# National Institute for Health and Care Excellence

# IP1733 Swallowable gastric balloon capsule for weight loss

**IPAC dates: 14/05/20 and 13/08/20**

| Com. no. | Consultee name and organization | Sec. no. | Comments | Response<br>Please respond to all comments |
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| 1 | Consultee 1<br>NHS professionals<br>British Dietetic Association | **1** | 1.1 We are in agreement with this recommendation. The evidence at present is of low quality and lacks direct comparison with best practice.<br><br>1.2 Agree with recommendation. It appears that although there is short term weight loss, the evidence showing long term maintenance is limited and therefore further research is required. We would suggest it would be good for research to include groups of patients that need rapid weight loss for other procedures such as fertility treatment/IVF, transplantation or orthopaedic operations. | Thank you for your comments.<br>IPAC considered the suggestion regarding the groups of interest in future research but decided not to amend 1.3 as there may be many other groups who need rapid weight loss. The committee agreed for research purposes all groups who need rapid weight loss need to be assessed. |
| 2 | Consultee 1<br>NHS professionals<br>British Dietetic Association | **2.1** | 2.1 We support the use within people with overweight or obesity however please note that overweight is defined to BMI 29.9 kg/m2 and not 30kg/m2 as this is the threshold for obesity. “Long-term survival” is not a typical phrase, we would therefore suggest alternative phrasing. | Thank you for your comments.<br>IPAC considered your comment and amended 2.1. |
| 3 | Consultee 1<br>NHS professionals<br>British Dietetic Association | **2.2, 2.3** | 2.2 "It’s considered only if they have not lost enough weight using non-surgical measures. Surgical procedures aim to help people lose weight either by restricting the size of the stomach, for example, gastric banding or sleeve gastrectomy, or by reducing someone’s capacity to absorb food, for example, Roux-en-Y gastric bypass or other diversion procedures, or | Thank you for your comments.<br>.<br><br>IPAC considered your comment and amended 2.2 and 2.3. |

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| | | | both"<br><br>We appreciate that NICE are trying to use lay terms but we do not agree with this wording. Bariatric surgery is considered if the patient has not achieved or maintained adequate, clinically beneficial weight loss. Procedures such as sleeve gastrectomy and Roux-en-y gastric bypass affect the physiology and gut hormone response so that people feel less hungry and are satiated sooner. Absorption of micronutrients is affected following the sleeve gastrectomy and Roux-en-y gastric bypass but there is no malabsorption of fat, protein or carbohydrate unless the person has had a long limbed bypass. The mechanism of action is not by food malabsorption.<br><br>2.3 “minimally invasive”. Sleeve gastrectomy, gastric band and Roux-en-y gastric bypass have been performed by laparoscopic minimally invasive procedures for years. Endoscopic intragastric balloons, gastrointestinal bypass sleeves, endoscopic sleeve gastroplasty and endoluminal restrictive surgical techniques are undertaken by endoscopy which is not classed as a minimally invasice procedure to my knowledge. We are unaware of evidence for the statement “induce weight loss by increasing satiety, reducing the amount of food eaten or absorbed (or both), and delaying gastric emptying”. | |
| 4 | Consultee 1<br>NHS professionals<br>British Dietetic Association | **2.4** | 2.4 We are in agreement that the swallowable gastric balloon be used in conjunction with supervised nutrition and behaviour modification programme. We recommend that this should be a qualified, registered healthcare professional and preferably a registered dietitian. In addition we would suggest recommending follow-up up to 12 months. “Swallowable gastric | Thank you for your comment.<br>This section of the guidance is intended to be a brief summary description of the way the procedure is typically done.<br>IPAC considered your comment and amended 2.4. |

