National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Dexamethasone intravitreal implant for treating diabetic macular oedema in people without a pseudophakic lens (part review of TA349)

Response to consultee and commentator comments on the draft remit and draft scope (pre-referral)

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Comment 1: the draft remit

Section	Consultee/ Commentator	Comments [sic]	Action
Wording	AbbVie	Yes, the draft remit appropriately reflects the issue(s) of clinical and cost effectiveness about this technology that NICE should consider.	Thank you for your comment. No action required.
	Alimera Sciences Ltd.	1. **Wording: *"within its marketing authorisation"* -** The indication for Ozurdex is, "visual impairment due to diabetic macular oedema (DMO) who are pseudophakic or who are considered insufficiently responsive to, or unsuitable for non-corticosteroid therapy". This needs to be reflected more appropriately in the draft remit/appraisal.	Thank you for your comment. This appraisal is a partial review of the guidance produced for TA349, where dexamethasone intravitreal implant was recommended for people with diabetic macular oedema who have a pseudophakic lens. The remit of this

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			appraisal is to consider the clinical and cost effectiveness of dexamethasone intravitreal implant for people who do not have a pseudophakic lens but still meet the conditions of the marketing authorisation. No action required.
	Macular Society	Yes	Thank you for your comment. No action required.
	Novartis Pharmaceuticals UK Limited	The remit is appropriate.	Thank you for your comment. No action required.
Timing Issues	AbbVie	High Currently, there are limited treatment options for patients with phakic DMO who are insufficiently responsive to, or unsuitable for non-corticosteroid treatment. Approximately, 40% of patients with DMO do not respond completely or are suboptimal responders to anti-VEGF.[1,2]	Thank you for your comment. No action required.
	Alimera Sciences Ltd.	2. **Timing: Alimera believe this review should be urgent.** Ophthalmology services in the UK were already struggling with resource pressures prior to the COVID-19 pandemic and this was widely reported in both journals[i] and the media.[ii,iii] Backlogs have only been worsened by the pandemic.[13] Access to alternative	Thank you for your comment. No action required.

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		treatments that are less burdensome compared to the comparator anti-VEGF treatments may assist with reducing pressure on ophthalmology services.	
	Macular Society	Not urgent	Thank you for your comment. No action required.
	Alimera Sciences Ltd.	3. **Lens status is not a major determinant in reduction of DMO.** Cataract surgery is a relatively common and low-risk surgical procedure with high success rate in the NHS.[iv] In TA613 clinical experts identified that, in some cases, people continue to have anti-vascular endothelial growth factors (anti-VEGFs), even if they do not work well. A recent consensus publication[v] reinforced this identifying that insufficient attention has been paid to considering clear guidance for appropriate timely conversion of patients with DMO and an insufficient response to anti-VEGF treatment to other alternative treatments such as intravitreal corticosteroid therapy. As a result, there is a risk that patients may continue to receive anti-VEGF treatment after it has failed to produce a sufficient therapeutic benefit. Adopting a clearer stopping rule for current (anti-VEGFs) treatments and an earlier switch to steroid therapy may allow for improved outcomes that focus on protecting the retina against irreversible damage, irrespective of lens function. See points 16/17/18/19 under 'Equality'.	Thank you for your comment. The remit for this appraisal is to appraise the clinical and cost effectiveness of dexamethasone intravitreal implant within its marketing authorisation for treating diabetic macular oedema in people without a pseudophakic lens. No action required.

