NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE
Patient/carer organisation statement (STA)

Dexamethasone intravitreal implant for treating diabetic macular oedema

1. About you and your organisation

Please note: this is a joint response from Royal National Institute of Blind People (RNIB), Macular Society and Diabetes UK.

Your name: Clara Eaglen
Name of your organisation: RNIB
Your position in the organisation: Policy and Campaigns Manager
Brief description of the organisation: RNIB is the UK's leading charity offering information, support and advice to almost two million people with sight loss. We have over 12,000 members throughout the UK and 80 per cent of our Trustees are blind or partially sighted. We encourage members to get involved in our work and regularly consult them on matters relating to Government policy and ideas for change.

Name: [redacted]
Name of your organisation: Macular Society
Your position in the organisation: [redacted]
Brief description of the organisation: Macular Society is the specialist UK charity for people living with macular conditions. We are the largest patient member organisation in the eye care sector with nearly 16,000 members. We offer a range of support and information services to people with central vision loss, as well as their families and carers. We provide information for health professionals, campaign for better services, sponsor research and raise awareness of macular degeneration and its prevention.

Name: [redacted]
Name of your organisation: Diabetes UK
Your position in the organisation: [redacted]
Brief description of the organisation: Diabetes UK is the leading charity that cares for, connects with and campaigns on behalf of every person affected by or at risk of diabetes. We help people manage their diabetes effectively by providing information, advice and support. We campaign with people with diabetes and with

healthcare professionals to improve the quality of care across the UK's health services. We fund pioneering research into care, cure and prevention for all types of diabetes. We are a growing community with more than 300,000 supporters nationwide – including people with diabetes, their friends and families

2. Living with the condition
What is it like to live with the condition or what do carers experience when caring for someone with the condition?

i. The patient perspective:

Diabetic macular oedema affects central vision and has a big impact on the day-to-day lives of patients, carers and their families. This condition does not affect the peripheral vision, so the patient will not go completely blind.

The emotional impact of sight loss through diabetic macular oedema will vary from individual to individual. However, many of the patients we have spoken to expressed significant fear of losing their sight - a reaction which they said was similar to bereavement.

As well as the emotional toll, sight loss due to diabetic macular oedema can impact on a person's life in many ways. Some of these impacts are summarised below:

- Forced early retirement from paid employment as this condition tends to affect a younger cohort of people (ie the working age population) compared to other eye conditions such as age-related macular degeneration
- Loss of income and dependence on benefits
- Loss of driving licence and subsequent loss of independence
- Increased costs for visual aids, transport and domestic help
- Increased risk of falls and accidents
- Dependence on family members, who often have to give up significant time to care for their loved one. In some cases having to give up paid employment themselves.
- Loss of confidence and self-esteem
- Social isolation (due to difficulties in undertaking social activities such as reading menus in restaurants etc)
- Clinical depression requiring NHS treatment

In addition to these, sight loss can hamper a person's ability to self manage their diabetes. Most diabetics undertake daily activities in order to manage their condition. If they have vision loss they may require specifically developed technologies, assistance, or may even need to learn new techniques to undertake these daily activities. Vision loss means it is harder for a diabetic patient to:

- Self administer insulin or use an insulin pump (where required)
- Take tablets to manage their blood glucose levels (where required) and monitor their glucose levels at home
- Check their feet daily for discolouration, as this could be a warning sign of a foot ulcer. The more significant the vision loss the more difficult this will be for the patient.
- Stay active to maintain a healthy weight
- Eat a healthy, balanced diet and read food labels to identify products that are high in fat, salt and sugar. Patients may find it hard to read 'use by dates' on products or read cooking instructions.

Poor self-management of diabetes increases a person's risk of developing/progressing the long term complications of the condition (i.e. kidney disease, retinopathy, cardiovascular disease and amputations).