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| | | | balloon capsule for weight loss is a minimally invasive procedure". This is incorrect. There are no surgical incisions. | |
| 5 | Consultee 1<br>NHS professionals<br>British Dietetic Association | **3.5** | 3.5 We are in agreement with this comment it would benefit from clarity what you mean by "surgery". Does this mean bariatric surgery or other surgeries such as hip operations or transplantation? In addition we feel other areas could be included such as IVF/fertility, all referral criteria have a weight related limit on access to the service. | Thank you for your comment.<br>IPAC considered your comment about adding clarity to the statement in 3.5 and amended it. |
| 6 | Consultee 2<br>Company<br>Allurion | | We are disappointed the Committee continues to recommend that the Elipse "Swallowable Gastric Balloon Capsule" should only be used in the context of research.<br>We wish to provide additional evidence that demonstrates Allurion's Elipse balloon safety and clinical effectiveness including sustained weight loss. We therefore present data from 4 additional studies that have been completed during the development of this IPG.<br>Please note that the ENLIGHTEN Clinical Study Report is HIGHLY CONFIDENTIAL. We are willing to share this with the committee as it provides the highest (level 3) clinical data that the committee is looking for. However, as per FDA guidance, this should not be published or enter the public domain.<br>1. **ENLIGHTEN Clinical Study Report (2020)**.<br>A Randomized, Multi-Center, Phased, Pivotal, Safety and Efficacy Study Comparing the Elipse Gastric Balloon System vs Sham for the Treatment of Obese Adults -A double-blind study conducted in 416 subjects in USA. *Submitted to FDA for PMA approval in USA.* | Thank you for your comments and providing additional evidence.<br>**Ienca et al (2020) study of 1770 patients** (published online) is added to table 2 in the overview. IPAC reviewed the new evidence, considered comments and amended recommendations in section 1.1.<br>**Enlighten clinical study report (2020)** is an unpublished RCT study comparing Elipse gastric balloon versus sham. .<br>**Ienca et al IFSO 2020 of 509 patients and Raftopoulos et al (2019)** are conference abstracts only. These are not normally considered adequate to support decisions on efficacy unless they contain important safety data. The safety outcomes reported in these abstracts are those which are described in the available evidence (Ienca et al 2020).<br>Studies that have not been published or accepted for publication by peer review are not normally selected for presentation to the Committee. Therefore, the above studies are not included in table 2 of the |

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| | | | 2. **Ienca et al (2020**). The Procedureless Elipse Gastric Balloon Program: Multicenter Experience in 1770 Consecutive patients. -A multicenter, prospective, non-randomised, open label registry study with 1,770 patients (*in press Obesity Surgery, 2020).*<br>3**. Ienca et al (2020) Abstract**. Elipse Gastric Balloon System for Weight Loss: Short and Long-Term Multicenter Results in 509 Patients after Balloon Treatment, and 1 Year after Balloon Passage.<br>*Submitted to the International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO) Miami USA July 2020.*<br>4. **Raftopoulos et al (2019) Abstract**. An Intensive 16-week Nutritional, Exercise and Behavior Modification Program: Comparison With or Without the Elipse Intragastric Balloon -A 2-centre study comparing intense medical weight loss (IMWL) plus Allurion Balloon with IMWL alone.<br>*Abstract 1978. Presented at American College of Surgeons Clinical Congress San Francisco, United States, 2019.* | overview. IPAC may review the guidance upon publication of this evidence in peer reviewed journals. |
| 7 | Consultee 2<br>Company<br>Allurion | **1, 3** | **SAFETY**<br>We note the statement made in draft recommendation 1.1 that “the evidence shows infrequent but potentially serious adverse events”. We are concerned that whilst any adverse event is always regrettable the actual numbers of patients that experience such events following treatment with Elipse are, given the significant health issues these patients already face, within reasonable and expected limits. | Thank you for your comments and providing additional evidence.<br>**Ienca et al 2020 study of 1770 patients** (published online) is added to table 2 in the overview.<br>IPAC reviewed the new evidence, considered comments and amended recommendations in section 1.1. |

