National Institute for Health and Care Excellence

IP1817 Transvaginal laser therapy for urogenital atrophy

IPAC date: 11 March 2021

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
1	Consultee 1 Patient	**General**	In 2015 aged 53, I started to notice a variety of changes occurring within my body, coupled with heavy, unpredictable periods. Over the next 4 years I made more frequent appointments at the GP to discuss vaginal discomfort (dryness, soreness, bleeding, itchiness, sharp pains, heaviness) and was diagnosed with a variety of conditions such as Hostile Vagina, Thrush, Eczema, Atrophy and it transpired, an underactive Thyroid. My sleeping patterns were chaotic, often with only 3-4 hrs per night – leaving me blurry eyed for the next working day and throwing irrationality on a mammoth scale into the mix. By 2019 things had become intolerable. Penetrative sex was no longer an option, as I was unbearably tender and tearing at a simplest of touch and by then I was noticing blood on my toilet paper each time I visited the bathroom; I was weepy, moody, tired and concerned that I had no understanding as to what was going on with my body and felt there were huge information gaps on the internet and from the GP's surrounding the Menopause, to help me understand the transition I was going through. My research proved to be futile and inconclusive; By mid - 2019, and yet another GP appointment, I was then referred to a specialist. At this point, five-years into the decline and my increasing medical appointments, I felt traumatised and genuinely feared for what was to come for my future; In non-medical circles, few women speak candidly of their menopause, other than reference to hot flushes, HRT, weight gain; I had fully anticipated hormonal	Thank you for your comment. The Committee very much welcomes hearing from patients who have undergone this procedure and considered your experience and views in their deliberations.

			changes and looked into homeopathy for potential support, but nobody had primed me for the vaginal changes that can, do, and certainly in my case, did occur. My initial consultation was thorough, consisting of a full historic account/discussion of my journey, along with a vaginal examination. I was then given a detailed explanation as to “what had gone on”, “what was going on”, and what options were available to support me moving forward. It was only at this point that I dared to believe there could be a solution for me to have hope of a “near normal” future for me and for my husband and craving a sense of normality as quickly as possible, I opted for Mona Lisa Touch. I was given the Mona Lisa Touch information-fact sheet to take away and digest, along with contact details to arrange for the procedure to start in early January 2020. I was extremely nervous going into my first session, predominantly because of the unknown, but also had a great sense of relief that I was on a new journey, with belief and great faith that my condition would improve as a result; It was explained to me that we would meet prior to each session to discuss and understand progress made between sessions; The procedure itself was “a little uncomfortable” at most and to my surprise, immediately after, I was able to walk normally, drive myself home and didn’t experience any side effects. In fact, after my second session I went straight to the gym on my way home, albeit for a swim. My physical symptoms started to improve almost immediately, and I began to feel mentally stronger too. I went on to have 4 Mona Lisa Touch sessions in total and believe the procedure (coupled with HRT) has been a real life-changer for me. Jan 2021, and one year on from my initial Mona Lisa Touch procedure, my vagina continues to be trouble free and I haven’t had need to visit the Drs in the past year. Sexual intercourse is back on the menu and our element of intimacy has returned,	

			which is such a powerful, unspoken, all forgiving communication that we both felt robbed of, way before our years. I no longer bleed after visiting the bathroom. It was a considerable financial outlay for us, and beyond the reach of many, but I believe it was the best decision we have ever made; My health, my life and our lives, have been totally transformed.	
2	Consultee 2 NHS Professional	**1.1**	Having carefully read the entire draft document we cannot see how the committee have drawn up their recommendations. The statement that 'evidence on the long term safety and efficacy of transvaginal laser therapy for urogenital atrophy is inadequate in quality and quantity. Therefore, this procedure should only be used in the context of research' is plainly not what the studies which have been included in the literature search demonstrate. There are high quality randomised control trials using both sham and the 'gold standard' low dose local vaginal oestrogen as comparators which demonstrate that laser therapy is at least as good as the alternatives and better than sham. The duration of efficacy of therapy ie 12-18 months is reasonable and compares with other therapies that have to be repeated regularly to maintain efficacy (oestrogen has to be taken indefinitely to maintain its efficacy). Therefore, we feel that to recommend laser therapy only in clinical trials for GSM would deprive women who are unable to use topical oestrogen of a very valuable reasonably safe and efficacious treatment.	Thank you for your comment. Section 1.1 of the draft guidance has been changed to state that there are no short-term safety concerns.
3	Consultee 2 NHS Professional	**1**	We feel that patient selection is of paramount importance and the NICE recommendation should consider which women will be most suitable for therapy who are unable to have (or have not responded to) other forms of treatment. All of these women should have undergone review by a multidisciplinary team including gynaecologists, nurse specialists and physiotherapists to ensure that all patient education, counselling and conservative therapies have been exhausted and potential patients should be	Thank you for your comment. The draft recommendations state that this procedure should only be done in the context of research. The procedure should therefore be done under the scrutiny and governance of a research ethics committee.

