NATIONAL INSTITUTE FOR CLINICAL EXCELLENCE

Appraisal of the use of fluid-filled thermal balloon and microwave endometrial ablation techniques for heavy menstrual bleeding

Decision of the panel

1. Introduction

1.1 An appeal panel was convened on 26th January 2004 to consider appeals against the Institute's Final Appraisal Determination (FAD), to the NHS, on the use of fluid-filled thermal balloon (TBEA) and microwave endometrial ablation (MEA) techniques for heavy menstrual bleeding.

1.2 The appeal panel comprised Professor Sir Michael Rawlins (chair of the appeal panel and chair of the Institute), Mercy Jeyasingham (non-executive director), Professor Leon Fine (non-executive director), Gill Donovan (patient representative) and Dr David Webster (industry representative).

1.3 An appeal had been lodged by the following appellant:

- Microsulis Medical Ltd ("MML")

1.4 The appellant was represented by Leading Counsel at the hearing.

1.5 In addition the following individuals involved in the appraisal were present and available to answer questions from the appeal panel: Professor David Barnett (chair of the Appraisal Committee), Dr Carol Longson (Appraisals Programme Director), Professor Robert Shaw CBE (expert advisor to the Appraisal Committee), Dr Sunil Angris (member, Appraisal Committee), Dr Ken Stein (Peninsular Technology Appraisal Group)

1.6 Nina Pinwill (appraisal project manager), Cathryn Fuller and the Institute's legal advisor (Stephen Hocking) were also present.

1.7 The three grounds on which the appeal panel can hear an appeal are:

1) The Institute has failed to act fairly and in accordance with its procedures

2) The Institute has prepared guidance which is perverse in the light of the evidence submitted.

3) The Institute has exceeded its legal powers.

2 Appeal Ground One: The Institute has failed to act fairly and in accordance with the Appraisal Procedure set out in the Institute's Interim Guidance to Manufacturer and Sponsors.

The appellant made no appeal under this ground.

3 Appeal Ground Two: The Institute has prepared guidance which is perverse in the light of the evidence submitted.

3.1 The appellants alleged that there was no clinical, scientific or statistical evidence to support the assumption underlying the guidance that the referral threshold for second-generation endometrial ablation should be the same as that for hysterectomy or first-generation endometrial ablation. MML claimed that, in recommending medical treatment before any form of surgical intervention, the Appraisal Committee had assumed the same threshold of referral for second-generation endometrial ablation was being applied as for hysterectomy or first-generation endometrial ablation.

MML also alleged that FAD 1.1 implied an earlier, non-surgical intervention should always be used before recourse to thermal balloon endometrial ablation (TBEA) or microwave endometrial ablation (MEA). MML proposed that FAD 1.1 should make it clear that second

generation endometrial ablation techniques might sometimes be valid as immediate alternatives to medical intervention.

Professor Shaw agreed that there might, occasionally, be situations where direct referral for surgical treatment was appropriate and Professor Barnett accepted this.

The Appeal Panel reminded itself that the Institute's guidance was advisory and not mandatory. The panel considered it had not been the intention of the Appraisal Committee to deny physicians the opportunity to recommend surgical intervention, without a trial of medical therapy, even though this was not appropriate in most circumstances. The Appeal Panel did not, therefore, consider that the committee had acted perversely.

Nevertheless, the Appeal Panel agreed that there was a real danger that the FAD would not be interpreted consistently with the Appraisal Committee's intentions, and considered that the Appraisal Committee's intentions would be better reflected in the FAD if (as suggested by Professor Barnett) the last part of paragraph 1.1 were to be redrafted as follows:

"Fluid-filled thermal balloon endometrial ablation and microwave endometrial ablation are recommended as treatment options for women with heavy menstrual bleeding in cases where it has been decided (by the woman and the clinician responsible for her treatment) surgical intervention is appropriate for the management of the condition".

The Appeal Panel rejected the appeal on this point but draws the attention of the Guidance Executive to the recommended rewording of FAD 1.1.

3.2 MML alleged that the term "normal menstrual bleeding" in FAD 1.2 was misleading since "normal" in this context is highly subjective and varies from woman to woman.

Professor Shaw accepted this and explained that the term "eumenorrhoea" was rarely used by gynaecologists

outside the context of designing and reporting clinical trials. Professor Barnett agreed that the appellants proposed wording in FAD "reduced menstrual bleeding" would correctly express the Appraisal Committee's intention.

The Appeal Panel did not consider the use of the term "normal menstrual bleeding" perverse and rejected the appeal on this point, but draws the attention of the Guidance Executive to its recommendation that FAD 1.2 is reworded and that "normal menstrual bleeding" is replaced with "reduced menstrual bleeding" in this section. The Appeal Panel also considered that the term "eumenorrhoea" should be removed from FAD 1.2 as well as elsewhere in the document.

The Appeal Panel rejected the appeal on this point but draws the attention of the Guidance Executive to its recommendation that these changes be made.