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| | | | The additional evidence included in this consultation response provides new data to show the small numbers of SAEs across 3 studies that enrolled a very significant number of patients, including the ENLIGHTEN study. We ask that the Committee carefully evaluate their recommendation both in the light of this new evidence and the studies already included in the draft IPG.<br>**Ienca et al (2019)** collected data from 1770 consecutive patients in a large multi-center population who had started treatment with an Elipse Balloon. Mean weight at baseline was 94.6 ± 18.9 kg and mean BMI 34.4 ± 5.3kg/m2.<br>Safety was measured via the prospective collection of adverse event and complication data associated with the use of the Elipse System in the 19 participating centers. All patients had to have previously failed dietary treatments.<br>The following complications were reported.<br>• 3/1770 patients (0.17%) with small bowel obstruction (all occurring in 2016 with a previous version of the Elipse balloon, none with the current version)<br>• 52/1770 patients (2.9%) with intolerance requiring endoscopic removal<br>• 11/1770 (0.6%) with early balloon deflation<br>• 1/1770 patient (0.06%) with gastric perforation - laparoscopic surgical repair<br>• 1/1770 patient (0.06%) with oesophagitis - endoscopic removal | **Enlighten clinical study report (2020)** is an unpublished RCT study comparing Elipse gastric balloon versus sham. **Ienca et al IFSO 2020 of 509 patients and Raftopoulos et al (2019)** are conference abstracts only. These are not normally considered adequate to support decisions on efficacy unless they contain important safety data. The safety outcomes reported in these abstracts are those which are described in the available evidence (Ienca et al 2020).<br>Studies that have not been published or accepted for publication by peer review are not normally selected for presentation to the Committee. Therefore, the above studies are not included in table 2 of the overview. IPAC may review the guidance upon publication of this evidence in peer reviewed journals. |

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| | | | • 1/1770 patient (0.06%) with pancreatitis - endoscopic removal<br>• 1/1770 patient (0.06%) with gastric outlet obstruction - endoscopic removal<br>• 1/1770 patient (0.06%) with delayed intestinal balloon transit<br>• 1/1770 patient (0.06%) with gastric dilatation - resolved by 24hr liquid diet<br>• 4/1770 spontaneous balloon hyperinflations.<br><br>Authors of this prospective study of obese patients concluded that on the basis of this data the Elipse Balloon demonstrated an excellent safety profile.<br><br>**ENLIGHTEN Clinical Study Report**. This important and significant randomized double-blind trial that compared Elipse with a sham treatment in adults with a body mass index [BMI] between 30 and 40 kg/m2. These patients had been unsuccessful in losing weight within the 24 months prior to enrollment, but were otherwise generally healthy. The study's objective was to evaluate both the safety and effectiveness of Elipse balloon.<br>This study enrolled 416 subjects who were randomized 2:1 to either receive Elipse or a sham procedure. After 24 weeks, patients in the Sham group were able to cross over to the Elipse arm. All subjects were followed up for 48 weeks after initial placement procedure.<br>Information provided in-confidence to NICE [redacted] | |

