

**National Institute for Health and Care Excellence**  
**IP1087 High-intensity focused ultrasound for glaucoma**  
**IPAC 11/07/19**

Com . no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
1	Consultee 1 Company EYE TECH CARE	<b>Specialist advice</b>	<p>Specialist advisor – Gus GAZZARD (Royal College of Ophthalmologist (RCO))</p> <p>7.1 Other information. -&gt; Conflict of interests in all paper authors</p> <p>Seven studies were selected by NICE in the literature review conducted in January 9th, 2019. There is no “conflict of interest” vis-à-vis the manufacturer for the authors listed below:</p> <ul style="list-style-type: none"> <li>- Giannaccare G (Ref #4 and #5) – Graefe’s archive for Clinical and experimental Ophthalmology 2017 / Ophthalmic research 2018</li> <li>- De Gregorio A (Ref #6) - Graefe’s archive for Clinical and experimental Ophthalmology 2017</li> </ul>	<p>Thank you for your comment.</p> <p>The specialist adviser’s comments about conflicts of interest are considered by the committee alongside their review of the evidence summarised in the overview, and the committee also has access to the full-text papers described in table 2 of the overview.</p> <p>The overview states that there is no conflict of interest for the 3 studies cited. This was based on the information provided in these journal articles which did not declare any conflicts of interest.</p>
2	Consultee 1 Company EYE TECH CARE	<b>Specialist advice</b>	<p>Specialist advisor – Kin Sheng LIM (Royal College of Ophthalmologist (RCO))</p> <p>4.2 Efficacy outcome for HIFU procedure. -&gt; Poor. Less than 15% reduction of pressure at 3 months from baseline (both wash-out pressure)</p>	<p>Thank you for your comment.</p> <p>The specialist adviser’s comments are considered by the committee alongside their</p>

			<p>Results cited by the advisor are not in line with those published in the literature selected by NICE wherein mean IOP reduction ranged between 22% and 36% at month-3, month-6 or month-12.</p> <p>Moreover, Posarelli et al (see below) published in May 2019 a review of efficacy results on HIFU with similar results with IOP reduction between 26% and 36%, 6, 12 and 24 months after HIFU procedure.</p> <p>Likewise, Torky et al published in April 2019 a mean IOP reduction at 1 year of 42%.</p> <p>None of the authors in the latter references have any conflict of interest in regard to the product.</p> <p>The low efficacy observed by Lim et al might be due the fact that 60 % of the 30 patients enrolled were of African origin whereas any other study published so far had been conducted with Caucasian and Asian patients.</p> <p>Ref: Posarelli et al. High Intensity Focused Ultrasound (HIFU) procedure: the rise of a new non-invasive glaucoma procedure and its possible future applications. <i>Surv Ophthalmol</i> 2019 May 21. doi: 10.1016/j.survophthal.2019.05.001. [Epub ahead of print]</p> <p>Ref: Torky et al. Safety and Efficacy of ultrasound ciliary plasty as a primary intervention in glaucoma patients. <i>Int J Ophthalmol</i> 2019 Apr 18. Doi: 10.18240/ijo.2019.04.12</p>	<p>review of the evidence summarised in the overview.</p> <p>The review article by Posarelli et al. (2019) has been added to the appendix of the overview.</p> <p>The case series by Torky et al. (2019) was identified in the updated literature search and has been added to table 2 of the overview.</p>
3	<p>Consultee 1 Company EYE TECH CARE</p>	<p><b>Specialist advice</b></p>	<p>NICE Guidance draft Specialist adviser's opinion</p> <p>EYE TECH CARE welcomes feedback from consultants about its HIFU procedure for glaucoma as part of the NICE Guidelines process. As stated in the "interventional procedures guidelines", specialist advisers provide advice and give their personal opinion that complements findings from published studies selected during the literature review conducted in January 2019.</p> <p>Among the NHS experts contributing herein: one has performed just four procedures; another used exclusively the first-generation product and has not conducted a HIFU treatment since 2014; and a third adviser's experience is limited to scientific research whereby the majority of patients</p>	<p>Thank you for your comment.</p> <p>Specialist advisers are nominated by the relevant specialist society.</p> <p>For this procedure, 6 specialist advisers were nominated by either the UK and Éire Glaucoma Society or the Royal College of Ophthalmologists, and 3 questionnaires were received.</p>

