

# TRENDS IN UROLOGY GYNAECOLOGY & SEXUAL HEALTH

MEETING REPORT

## Practical management of low sexual desire in surgically menopausal women

**H**ypoactive sexual desire disorder (HSDD) and its possible treatments are genuinely misunderstood, with few resources available to support clinicians (in both primary and secondary care). In a recent survey of clinicians, common reasons for the lack of support of patients with sexual dysfunction were shortage of training, and limited patient awareness and counselling.<sup>1</sup>

To help tackle the problem of managing low sexual desire among surgically menopausal women, an HSDD resource pack for physicians in primary and secondary care was developed under the guidance of a multidisciplinary group of UK specialists, with support from Procter & Gamble Pharmaceuticals UK Ltd. This important new resource was made available to all delegates attending the British Menopause Society Annual Meeting. At the conference, four of the key contributors to this resource, Miss Joan Pitkin (Chairperson), Professor Janice Rymer, Mr Nick Panay, and Mr Mike Cust (speaker credentials can be found on page 4) discussed how this pack can support clinicians in the practical management of women with low sexual desire.

### The impact of low sexual desire

Reduced sexual desire is a common symptom in surgically menopausal women. For these women (bilaterally oophorectomised and hysterectomised), the onset of sexual dysfunction is often abrupt as the result of a dramatic decline in the levels of ovarian hormones including testosterone, and low sexual desire may be a key consequence of testosterone loss.

**Bms**  
Meeting the  
challenge of  
menopause

To help physicians identify, educate and treat HSDD patients appropriately, a new resource pack has been developed so that physicians can benefit from the combined experience of an expert team. Professor Janice Rymer introduced the core elements of the resource pack, which include:

**Patient Care Pathway** – a carefully crafted guide to the management of women at risk of, or presenting with, HSDD

**Memory Stick** containing:  
**Physician Slide Kit** which outlines the evidence for the impact of surgical menopause on sexual function, the prevalence, impact, potential causes, and the evaluation and treatment of HSDD; and **Patient Case Finding Algorithms** which have been adapted for primary and secondary care

**Brief Profile of Female Sexual Function (B-PFSF)<sup>®</sup> questionnaire** which is designed for women who are experiencing low sexual desire that is concerning to them to help them decide whether or not to consult a physician

**Patient Education Leaflet** which can be used with patients both pre- and post-TAH & BSO, and includes useful contact details for associations and support groups who can provide further helpful information

Copies of the pack (or any element of the pack) can be obtained by healthcare professionals at no charge by e-mailing: [HSDD@nbggroup.co.uk](mailto:HSDD@nbggroup.co.uk)

For some women, low sexual desire can have a significant impact on general well-being and their sexual relationships, leading to distress (Box 1).

*‘The consequences of HSDD are important at any age but for young women who have had a total abdominal hysterectomy (TAH) with*

*bilateral salpingo-oophorectomy (BSO), the impact of HSDD can be disastrous.’*  
[Miss Joan Pitkin]

Recognising the specific nature of this condition, HSDD was defined in the DSM-IV as a condition characterised by persistent or recurrent deficiency and/or

**Box 1. The impact of low sexual desire**

*"I made up excuses to avoid having sex. I avoided doing anything that would get my partner sexually excited"*

*"I dreaded having sex....having sex was a chore..."*

*"I felt distressed about sex and I was frustrated about my sex life"*

*"I felt sexually numb...it was difficult for me to get aroused. Sex was not satisfying or fulfilling"*

These statements (not verbatim quotes) were developed based on interviews with women with low sexual desire which caused them distress and were used to validate the Profile of Female Sexual Function (PFSF)<sup>2</sup>, an instrument that distinguishes between these two groups of women.

absence of sexual thoughts/fantasies and/or receptivity to sexual activity that causes distress or interpersonal difficulty.<sup>3</sup>

The introduction of Intrinsa▼ (a transdermal testosterone patch), the first medically approved treatment for HSDD in surgically menopausal women younger than 60 years of age,

has highlighted many issues on the identification and management of female sexual dysfunction.

*Role of androgens in female sexual function*

Androgens have an important role in female sexual function, improving well-being, sexual desire, arousal and

orgasm, as well as playing a key physiological role in bone physiology and muscle mass. Reduced levels of testosterone in postmenopausal women are associated with loss of libido, decreased sexual activity, diminished feelings of physical well-being and fatigue.<sup>4</sup>

A recent European survey among 1356 women found that surgically menopausal women were significantly more likely to develop HSDD than premenopausal or naturally menopausal women ( $p=0.001$ ).<sup>5</sup> One in three surgically menopausal women with low sexual desire reported associated distress and were classified as having HSDD.

