Australian Government
Department of Health
Therapeutic Goods Administration

Urogynaecological Devices Working Group

Minutes

Meeting 2

22 October 2013

Teleconference

TGA Health Safety Regulation

Contents

The second meeting of the Urogynaecological Working Group (UDWG) was held on 22 October 2013 by teleconference, commencing at 6.30pm AEST.

Participants

Members: [redacted]

TGA officers: Dr Jane Cook (Chair) – Head, Office of Product Review (OPR)

Ms Pamela Carter, Director, Device Monitoring and Vigilance, OPR

Dr Rhianna Thompson, Medical Officer, Device Monitoring and Vigilance, OPR

Secretariat: Mr Craig Davies, Secretary, Advisory Committee on the Safety of Medical Devices, OPR

Item 1 Administrative arrangements

1. 1 Welcome and apologies

The Chair welcomed members to Meeting 2 of the UDWG.

1.2 Apologies

Apologies were received from [redacted] who was unable to participate in this meeting due to unforeseen circumstances.

1.3 Disclosure of interest declaration forms

Members submitted disclosure of interest forms for the item under consideration prior to the teleconference. There were no declarations of interest made for this meeting.

Item 2 Minutes of the previous meetings

2.1 UDWG1 Minutes

Members ratified the draft Minutes from Meeting 1 subject the Working Group's advice under Item 3 being amended as indicated at Attachment A.

2.2 Matters arising from UDWG1 Minutes

Members noted the status of the matters arising from UDWG1 and that some would be further discussed in items below.

A member asked whether the TGA had been able to consider the feasibility/ appropriateness of the Working Group's suggestion to re-classify **all** urogynaecological mesh devices as Class III medical devices under the current legislation.

The Chair advised that the TGA had further discussions about this suggestion since UDWG1 and has reached the view that at this time, there is insufficient evidence to support a change in classification. More specifically, the data isn't robust enough to determine if there's a significant problem with the actual devices or whether there are problems in particular patient groups or if the problems are as a result of the manner in which the devices are being used in some circumstances. The TGA's preference, at this time, is for the Working Group to further consider some of the other risk mitigation strategies being discussed.

The members noted that companies are now promoting newer products with claims of similarity to older products. This raises concerns as to whether old problems will be repeated and whether the newer products will result in a new wave of adverse events. The Working Group also expressed concerns about the lack of clinical data provided by companies to support the use of their products and also in relation to the paucity of data addressing complication rates. The Chair advised that the TGA's pre-market regulatory framework does not allow for the evaluation of comparative efficacy data nor is there a mandatory number of procedures required in a clinical study as part of a device's marketing approval process.

Item 3 Post market review of urogynaecological mesh devices

3.1 Overview of *Instructions for Use* and training material submitted to the TGA

Background

In considering issues relating to the safety and performance of urogynaecological surgical mesh devices, the Working Group has noted that the quality, quantity and actual supply of Instructions for Use (IFU) and training materials are variable between the manufacturers of mesh devices.

During UDWG1, it was agreed that the TGA would present to the Working Group a review of IFUs and training material for devices currently in use and to provide the committee with examples of these items.

Instructions for Use

The TGA reviewed the IFUs that have been provided and summaries of Stress Urinary Incontinence (SUI) devices and Pelvic Organ Prolapse (POP) devices were included in the agenda papers. [redacted]

Several of the IFUs were of satisfactory quality and included all or most of the expected information regarding warnings, contraindications and adverse events. It was noted that diagrams are present in some instructions. An example of an acceptable IFU was included in the agenda papers.

However, the meeting was also advised that there are several IFUs which have very brief instructions and don't include some of the known adverse events such as dyspareunia, erosion and, in the case of SUI devices, whether the device can be used when the patient also has other pelvic floor problems such as cystocele. An example of a poorly written and constructed IFU was also included in the agenda papers.

The Working Group was advised that the majority of IFUs meet the requirements of EP13 however; there are some areas for improvement in several. There is inconsistency with the quantity and quality of the information provided; specifically in the area of adverse events and information on how to perform the surgery using the devices and instruments provided.

Training material

The Working Group noted there was a wide variation in the material submitted. [redacted]

Additionally, minimal and inadequate information or electronic only training materials were supplied by - [redacted] and TFS.