Finally, diabetic patients often have to attend multiple medical appointments each year, which can have a huge impact on their life. Some may only need an annual check with their GP and one with the diabetic retinopathy screening service, while others may have multiple appointments each month. As many diabetic patients are of working age, they have to take time off work to attend these appointments or to self-manage their condition. Some patients report that this causes anxiety as they can sense that their work colleagues are not that understanding about their absences. Sight loss from diabetic macular odema causes additional difficulties in getting to and from these medical appointments, as it is much harder to get out and about on public transport and many patients will no longer be able to drive.

ii. The carer perspective:

Caring for a person with diabetic macular odema can be a large undertaking. Many patients are cared for by their loved ones (spouses or children) and for the carer the impacts could include:

- Taking on responsibility for many of the household tasks that the patient is no longer able to accomplish (ie cooking, cleaning, gardening, ironing etc)
- Helping the patient self-manage their diabetes through organising their tablets or helping them to inject insulin (where required)
- Driving the patient to and from numerous medical appointments, especially to the eye clinic where drops are administered blurring the vision
- Offering practical and emotional support to the patient, which in turn can impact on the mental health of the carer

3. Current practice in treating the condition

Which treatment outcomes are important to patients or carers? (That is, what would patients or carers like treatment to achieve?) Which of these are most important? If possible, please explain why.

Stopping the patient's sight deteriorating is the most important outcome. This relates to visual acuity as well as visual function (ie the amount of useful vision that is maintained so that the patient can continue their day to day activities. Patients are interested in what they can continue to do, such as drive, rather than how many letters they can read on an eye chart).

Most would also like an improvement in their vision.

All would prefer treatments with a low risk of complications and limited/no side effects.

What is your organisation's experience of currently available NHS care and of specific treatments for the condition?

Collectively RNIB, Macular Society and Diabetes UK have a huge amount of experience of currently available treatments for diabetic macular oedema. This experience has been gained through:

- Daily conversations with patients who are living with and being treated for diabetic macular odema
- Discussions with clinicians and patients to examine the treatment of diabetic macular oedema in the UK and its impact on patient's quality of life

- One to one discussions with clinicians and trial patients who have used dexamethasone intravitreal implant to treat diabetic macular odema
- Reading published research
- The Summary of Product Characteristics for each treatment

How acceptable are these treatments and which are preferred and why?

In terms of current treatments, ranibizumab is well tolerated by patients and preferable to laser, which causes scarring. Although patients are apprehensive about intravitreal injections, the thought of losing their sight makes the procedure bearable. More details on the acceptability and preferences of current treatments are covered in section four below.

4. What do patients or carers consider to be the advantages of the treatment being appraised?

Please list the benefits that patients or carers expect to gain from using the treatment being appraised.

We believe the advantages of dexamethasone intravitreal implant are:

- the safe and effective treatment of diabetic macular odema
- reduced burden for the patient and NHS due to the long-acting nature of the treatment
- the provision of another choice of treatment, which can save the patient's sight if they do not respond to current approved therapies

Further information on these advantages is summarised below:

i. Safe and effective treatment for diabetic macular oedema

Data from the MEAD study shows that dexamethasone intravitreal implant is an effective and safe treatment in comparison to sham intravitreal injections.

ii. Reduced burden for the patient and NHS

The implant is long-acting and in the MEAD trial patients received treatment in intervals of six months and over. We are aware, but

do not have robust evidence, that this interval may be shorter in routine practice and have spoken to patients who have been injected every four months.

Either way, dexamethasone intravitreal implant will provide longer follow-up intervals compared with current NICE approved treatments. This will in turn reduce the:

- number of hospital visits for the patient and their carer
- number of leave requests required by the patient to attend hospital appointments (ie reducing the burden to the employer)
- caseload in the hospital eye department (ie reducing the burden on health professionals)

iii. Patient choice

Dexamethasone intravitreal implant provides patients with another choice of treatment for diabetic macular odema which can save their sight if they do not respond to current approved treatments.

