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(Impotence)

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UROLOGICAL SOCIETY OF
AUSTRALIA AND NEW ZEALAND
ABN 64 890 438 680

4 September 2009

Ms Penny Wijnberg
Senior Research Officer
Standing Committee on Health and Ageing
House of Representatives
Parliament House ACT

By email

Dear Ms Wijnberg

Please find attached material to be included as written submissions from the Urological Society of Australia and New Zealand (USANZ) to the House of Representatives Roundtable Forum on Impotence Medications.

The Urological Society of Australia and New Zealand (USANZ) is the peak specialist medical body treating disorders of the urinary tract and male reproductive system. Urologists assess and treat all aspects of erectile dysfunction, from counselling through to the medical and surgical management of the condition. USANZ is a thought leader and advocate to the wider community in all aspects of urological well-being.

In the first instance, USANZ seeks to alert the Committee to a subtle but increasingly relevant issue pertaining to AMI and the impact of its conduct on the wider community. USANZ feedback to date indicates that there is an adverse effect that extends beyond the middle to older aged male demographic. There is evidence that adolescent males are seeking inappropriate treatment and experiencing psychological distress directly as a result of AMI's campaign promoting "longer lasting sex". USANZ believes that this marketing is inappropriately targeting impressionable and vulnerable young men who are unaware of the health consequences of unnecessary intervention. It is well established that premature ejaculation in this demographic is common and resolves in the vast majority of occasions with sexual experience and/or appropriate medical counselling.

The USANZ submission includes this letter and three other documents. The first attached document is closely related to the opening statement I made in session one in Canberra. The text of this document is appended below.

The second document, labelled AMI Letter, is a de-identified letter from a patient treated by a Queensland Urological colleague. The patient has detailed his adverse experience with AMI in a comprehensive letter which I wish to table. I have spoken with him personally and he would like to identify himself and speak publicly about his

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contact with AMI, though he is concerned about potential legal complications related to a deed he was required to sign before a refund was provided to him.

The third document is an email from another colleague, Dr Steve Brough from Tasmania, describing his experience when he rang the AMI Clinic number requesting information on the composition of a drug prescribed by an AMI doctor. USANZ notes the response by the AMI Clinic employee to Dr Brough's enquiry is at odds with Mr Doyle's statement to the Committee that AMI will make freely available information regarding the composition of the agents prescribed by AMI. I refer to Mr Doyle's statement to the Roundtable Forum as recorded in Hansard where he said "We are quite happy to advise what the active ingredients are in the formulations."

USANZ would also like to provide material to the Committee in support of our statements regarding the deficiencies in the standard of care being provided by AMI. These deficiencies are firstly related to the method of telephone assessment used by AMI employees of erectile dysfunction patients, and secondly to the selection of therapeutic agents employed by AMI as first and second line therapies.

USANZ holds that the practice of assessing new patients with erectile dysfunction without a face to face appointment is fundamentally flawed. USANZ wishes to table two publications in support of this. The first is the **EAU Guidelines on Erectile Dysfunction: An Update (May 2006)**. The European Association of Urology is one of the 2 premier educational bodies in the international urological domain, representing some 12000 urologists. The document I refer to can be found in full at http://www.europeanurology.com/article/S0302-2838%2806%2900088-1/pdf/EAU+Guidelines+on+Erectile+Dysfunction%3A+An+Update. I would like to draw the attention of the Committee to two key points. The first point emphasises the importance of a focused urological examination and laboratory investigations in the assessment of a new patient with erectile dysfunction. These "best practice" guidelines demonstrate the inadequacies and the potential for mis-diagnosis of the telephone assessment conducted by AMI doctors, where no such physical examination or laboratory assessment is performed. The guidelines note inter-alia:

A focused physical examination must be performed on every patient, with particular emphasis on the genitourinary, endocrine, vascular, and neurologic systems. The physical examination may reveal unsuspected findings, such as Peyronie disease, prostatic enlargement, or cancer as well as signs and symptoms indicative of hypogonadism (small testes, alterations in secondary sexual characteristics, diminished sexual desire, changes in mood, fatigue syndrome, reduced physical performance) [7]. Blood pressure and heart rate should be measured if not assessed in the previous 3–6 mo. Particular attention must be given to patients with cardiovascular disease (see Section 2.2).