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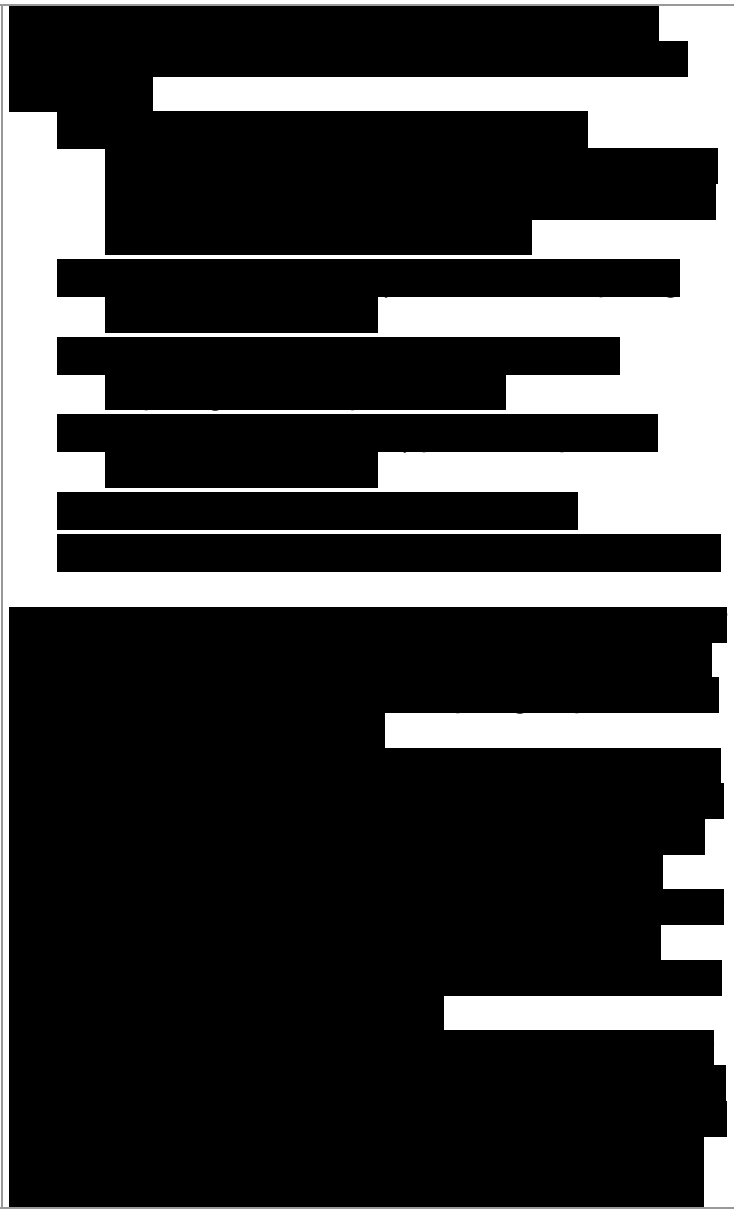
| | | |  | |

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| | | | [redacted] This contrasts with the findings of a meta-analysis of 80 studies involving 8506 patients receiving a traditional Orbera endoscopic intragastric balloon. The rate of obstruction for Orbera endoscopic balloon patients was 0.3%[i].<br>**Ienca et al (2019 Abstract)** evaluated the short and long-term efficacy of Elipse at 4 months and 1 year after balloon passage for 509 patients in 9 centres. Mean weight and BMI before the procedure were 102.6 ± 21.3kg and 35.9 ± 5.8kg/m2.<br>This abstract listed the following observed adverse events<br>• 1/509 patient (0.2%) with gastric perforation - laparoscopic surgical repair<br>• 6/509 patients (1.2%) with intolerance requiring endoscopic removal<br>• 1/509 patient (0.2%) with gastric dilation<br>• 1/509 patient (0.2%) with gastritis<br>• 7/509 patients (1.3%) with emesis excretion<br>Authors concluded that for the large size of the patient cohort included in this data there were very few adverse events.<br><br>The MHRA system recorded 2 alerts. One in 2016 was device related and another in 2018 related to the filler kit. No details are available. | |
| 8 | Consultee 2<br>Company<br>Allurion | **3.3** | **Adverse Events evaluated during drafting of the IPG.**<br>We recognise that studies report patients experiencing nausea and vomiting and note that | Thank you for your comments.<br>**IPAC removed 'nausea and vomiting' as key safety outcomes from section 3.3 in** |