The implant's licence states that: '"Ozurdex® is indicated for the treatment of adult patients with visual impairment due to diabetic macular oedema who are pseudophakic or who are considered insufficiently responsive to or unsuitable for non-corticosteroid therapy." This wording is very flexible and beneficial to patients, as some may be unsuitable to attend the eye clinic regularly due to other commitments (ie work, looking after dependents etc); so having a long-acting treatment option available based on their lifestyle needs is extremely helpful.

Please explain any advantages that patients or carers think this treatment has over other NHS treatments in England.

Ranibizumab has been approved to treat any eye (with diabetic macular oedema) that has a central retinal thickness of 400 micrometres or more at the start of treatment. This means that anyone with diabetic macular odema and a central retinal thickness of less than 400 micrometres has no approved anti-VEGF treatment option. We hope that dexamethasone intravitreal implant will be made available to patients with diabetic macular odema regardless of the thickness of their retina. We appreciate that the licence for this treatment imposes other restrictions on its use (ie for use in pseudophakic patients).

Fluocinolone acetonide intravitreal implants have been approved for use on the NHS but only in patients whose diabetic macular oedema is insufficiently responsive to available therapies, therefore we are not going to compare this to the treatment with dexamethasone intravitreal implant.

Now that pharmacological treatments are available, laser photocoagulation therapy is being used less and less. In the past, patients reported being treated with laser and that it helped prevent further sight loss but caused scarring. Scarring is a major disadvantage and something that does not happen with dexamethasone intravitreal implant.

As mentioned above, we believe the long-acting nature of dexamethasone intravitreal implant is helpful for patients.

As also mentioned above, current treatments do not work in all patients. Therefore, another option (i.e. dexamethasone intravitreal implant) could save the sight of an unresponsive patient.

Case study:

Patient A is 65 years old, retired and was diagnosed with diabetic macular odema in both eyes in 2007.

How was the patient's diabetes diagnosed?
The patient was diagnosed with diabetes in 2000. They went to see a nurse and had their urine checked. This was followed by a blood test. They suspected they may develop diabetes as their maternal grandmothers had the condition. Initially they were prescribed tablets to control their blood glucose levels but this had little effect. They admitted that initially they were not as careful as they should have been (in relation to self management) and really regret that now. They just did not realise how hard it would be to manage their blood glucose and how quickly the complications of diabetes could set in. After a year they were sent to the hospital to change their medications and this helped reduce their blood pressure and control their blood glucose level.

What was the impact of living with diabetes?
The patient said they have to be very strict and diligent when it comes to self management. They are allowed no sugar, no fizzy

drinks and no sweets. They have to eat three small meals a day and carry bananas and apples around with them to eat in case their blood sugar level suddenly drops. They can often feel their feet itching due to the condition and are very anxious about the serious complications related to the disease (such as blindness, kidney disease and heart disease). The patient said this motivates them to really take control of their condition as they want to stay in this world. They also said they have lost weight in order to be healthier and check their blood glucose levels at home on a regular basis. They also attend multiple health appointments at their local GP practice and hospital.

How was their diabetic macular oedema diagnosed and how was it treated?
The patient said they always attend their annual sight test at the diabetic retinopathy screening service. In 2007, they recall not being able to see very well - their left eye was not clear and made the world look foggy. Following their screening appointment, they were told that they had fluid at the back of their left eye. They recall being extremely frightened about going blind and (at the time) had not realised that diabetes could cause such significant sight loss. Initially they had laser on their eye but this did not work well. Over the years they were switched to anti-VEGF treatment but this again was of little benefit. Finally they joined the MEAD clinical trial and were given a dexamethasone intravitreal implant. They remember the needle feeling bigger than the one used to administer anti-VEGF treatment and that it was a bit more painful. This time the treatment worked, creating a noticeable difference in their vision. During the course of the trial they needed a cataract operation but did not mind as the treatment was so beneficial. They would recommend the implant and felt they received a very good experience.