There is now good evidence to show that the restoration of physiological levels of testosterone in appropriately selected surgically

**Brief Profile of Female Sexual Function (B-PFSF)<sup>®</sup>**

This questionnaire was designed for women who are experiencing low sexual desire that is concerning to them to help them decide whether or not to consult a physician. In this questionnaire you will be asked about your sexual feelings and sexual activity and some concerns you may have about your level of interest in sex during the past 2–3 months. Read each statement carefully and circle the number that best corresponds to your experience over the past 2–3 months. Then, add the numbers together for a total score and record the score in the box at the bottom of the questionnaire.

	Never	Seldom	Sometimes	Often	Very Often	Always
I felt like having sex	0	1	2	3	4	5
I was unhappy about my lack of interest in sex	5	4	3	2	1	0
Getting aroused took forever	5	4	3	2	1	0
I felt sexually numb	5	4	3	2	1	0
I lacked sexual desire	5	4	3	2	1	0
I felt disappointed by my lack of interest in sex	5	4	3	2	1	0
I reached orgasm easily	0	1	2	3	4	5

Please add up the responses to the questions above and record the Total Score here:

This questionnaire is not intended to be a substitute for professional medical advice or a medical diagnosis. Always seek the advice of your physician or healthcare provider regarding questions you may have about any medical condition including Hypoactive Sexual Desire Disorder. Sharing the results of this questionnaire with your physician may help you to start a conversation with him or her about your concerns.

A Total Score between 0 – 20 indicates that you may have low sexual desire that is concerning or distressing (also known as Hypoactive Sexual Desire Disorder). This is something that you may want to discuss with your physician.

**Figure 1.** The B-PFSF questionnaire; copies of the questionnaire can be obtained by healthcare professionals at no charge by emailing: HSDD@nbgroup.co.uk (©Procter & Gamble Pharmaceuticals, Inc. All rights reserved.)

menopausal women improves many important aspects of female sexuality.<sup>6,7</sup> In two carefully designed phase III multicentre studies in surgically menopausal women on concomitant oestrogen therapy, treatment with transdermal testosterone 300mcg/day, alleviated many of the symptoms of HSDD.<sup>6,7</sup> Treatment significantly increased the frequency of satisfying sexual activity and sexual desire, and reduced distress, as well as improving all other efficacy endpoints including: arousal, pleasure, orgasm, responsiveness and self-image.<sup>6</sup>

Recent models of female sexual arousal recognise the many factors (hormonal as well as other, external, factors) that can impact on emotional status and so determine a woman's sexual responsiveness.<sup>8</sup> The key to the successful treatment of HSDD with low-dose testosterone therapy is the

identification of the appropriate candidates for whom all other problems that influence sexual desire and satisfaction have been identified and treated.

### The HSDD resource pack - Putting the theory into practice

The following sections describe the main components of the HSDD resource pack and the way in which each can be used in practice.

#### The Patient Care Pathway

'The *Patient Care Pathway* is a ready-made tool to help identify and guide the management of women at risk of, or presenting with HSDD' (see pages 4 and 5), said Mr Panay in introducing this component of the HSDD resource pack.

Appropriate identification and diagnosis of HSDD among surgically

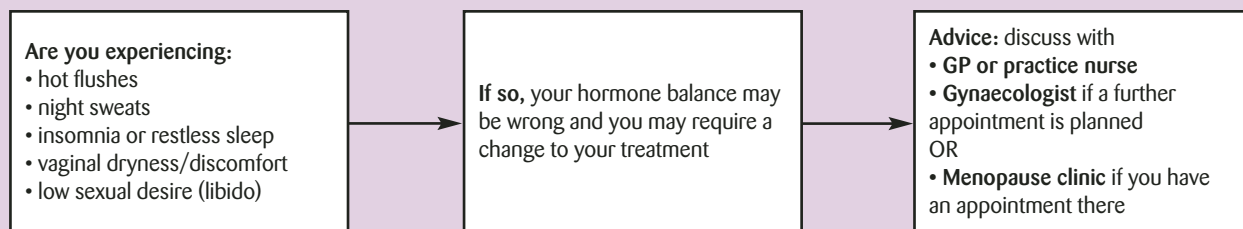
#### Box 2. Criteria for referral

- Complex psychosexual issues
- Concomitant medical conditions
- Complex hysterectomy, e.g. severe endometriosis,
- Malignancy
- Premature ovarian failure (<40 years)
- Unwilling to take or contraindicated to take oestrogen
- Non-surgically menopausal woman with HSDD

menopausal women is an important first step. The Brief Profile of Female Sexual Function (B-PFSF)<sup>©</sup> questionnaire is a useful tool to identify patients at risk of HSDD because it helps patients to identify and express the nature and severity of their sexual dysfunction prior to a formal assessment by the physician (see Figure 1).<sup>9</sup> However, the results of the B-PFSF questionnaire should