			discussed at an multidisciplinary team meeting prior to initiation of therapy.	
4	Consultee 2 NHS Professional	**Overview**	In some of the descriptions of trial outcomes, no context or critique of findings has been considered. for example on page 6 under the section on FSFI it reports that the results here were not statistically significant in any of the trials but this is not uncommon and female sexual function is so multifactorial in nature that this is not an unexpected finding in line with all other therapies.	Thank you for your comment. The overview summarises the outcomes that are published in the literature. The committee discussed the evidence with advice from a professional expert.
5	Consultee 2 NHS Professional	**Overview**	on page 7 the patient satisfaction scores detailed are actually very high in comparison to other therapies and should be considered as very positive.	Thank you for your comment.
6	Consultee 2 NHS Professional	**Overview**	on page 8 under the safety summary to have only had 4 safety cases reported when there have been hundreds of women in the systematic reviews reported demonstrates excellent safety. it should also be noted that in the review of the cases that had issues, many of these women went on to need multidisciplinary input particularly for physio or appropriate counselling and education about lubricants / devices etc. In reality, these women were maybe not the most suitable women for laser therapy and would have benefited form a multiprofessional approach in the first place. This again highlights the importance of patient selection and the need to ensure that all conservative therapies have been considered prior to consideration of laser therapy.	Thank you for your comment. Section 1.1 of the draft guidance has been changed to state that there are no short-term safety concerns.
7	Consultee 3 Specialist Society BSUG	**General**	IP1817 Transvaginal laser therapy for urogenital atrophy: • The IPG considers vaginal laser in the treatment of GSM but does not give consideration to other energy-based devices such as Radiofrequency treatment which is possibly used more than laser commercially for this indication.	Thank you for your comment. The remit of this guidance is transvaginal laser therapy. Other energy-based devices for this indication would be considered for

				guidance if they were notified to the IP programme.
8	Consultee 3 Specialist Society BSUG	**1.1**	• The recommendation from the IPG is that this should only be permitted as part of a larger robust clinical trials however several of our members have put in Grant applications to the NIHR and RfPB which have been turned down. How are we to generate the evidence if there is no consideration of funding for research? We would request NICE make a recommendation for a called grant to investigate this intervention. We would also propose that generating reliable data can take several years however gathering observational data should be a priority for anyone undertaking these procedures as they are sufficiently established in clinical practice and are being widely used. Unless there is a mandate to stop use this will continue, so it makes more sense to encourage data collection and reporting of outcomes. • Making practical recommendations therefore is likely to be more beneficial as laser is already being widely used “off label” and no doubt will continue to be so despite the guideline.	Thank you for your comment. The Committee considered this comment but decided not to change the guidance.
9	Consultee 3 Specialist Society BSUG	**1**	• The IPG does not discuss who should be performing these studies. There should be guidance on qualifications and training clinicians undertaking these procedures should be able to demonstrate as well as the outcomes they should be required to collect as part of this process. • There is a need for appropriate training before using the device. In particular, anyone using the device should be a) able to make the appropriate diagnosis, b) examine the patient appropriately and c) understand and deal with any potential complications. Although the scientific papers are conducted largely by gynaecologists, many of the commercial users of these devices are from a wide variety of health care disciplines such as primary care and dermatology, some are done by nurses or allied health assistants and in some instances by aesthetic practitioners with	Thank you for your comment. The draft recommendations state that this procedure should only be done in the context of research. The procedure should therefore be done under the scrutiny and governance of a research ethics committee.