Comment 2: the draft scope

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Background information	AbbVie	The background information is accurate. However, the gap in the treatment pathway of phakic DMO patients who are insufficiently responsive to, or unsuitable to non-corticosteroid is missing and will be worth highlighting. "Approximately 40% of patients with DMO do not respond completely or are suboptimal responders to anti-VEGF1,2 yet many of these patients continue to receive frequent anti-VEGF injections, given the lack of effective alternative treatment options."	Thank you for your comment. The scope is intended to be a broad outline of the disease area. The treatment pathway and available treatments will be considered by the committee. No action required.
	Alimera Sciences Ltd.	4. **Already existing backlogs in Ophthalmology services have been exacerbated by COVID-19.** Ophthalmology is a resource heavy NHS service, and recorded the highest level of outpatient activity of all NHS services in 2019-20 with 7.9 million attendances.[vi] Chronic conditions (e.g. cataract development, glaucoma, age related macular oedema, diabetic macular oedema) have been severely delayed during this prolonged pandemic period leading NHS England leadership to requested all healthcare systems aim for top quartile performance in productivity on high-volume clinical pathways systems with greatest COVID-19 back logs. Ophthalmology is one of the top 4 priority areas.[vii] 5. **Due to COVID-19 backlogs, less clinically burdensome pharmacological options for the treatment of DMO might need to be prioritised due to the changing clinic environment in the real world.** Frequent injections are required with anti-VEGF treatments. These treatments are also indicated for the treatment nAMD as well as DMO (TA274 and TA346). These treatments represent a key area of clinical burden for Ophthalmology services, including phakic DMO patients.	Thank you for your comments. The scope is intended to be a broad outline of the disease area. The remit for this appraisal is to appraise the clinical and cost effectiveness of dexamethasone intravitreal implant within its marketing authorisation for treating diabetic macular oedema in people without a pseudophakic lens. In TA613, fluocinolone acetonide intravitreal

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		6. ***"For eyes with a CRT of less than 400 micrometres, laser photocoagulation may be a treatment option".*** NICE TA613 identified that the fluocinolone acetonide intravitreal implant can also be used in sub-400 microns. There is no restriction on the CRT value in the indication for this product. 7. ***"…TA613, fluocinolone was not recommended for treating chronic diabetic macular oedema that is insufficiently responsive to available therapies in an eye with a natural lens (phakic eye)".*** More clarity should be provided here. Due to a lack of clinical evidence, the cost-effectiveness estimates for fluocinolone acetonide intravitreal implant were uncertain. Despite this, 3.17 states *"the clinical experts stated that the fluocinolone acetonide intravitreal implant would be a substantial change in treating diabetic macular oedema in phakic eyes with symptomatic cataract because the long-lasting effect reduces the need for repeated treatment and reduces treatment and follow-up burden. The committee concluded that fluocinolone acetonide intravitreal implant might be beneficial for the people with phakic eyes and symptomatic cataract but that it had not been shown evidence of any additional benefits that were not captured in the measurement of QALYs."* 8. As stated in point 3 above, **lens status is not a major determinant in the reduction of DMO.** Adopting a clearer stopping rule for current (anti-VEGFs) treatments and an earlier switch to steroid therapy may allow for improved outcomes that focus on protecting the retina against irreversible damage, *irrespective* of lens function.	implant was not recommended for treating diabetic macular oedema in people without a pseudophakic lens. No action required
	Macular Society	Good	Thank you for your comment. No action required.

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	Novartis Pharmaceuticals UK Limited	This information is accurate and complete.	Thank you for your comment. No action required.
	Roche Products Limited	For completeness, the population covered by the NICE recommendation for the fluocinolone acetonide implant in TA301 should be included.	Thank you for your comment. TA301 recommends fluocinolone acetonide intravitreal implant only in people with pseudoophakic lens, so it is not relevant to this topic. No action required.
The technology/ intervention	AbbVie	The description and/or mechanism of action of the technology is accurately reflected.	Thank you for your comment. No action required.
	Alimera Sciences Ltd.	9. **"…delivers dexamethasone to the posterior segment of the eye for up to 6 months."** Recent findings from the prospective, multicentre, AUSSIEDEX study highlighted the mean number of DEX injections over 52 weeks was 2.4 (95% CI 2.2 to 2.5), ranging from 1 to 4 (median, 2.5); 49 (25.0%) patients received 1 injection, 49 (25.0%) received 2 injections, 75 (38.3%) received 3 injections and 23 (11.7%) received 4 injections.[viii] Alimera are also not aware of any human vitreous pharmacokinetic data to support a 6-month duration of the dexamethasone implant in the eye,[ix] and this is also reflected in the available pharmacodynamic data which suggests retreatment is likely to occur from Month 3 or 4.[x,xi]	Thank you for your comment. The rationale for conducting the partial review appraisal can be found in the review decision paper. No action required.