#### After your surgery...

As a result of your operation (hysterectomy and removal of both ovaries), you may have noticed some changes (see below). If these changes occur, they may come on immediately or perhaps after some months.



#### Tips for discussing symptoms with your doctor:

- Be specific about your symptoms (e.g. night sweats, vaginal dryness, low sexual desire). It can help your doctor determine what's best for you.
- To help you speak openly with your doctor, here are some ideas for starting the conversation:

"Since my operation I have started feeling pain/discomfort during sex. Is this normal?"

"My partner finds it frustrating that I'm never 'in the mood', is there anything I can do about this?"

"Is not wanting sex a normal result of my surgery?"

"Could the menopause have affected my sexual desire?"

"Since the surgery, my partner and I have not been as physically

intimate as we were beforehand. Is there anything I can do to increase my sex drive?"

If you are concerned by your loss of sexual desire please visit [www.desireandmenopause.co.uk](http://www.desireandmenopause.co.uk) for further information. There you can assess your sexual desire using a Brief Patient Questionnaire. Take a copy of the completed questionnaire with you to your doctor's appointment as it may help you start a conversation about your sexual concerns.

You may find it helpful to contact one of the following organisations for further information:

**Daisy Network:** 0845 122 8616

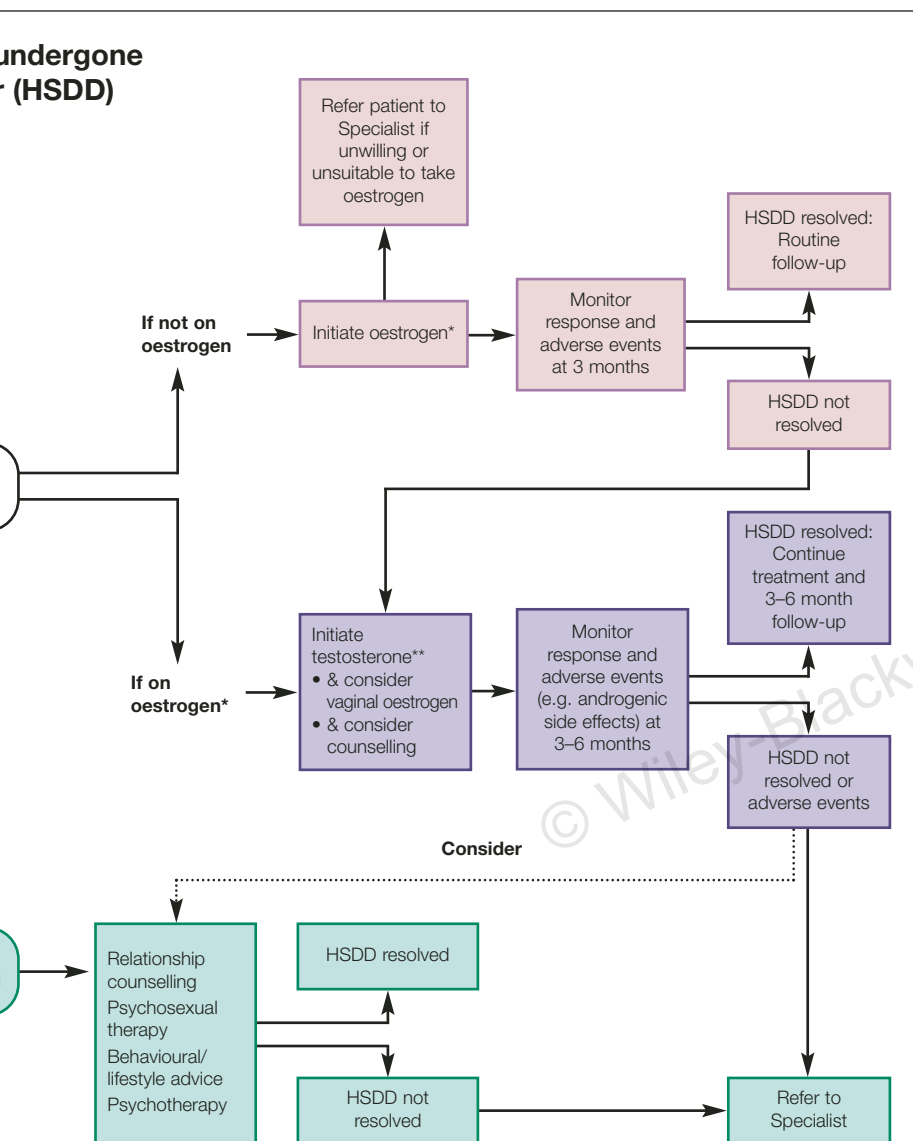
**Menopause Matters:** [info@menopausematters.co.uk](mailto:info@menopausematters.co.uk)