The training materials for some devices were limited in scope and limited information was provided about access to training or preceptorship programs. There was also no information about access to training for Australian surgeons in some [redacted]

Examples of both adequate and inadequate training material were included in the agenda papers. The Working Group was also advised that detailed training which appears to be appropriate and adequate (as it included hands-on workshops/ preceptorship-style training/ RANZCOG accredited training) was provided by: [redacted]

An example of an appropriate and adequate training program was included in the agenda papers.

The Working Group noted that the training material is variable, with very few manufacturers having a thorough program that includes video/DVD procedures, detailed instructions, face-to-face training conducted by the manufacturer or another surgeon accredited to teach these procedures and continuing education and preceptorship programs. It was also noted that several manufacturers seem to rely on the surgeon having surgical experience with other devices or with native tissue repairs.

The working group's advice on a number of specific questions asked by the TGA is detailed below.

Advice

Given the variable quality and quantity in the IFUs, does the UDWG have advice regarding what should be a minimum data set in the IFUs?

The Working Group suggested that the TGA could develop a template or proforma for training and educational material for health care professionals (based on the acceptable material included in the agenda papers). This template / proforma should distinguish between 'training' and 'education'; and be sent to the sponsors/manufacturers with the advice that this is the minimum level of information to be provided with their devices in the Australian market which is likely to comply with the relevant EPs for safety and performance.

It was also suggested that a template be developed which manufacturers could use to develop patient information leaflets for doctors to hand out to their patients.

[redacted] Therefore a template for an IFU should include relevant information populated under the following headings –

- Cautions / General Warnings;
- Device description;
- Intended purpose;
- Contraindications;
- Directions (include relevant warnings)
  - Prior to use
  - Steps in use
  - Tension mesh / Sleeve removal
- Post procedural warning/s;
- Potential complications;
- Precautions;
- Storage;
- Warranty;

and a template for a training and educational program intended for urogynaecologists, surgical gynaecologists and urologists should include relevant information under the following headings -

- Surgeon training options;
  - Cadaver workshops
  - Proctor and preceptor training networks
  - Speaker programs
  - Technique 'spotlights' and procedural steps, including videos / DVDs which illustrate step-by-step instructions
  - Directions for use
- Virtual Education Forums which include a variety of educational and training tools designed to enhance urogynaecology knowledge and product techniques;
- Territory manager training; and
- Patient resources.

The meeting also discussed whether there was the capacity to mandate that manufacturers provide a 'patient card' with the products for surgeons to complete and return to the company with details of the implant's use. The meeting was advised that the US FDA mandated this for active implantable devices approximately 20 years ago and the issue is currently being considered by the International Medical Devices Regulators Forum (IMDRF). This type of change to practice is slowly evolving and will be most likely driven by market forces.

A member asked whether any such patient card could be mandated to be returned to and logged by the TGA. The meeting was advised this is not possible as it is not within the TGA's legislative bounds to establish (quasi) product registries. It was also noted that the previous Government had committed $1.4 million per year for breast implant and cardiac device registries.

As the training material provided is vastly different between manufacturers, does the UDWG have advice regarding what amounts to adequate training of surgeons by sponsors and manufacturers?

The Working Group was reminded that the scope of the therapeutic goods legislation does not extend to 'medical practice issues' and considered that an adequate amount of training would be jointly determined by the adequacy of the training material provided by the companies, the requirements set by the relevant professional organisations and the standards of accreditation set by the hospitals where these procedures are carried out.

In this regard, a member advised the meeting that some hospitals require surgeons to firstly observe a certain number of procedures and then perform a certain number under supervision before being granted accreditation to perform the procedures alone.

The meeting was also advised that documentation relevant to this issue is currently under consideration by the Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG).

3.2 Separating Medicare item numbers for native tissue and mesh repairs and for primary repair, or surgery for recurrent symptoms.

Background

During UDWG 1, the TGA undertook to have a discussion with the Department of Health's Medical Benefits Division (MBD) regarding the possibility of establishing separate Medicare item numbers for NT and mesh repairs and for primary repair, or surgery for recurrent symptoms. The meeting was advised that TGA and MBD staff held a teleconference on 24 September 2013 in which MBD advised that if a proposal was developed and submitted to MBD, separation of item numbers would be considered. To assist with this process, the Working Group considered a paper which outlined the benefits and limitations of expanding the current Medicare item numbers to differentiate between urogynaecological procedures involving mesh devices and native tissue repairs.