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| | | | professional experts and the committee considered these to be key safety outcomes. We appreciate these are unpleasant symptoms for patients, but we are unclear why these are viewed as a safety issue as these are inherent to all intragastric balloons. The vast majority of these events are mild and transient in nature and resolve within 1 week. These are generally well controlled with liquid diet or medications. In rare instances, at the end of residence time, the Elipse balloon may be vomited instead of passing. Although startling to the patient, this occurrence has not been associated with any reported adverse events. Given that these events are mild and transient, and not associated with any adverse events, we would like to suggest that these are removed as a safety outcome.<br>We recognise that gastrointestinal obstruction and perforation would be considered safety outcomes.<br>We agree that early balloon deflation would prevent patients from receiving the full course of therapy<br>Having reviewed the relevant data summarised in the IPG overview document we ask the committee to re-examine the number, and severity of the adverse events presented to them, as we believe they would generally be considered to lie well within acceptable limits. We take this view in part due to the ASGE and American Society for Metabolic and Bariatric Surgery having stated that when balancing risk against efficacy the risk associated with alternative, but endoscopic bariatric therapies should equate to a ≤5% incidence of serious adverse events[i].<br>We represent the data related to untoward events, and included in the IPG evaluation, here to highlight once again their infrequency. We invite the | **the guidance and added a committee comment related to this in section 3.6.**<br>The **American Society for Gastrointestinal Endoscopy (ASGE) Bariatric Endoscopy Task Force systematic review and meta-analysis** assesses the Preservation and Incorporation of Valuable endoscopic Innovations (PIVI) thresholds for adopting endoscopic bariatric therapies. This document states that 'the 2 endoscopic bariatric procedures (orbera balloon and endobarrier) evaluated had <5% incidence of serious adverse events as set by the PIVI threshold indicating acceptable safety profiles'.<br><br>IPAC reviewed the new evidence, considered comments and amended recommendations in section 1.1. |

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| | | | committee to balance these occurrences against the risk to patients of having no or more invasive interventions.<br>**References**<br>Abu Dayyeh et al (2015) ASGE Bariatric Endoscopy Task Force systematic review and meta-analysis assessing the ASGE PIVI thresholds for adopting endoscopic bariatric therapies. Gastrointestinal Endoscopy 82(3) 425-438.<br><br>Al-Sabah.<br>• 1/135 patient (0.7%) small bowel obstruction<br>• 1/135 patient (0.7%) intolerance requiring endoscopic removal<br>• 3/135 patients (2.2%) with early balloon deflation<br>• 1/135 patient (1.5%) with emesis excretion<br><br>Jamal MH.<br>• 1/112 patient (0.9%) small bowel obstruction<br>• 6/112 patients (5.4%) intolerance requiring endoscopic removal<br>• 3/112 patients (2.7%) with early balloon deflation<br>• 6/112 patients (5.4%) with emesis excretion<br>Al Sabaie.<br>• 5/51 patients (9.8%) intolerance requiring endoscopic removal<br>• 1/51 patients (2%) with early balloon deflation<br>• 1/51 patients (2%) with emesis excretion<br><br>Genco. | |

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| | | | • 1/38 (2.63%) endoscopic removal due to binge eating.<br><br>Machytka (2017).<br>• 2/34 patients (5.88%) intolerance requiring endoscopic removal<br>• 4/34 patients (12%) with emesis excretion | |
| 9 | Consultee 2<br>Company<br>Allurion | **3** | **Sustained Weight Loss**<br>The draft IPG raised questions about the degree of evidence for sustained weight loss. We recognise that Jamal et al's paper (112 patients) was the only one included in the evaluation with 12 month + follow-up. We ask the committee to look again at this study as it showed that at last day of follow up, which was at least a year from the time of balloon excretion and a mean of 19.6 months, weight loss had been maintained in 72% of the patients. Importantly, patient's average weight in kg and average BMI kg/$m_2$ had both reduced statistically from baseline (p=0.014 & p=0.001).<br>Three of the additional studies included in this response provide further evidence that the weight loss achieved by patients following treatment with Elipse is maintained in the longer term and we ask that the Committee consider this new evidence.<br>**ENLIGHTEN Clinical Study Report**<br>This study's co-primary effectiveness endpoints were first measured at 16 weeks and the intent to treat population was the primary population for analysis.<br>Information provided in-confidence to NICE [redacted] | Thank you for your comments.<br>**IPAC reviewed the new evidence, considered comments and amended recommendations in section 1.1.**<br>.<br>**Enlighten clinical study report (2020)** is an unpublished RCT study comparing Elipse gastric balloon versus sham.<br>**Ienca et al 2020 (of 509 patients) and Raftopoulos et al 2019** are conference abstracts and are not considered adequate to support decisions on efficacy unless they contain important safety data. The safety outcomes reported in these abstracts are those which are described in the available evidence (Ienca et al 2020).<br><br>Studies that have not been published or accepted for publication by peer review are not normally selected for presentation to the Committee. Therefore, the above studies are not included in table 2 of the overview. IPAC may review the guidance upon publication of this evidence in peer reviewed journals. |