			no medical qualification. The situation is even less regulated in many other countries.	
10	Consultee 3 Specialist Society BSUG	**General**	• In women who have had breast or other cancers and are therefore deemed to be unsuitable for low dose local oestrogen therapy there definitely appears to be a role for this intervention as it has been shown to be equivalent to oestrogen.	Thank you for your comment. Section 3.5 of the draft guidance currently states 'The committee was informed that the procedure may have a role for patients who are unable to use topical oestrogen.'
11	Consultee 3 Specialist Society BSUG	**General**	• Several Hospitals have received NHS funding to carry out laser in specific cases (h/o breast cancer etc). Thus, there is already a precedent for use on a named patient basis. If used on a named case basis, special arrangements should be in place regarding consent of patients regarding its limited evidence and maintenance of a database of treatment and regimes used (laser type, power, frequency, pulses, passes etc) as well as side effects and outcomes (up to 24 months).	Thank you for your comment. The Committee considered this comment but decided not to change the guidance.
12	Consultee 3 Specialist Society BSUG	**1**	• The emphasis needs to be on long term safety and outcome as was evident from the Cumberlege review into the use of mesh. The longer follow ups in the studies used for evidence is up to 24 months but it would be interesting to know if the use of Laser influences the quality of the vaginal skin and also its impact for any future surgical interventions. It is therefore important to know that the use of Laser will not limit future surgical interventions or cause more damage.	Thank you for your comment. Section 1.2 of the draft guidance states that further research should report long-term safety and efficacy outcomes.
13	Consultee 3 Specialist Society BSUG	**General**	• For those women unable to use or benefit from vaginal oestrogen there are alternative options such as ospemifene which could be used before resort to invasive laser therapy.	Thank you for your comment. The overview states: 'The main treatments for urogenital atrophy are vaginal oestrogen, and

				non-hormonal lubricants and moisturisers.'
14	Consultee 3 Specialist Society BSUG	**Overview**	• The document mentions that typically 3 sessions would be performed, but this tends to range from 3-5 and will often require top ups at regular intervals as the positive effects are reversible.	Thank you for your comment. The wording in the overview has been changed to 'typically 3 to 5 sessions, with further top up sessions as necessary'. Section 1.2 of the draft guidance states that further research should report the type of laser and energy used and treatment protocols.
15	Consultee 3 Specialist Society BSUG	**1.2**	Recommendation 1.2: There is a need for standardisation of protocols. Many of the studies used different treatment intervals and settings.	Thank you for your comment. Section 1.2 of the draft guidance states that further research should report details of treatment protocols.
16	Consultee 4 NHS Professional	**1.1**	I am in general agreement with the preliminary recommendations which are appropriate given the limited evidence. Please see recent editorial: Hillard TC, Nappi R Climacteric 2020;23(suppl 1) pS1-S2 **https://doi.org/10.1080/13697137.2020.1828855**	Thank you for your comment. Consultee agrees with main recommendation.
17	Consultee 4 NHS Professional	**1.2**	Recommendation 1.2: There is a need for standardisation of protocols. Many of the studies used different treatment intervals and settings which seem at the operators discretion. It is difficult to compare and interpret results scientifically when there is so much variation. This is particularly pertinent with respect to repeat courses of treatments.	Thank you for your comment. Section 1.2 of the draft guidance states that further research should report details of treatment protocols.