It was noted that the TGA does not collect data on product usage but supply figures have previously been provided by sponsors on a case by case basis and this information was again included in the agenda. Medicare Australia collects data about procedures performed in the public hospital setting through Medicare item numbers, but in the case of urogynaecological procedures the current Medicare item number descriptors do not differentiate between native tissue and mesh repairs, or between primary and subsequent repairs. As a result, current Medicare data cannot be used to infer information about the usage of urogynaecological mesh in Australia or to make comparisons with the rates of adverse events reports.

Additionally, whilst Medicare funds treatment and accommodation for public patients in public hospitals these encounters are not captured via the Medical Benefits Schedule (MBS) statistics. The MBS does not collect data on public patients in public hospitals, or on patients attending Accident and Emergency clinics and public outpatient departments of hospitals. Medicare statistics also exclude services provided to Department of Veterans' Affairs patients and some compensation cases. Medicare estimates that approximately 50% of surgeries of interest would be captured by the MBS data due the public/private mix of cases.

It was also noted that MBS data is not currently set up to collect data for non-Medicare related purposes. The MBS data is linked to payments and if there is no payment claim made then no data is available. There can also be variation in how services are provided to patients between states, hospitals, medical specialty etc.

The Working Group was advised that Medicare Australia is able to provide health-related statistics based on the items and groups in the MBS. The statistics are based on claims made to Medicare by eligible health professionals for their services to patients eligible for Medicare benefits. The data collected allows for the identification and analysis of trends and more complex reports can be requested from Medicare Australia.

As outlined above, the current MBS item numbers do not differentiate between primary and secondary repair nor mesh and native tissue repair. The current MBS items (14) that relate to Pelvic Organ Prolapse and Stress Urinary Incontinence repairs by various approaches were listed in the agenda papers.

The Working Group noted that any amendment to the MBS requires formal regulatory change and as part of the process, advice would be sought from the Medical Services Advisory Committee (MSAC). Expanding the number of MBS items would allow the MBS to collect data on the usage patterns of urogynaecological mesh devices in Australia. There would be a time lag before useful data could be collected as the new item numbers need to be introduced and adopted into common practice. There would then be a subsequent delay before enough data was collected to be able to infer trends in mesh use. Eventually the data collected may allow the determination of the proportion of mesh to non-mesh procedures being undertaken in Australia, depending upon appropriate claiming by health professionals.

As the quality of the data also relies on the adoption of the new item numbers by health professionals, collaboration between the relevant colleges will be required to promote proper use and reinforce the need for correct item number selection. Their support for the changes will also need to be provided in order for MSAC to consider the changes being proposed.

It was also noted there are legal implications if the wrong MBS item number is used as health professionals are legally responsible for services billed under their provider number in their name.

The current wording of the MBS items have mesh and non-mesh items included under the one number. This was originally put in place to prevent incorrect Medicare claims and simplify the MBS item numbers. There is the potential that by expanding the MBS item numbers this issue of incorrect Medicare claims could be reintroduced.

Currently repairs with or without mesh attract the same fee from Medicare. It was proposed that whilst the MBS item numbers could be split to differentiate mesh from native tissue repairs the same fee should continue to apply to both procedures to prevent influencing current practice. Current MBS item numbers cannot be divided in the current system (eg. 35570a, 35570b) and the number of items available in the current section is limited. This means that new item numbers will need to be found elsewhere in the schedule either for all or some of the prolapse and incontinence items.

It was hypothesised that the expansion of MBS item numbers could also provide a cost effective alternative to setting up a formal registry similar to the National Joint Replacement Registry (a registry funded by the Department of Health), although the data from MBS item number usage would be much more limited than that provided by a registry.

The Working Group noted the following benefits from expanding the current MBS item numbers -

- MBS data will allow for the inference of patterns of usage of urogynaecological mesh devices in Australia;
- The data will allow for gross differentiation between primary and secondary repair;
- The data can be used to assist product safety monitoring; and
- It is more cost effective than establishing a national registry.

However, the following limitations with this approach were also noted -

- MBS statistics only capture approximately 50% of surgeries;
- There will be a delay before changes can be incorporated into the MBS;
- The changes will only be effective if there is uptake of the new MBS item numbers among health professionals;
- Results will be limited in the first few years of data collection as adequate data collection before inferences such as to mesh usage can be made will take time; and
- Related MBS item numbers will not be sequential and this may cause confusion.