Laboratory testing must be tailored to the patient's complaints and risk factors. All patients must undergo a fasting glucose and lipid profile if not assessed in the previous 12 mo. Hormonal testing must include a morning sample of total testosterone (bioavailable or calculated-free testosterone is more reliable to establish the presence of hypogonadism, ie, these tests are preferable to total testosterone if available). Further laboratory tests must be considered only in selected patients (eg, prostate-specific antigen [PSA] for detection of prostate cancer). Additional hormonal tests (eg, prolactin, follicle-stimulating hormone [FSH], luteinizing hormone [LH]) must be carried out when low testosterone levels are detected. If any abnormality is observed, further investigation by referral to another specialist may be necessary [11]. Minimal diagnostic evaluation (basic work-up) in patients with ED is presented in Fig. 1.

The second point relates to the agents used by AMI to treat erectile dysfunction patients. USANZ holds that the use of an agent other than an oral phosphodiesterase (PDE5) inhibitor (such as Viagra, Levitra or Cialis) as first line therapy is

inappropriate clinical practice for the vast majority of patients, and falls below the minimum standard of care expected from a registered medical practitioner. This belief is consistent with international practice. Listed below is an extract from the EAU Guidelines with a reference comparing the relative effectiveness of PDE5 inhibitors to apomorphine, the primary compound in the "nasal delivery technology" offered by AMI. Whilst the reference below in paragraph 4 comparing PDE5 inhibitors (in this study sildenafil (trade name Viagra)) to apomorphine refers to the sub-lingual (oral) form of apomorphine, the conclusions regarding the comparative effectiveness of PDE5s are also relevant to nasally delivered apomorphine. The guidelines state:

3.4. First-line therapy

3.4.1. Oral pharmacotherapy

Phosphodiesterase type 5 (PDE5) is an enzyme that hydrolyzes cyclic guanosine monophosphate (cGMP) in the cavernosum tissue of the penis. Inhibition of PDE5 results in increased arterial blood flow leading to smooth muscle relaxation, vasodilatation, and penile erection. Three potent selective PDE5 inhibitors are currently licensed with proven efficacy and safety for the treatment of ED.

3.4.1.7. Apomorphine sublingual

Apomorphine is a centrally acting drug (dopamine agonist, mainly D2) that improves erectile function by enhancing the natural central erectile signals that normally occur during sexual stimulation. It is administered sublingually on demand in 2- or 3-mg doses. Apomorphine has been approved for ED treatment in many countries but not in the United States.

Efficacy rates (erections hard enough for intercourse) range from 28.5% to 55% [39]. Due to rapid absorption, 71% of erections are achieved within 20 min. The most common adverse events are nausea (7%), headache (6.8%), and dizziness (4.4%). Apomorphine is not contraindicated in patients taking nitrates or antihypertensive drugs of all classes and it does not affect vital signs.

Comparative studies clearly show that apomorphine is associated with significantly lower efficacy and satisfaction rates than sildenafil [40]. Today, the use of apomorphine is limited to patients with mild to moderate ED or psychogenic causes due to reduced efficacy rates. It also may represent a first-line treatment in patients with certain contraindications (eg, use of nitrates) for the use of PDE5 inhibitors.

USANZ wishes to ensure the committee appreciates the significance of the statement "Comparative studies clearly show that apomorphine is associated with significantly lower efficacy and satisfaction rates than sildenafil [40]. Today, the use of apomorphine is limited to patients with mild to moderate ED or psychogenic causes due to reduced efficacy rates." These best practice guidelines confirm that the use of apomorphine containing compounds in preference to PDE5 inhibitor agents as a first line agent represents inappropriate clinical practice for the vast majority of men with erectile dysfunction.

The other leading international educational body is the American Urological Association (AUA). The AUA has over 16500 members internationally. The second document for tabling before the Committee is the **Management of Erectile Dysfunction ('05/Updated '06)** and can be found at http://www.auanet.org/content/guidelines-and-quality-care/clinical-guidelines/main-reports/edmgmt/chapter1.pdf. This document also defines best practice management of men with erectile dysfunction. USANZ draws the Committee's attention to the AUA reference to the initial patient contact:

The typical initial evaluation of a man complaining of ED is conducted in person and includes sexual, medical, and psychosocial histories as well as laboratory tests thorough enough to identify comorbid conditions that may predispose the patient to ED and that may contraindicate certain therapies.

The AUA document goes on to describe the role of a physical examination:

A focused physical examination evaluating the abdomen, penis, testicles, secondary sexual characteristics and lower extremity pulses is usually performed.