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| | | | [redacted]<br>**Ienca et al (2020 Abstract)**<br>One year follow up data was available for 509 patients. After 4 months of treatment, weight loss, % Total Body Weight Loss (TBWL), % Excess Weight Loss (EWL) and BMI loss (BMIL) were 14.4 ± 7.7kg, 13.9 ± 6.4%, 55.5 ± 36.9% and 5.1 ± 2.6kg/m2 respectively. One year after balloon passage, weight loss, %TBWL, %EWL and BMIL were 14.1 ± 11.7kg, 13.3 ± 9.9%, 50.8 ± 44.0% and 4.9 ± 4.0kg/m2 respectively.<br>These results show that for this large cohort of patients, 95% of %TBWL was maintained at 12 months after balloon passage.<br>**Raftopoulos et al (2019).** This study, currently published as an abstract, makes an important contribution to the evidence of Elipse's effectiveness in both the short and [i] Abu Dayyeh et al (2015) ASGE Bariatric Endoscopy Task Force systematic review and meta-analysis assessing the ASGE PIVI thresholds for adopting endoscopic bariatric therapies. Gastrointestinal Endoscopy 82(3) 425-438.<br>long term due in part to its comparison with patients receiving Intense Medical Weight loss treatment (IMWL). 97 patients received Elipse + IMWL and 413 IMWL alone. | |

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| | | | Statistically significant differences in % TBWL were observed at 16 weeks (p<0.0001) between Elipse + IMWL (14.3%) vs IMWL alone (6.36%).<br>Greater than 10% TBWL was achieved in 85.2% of the Elipse + IMWL group and 8.2% of the IMWL alone (p<0.0001) and 17.1% of the Elipse + IMWL group had a >20% TBWL vs 0.05% of the IBWL group (p<0.0001).<br>At the presentation of the abstract, the authors noted that 12 months after balloon placement the %TBWL for Elipse + IMWL was 13.32%. More importantly, 93% of weight loss was maintained at 1 year for those patients in the Elipse + IMWL group.<br>These statistics provide further evidence of Elipse's ability to support sustained weight loss and we would ask the committee to consider these findings. | |
| 10 | Consultee 2<br>Company<br>Allurion | **1** | **Conclusion**<br>We are disappointed that the draft recommendations suggest that Elipse treatment should only be used in research. We have provided new evidence that demonstrates both safety and long term effectiveness of this product, as well as highlighting the low incidence of adverse events in literature evaluated by NICE. Conventional bariatric surgery and alternative minimally invasive procedures currently used in the NHS have been shown to carry higher risks for patients related to anaesthesia and more invasive methods of device deployment. We therefore ask the Committee to reconsider their draft recommendations. | Thank you for your comments.<br><br>**IPAC reviewed the new evidence, considered comments and amended recommendations in section 1.1.** |
| 11 | Consultee 2<br>Company<br>Allurion | **3** | In addition, I am attaching two extremely relevant publications last week in *Obesity Surgery* that strongly support the efficacy and safety of the Elipse balloon. NICE, in their earlier communication, had specifically | Thank you for your comments.<br>The 2 studies (Ienca 2020, Vantanasiri 2020) have been reviewed by IPAC and |

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| | | | asked for these studies before it could make a stronger endorsement of the Elipse balloon. I respectfully submit these to be reviewed by the committee before their final decision.<br>1. Ienca et al. Multicenter Registry Study of 1770 Elipse patients.<br>2. Vantanasiri et al. Review and Meta-Analysis from Mayo Clinic of Elipse Studies with a combined 2013 Elipse patients.<br>  Ienca Multicenter Registry Study.pdf  Mayo Clinic Elipse Meta-Analysis Study | then added to table 2 in the overview of evidence.<br><br>**IPAC reviewed the new evidence, considered comments and amended recommendations in section 1.1.** |

*"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."*