The patient said that their eye condition has had an impact on their family - their nieces and nephews have had to take time off work to help them attend medical appointments. Their family has also 'been there' offering emotional support when the patient has needed it the most.

If you know of any differences in opinion between patients or carers about the benefits of the treatment being appraised, please tell us about them.

Most of the patients we interviewed felt dexamethasone intravitreal implant was beneficial and stopped their vision loss/improved their vision. However, some were unhappy with the side effects and were unable to comment on perceived benefits in these cases.

Some patients were highly complimentary and said they would recommend the treatment as it improved their vision; this was despite needing a cataract operation as a result of using the long-acting steroid (phakic patients were permitted to take part in the clinical trial). However, a couple of patients felt they would not want to use this treatment option again due to the risk of increased intraocular pressure, increased risk of developing glaucoma and increased risk of developing a cataract.

One patient had to have a cataract operation as a result of the treatment and was very unhappy about it but still felt the treatment may be suitable for other patients. Another patient stated that there is no point being treated for a condition only to develop another.

As the licence states that "Ozurdex® is indicated for the treatment of adult patients with visual impairment due to diabetic macular oedema who are pseudophakic .." the risk of developing cataract will at least be removed.

The negative feedback about this treatment highlights the need for patient choice. It is so important that patients fully understand the advantages and disadvantages of various treatments and are able to make an informed choice.

5. What do patients and/or carers consider to be the disadvantages of the treatment being appraised?
Please list any concerns patients or carers have about the treatment being appraised.

i. Side effects and complications

As mentioned above, patients report that the disadvantages to be the risk of increased intraocular pressure, increased risk of developing glaucoma and increased risk of developing a cataract.

ii. Injecting the implant into the eye

All of the patients we spoke to said that the thought of receiving an injection in their eye (ie to insert the implant) had caused anxiety initially. However, they reported that the unpleasant thought was much worse than the reality. The general consensus was that the injections were not a problem if they prevented sight loss. Many patients complimented hospital staff and said they were taken through the process step-by-step and had received all the necessary information before going through the treatment.

Most did not have any side effects except for temporary floaters and some said they felt pain in their eye when the anaesthetic wore off.

(Please note: patients express the same concerns about the current anti-VEGF treatment ranibizumab).

iii. Comparison of an anti-VEGF injection and implant injection

Some patients who had received the anti-VEGF treatment ranibizumab for diabetic macular odema said that the dexamethasone intravitreal implant injection felt bigger than anti-VEGF injection. They also said it caused a little more eye pain. However, many felt this was not a significant problem and believed the benefits of the long-acting treatment outweighed these disadvantages.

If you know of any differences in opinion between patients or carers about the disadvantages of the treatment being appraised, please tell us about them.

Some patients felt that the disadvantages were no problem if it meant their sight would be saved and they could get longer-acting treatments. A much smaller number felt the disadvantages outweighed the benefits. Each individual responds differently and this is why patient choice is so important.

6. Patient population
Are there any groups of patients who might benefit more from the treatment than others? If so, please describe them and explain why.

As far as we are aware, dexamethasone intravitreal implant appears to work equally well in all groups of patients. The

exception is those who are phakic or have existing issues with intraocular pressure control or have glaucoma. Patient selection is therefore important in the use of this treatment.

Are there any groups of patients who might benefit less from the treatment than others? If so, please describe them and explain why.

As mentioned above phakic patients or those who have existing issues with intraocular pressure control or glaucoma will benefit less from the treatment.

7. Research evidence on patient or carer views of the treatment
Is your organisation familiar with the published research literature for the treatment?

x Yes ☐ No

If you answered 'no', please skip the rest of section 7 and move on to section 8.

Please comment on whether patients' experience of using the treatment as part of their routine NHS care reflects the experiences of patients in the clinical trials.

