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

Aflibercept 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 patients who have used aflibercept to treat diabetic macular oedema
- Reading published research
- The Summary of Product Characteristics for each treatment

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

Anti-VEGF treatment 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 aflibercept are:

- the safe and effective treatment of diabetic macular odema
- a fixed dosing regimen which means that patients and their carers know when an injection will be administered
- 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 VIVID and VISTA studies show that aflibercept is an effective and safe treatment in comparison to laser photocoagulation.

ii. The fixed dosing regimen

The posology for aflibercept for the treatment of diabetic macular oedema states that:
'Eylea treatment is initiated with one injection per month for five consecutive doses, followed by one injection every two months. There is no requirement for monitoring between injections. After the first 12 months of treatment with Eylea, the treatment interval may be extended based on visual and anatomic outcomes. The schedule for monitoring should be determined by the treating physician'.

The posology for this treatment is helpful for patients as they will know exactly when they will get an injection in year one (rather than attend a monitoring appointment and then find out if they need an injection or not).

The treat and extend posology means that each patient can work with their clinician to identify appointment timeframes that meet their individual needs - patients report that this is reassuring as they feel that their care is being planned around them.

If appointment intervals can be extended this will 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 eye department (ie reducing the burden on health professionals)

iii. Patient choice

Aflibercept 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.

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 aflibercept will be made available to all and treat any patient with diabetic macular odema regardless of the thickness of their retina.

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 aflibercept.

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 aflibercept. Also laser has inferior efficacy to aflibercept.

As mentioned above, we believe the posology for aflibercept is helpful for patients.

As also mentioned above, current treatments do not work in all patients. Therefore, another option (i.e. aflibercept) could save the sight of an unresponsive patient. One patient we spoke to said there was a noticeable improvement in their vision when they were switched from ranibizumab to aflibercept (see case study below). We are aware of emerging evidence relating to switching patients and believe that some will benefit from aflibercept in comparison to ranibizumab and vice versa.

Case study:

Patient A is 53 years old, worked as a carer and was diagnosed with diabetic macular odema in both eyes in 2008.

How was the patient's eye condition diagnosed?
The patient had been living with undiagnosed diabetes and had noticed blurred vision in their right eye. Following a visit to their GP and a number of tests they were diagnosis with diabetes in 2008. They were asked to attend a diabetic retinopathy screening appointment and were then referred to their local eye clinic. This is how they were diagnosed with diabetic macular odema. The patient said that they were really, really worried about going blind. Especially as their diabetes was not well controlled and the vision in their left eye had deteriorated too.

The impact of the condition on the patient's daily life:
As well as the huge anxiety caused by the deterioration of their vision, they had problems with day to day activities. It took them much longer to see the number on the front on the bus, which they used to be able to read at a distance. They also noticed that their eyes got very tired and sore when reading for any length of time. Although they did not drive, they were worried that losing their sight would stop them getting out and about and stop them caring

for their sick mother. At this stage the condition had a big impact on their life and they were worried it would become debilitating.

What treatment did they have?
Initially they were treated with laser but this was not effective as it caused scarring. Several years later (they could not remember the exact date) they were given anti-VEGF injections. They had five injections in their left eye and 10 in their right. Although they did not notice an improvement in their vision, which they would have liked, they were happy that their sight did not deteriorate further. This was reassuring.

Recently the patient switched to aflibercept injections and noticed an improvement within a couple of months. At first they wondered if they were imagining it. However, they were able to read more letters on an optician's chart (they could read a whole line more) and scans showed an improvement. The patient also reported that they could see text/objectives more clearly. To date they have had two aflibercept injections in their right eye and one in the left. Further injections are planned and they have said that they are not getting such sore eyes when reading.

What impact has the condition had on their quality of life following treatment?
After treatment with aflibercept, the patient said that their condition is no longer a massive problem and they do not fear going blind. They can now see better, which helps them undertake day to day tasks better. They said they were lucky as their sibling takes them to and from hospital appointments, however, they felt this would be burdensome without that support. In summary, the patient said that aflibercept injections are wonderful and make all the difference to their life.

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.

We are not aware of any differences in opinions.

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.

All of the patients we spoke to said that the thought of receiving an injection in their eye 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 anti-VEGF treatment ranibizumab).

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.

We are not aware of any differences in opinions.

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, aflibercept appears to work equally well in all groups of patients.

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

We do not feel there are any groups of patients who would benefit less from this 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. Therefore, it is unlikely that patients will all get treatment in line with clinical trial intervals. Clinicians are of course doing all they can to treat their patients, even putting on extra clinics in their free time (at evenings and weekends) and patients are extremely grateful for this.

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 intravitreal injections, 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 aflibercept 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.
- Aflibercept 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 aflibercept is a safe and effective treatment for diabetic macular odema and we believe it should be approved for use by NHS patients.
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. Aflibercept will be particularly beneficial to patients who have not responded to current NICE approved treatments. Aflibercept increases patient choice for the treatment of diabetic macular odema.
4. The posology for this treatment is beneficial for patients as they will know exactly when they will get an injection in year one rather than attend a monitoring appointment and then find out if they need an injection or not.
5. The licence for the treatment means that after year one, the patient can work with their clinician to create a treatment 'plan' with timeframes tailored to their needs - patients report that this is reassuring as they feel that their care is being planned around them.