**The Hysterectomy Association:** 0871 781 1141

**Womens Health Concern:** 0845 123 2319

Figure 2. The 'After your surgery' patient information leaflet found in the HSDD resource pack; copies of the leaflet can be obtained by healthcare professionals at no charge by emailing: [HSDD@nbggroup.co.uk](mailto:HSDD@nbggroup.co.uk)





SHBG levels.<sup>6</sup>  
 tibolone alone is recommended.<sup>11</sup>

## References

1. Tanna N, *et al.* (2002) *Climacteric* 5 (S1): 197.
2. Utian. (2005) *Men Man* Jan/Feb: 10-22.
3. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders: DSM-IV-TR*. 4th ed. Arlington, Va; 2000.
4. Basson R, *et al.* (2000) *Journal of Urology*; 163: 888-893.
5. Rust J, *et al.* (2007) *Gynaecol Endocrinol*; 23(11): 638-644.
6. Serin IS. (2001) *Europ J Obs Gynae Reprod Biol*; 99:222-225.
7. Simon J, *et al.* (2005) *J Clin Endocrinol Metab*; 90: 5226-5233.
8. Buster JE, *et al.* (2005) *Obstet Gynecol*; 105: 944-995.
9. Davis SR. (1995) *Maturitas*; 21: 227-236.
10. Burger HG, *et al.* (1987) *BMJ*; 294: 936-937.
11. Rymer J. (1998) *Gynaecol Endocrinol*; 12: 213-220.

Copies of the patient care pathway can be obtained by healthcare professionals at no charge by emailing: HSDD@nbgroup.co.uk

If HSDD is not resolved following low-dose testosterone therapy, then the patient should be referred to a specialist clinic (or for relationship counselling, psychosexual therapy or lifestyle advice, as appropriate).

## Patient case finding - practical solutions after surgery

Among women who were sexually active, the long-term effects of surgery on their sex lives can lead to significant personal distress. Embarrassment and ignorance about the availability and appropriateness of treatment mean that many patients find it difficult to talk about their sexual problems. Although the surgery should resolve whatever problem for which it is warranted and therefore improve their quality of life dramatically, many women are not aware that loss of libido is an adverse effect of their surgery until after they have left specialist care. In his presentation, Mr Mike Cust discussed some practical solutions to the identification of patients with HSDD.

Healthcare providers within specialist centres need to be encouraged to regularly counsel and question patients about sexual function as an essential step in establishing a dialogue with patients before surgery (as part of the process of gaining patient consent) and after surgery.

The HSDD resource pack provides a useful 'After your surgery' *Patient Information Leaflet* (see Figure 2), which has been designed to inform patients as well as encourage a dialogue between patients and physicians.

## Supporting surgically menopausal women in secondary care

Within secondary care, the post-operative evaluation in particular provides an important opportunity to support women at future risk of developing HSDD and informs women about the potential menopausal