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		10. **"There is new evidence supporting the clinical and cost effectiveness of dexamethasone intravitreal implants for people with *phakic* (natural) lenses."** Please can NICE clearly outline: a. Exactly what type of data this is i.e. RCT? RWE? Retrospective? Direct? Indirect? b. How the studies were conducted c. Exactly what the lens status and entry criteria were for the study population d. If, and where, this data is published e. If it is generalisable to people with diabetic macular oedema in phakic eyes with symptomatic cataract seen in the NHS (see TA613 clinical evidence recommendations).	
	Macular Society	Yes	Thank you for your comment. No action required.
	Roche Products Limited	Abbreviation for diabetic macular oedema should be consistent with the background section, DMO not DME.	Thank you for your comment. The abbreviation in the technology section is consistent with the wording in the marketing authorisation, but we have removed the abbreviation to avoid any confusion. No action required.

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Population	AbbVie	Three elements of the patient population definition will need correction; 1. Ozurdex's licence is not restricted to "chronic" DMO patients, therefore, the term chronic should be removed. 2. The definition does not capture patients with phakic DMO who are "unsuitable" for non-corticosteroid treatment. 3.In alignment with NICE TA 349, the target patient population are those insufficiently responsive to, or unsuitable for "non-corticosteroid treatments" and not "available therapies" The population should rather be defined as - patients with phakic DMO who are unsuitable for, or insufficiently responsive to non-corticosteroid treatment.	Thank you for your comment. The population section has been updated.
	Alimera Sciences Ltd.	11. **Please define the exact lens status of the patients *'without a pseudophakic lens'***. a. For example, are they phakic without evidence of cataract development on initiation? Understanding the lens status in the new data that has triggered review would be useful to include in the scope.	Thank you for your comment. The rationale for conducting the partial review appraisal can be found in the review decision paper. No action required.
	Macular Society	Yes, the population is defined appropriately. No	Thank you for your comment. No action required.
	Novartis Pharmaceuticals UK Limited	Appropriate.	Thank you for your comment. No action required.

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Comparators	AbbVie	The list of comparators for the insufficiently responsive patient population is complete and reflects the current NHS practice, albeit decreasing use of laser photocoagulation for DMO within the NHS.[1] For the phakic DMO patients who are unsuitable for non-corticosteroid treatment (identified in the above section), watch and wait should be added as the most suitable comparator, consistent with the comparator included in NICE TA349.	Thank you for your comment. Watch-and-wait has been added as a comparator for people who are unsuitable for treatment with both anti VEGFs and laser photocoagulation.
	Alimera Sciences Ltd.	12. **Fluocinolone acetonide intravitreal implant has been omitted as a comparator.** Two recent systematic reviews of real-world evidence have included phakic patients, highlighting that fluocinolone acetonide intravitreal implant is used commonly in clinical practice in phakic patients. Kodjikian et al (2021) included 353 phakic eyes, and Fallico et al (2021) included 235 phakic eyes. Both the reviews provided independent analysis confirming strong consistency in outcomes in the real world with that shown within randomised placebo-controlled trials. This consistency was across primary outcomes of mean change of best corrected visual acuity (BCVA) at 24 months, and secondary outcomes of 36-month mean BCVA, mean central macular thickness (CMT) change, rates of eyes receiving supplementary intravitreal therapy, cataract surgery, intraocular pressure (IOP)-lowering drops and glaucoma. 13. **Two recent UK clinical expert consensus guidelines[5,xii] have included both fluocinolone acetonide *and* dexamethasone implants in their recommendations.** The first publications does not specify lens status as a decision factor in the pathway flow chart and it determines efficacy and burden of treatment (which impacts efficacy) as the 2 decision factors on which to base treatment choice.[5]	Thank you for your comment. The remit for this appraisal is to appraise the clinical and cost effectiveness of dexamethasone intravitreal implant within its marketing authorisation for treating diabetic macular oedema in people without a pseudophakic lens. In TA613, fluocinolone acetonide intravitreal implant was not recommended for treating diabetic macular oedema in people without a