3.3 MML alleged that the guidance perversely singles out eumenorrhoea as a possible preferred outcome but fails to take account of patient satisfaction even though such satisfaction is a widely used primary outcome in RCTs for heavy menstrual bleeding.

Professor Shaw emphasised that whilst amenorrhoea was the only possible outcome after hysterectomy, the experience of gynaecologists was that some women would prefer to retain their menses if this was possible. Dr Angril concurred with this view. Professor Barnett stated that the Appraisal Committee had had regard to patient satisfaction as a desired outcome of treatment.

The Appeal Panel noted that FAD 1.2 included, in the possible desired outcomes of treatment, both eumenorrhoea and amenorrhoea. The panel did not consider that the Appraisal Committee had acted perversely by including these two possible outcomes, and considered that that it had been aware of the importance of patient satisfaction.

The Appeal Panel dismissed the appeal on this point.

3.4 MML alleged that the FAD wrongly ignores a key factor differentiating MEA from TBEA: namely MEA's application to the vast majority of uteri and TBEA's serious limitations in this regard. Moreover, MML considered that the contraindications on the use of MEA in FAD 3.4 also applied to TBEA.

Professor Barnett explained that the Appraisal Committee had recognised the practical limitations of the use of TBEA, and had expressed these in FAD 3.2. Both he and Professor Shaw, however, agreed that the FAD was in error to have omitted the fact that TBEA, as well as MEA, were both contraindicated in women who had had a classical Caesarean section or if uterine surgery had left a scar where the uterine wall was less than 8 mm thick. Professor Barnett pointed out that in FAD 3.4 the guidance indicated that MEA could be used, successfully, in women with an irregular uterine cavity.

The Appeal Panel did not consider that the Appraisal Committee had been perverse in their consideration of this matter. The panel considered that, in the main, the differences between the procedures had been appropriately described; but that the misstatement in the FAD, should be rectified and that the contraindications to MEA (FAD 3.4) should also be included as contraindications to TBEA (FAD 3.2).

The Appeal Panel rejected the appeal on this point but draws the attention of the Guidance Executive to its recommendation that the misstatement, noted above, be rectified.

3.5 MML alleged that the FAD (2.10) failed to issue proper guidance on the difficulty of use of first generation endometrial ablation techniques.

Professor Barnett explained that the Appraisal Committee considered the comments in FAD 2.10 adequately summarised the difficulties in using first generation

endometrial ablation techniques. Professor Shaw concurred.

The Appeal Panel considered that the summary information in FAD 2.10 satisfactorily explained the position, and that the Appraisal Committee had not perversely underestimated the difficulties involved in the first generation techniques.

The Appeal Panel rejected the appeal on this point.

3.6 MML claimed that the FAD failed to demonstrate an understanding of the science of thermal ablation and the general risk associated with performing endometrial ablation on thin uterine walls.

Noting Professor Barnett's and Professor Shaw's comments in paragraph 3.4 (above), the Appeal Panel concluded that the Appraisal Committee had not been perverse; and considered that the change recommended in paragraph 3.4 would rectify the misstatement.

The Appeal Panel rejected the appeal on this point but draws the attention of the Guidance Executive to its recommendation that the misstatement be rectified.

3.7 In describing the use of priming agents (FAD 3.4), MML claimed that the reason for administration was unconnected with the size of the uterus.

Professor Barnett agreed that this had been incorporated in error, and that the words "particularly if the uterus is large" should be removed.

The Appeal Panel considered that the Appraisal Committee had not acted perversely but that the above words were incorrect and should be removed.

The Appeal Panel rejected the appeal on this point but draws the attention of the Guidance Executive to its recommendation that the error be rectified.

3.8 MML claimed that the analysis of the cost effectiveness data as between TBEA and MEA does not compare like with like. In particular, FAD 3.7 includes only the capital costs and not the placement costs for MEA whilst both the capital and ongoing costs for TBEA are quoted.

Professor Barnett agreed that the Appraisal Committee had been aware of the placement costs of MEA and that it would be appropriate for this to be included in the FAD.

The Appeal Panel considered that the Appraisal Committee had not acted perversely but the placement cost for MEA (about £280 per treatment with no capital cost) should be stated in parentheses at the end of FAD 3.7.

3.9 MML alleged that section 4 of the FAD failed to distinguish between the quality and weight of the RCTs used as evidence to illustrate the clinical and cost effectiveness of TBEA ,on the one hand, and MEA on the other. The latter were markedly superior.

Professor Barnett explained that the Appraisal Committee had considered, most carefully, the quality of the trials with both technologies. The summaries of the studies in section 4 of the FAD were factually correct. The committee were aware of the strengths and weaknesses of all the studies but, as stated in FAD 4.3.1, it was unable to distinguish between the clinical effectiveness of TBEA and MEA on the available data. The committee had concluded that a head-to-head comparison was needed to resolve this issue (FAD 5.1).

The Appeal Panel noted Professor Barnett's comments. The panel also noted that the Peninsula Technology Assessment Group (TAG) had tabulated a summary of the quality of the included studies (pp 57). The panel did not therefore consider that the Appraisal Committee acted perversely in their appraisal of the clinical effectiveness of the second generation endometrial ablation techniques.