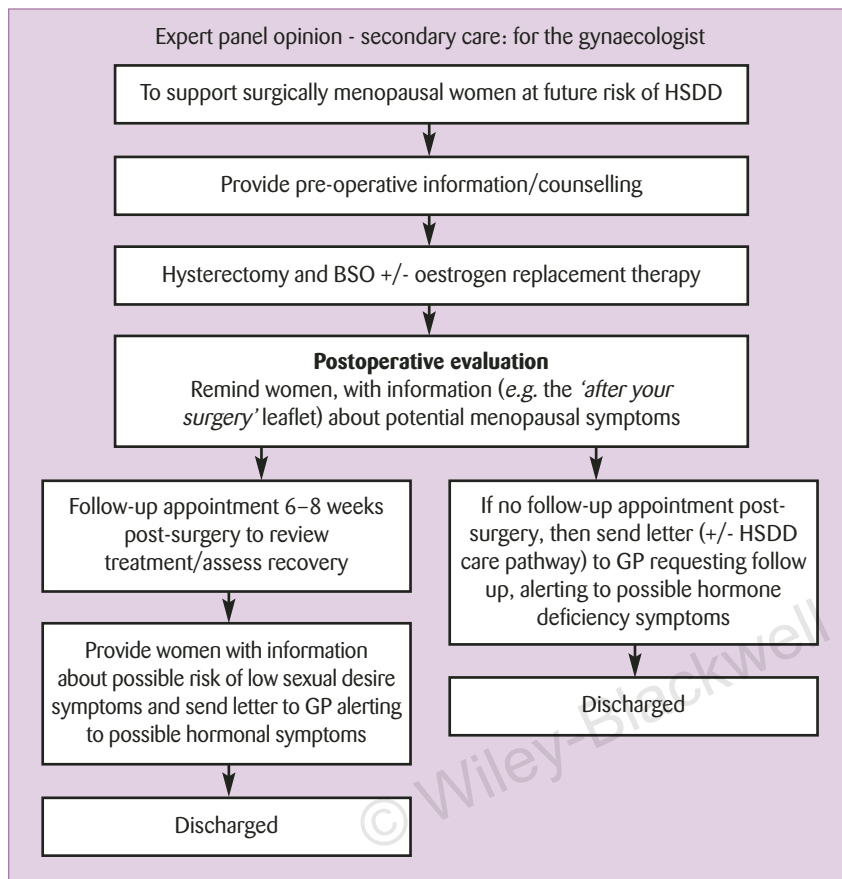


Figure 3. Algorithm for secondary care to support surgically menopausal women at risk of HSDD

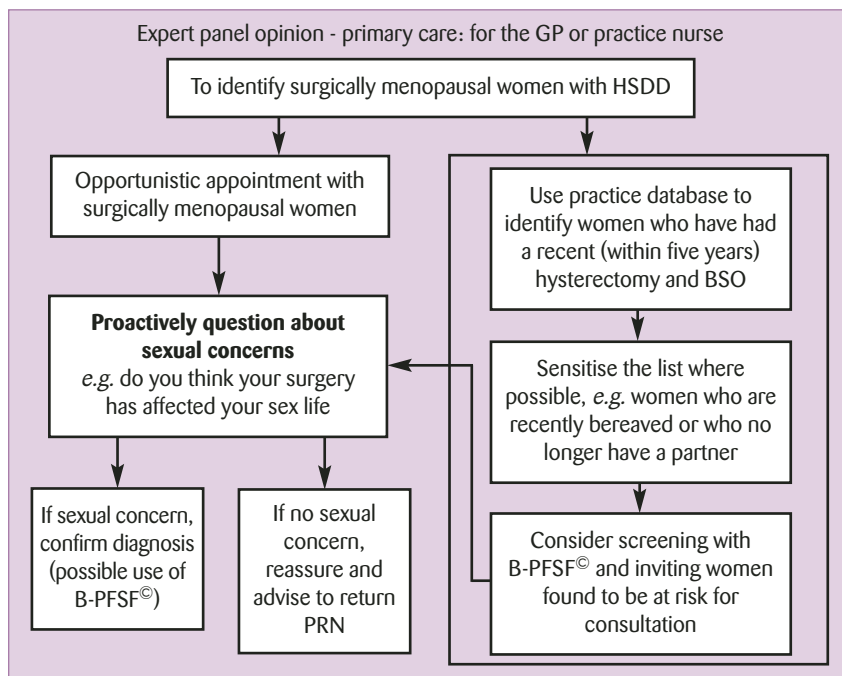


Figure 4. Algorithm for primary care to help identify women at risk of developing HSDD

symptoms. At discharge, primary care physicians should receive a copy of the HSDD *Patient Care Pathway* (either as a paper or electronic copy) with the discharge letter in order to ensure the ongoing support of patients in the months and years following surgery.

### Identifying HSDD in primary care

‘Primary care physicians are charged with the more difficult task of identifying women who have had TAH +/- BSO and who may have developed HSDD,’ (Figure 3) observed Mr Cust. Presentation of women with HSDD is likely to be delayed after discharge from hospital and so primary care practices should encourage women to return for a check-up at 6–12 weeks and between six and 12 months after discharge. However, an audit of the practice records may be the only way to identify ‘at risk’ women with a recent history (up to five years ago) of TAH +/- BSO. Healthcare providers should be sensitive to the patients’ current circumstance (*i.e.* recent bereavements, or women who no longer have a partner) when considering the relevance of HSDD screening with the B-PFSF questionnaire before inviting women for a consultation (Figure 4).