18	Consultee 4 NHS Professional	**1**	Draft Recommendations: It would be helpful to have an additional recommendation about who should be doing these procedures and the training required. In particular anyone using the device should be a) able to make the appropriate diagnosis, b) examine the patient appropriately and c) understand and deal with any potential complications. Although the scientific papers are conducted largely by gynaecologists, many of the commercial users of these devices are from a wide variety of health care disciplines such as primary care and dermatology, some are done by nurses or allied health assistants and in some instances by aesthetic practitioners with no medical qualification. The situation is even less regulated in many other countries. As with other surgical devices some guidance on who should be doing them or who should not be doing them would be helpful.	Thank you for your comment. The draft recommendations state that this procedure should only be done in the context of research. The procedure should therefore be done under the scrutiny and governance of a research ethics committee.
19	Consultee 4 NHS Professional	**3.5**	Committee Comments section 3.5. The phrase "unable to use vaginal oestrogen" is commonly used in laser study protocols. Firstly it is unclear how this conclusion is reached in many situations and whether a documented trial of oestrogen therapy has occurred. There are very few women in whom vaginal oestrogen is genuinely contraindicated. Secondly if vaginal oestrogens cannot be used there are recognised non-invasive alternatives such as DHEA or ospemifene which could be used before a resort to invasive laser therapy.	Thank you for your comment. The Committee considered this comment but decided not to change the guidance.
20	Consultee 5 Fotona Company	**General**	Comments to the NICE draft guidance Vulvovaginal atrophy (VVA) or more appropriately genitourinary syndrome of menopause (GSM) is a prevalent condition which, with increasing life expectancy, will affect more and more women. There are many treatment options available for otherwise healthy women, however women are often expressing concerns over lack of efficacy, tolerability and acceptability of these treatments, therefore newer treatment modalities are needed.	Thank you for your comment.
21	Consultee 5 Fotona	**3.1**	Comment to point 3.1 of the Draft Guidance Since the initial Structured Information Request (SIR) that the Fotona Company provided to the National Institute for Health and	Thank you for your comment.

	Company		Care Excellence's (NICE) interventional procedures programme, several new publications pertaining to the use of transvaginal laser therapy for urogenital atrophy have been published. Two of those, Gambacciani et al.1 and Gaspar et al.2 have been mentioned in the first SIR (under Chapter 8). Effects of non-ablative vaginal erbium laser in the skin and vaginal wall have been summarized in a recent review of Hympanova et al.6. A newly published study by Gaspar et al.2 further confirmed favourable histological changes in the vaginal wall of women with severe vaginal atrophy following the vaginal erbium laser treatment. The results of the study show that there was an increase in the epithelial thickness, accompanied also by a significant increase in the glycogen load, new papillae, and neo-angiogenesis in the lamina propria with capillaries reaching the epithelium. Vaginal health index score (VHIS) and the maturation value were significantly improved. Along with histological changes, the patients reported significantly diminished pain during intercourse, significant improvement regarding dryness and irritation and very much improved was sexual function, which was evident from significant changes in Female Sexual Function Index (FSFI) scores. Vaginal dryness, burning and dyspareunia are the most bothersome symptoms of GSM, which can lead to impaired sexual function of postmenopausal women and can negatively influence their overall quality of life. A retrospective study by Gambacciani et al.7 included 1081 sexually active postmenopausal women, who complained about symptoms and signs of GSM and the presence of impaired sexual life. Symptoms of sexual dysfunction were assessed using a standardized Female Sexual Function Index (FSFI) and Female Sexual Distress Scale - revised (FSDS-R). The results of the study on this large cohort of patients confirmed a positive effect of vaginal laser treatment on GSM-related sexual function distress (FSD). According to the authors7 and known favourable effects the laser has on the vaginal tissue2,8–10, the tissue restoration lead to better sexual activity and satisfaction.	Section 3.1 of the draft guidance describes the evidence that was included in the rapid review. Ref.1 (Gambacciani et al., 2020) has been added to the key evidence summary. Ref. 2 (Gaspar et al., 2020) has been added to the appendix. Ref. 6 (Hympanova et al., 2020) has been added to the appendix. Ref. 7 (Gambacciani et al., 2020) has been added to the key evidence summary. Ref. 8 (Lapii et al., 2017) refers to patients with stress urinary incontinence, which is covered by a separate Interventional Procedures guidance. Ref. 9 (Lapii et al., 2017) refers to patients with stress urinary incontinence, which is covered by a separate Interventional Procedures guidance. Ref. 10 (Lukac et al., 2018) discusses the mechanism of tissue regeneration but does not report