The AUA document also includes an evidence based approach to the implementation of treatment strategies:

Initial Management and Discussion of Treatment Options with Patients

Recommended Therapies and Patient Information

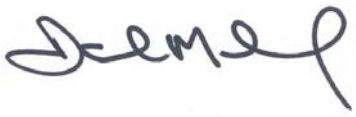
Standard: The management of erectile dysfunction begins with the identification of organic comorbidities and psychosexual dysfunctions; both should be appropriately treated or their care triaged. The currently available therapies that should be considered for the treatment of erectile dysfunction include the following: oral phosphodiesterase type 5 [PDE5] inhibitors, intra-urethral alprostadil, intracavernous vasoactive drug injection, vacuum constriction devices, and penile prosthesis implantation. These appropriate treatment options should be applied in a stepwise fashion with increasing invasiveness and risk balanced against the likelihood of efficacy.
[Based on review of data and Panel consensus.]

The best practice guidelines from the AUA describe the stepwise introduction of therapies, confirming the role of PDE5 inhibitors as the first line agent. It is of significance that apomorphine is not listed as a therapeutic option in the AUA Guidelines as it is not approved for use in the United States.

In summary, the two leading international urological education and accreditation bodies, the EAU and the AUA, have published best practice guidelines which concur with the USANZ position that a physical examination and basic laboratory investigations are both important components of the assessment of a new patient with erectile dysfunction. In the guidelines there is also concordance with the USANZ position that PDE5 inhibitors should be the first line agent for the majority of men with erectile dysfunction where pharmacological therapy is indicated.

USANZ appreciates the opportunity of making a submission to the House of Representatives Committee and is willing to act as an ongoing resource to the Committee with regards to this important issue if requested.

Yours sincerely



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President
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Material Presented to the Roundtable Forum 21 August 2009

I would like to thank the House of Representatives Standing Committee for the opportunity to speak on the subject. The practices of commercial impotence clinics have been a concern of mine and of my professional body for some time.

Urologists are medical specialists who treat disorders of the urinary and reproductive systems. We work in conjunction with general practitioners who, in an ideal model, should be the first contact point for men with ED. We address all aspects of the management of ED from the initial assessment and diagnosis, through to management including counselling, medical therapy and surgical options. As such, I believe urologists are well placed to comment on this topic.

Commercial ED clinics are a story of bad medicine and bad marketing.

ED is common, and becomes more common as men age. The diagnosis includes disorders of libido (sexual desire), erection and ejaculation. There is no one size fits all treatment. In younger men, the condition is often an issue of confidence and counselling is all that is required. As men age, other important medical conditions may be present, including heart and other vascular disease, diabetes, obesity and disorders of the nerve and hormone systems.

The practice of telephone assessment is incomplete and inappropriate. The qualifications of call centre operatives are unknown. No basic physical examination or blood tests are performed. No assessment of the common associated medical conditions is undertaken. Australian men do not often visit doctors. A telephone interview is a lost opportunity for a doctor to assess and implement basic preventative strategies with regards to alcohol and smoking habits, obesity, blood pressure and cholesterol management. The psycho-social aspects of ED are not addressed.

The treatment strategies employed by commercial ED clinics are a similar sad tale. Men are enticed into anonymously calling the ED clinics by clever advertising which promises a quick and simple fix. These men are often too embarrassed to speak to their GP. The reality is that the nasal delivery system rarely works. Apomorphine has been extensively evaluated by the medical and pharmaceutical communities and has shown to be less effective and to have more side effects than comparable agents. As a result men who have signed expensive contracts ultimately end up with injectable agents. These are expensive and poorly tolerated and have high treatment drop out rates.

It is appalling that these men are never offered oral agents such as Viagra, Levitra and Cialis as first line medical therapy. These drugs are effective, safe and relatively inexpensive. Many patients of mine who have been treated by commercial ED clinics before I see them are dismayed to learn that a simple tablet is all they need to treat their problem.

Patient selection is also a concern. I know of a 17 year old boy prescribed injectable agents by AMI to treat premature ejaculation. There is no medical evidence to support this and counselling should be the first line of therapy. We have seen AMI initiate a marketing campaign to treat female sexual dysfunction. There are claims on the AMI

website that disorders of desire, arousal, orgasm and painful intercourse can be addressed. There is limited or no evidence that drug therapy is indicated for any of these conditions. The best evidence supports counselling and simple non-drug therapies for these conditions.

Let me finish with a story of a 45 year old patient of mine. He was using injectable agents from an ED clinic. This was not the appropriate agent as counselling or an oral tablet would have been effective for what was, at the time, a mild problem. He developed a prolonged erection which permanently damaged his erectile function. He now is completely impotent as a result of this poor management.

We need to develop a system which will assess and treat men with ED appropriately, and one which will protect them from aggressive commercial enterprises.

Dr David Malouf
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