### Engaging with the patient

The doctor-patient relationship is crucial to uncover sexual problems.<sup>10</sup> Sexual well-being is relevant to quality of life and health. Despite this, sexual health problems remain infrequently diagnosed and therefore frequently untreated.<sup>1</sup>

One of the key goals of the HSDD resource pack is to help physicians facilitate a meaningful discussion with patients who are at risk of HSDD. ‘Regardless of the outcome of this discussion, the simple acknowledgement of HSDD by the physician is likely to help many surgically menopausal women address this difficult and

### Box 3. Helpful questions to initiate the sexual conversation

- Since your operation, has your love/sex life changed?
- Has this bothered you? If you have a partner, have any comments been made?
- Are you happy/satisfied with your love life?
- Do you still fancy/get turned on by/find attractive/desire your partner?
- Are you in a relationship in which you are having sex?
- Are there difficulties or is there anything you would like to discuss?
- Are you experiencing any pain during sex/sexual activity?

embarrassing problem,' remarked Miss Pitkin.

A recent survey showed that embarrassment is the primary reason for patients not initiating a discussion with their physician.<sup>11</sup> Many women (up to 78%) would have been happy to talk if the physician had initiated the discussion; more than 95% of women across all age groups considered that they would be happy to talk to their physician if he or she was professional, comfortable with the topic, kind and understanding. Developing a good rapport with the patient is the key to effective communication.

#### *Causes of women's sexual dysfunction*

Women's sexual dysfunction can be due to one or a number of factors in combination, including difficulties relating to desire, arousal, orgasm, vaginismus or pain with attempted or completed intercourse. In order to assess the cause of sexual dysfunction, physicians need to collate information from:

- full general medical and gynaecological history
- medication review
- examination, including: atrophic change, urogenital (leakage with coitus), muscle tone, deep pain trigger points

- lifestyle risk factors
- some psychosexual and relationship history (e.g. sexual abuse).

In order to ease the potential discomfort associated with an assessment of HSDD, the expert panel recommended the following structure for a dialogue with the patient:

- Start with a review of the physical symptoms:
  - acknowledge whether or not vaginal dryness/soreness is present
  - ask if there is any discomfort
  - ask if this is an issue.
- Then expand on this to enquire about:
  - change in desire
  - ease of arousal.

Further in-depth management will depend on your level of expertise as a clinician.

'Remember, it is important to respond positively to patients' concerns, reinforcing the common nature of the problem,' observed Miss Pitkin. 'If asked sensitively, women will generally appreciate being asked about sexual problems. Don't believe that 'it's too complex to address' and don't be too focused on finding a solution at first visit. Sex problems can take more than one consultation to resolve.'

Many factors may impact on a woman's sexual responsiveness, including her social and cultural construct, her religious beliefs, sexual orientation and whether there are any partner problems. In addition, some patients may have partners who are sexually impotent due to diabetes, hypertension, radiotherapy or extensive surgery for prostate tumours. 'For these women, they may wish to be faithful and loving and find another way around the problem,' remarked Miss Pitkin. In some instances, however, it may be useful to ask the couple about their sexual problems in order to define the nature, duration and context of the problem, the sexual response

(e.g. a woman can have dyspareunia and still have sexual arousal), the reaction from the partner, previous treatment or self-help, and the reason why the couple are seeking help now.

#### *Approaching the topic*

Good opening questions suggested by the expert panel include: 'Is this something that bothers you? I'd be pleased to talk with you about it.' Other helpful questions to initiate discussions about sex with your patient are outlined in Box 3.

The HSDD resource pack also provides a B-PFSF questionnaire to screen patients and help them to initiate the discussion if they believe that there is a problem (Figure 1). 'However, the questionnaire was not designed to bypass a conversation with the physician. Any patient who scores less than 20 out of a possible total score of 35 should be assessed further for HSDD,' said Miss Pitkin, reiterating a point made earlier by Mr Panay.

#### *Topic avoidance by physicians*

Some of the commonly reported reasons from physicians for not initiating such discussions are embarrassment, conservative sexual beliefs and time constraints, as well as insufficient knowledge about either the physiology of arousal mechanisms or specific sexual profiles. 'Whatever your reservations, don't forget that surgically menopausal women will appreciate the opportunity to discuss these problems with you. If you feel ill-equipped to deal with her problems, take comfort in the fact that there is always somewhere else to refer patients on to including: gynaecology units, psychosexual counsellors, marriage guidance counsellors, life coaches, sex therapists and social services,' concluded Miss Pitkin.