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		The second publication recommends both long acting steroid treatments in phakic eyes.[12] With consensus from clinical opinion leaders recommending both treatments in UK clinical practice, **omitting fluocinolone acetonide seems to ignore current clinical practice.**	pseudophakic lens, so it is not a comparator for this population. The comparators and standard clinical practice will also be considered by clinical experts as part of the appraisal process. No action required
	Macular Society	Yes	Thank you for your comment. No action required.
	Novartis Pharmaceuticals UK Limited	As outlined in the background section, the listed comparators are comparators recommended in different populations so the appropriate comparators for this appraisal will defined by the population the company is submitting for appraisal. Anti-vascular endothelial growth factors (VEGFs) are the standard of care for the treatment of visual impairment due to DMO with central retinal thickness (CRT) greater than 400 micrometers. They are unlikely to be considered comparators for dexamethasone. A consensus statement by The Royal College of Ophthalmologists describes anti-VEGF as first-line treatment if the eye has a central foveal of 400 micrometers or more. The consensus also recommends switching Anti-VEGF before steroids for tachyphlaxis.[1] Unlicensed bevacizumab is not an appropriate comparator for this topic as it is neither standard of care nor has a marketing authorisation in the UK for DMO.	Thank you for your comment. The comparators and standard clinical practice will be considered by clinical experts as part of the appraisal process. No action required.

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		Additionally, laser photocoagulation alone is not considered standard of care for the treatment of centre involving DMO. The Royal College of Ophthalmologists Consensus Guideline only recommends the use of laser for non-centre involving DMO.[1] 1. Amoaku, W.M., Ghanchi, F., Bailey, C., Banerjee, S., Banerjee, S., Downey, L., Gale, R., Hamilton, R., Khunti, K., Posner, E. and Quhill, F., 2020. Diabetic retinopathy and diabetic macular oedema pathways and management: UK Consensus Working Group. *Eye*, *34*(1), pp.1-51.	
Outcomes	AbbVie	Yes, the listed outcome measures capture the most important health benefits (and harms) associated with the technology.	Thank you for your comment. No action required.
	Alimera Sciences Ltd.	14. **Additional outcomes should include:** a. Elevated IOP as an adverse event b. Time to cataract development c. Time to cataract extraction procedure d. Clinic burden of intravitreal injection e. Patient/carer burden of intravitreal injection f. Mean average BCVA (area under the curve) g. Mean average CST (area under the curve)	Thank you for your comment. The outcomes in the scope are not intended to be an exhaustive list and appropriate outcomes will be considered by the committee. No action required.
	Macular Society	Yes	Thank you for your comment. No action required.
	Novartis Pharmaceuticals UK Limited	Appropriate.	Thank you for your comment. No action required.

