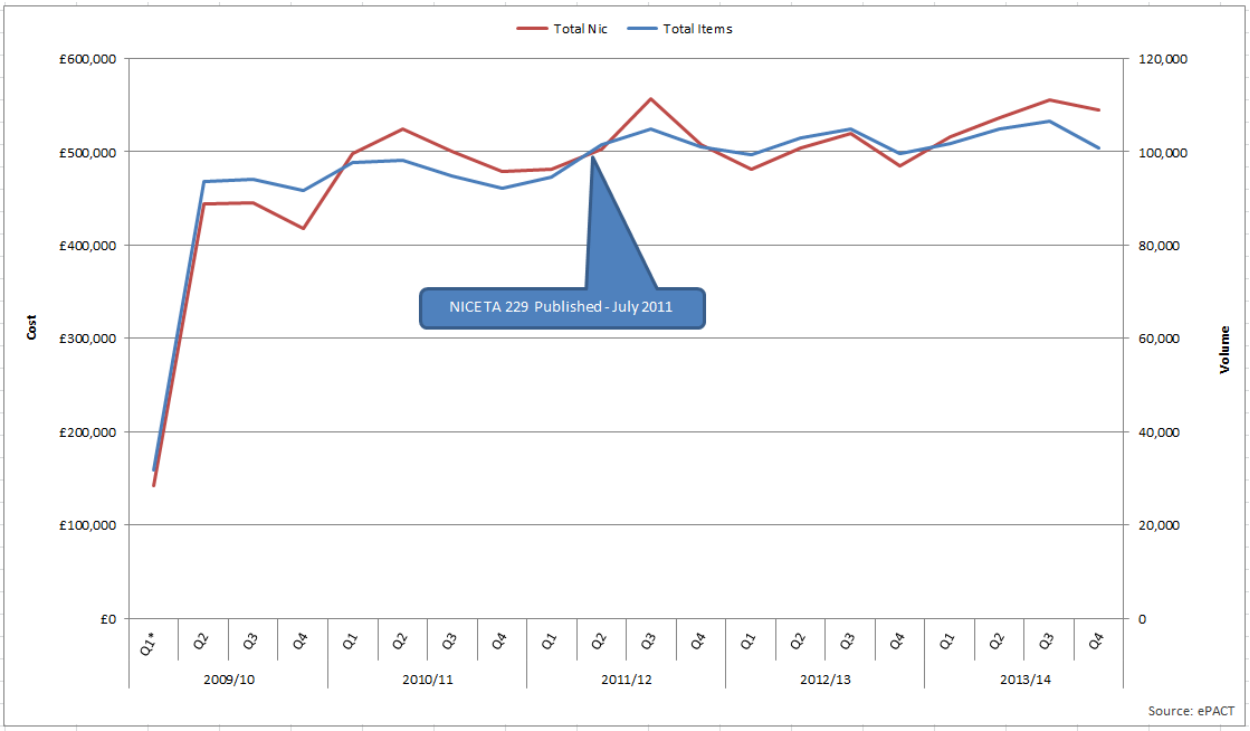
This section presents electronic prescribing analysis and cost tool (ePACT) data on the net ingredient cost (NIC) and volume of dexamethasone prescribed in hospitals and or the community and dispensed in the community in England between April 2009 and March 2014.

Figure 1 Cost and volume of dexamethasone prescribed in hospital and dispensed in the community in England between April 2009 and March 2014.



*Q1 2009/10 has incomplete data

Figure 2 Cost and volume of dexamethasone prescribed and dispensed in the community in England between April 2009 and March 2014.



*Q1 2009/10 has incomplete data

Hospital Pharmacy Audit Index data

This section presents Hospital Pharmacy Audit Index (HPAI) data on the net ingredient cost (NIC) and volume of drugs prescribed and dispensed in hospitals in England. There was no data available for dexamethasone.

2. Implementation studies from published literature

No uptake information was found on the uptake database website for TA 229.

3. Qualitative input from the field team

The field team recorded one piece of relevant feedback in relation to this guidance. A trust reported some difficulty in getting the commissioning PCT to agree to the use of this treatment. They also reported that there has been some local concern expressed over the actual clinical effectiveness of the drug.

4. Implementation studies from shared learning

A search of the shared learning website highlighted no examples of TA229 being implemented.

Appendix A: Healthcare activity data definitions

ePACT

Prescribing analysis and cost tool system

This information comes from the electronic prescribing analysis and cost tool (ePACT) system, which covers prescriptions by GPs and non-medical prescribers in England and dispensed in the community in the UK. The Prescription Services Division of the NHS Business Services Authority maintains the system. PACT data are used widely in the NHS to monitor prescribing at a local and national level. Prescriptions dispensed in hospitals, mental health units and private prescriptions, are not included in PACT data.

Measures of prescribing

Prescription Items: Prescriptions are written on a prescription form. Each single item written on the form is counted as a prescription item. The number of items is a measure of how many times the drug has been prescribed.

Cost: The net ingredient cost (NIC) is the basic price of a drug listed in the drug tariff, or if not in the drug tariff, the manufacturer's list price.

Data limitations (national prescriptions)

PACT data do not link to demographic data or information on patient diagnosis. Therefore the data cannot be used to provide prescribing information by age and sex or prescribing for specific conditions where the same drug is licensed for more than one indication.