## References

- Athanasiadis L, Papaharitou S, Salpiggidis G, *et al.* Educating physicians to treat erectile dysfunction patients: development and evaluation of a course on communication and management strategies. *J Sex Med* 2006;3:47–55.
- McHorney CA, Rust J, Golombok S, *et al.* Profile of female sexual function: a patient-based, international, psychometric instrument for the assessment of hypoactive sexual desire in oophorectomised women. *Menopause* 2004;11:474–83.
- Basson R, Berman J, Burnett A, *et al.* Report of the international consensus development conference on female sexual dysfunction: definitions and classifications. *J Urol* 2000;163:888–93.
- Mazer NA. Testosterone deficiency in women: etiologies, diagnosis, and emerging treatments. *Int J Fertil* 2002;47:77–8.
- Dennerstein L, Koochaki P, Barton I, *et al.* Hypoactive sexual desire disorder in menopausal women. *J Sex Med* 2006;3:212–22.
- Simon J, Braunstein G, Nachtigall L, *et al.* Testosterone patch increases sexual activity and desire in surgically menopausal women with hypoactive sexual desire disorder. *J Clin Endocrinol Metab* 2005;90:5226–33.
- Buster J, Kingsberg SA, Aguirre O, *et al.* Testosterone patch for low sexual desire in surgically menopausal women: a randomised trial. *Obstet Gynecol* 2005;105:944–52.
- Dennerstein L, Leher P, Burger H, Guthrie J. Sexuality. *Am J Med* 2005;118 (Suppl 12B):59–63.
- Rust J, Derogatis L, Rodenberg C, *et al.* Development and validation of a new screening tool for hypoactive sexual desire disorder: The Brief Profile of Female Sexual Function (B-PFSF). *Gynecol Endocrinol* 2007;23:638–44.
- www.fsdeducation.eu; Educational Slide Sets, Module 1 : Menopause Transition.
- Nusbaum MR, Helton MR, Ray N. The changing nature of women's sexual health concerns through the midlife years. *Maturitas* 2004;49:283–91.

Intrinsa ▼ 300 micrograms/24 hours transdermal patch

**ABBREVIATED PRESCRIBING INFORMATION:**

**PRESENTATION:** Patch of 28 cm<sup>2</sup> contains 8.4 mg testosterone and provides 300 micrograms of testosterone/24 hrs. **INDICATIONS:** Intrinsa is indicated for the treatment of hypoactive sexual desire disorder (HSDD) in bilaterally oophorectomised and hysterectomised (surgically induced menopause) women receiving concomitant estrogen therapy. **DOSAGE AND ADMINISTRATION:** 300 micrograms/24 hrs by applying one patch at a time, twice weekly on a continuous basis, to a clean, dry area of skin on the lower abdomen below the waist (replace with a fresh patch every 3–4 days). A skin site with minimal wrinkling and not covered by tight clothing is recommended. The site should not be oily, damaged, or irritated. No creams, lotions or powder should be applied to the skin where the patch is to be applied. Rotate application site with an interval of at least 7 days between applications. Do not apply to the breasts or other body regions. Concomitant estrogen treatment: Prior to therapy, and during re-evaluation, consider the use and restrictions associated with estrogen therapy. Not recommended for patients treated with conjugated equine estrogen (CEE). Duration of treatment: Re-evaluate treatment response within 3–6 months of initiation and consider discontinuation of therapy in patients who do not experience a meaningful benefit. Re-evaluate every 6 months thereafter. The efficacy and safety of Intrinsa have not been evaluated in studies of longer duration than 1 year. Children and adolescents: Not for use in children and adolescents. **CONTRAINDICATIONS:** Hypersensitivity to testosterone or any of the excipients. Known, suspected or past history of cancer of the breast or known or suspected estrogen-dependent neoplasia, or any other condition consistent with the contraindications for the use of estrogen. **PRECAUTIONS:** Regularly monitor patients for potential androgenic undesirable effects (e.g. acne, changes in hair growth or hair loss). Patients should be advised to self assess. Signs of virilization, such as voice deepening, hirsutism or clitoromegaly, may be irreversible and discontinuation of treatment should be considered. In clinical trials these reactions were reversible in the majority of patients. Discontinue use of the patch if severe skin erythema, local oedema and blistering occur at application site. The long-term effect of testosterone treatment on the breast, endometrium and cardiovascular system are unknown. Monitor in accordance with currently accepted screening practices and individual patient needs. Carefully monitor blood pressure and weight in patients with cardiovascular risk factors, (particularly hypertension, and known cardiovascular disease). In diabetics, testosterone may decrease blood glucose and therefore insulin requirements. Oedema (with or without congestive heart failure) in patients with pre-existing cardiac, renal, or hepatic disease is not expected from the low dose of testosterone delivered by Intrinsa. Recommended for use in surgically menopausal women up to the age of 60. Intrinsa cannot be recommended in naturally menopausal women. Androgens may decrease levels of thyroxin-binding globulin, resulting in decreased total T4 serum levels and increased resin uptake of T3 and T4. Free thyroid hormone levels remain unchanged, however, and there is no clinical evidence of thyroid dysfunction. **INTERACTIONS:** Concomitant use of testosterone with