			<p>enrolled were made up predominantly of non-Caucasian origin (African or of African descent) where it is widely documented that glaucoma is more challenging to treat.</p>	<p>NICE seeks specialist advisers who have a range of experience with the procedure. Their role is to provide their opinion about interventional procedures and not to advise on the published research. The latter is summarised in the overview and assessed independently by IPAC.</p> <p>The committee notes your comments about the specialist advisers.</p>
4	<p>Consultee 1 Company EYE TECH CARE</p>	<p><b>Section 1</b></p>	<p>Evidence on safety and efficacy of High Intensity Focused Ultrasound is inadequate in quality and quantity. Therefore, this procedure should be used only in the context of research Specialist</p> <p>Since the review of the literature for IP1087, new evidence of the efficacy and safety of HIFU has been published (see below) and further manuscripts are in preparation. EYE TECH CARE believes this evidence added to existing studies should be considered by NICE in the review process.</p> <p>The fact that the company has to date focused limited effort in the clinical research and marketing of the procedure in the UK should not obscure the fact that over 10,000 glaucoma treatments have been carried out worldwide using HIFU, and more than 20 papers in peer-reviewed journals have been published by researchers from three continents.</p> <p>The company wishes to point out that:</p> <ul style="list-style-type: none"> <li>- HIFU technology is being used in an ever-growing number of medical specialties for a plethora of indications (ref. <a href="https://www.fusfoundation.org/the-technology/overview">https://www.fusfoundation.org/the-technology/overview</a>)</li> </ul>	<p>Thank you for your comment.</p> <p>The review article by Posarelli et al. (2019) has been added to the appendix of the overview.</p> <p>The case series by Torky et al. (2019) was identified in the updated literature search and has been added to table 2 of the overview.</p>

			<p>- Our technique, marketed under the name Ultrasound Cyclo Plasty), is the second iteration of treatment by HIFU. The first device marketed under the name of Sonocare (Sonocare Inc.) in the 1980's and 1990's, although eventually discontinued, was FDA-approved.</p> <p>EYE TECH CARE is at NICE's disposal to provide the required information and to assist in the review.</p> <p>References</p> <p>Posarelli et al. High Intensity Focused Ultrasound (HIFU) procedure: the rise of a new non-invasive glaucoma procedure and its possible future applications. <i>Surv Ophthalmol</i> 2019 May 21. doi:10.1016/j.survophthal.2019.05.001. [epub ahead of print]</p> <p>Torky et al. Safety and Efficacy of ultrasound ciliary plasty as a primary intervention in glaucoma patients. <i>Int J Ophthalmol</i> 2019 Apr 18. Doi: 10.18240/ijo.2019.04.12</p>	
5	Consultee 2 International Expert on Glaucoma	1.1	<p><b>Section 1: Evidence on safety and efficacy of High Intensity Focused Ultrasound is inadequate in quality and quantity. Therefore, this procedure should be used only in the context of research.</b></p> <p>With regards to the HIFU procedure for glaucoma:</p> <ol style="list-style-type: none"> <li>1. Our department has performed over 400 procedures since 2012. We consider it to be routine option in the treatment of glaucoma for patients who are refractory to medication and/or surgery or who are poor candidates for surgery with a high risk of complications.</li> <li>2. At the French National Ophthalmology Meeting in May 2019 we presented 3 years follow-up from two centers in France on the 2nd generation HIFU product which has been commercially available since April 2015. A total of 104 patients with 58% having Primary Open Angle Glaucoma and 31% having secondary OAG were enrolled with 36 months follow-up being available for 74 patients. 49% of the patients had previous filtering surgery, 28% laser trabeculoplasty. The average IOP baseline was 27.6 +/- 8.9 mmHg on 3.0 medications. With regards to serious complications no phthisis was observed, 3% had transient hypotony, 3% macular edema and 5% corneal edema. Mild mydriasis occurred in 17% of the patients, hyperemia/chemosis in 30%, 40% had transient inflammation of the anterior chamber and 63% had keratitis. Efficacy at 36 months follow-up was found to be an average IOP of 17.0 +/- 6.8 mmHg corresponding to</li> </ol>	<p>Thank you for your comment and summarising the findings presented at the French meeting in May 2019.</p> <p>Conference abstracts are not normally considered adequate to support decisions on efficacy and are not generally selected for presentation in the overview, unless they contain important safety data.</p> <p>Procedures with 'research only' recommendation may be reassessed when relevant new research is published.</p>

			<p>a 33% reduction versus baseline. Medication was slightly reduced to 2.8. The response rate defined as IOP reduction greater than 20% without additional medication was 55% at 36 months.</p> <p>These results are currently being prepared for publication in an international journal and they are consistent with previously published series of patients</p>	
6	<p>Consultee 3 Royal College of Ophthalmologists</p>	<b>Overview</b>	<p>Please use correct acronym for The Royal College of Ophthalmologists, it should be RCOphth not RCO.</p>	<p>Thank you for your comment. We apologise for this error. The acronym will be changed in the overview.</p>
7	<p>Consultee 4 The College of Optometrists</p>	<b>General</b>	<p>Cases of glaucoma and glaucoma-related conditions are often identified through routine NHS Sight Tests or Private Eye Examinations by community optometrists. These cases have traditionally been referred to the Hospital Eye Service for further investigation and currently are referred into triage or referral refinement services. Community optometrists need to be involved of changes of treatment plan. There are a growing number of optometrists who support the provision of glaucoma services in community and hospital settings, including monitoring and management of low and medium risk people affected by glaucoma. Independent prescribing optometrists with the highest level specialist training, competence and experience may also be prescribing treatments for glaucoma.</p>	<p>Thank you for your comment.</p>

*"Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees."*