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Economic analysis	AbbVie	The time horizon will be set at a value that is considered sufficiently long to capture all important differences in costs and outcomes, specifically in terms of reaching (or avoiding) the impact of severe visual impairment.	Thank you for your comment. No action required.
	Alimera Sciences Ltd.	15. **Tighter emphasis on real-world clinical practice and patient reported outcome measures.** It is difficult to comment upon the economic analysis until we know the type of new data for the product in question. It would be beneficial to place tighter emphasis upon healthcare resource use, patient reported outcome measures (rather than just BCVA/CRT) and real-world comparison due to the frequency of injections required for suggested anti-VEGF comparators that may not be injected in line with evidence and SPC in the real world. The latter point is especially relevant in light of the COVID-19 backlogs mentioned in point 4.	Thank you for your comment. This section of the scope is intended to outline the broad approaches that need to be considered. Evidence submissions can elaborate on how the data will be used in the economic analysis. No action required.
Equality and Diversity	AbbVie	The proposed scope and remit do not exclude any people protected by the equality legislation, lead to a recommendation that has a different impact on people protected by equality legislation than on the wider population or lead to recommendations that have an adverse impact on people with a particular disability or disabilities.	Thank you for your comment. No action required.
	Alimera Sciences Ltd.	16. **The recently published PHE Atlas of variation in risk factors and healthcare for vision in England[xiii] highlights some very important trends meaning patients with DMO may have been adversely impacted by the favouring of anti-VEGF drugs treatment in DMO phakic patients.** Since the onset of the coronavirus (COVID-19) pandemic in March 2020, clinical risk stratification has prioritised patients receiving treatment with anti-VEGF drugs (new and ongoing) for high-risk conditions such as wet	Thank you for your comment. Issues related to COVID-19 are not considered equalities issues under the Equality Act 2010. Where relevant and appropriate, protected

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		AMD, above all other indications. Patients classified as having medium and low risk clinical conditions had their management delayed or rescheduled for at least 3 to 6 months later. This is reflected in the significant reduction in intravitreal injection therapy activity. Patients who need intravitreal injection therapy are more likely to have been classified as being clinically vulnerable to COVID-19 infection or shielding due to systemic comorbidities or their age. Patients may also have been reluctant to attend a hospital clinic especially during the first wave (and possibly subsequent waves). A pronounced drop in first injection activity was seen and could also be attributed to the rescheduling of treatment for new patients presenting with medium and low risk retinal conditions for several months later. Subsequent waves not reported in the vision Atlas of Variation will have only added to the delays and backlog particularly in the management of retinal conditions other than AMD. 17. ***"New pathways developed to manage the backlogs should be reviewed for their impact on mitigating risk for irreversible disease progression; reducing delays and acceptability to patients."***[12] The above should be taken into account in ID3951 as patients may have faced irreversible damage to the retina if they did not receive the correct frequency of anti-VEGF injections, whether phakic or pseudophakic. Access to longer acting implanted steroid treatment (irrespective of lens function) may have reduced the risk of this potential harm. 18. **Limited access to cataract surgery during the COVID-19 pandemic[xiv,12] further complicated the access to treatment issues outlined in point 16 for *phakic* DMO patients**. They may have been unable to access frequent enough anti-VEGF treatment to prevent irreversible deterioration in retinal function, but they may also have been denied access to a switch to a long-acting steroids due to their	characteristics as stated in equality legislation will be considered by the committee during the appraisal. No action required.

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		phakic lens status after the recommendations of TA349 and TA613. This may have increase the risk of irreversible DMO disease progression for phakic patients who did not receive their anti-VEGF treatment. ID3951 should take into account the adverse impact previous TA decisions for phakic DMO patients may have had during the COVID-19 pandemic. 19. **It is with reference to the above this adverse impact that Alimera Sciences believe NICE should approach ID3951 with urgency in their timelines.**	
	Roche Products Limited	If a person is registered as blind or partially sighted they are considered disabled, as stated in the Equality Act 2010. Therefore, the patient population addressed in this submission is a protected group under this act.	Thank you for your comment. Where relevant and appropriate, protected characteristics as stated in equality legislation will be considered by the committee during the appraisal. No action required.
Other considerations	Macular Society	Aflibercept has not been included as a possible previous treatment.	Thank you for your comment. Aflibercept has been added as a possible prior treatment.
	Roche Products Limited	The availability and cost of biosimilar and generic products should be taken into account in any future appraisal of dexamethasone.	Thank you for your comment. Reference to the availability and cost