This treatment is not yet in routine use so we are unable to comment.

However, we would like to note that many eye clinics in England are under huge pressure to deliver services and unable to keep up with demand. In some cases treatment intervals are being extended beyond clinically appropriate timeframes due to the sheer number of patients. This has been identified by recent research carried out by both RNIB and Macular Society. Dexamethasone intravitreal implant could help ease some of these problems, as patients will need fewer visits to the eye clinic, meaning reduced burden for the patient and the NHS. This in turn could result in patients receiving optimal treatment in clinically appropriate timeframes.

Also, in routine practice each patient's needs will determine the best choice of treatment for them and there will be many factors affecting that choice.

Do you think the clinical trials have captured outcomes that are important to patients? Are you aware of any limitations in how the treatment has been assessed in clinical trials?

Many relevant outcomes have been captured; however, trying to assess the impact of a sight condition on a patient's quality of life is notoriously difficult. NICE uses the EQ5D as the standard tool for measuring health outcomes but this is not a good instrument for use in patients with vision problems. This is why it is imperative that the NICE Committee takes patients' views into consideration alongside the clinical trial results.

If the treatment being appraised is already available in the NHS, are there any side effects that were not apparent in the clinical trials but have emerged during routine NHS care?

This treatment is not yet in routine use so we are unable to comment.

Are you aware of any relevant research on patient or carer views of the condition or existing treatments (for example, qualitative studies, surveys and polls)?

☐ Yes x No

8. Equality
Please let us know if you think that there are any potential equality issues that should be considered in this appraisal.

We do not believe there are any equality issues that should be considered.

Are there groups of patients who would have difficulties using the treatment or currently available treatments? Please tell us what evidence you think would help the Committee to identify and consider such impacts.

Other than the anxieties mentioned above about the use of the intravitreal implant injection, we do not believe there are any patients who would have difficulties using the treatment or the currently available treatments.

9. Other issues
Do you consider the treatment to be innovative?

☐ Yes x No

Are there any other issues that you would like the Appraisal Committee to consider?

We believe that dexamethasone intravitreal implant should be made available for clinicians to use as it is proven to be safe and effective.

If this treatment is approved, we would hope the resulting guidelines state that:

- Clinicians should not wait before treating patients. This will ensure they do not suffer needless, irreversible damage to their vision.
- Dexamethasone intravitreal implant should be made available for use in any eye (with diabetic macular odema) if deemed beneficial by the clinician and patient. It is important to treat monocular eye disease where possible as there is always the risk of developing another eye condition in the other, better seeing eye.
- Make clear if the treatment is to be used first line or second line, or should be used in a specific sequence. We believe the guidance should offer prescriptive clarification, for example: 'This treatment is approved as a first line option alongside other first line options for diabetic macular odema. This means the therapy must be made available to all NHS patients. It is for the clinician and patient to decide which of the treatments is most appropriate'.

10. Key messages
In no more than 5 bullet points, please summarise the key messages of your submission.

1. Clinical trials show that dexamethasone intravitreal implant is a safe and effective treatment for diabetic macular odema and we believe it should be approved for use by NHS patients. (Despite some patients' reservations about the side effects and complications of the treatment, most believe the advantages outweigh the disadvantages).
2. Preventing a patient's sight loss will help them self-manage their diabetes and, in turn, halt the progression/development of serious complications linked to the condition.
3. Dexamethasone intravitreal implant will be particularly beneficial to patients who have not responded to current NICE approved treatments.
4. Dexamethasone intravitreal implant increases patient choice for the treatment of diabetic macular odema.
5. The long-acting nature of the treatment will reduce the burden on the patient (as they will need less visits to the eye clinic); the burden on the employer (as patients need less time off of work to attend medical appointments); the burden on the carer (as they will not be required to take their loved one to medical appointments so regularly) and the burden on the NHS (as treatment intervals will be longer).