			Newly published papers since the submitted Structured Information Request are listed at the bottom of this document and marked in green.	any patient outcomes, so it does not fit the inclusion criteria for the overview.
22	Consultee 5 Fotona Company	**3.3**	Comment to point 3.3 of the Draft Guidance Neither in clinical studies, nor in clinical practice was there any report of the erbium vaginal laser to cause scarring or formation of fistulas. In a large safety study, conducted by Gambacciani et al.1, as a response to the FDA warning mentioned above, the safety of vaginal erbium laser procedures was evaluated in a large cohort of more than 43.000 patients that have been treated with the vaginal erbium laser in the past eight years. There have been no serious adverse events reported by none of the 535 users/practitioners who participated in the study, while most of the reported adverse events had the frequency of appearance lower than 1%. The highest occurring adverse event reported was vaginal discharge that appeared in approx. 4 % of the patients. Most importantly, all reported adverse events were mild to moderate and of transient nature. The authors conclude that vaginal erbium laser treatment appears to be safe and carries a very low risk profile. In their review of the existing literature on the vaginal laser treatment of GSM, Guo et al.11 investigated whether the evidence supports the 2018 Food and Drug Administration (FDA) safety communication12 cautioning against the use of vaginal laser devices for treating GSM. According to the authors, the evidence to justify the FDA warning was not found neither in the medical literature nor by searching relevant databases for adverse events (AE)11. The FDA warning regarding vaginal laser therapy appears to misrepresent the current evidence concerning vaginal laser therapy for the treatment of GSM. Authors state that it is possible AE exist that have not been reported in the mechanisms investigated by the authors and could be solely known to the FDA; therefore, the disclosure of such events to the	Thank you for your comment. The key safety outcomes are those that were considered by the committee to be the most important and include events that could potentially happen as well as those that have been reported. Ref.1 (Gambacciani et al., 2020) has been added to the key evidence summary. Ref 11. (Guo et al., 2020) has been added to the key evidence summary.

			medical community through clarification of the warning would be of great importance to allow for better monitoring and prevention. Further regulatory action based on this statement, without clarification of the risks, is effectively closing off the potential to explore an effective therapeutic option for a population of women with no other alternatives11. The authors also raise a question of disparities across sex differences by presenting several instances in which the FDA warned about the use of potentially beneficial treatment options for women, even though it was proven, that the risk in women was overestimated, while at the same time recommending far more risky treatments that were specifically aimed at men11. Some of the mentioned treatments that may have very frequent serious adverse effects in men, can be used without restrictions. The authors question whether the FDA demonstrates a pattern of suggesting women need to be kept from harm, even at the consequence of withholding beneficial treatment; whereas men can accept risk and participate in shared decision-making11. The authors appeal that the FDA, in a revision of their communication, has the opportunity to validate the millions of affected women by clarifying and publicly providing its specific concerns regarding the use of laser treatments specifically for GSM, so that women can participate in decision making for the best interest of their health.	
23	Consultee 5 Fotona Company	**3.5**	Comment to point 3.5 of the Draft Guidance There is a specific subgroup of women, namely breast cancer patients and breast cancer survivors in which some of the otherwise effective treatment options are contraindicated or controversial. The practitioners/oncologists do not feel confident to prescribe vaginal estrogen therapy in the fear of increased cancer recurrence, the possible interference with tamoxifen, or AIs and the fear of medical litigation3, leaving these patients with a limited number of treatment options that have short-term effectiveness. With its localized effect on the target tissue, vaginal laser treatment presents a valuable addition to the treatment armamentarium of the GSM, and could be offered as a first line treatment option. As such, it has been recently recommended as	Thank you for your comment. The Committee considered this comment but decided not to change the guidance. Ref. 4 (Robinson et al., 2020) refers to a conference discussion. Ref. 5 (Cagnacci et al., 2019) describes recommendations for