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		Aflibercept should be included in the 'previous treatment history' subgroup bullet. Disagree with the inclusion of patients without prior treatment, as dexamethasone should not be offered under those conditions. Laser photocoagulation would be more appropriate should a patient be contraindicated for anti-VEGF, the standard of care.	of biosimilar and generic products has been added. Aflibercept has been added as a possible prior treatment. The comparators and standard clinical practice will be considered by clinical experts as part of the appraisal process if the topic is referred for appraisal.
Innovation	AbbVie	Dexamethasone intravitreal implant has a mechanism of action that targets the multifactorial pathophysiology of DMO. This allows for approximately 6 months of corticosteroid treatment through a single intravitreal application. As such, DEX700 has a longer duration of action compared with the anti-VEGFs. In addition, DEX700 has a flexible retreatment criterion, allowing the optimization of treatment frequency based on the individual patient need. Further to this, patients with phakic DMO who are unsuitable for treatment with non-corticosteroids have no available pharmacotherapy treatment options and are treated with watch-and-wait; therefore, Dexamethasone intravitreal implant provides a pharmacological treatment option for these patients. For patients with phakic DMO who are insufficiently responsive to treatment with non-corticosteroids, Dexamethasone intravitreal implant offers a treatment option that improves patient outcomes and decreases the burden on patients and healthcare systems.	Thank you for your comment. The innovative nature of the technology will be considered by the appraisal committee based on evidence presented to it. No action required.

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		Dexamethasone intravitreal implant requires less frequent injections than current treatment options. A therapy requiring less frequent injections reduces the treatment burden on patients, thereby improving patient compliance and patient quality of life.[3] A reduction in the number of injections also will also reduce the resource use burden.[3] No, potential significant health related benefits are unlikely to be to be missed in the QALY calculation. 1. Data specific to phakic population from the MEAD trial 2. Ozurdex RWE collected since TA349 showing comparable outcomes in phakic and pseudophakic, data on benefits of early switch to Ozurdex from the anti-VEGF insufficiently responsive groups 3. Data from UK clinical practice on continued use of anti-VEGF.	
	Alimera Sciences Ltd.	20. **See comment 12.** Use of long-acting steroid implants for phakic DMO patients may assist clinics dramatically reduce the number of treatment visits, irrespective of a patients lens status, when compared to anti-VEGF treatment. 21. **See TA613, under 'Innovation 3.17'. The same could be concluded for dexamethasone implant, irrespective of lens status** (*"the clinical experts stated that the fluocinolone acetonide intravitreal implant would be a substantial change in treating diabetic macular oedema in phakic eyes with symptomatic cataract because the long-lasting effect reduces the need for repeated treatment and reduces treatment and follow-up burden."*	Thank you for your comment. The innovative nature of the technology will be considered by the appraisal committee based on evidence presented to it. No action required.

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		22. **Recent consensus guidelines published for the UK state:[5] *"these [DEX and FAc] implants require injection considerably less frequently than anti-VEGF**, their use can help clinics dramatically reduce the number of treatment visits needed. Although this is always welcome to ease capacity issues, it is especially valuable during a pandemic when clinics need to limit the number of patients in the clinic and the number of invasive procedures performed."*[5]	
	Macular Society	This technology is not innovative but the revision to the TA would expand the number of patients who could benefit. As younger patients are more likely to be phakic it would be younger patients who would benefit the most.	Thank you for your comment. The innovative nature of the technology will be considered by the appraisal committee based on evidence presented to it. No action required.
Questions for consultation	Alimera Sciences Ltd.	23. **Have all relevant comparators for dexamethasone intravitreal implants been included in the scope?** No. Please see points 12 & 13 above. 24. **Which treatments are considered to be established clinical practice in the NHS for diabetic macular oedema in people without a pseudophakic lens?** Please see points 12 & 13 above. **Does this differ for those with a central retinal thickness of less than 400 micrometres?** Please see point 6. NICE TA613 identified that the fluocinolone acetonide intravitreal implant can also be used in sub-400 microns as there is no restriction on the CRT value in the indication for this product.	Thank you for your comment. Please see responses in the relevant sections above. No action required