anticoagulants may increase their effect. Closely monitor patients receiving oral anticoagulants when testosterone therapy is started or stopped. **USE IN PREGNANCY AND LACTATION:** Intrinsa must not be used in women who are or may become pregnant or by breast-feeding women. Discontinue use in case of inadvertent exposure during pregnancy. **SIDE EFFECTS:** The adverse reaction most often reported (30.4%) was application site reactions. The majority of these adverse reactions consisted of mild erythema and itching and did not result in patient withdrawal. Hirsutism was also very commonly reported. Most reports concerned the chin and upper lip, were mild (≥ 90%), and less than 1% of all patients withdrew from the studies due to hirsutism. Other androgenic effects commonly reported were acne, voice deepening and alopecia. More than 90% of these reports were considered mild. These reactions were reversible in the majority of patients. Less than 1% of patients withdrew from the studies because of any of these reactions. All other common adverse events resolved in the majority of patients. During 6-month double blind exposure the following adverse reactions occurred in the treatment group (n=549) at a greater incidence than placebo (n=545) and were assessed by the investigators as possibly or probably related to Intrinsa treatment: Very common (≥1/10): hirsutism, application site reaction (erythema and itching) Common (≥1/100, <1/10): insomnia, migraine, voice deepening, abdominal pain, acnes, alopecias, breast pain, and increased weight. Uncommon (≥1/1000, <1/100): sinusitis, abnormal clotting factor, hypersensitivity, increased appetite, agitation, anxiety, disturbance in attention, dysgeusia, impaired balance, hyperaesthesia, oral paraesthesia, transient ischemic attack, diplopia, eye redness, palpitations, nasal congestion, throat tightness, diarrhoea, dry mouth, nausea, eczema, increased sweating, rosacea, arthritis, breast cyst, clitoral engorgement, enlarged clitoris, genital pruritus, vaginal burning sensation, anasarca, asthenia, chest tightness, chest discomfort, abnormal blood fibrinogen, increased heart rate, increased alanine aminotransferase, increased aspartate aminotransferase, increased blood bilirubin, abnormal liver function test, increased blood triglycerides. **PACK QUANTITY:** Cartons of 2, 8 and 24 patches. Not all pack sizes may be marketed. **BASIC COST:** £28.00 in UK. **MARKETING AUTHORISATION NUMBER(S):** EU/1/06/352/002. **EU LEGAL CATEGORY:** POM. **MARKETING AUTHORISATION HOLDER:** Procter & Gamble Pharmaceuticals UK Ltd, Rusham Park Technical Centre, Whitehall Lane, Egham, Surrey, TW20 9NW United Kingdom. Refer to Summary of Product Characteristics before prescribing.

Date of preparation: October 2008; INT-UK3240

UK: Adverse events should be reported. Reporting forms and information can be found at [www.yellowcard.gov.uk](http://www.yellowcard.gov.uk). Adverse events should also be reported to Procter & Gamble Pharmaceuticals UK Ltd on 0800 032 8701.  
Ireland: Reporting forms and information can be found at [www.imb.ie](http://www.imb.ie). Adverse events should also be reported to Procter & Gamble Pharmaceuticals UK Ltd on 1 800 88 29 37 (Ireland).

This supplement is sponsored by **Procter & Gamble Pharmaceuticals UK Ltd**

Printed and published by Wiley Interface – a division of John Wiley & Sons, The Atrium, Southern Gate, Chichester, West Sussex P019 8SQ. © John Wiley & Sons 2008.

The views expressed in this publication are not necessarily those of the publisher or Procter & Gamble Pharmaceuticals UK Ltd

Pr. 824

Date of preparation October 2008  
INT-UK3236