			a treatment for vulvo-vaginal atrophy by the Italian Menopause Society and advocated as a first line treatment for GSM by the most prominent urogynecological specialists at this year's meeting of the International Continence Society4,5.	diagnosing and treating vulvovaginal atrophy. It states: 'Laser therapy can be considered among the range of therapeutic options based on the woman's specific needs and preferences and is of particular interest to women in whom systemic or local hormone therapies are contraindicated.'
24	Fotona Company	**References**	References (newly published publications are bold) **1. Gambacciani M, Cervigni M, Gaspar A, et al. Safety of vaginal erbium laser: A review of 113,000 patients treated in the past 8 years. Climacteric. 2020;23(sup1):S28-S32. doi:10.1080/13697137.2020.1813098** **2. Gaspar A, Silva J, Calderon A, Di Placido V, Vizintin Z. Histological Findings after Non-ablative Er:YAG Laser Therapy in Women with Severe Vaginal Atrophy. Climacteric. 2020;23(sup1):S11-S13. doi:10.1080/13697137.2020.1764525** 3. Biglia N, Bounous VE, D'Alonzo M, et al. Vaginal Atrophy in Breast Cancer Survivors: Attitude and Approaches Among Oncologists. Clin Breast Cancer. 2017;17(8):611-617. doi:10.1016/j.clbc.2017.05.008 **4. Robinson DT, Cardozo L, Salvatore S, Iglesia CB, Shobeiri SA. If you can't Stand the Heat…. Appraising the Evidence for Thermal therapy in Lower Urinary Tract Dysfunction. In: ICS 2020 Online. ; 2020.** 5. Cagnacci A, Gallo M, Gambacciani M, Lello S. Joint recommendations for the diagnosis and treatment of vulvo-vaginal atrophy in women in the peri- and post-menopausal phases from the Società Italiana per la Menopausa (SIM) and the Società Italiana della Terza Età (SIGiTE). Minerva Ginecol. 2019;71(5):345-352. doi:10.23736/S0026-4784.19.04469-1 **6. Hympanova L, Mackova K, El-Domyati M, et al. Effects of non-ablative Er:YAG laser on the skin and the vaginal wall:**	Thank you for your comment. Please see responses to comments 21, 22 and 23.

			systematic review of the clinical and experimental literature. Int Urogynecol J. 2020. doi:10.1007/s00192-020-04452-9 **7. Gambacciani M, Albertin E, Torelli MG, et al. Sexual function after vaginal erbium laser: the results of a large, multicentric, prospective study. Climacteric. 2020;23(sup1):S24-S27. doi:10.1080/13697137.2020.1804544** 8. Lapii GA., Yakovleva AY., Neimark AI. Structural Reorganization of the Vaginal Mucosa in Stress Urinary Incontinence under Conditions of Er:YAG Laser Treatment. Bull Exp Biol Med. 2017;162(4):510-514. doi:10.1007/s10517-017-3650-0 9. Lapii GA, Yakovleva AY, Neimark AI, Lushnikova EL. Study of Proliferative Activity of Vaginal Epithelium in Women with Stress Urinary Incontinence Treated by Er:YAG Laser. Bull Exp Biol Med. 2017:1-4. doi:10.1007/s10517-017-3784-0 10. Lukac M, Gaspar A, Bajd F. Dual Tissue Regeneration : Non-Ablative Resurfacing of Soft Tissues with FotonaSmooth ® Mode Er : YAG Laser. J Laser Heal Acad. 2018;2018(1):1-15. **11. Guo JZ, Souders C, McClelland L, et al. Vaginal laser treatment of genitourinary syndrome of menopause: does the evidence support the FDA safety communication? Menopause. 2020;27(10):1177-1184. doi:10.1097/GME.0000000000001577** 12. FDA Warns Against Use of Energy-Based Devices to Perform Vaginal “Rejuvenation” or Vaginal Cosmetic Procedures: FDA Safety Communication | FDA. https://www.fda.gov/medical-devices/safety-communications/fda-warns-against-use-energy-based-devices-perform-vaginal-rejuvenation-or-vaginal-cosmetic. Published 2018. Accessed December 13, 2019.	

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