The Appeal Panel rejected the appeal on this point.

3.10 MML claimed that the phrase “defined inconsistently” (FAD 4.1.7) implied a criticism of the relevant RCTs and suggested that they contradicted or undermined each other.

Professor Barnett explained that whilst each trial was internally consistent there was inconsistency between studies.

The Appeal Panel had drawn the same interpretation from the FAD and did not consider that the Appraisal Committee had acted perversely or misrepresented the trials.

The Appeal Panel rejected the appeal on this point.

3.11 MML alleged that the FAD (4.2.3, 4.2.6, 4.3) failed to address the economic advantages that would result from the wider applicability of MEA than TBEA and the consequential benefits to NHS budgets.

Professor Barnett emphasised, again, that the Appraisal Committee had been unable to distinguish the clinical superiority of TBEA or MEA (FAD 4.3.2); nor had it been able to draw conclusions on their relative cost effectiveness (FAD 4.3.4). He emphasised that expert advice available to the committee indicated that there were potential advantages, to some patients, from both first and second generation techniques; and from the different second generation techniques, and that their availability would allow appropriate choices for individual patients.

It was clear to the Appeal Panel that this matter had been fully considered by the Appraisal Committee, and that their conclusions were not perverse.

The Appeal Panel rejected the appeal on this point.

3.12 MML contended that the statement (FAD 4.3.3) about the acceptability of applying endometrial ablation techniques under local anaesthesia was wrong. MML claimed that MEA is being performed widely in the NHS under local

anaesthesia, and that a considerable proportion of patients in the clinical trials of MEA had been managed in this manner.

Professor Shaw accepted that some centres were, indeed, using MEA under local anaesthesia but that the option to be treated under general anaesthesia would be preferred by many patients. Dr Longson indicated that the response from consultees suggested that the option to be treated under general anaesthesia was regarded as important.

The Appeal Panel considered that the choice between local and general anaesthesia was a matter for the woman and her surgeon. The panel considered that patient choice, in this regard, was important. Nevertheless, the statement in FAD 4.3.3 appeared to overstate the situation and the panel suggests that the final sentence should read "However they heard from consultees that the application of endometrial ablation techniques under local anaesthesia was by no means universal in the NHS".

The Appeal Panel rejected the appeal on this point but draws the attention of the Guidance Executive to its recommendation that this change be made.

3.13 MML contended that the FAD (4.3.4) falsely concluded that patient preferences for different outcomes render less relevant the differences between the overall effectiveness of TBEA and MEA.

The Appeal Panel noted Professor Barnett's responses in paragraph 3.11 (above). It also noted its conclusions in paragraph 3.14 (below). It considered that the appellant's complaint would be adequately resolved by the action recommended in paragraph 3.14 (below).

The Appeal Panel rejected the appeal on this point but draws the attention of the Guidance Executive to its recommendation in paragraph 3.14 (below).

3.14 MML contended that FAD 4.3.6 omits to advise on the treatment which gives the best amenorrhoea rates as an alternative to hysterectomy, and no other paragraph makes good the omission. MML also indicated that it took the greatest exception to the second sentence in FAD 3.6 suggesting the superiority of TBEA for women choosing eumenorrhoea rather than amenorrhoea as treatment for heavy menstrual bleeding.

Professor Barnett explained that Section 3 of the FAD attempted to describe the technologies, and did not reflect the evaluation of the Appraisal Committee. He accepted that, although accurate, the second sentence of FAD 3.6 might result in confusion and suggested that it be removed.

The Appeal Panel considered that, whilst this section of the FAD did not reflect the Appraisal Committee's evaluation, it could be misinterpreted. Whilst the committee had not acted perversely, the panel endorsed the proposal that the second sentence of FAD 3.6 be removed.

The Appeal Panel rejected the appeal on this point but draws the attention of the Guidance Executive to its recommendation about the proposed change to FAD 3.6.

3.15 MML contended that the audit criteria 1, 2 and 3 in the table within Appendix C falsely implied that TBEA can be offered to all women.

Although the audit criteria are not drawn up by the Appraisal Committee, the Appeal Panel nevertheless considered that some would be inappropriate in the light of its decision in paragraph 3.4 (above). It therefore advises the Institute to review the audit criteria, in their entirety, in the light of the decisions of the Appeal Panel.

3.16 MML pointed out to the Appeal Panel that there was an error in FAD 4.1.2 (the "normal" PBAC score should be 75 not 76).

Professor Barnett agreed with MML and apologised for the error.

The Appeal Panel thanked MML for drawing this error to the Institute's attention. The Guidance Executive would be recommended to effect the necessary change.

4. Appeal Ground Three: The Institute has exceeded its legal powers.

The appellant made no appeal under this ground.

5. Conclusions

5.1 The Appeal Panel dismissed all points in this appeal. The panel, however, draws the attention of the Guidance Executive to its recommendations in paragraphs 3.1, 3.2, 3.4, 3.6, 3.7, 3.8, 3.12, 3.13, 3,14, 3,15 and 3.16.