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		25. **Are the outcomes listed appropriate? Should disease severity and intraretinal and subretinal fluid be included as outcomes?** Please see point 14. We don't believe intra/subretinal fluid are as important as other factors listed (a) to (g). 26. **Are the subgroups suggested in 'other considerations appropriate? Are there any other subgroups of people in whom dexamethasone intravitreal implants are expected to be more clinically effective and cost effective or other groups that should be examined separately?** Please see the additional clarity on lens status requested in point 11. Without an understanding of the patients in the new data that triggered ID3951 we are unable to comment on subgroups. 27. **Where do you consider dexamethasone intravitreal implants will fit into the existing NICE pathways, Identifying and managing complications in adults with type 1 diabetes: eye disease and Identifying and managing complications in adults with type 2 diabetes: eye disease?** Both of these pathways need considerable development for DMO and omit a large amount of available clinical data and consensus on clinical practice in DMO. We would recommend that both guidelines produced by clinical opinion leaders in point 13. Adoption of these guidelines into NICE Pathways may help avoid some of the heightened barriers to steroid treatment outlined in both these publications that have been emphasised by the COVID-19 pandemic. 28. **NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others.**	

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		Please see comments on discrimination and adverse impact on DMO patients described in points 16-19. 29. **Do you consider dexamethasone intravitreal implants to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?** Yes. See points 20-22 30. **Do you consider that the use of dexamethasone intravitreal implants can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?** Please see comments requesting further information on the new data in points . We are unable to offer opinion until we understand the approach taken in the new study. 31. **Would it be appropriate to use the cost comparison methodology for this topic?** No comment. 32. **Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?** Yes. Please see comments in points 12 & 13. 33. **Is the primary outcome that was measured in the trial or used to drive the model for the comparators still clinically relevant?** It is impossible to comments because the trial and data used in the model are not outlined. See points 10 & 11. 34. **Is there any substantial new evidence for the comparator technologies that has not been considered?**	

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		Yes. Please see points 12 & 13. This RWE should be build into any comparison/CEA model, and fluocinolone acetonide intravitreal implant should be included as a comparator.	
	Novartis Pharmaceuticals UK Limited	**Which treatments are considered to be established clinical practice in the NHS for diabetic macular oedema in people without a pseudophakic lens? Does this differ for those with a central retinal thickness of less than 400 micrometres?** Standard of care for people without a pseudophakic lens (people with a phakic lens) are licensed anti-VEGF therapies, ranibizumab and aflibercept. NICE only recommends current anti-VEGF therapies in patients with a CRT greater than 400 micrometers. **Are the outcomes listed appropriate? Should disease severity and intraretinal and subretinal fluid be included as outcomes?** Anatomical outcomes such as subretinal fluid and intraretinal fluid or cyst would be appropriate for inclusion.	Thank you for your comment. The outcomes in the scope are not intended to be an exhaustive list and appropriate outcomes will be considered by the committee. No action required.
	Roche Products Limited	Are there any other subgroups of people in whom dexamethasone intravitreal implants are expected to be more clinically effective and cost effective or other groups that should be examined separately? DRCR.net Protocol U study, found the addition of dexamethasone to ranibizumab treatment compared with ranibizumab alone, in patients who were suboptimal responders to anti-VEGF, failed to provide any significant difference to the primary outcome for visual acuity; including the population included phakic eyes.	Thank you for your comment. No action required.

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Additional comments on the draft scope	Roche Products Limited	The second line positioning of dexamethasone is consistent with its evidence base. Roche is not aware of robust data demonstrating an overall clinical benefit over and above that provided by existing first-line agents	Thank you for your comment. No action required.