The working group's advice on a number of specific questions asked by the TGA is detailed below.

Advice

Does the UDWG agree that all relevant MBS item numbers for POP and SUI repairs by various approaches have been identified or can the working group identify any other relevant MBS item numbers that should be considered as part of this review?

The Working Group did not identify any additional MBS item numbers to those listed in the agenda papers which it considered should be part of this review.

Should all item numbers be split to differentiate between mesh and non-mesh procedures or only those item numbers related to POP repairs?

The Working Group agreed that the splitting of MBS item numbers should be limited to the following three (3) numbers - 35570, 35571 and 35573. Following discussion about item number 35597, it remained unclear as to whether there would be any benefit in splitting this item. Members agreed to further discuss this with colleagues and report back to the TGA.

Action – UDWG members to seek advice from colleagues as to whether there would be benefit in splitting MBS item numbers 35570, 35571, 35573 and 35597 and to report back to the TGA.

The Working Group also agreed that the MBS item numbers for bladder stress incontinence were already well defined and there was no need for any changes to these items.

If the UDWG agrees that the splitting should be limited to POP repairs, should the splitting cover all approaches or only those procedures by the vaginal approach?

The Working Group agreed that the splitting of MBS item numbers should be limited to the four (4) listed above which cover (i) anterior, (ii) posterior and (iii) anterior and posterior vaginal compartment repair, all by the vaginal approach; and (iv) sacral colpopexy.

Does the UDWG feel this approach will provide sufficient information to make inferences about mesh usage in the Australian setting?

The Working Group felt that the splitting of the four (4) item numbers listed above, to differentiate between mesh and non-mesh repairs, should provide some more useful information about the usage of urogynaecological mesh products in Australia and some information about revisions in the future.

What advice can the working group provide regarding the likely benefit that the differentiation of the MBS item numbers will have on the safety monitoring of these devices?

Despite the limitations discussed above about the scope of MBS statistics, the Working Group advised that by differentiating between mesh and non-mesh procedures, the TGA will still be able to gain a better understanding of the total number of mesh procedures being performed (compared to the information currently available). This would then provide a 'denominator' which could be used to calculate a better approximation of the overall number and rates of adverse events which are occurring with these devices; which in turn will further inform the TGA's approach to the ongoing safety monitoring of these devices.

Given that increasing the number of MBS item numbers increases the complexity of the schedule, does the working group feel that a further expansion of select MBS item numbers to differentiate between primary repair procedures from secondary repair procedures would provide any further useful information?

The Working Group considered that this question has been addressed in advice provided above.

As there will be the need for support from the relevant professional colleges / associations, can the UDWG provide advice on how this could be advanced?

UDWG members were generally of the view that their respective professional societies should be supportive of the proposal to split the three (3) MBS item numbers.

Following discussion, it was agreed that the TGA should write to the Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG), the Urological Society of Australia and New Zealand (USANZ), the Royal Australasian College of Surgeons (RACS) and the Urogynaecological Society of Australia (UGSA), seeking their written support of the proposal to split the three (3) MBS item numbers listed above, but also agreed that it would be prudent for members to firstly raise the proposal in an informal manner within their peer groups.

Action - UDWG members to informally raise the proposal to split the four (4) MBS item numbers listed above within their own professional societies and to advise the TGA of the feedback received.

Item 4 Next Meeting

The Chair advised that due to the continuing evaluation work being carried out by the TGA, it is likely that the next meeting will be scheduled sometime during late February – mid March 2014.

Members will be given plenty of advance notice and will again be asked to complete a Doodle Poll to assist with setting the date for UDWG Meeting 3.

Meeting close

The Chair closed the meeting at 8.15 pm and thanked members for their participation.

Dr Jane Cook
Chair
Urogynaecological Devices Working Group
December 2013

Attachment A

Draft Minutes Extract

Urogynaecological Devices Working Group (UDWG) Meeting 1: 27 August 2013

Secretary's note

During the second meeting of the UDWG on 22 October 2013, members suggested several amendments to the Advice for Item 3 outlined the draft Minutes from UDWG1. These amendments have been included in the extract below and were referred to members for final endorsement on 18 December 2013 and subsequent ratification of the UDWG1 Minutes.

From the information sourced for the review of urogynaecological mesh, there does not appear to be evidence of benefit, but there is evidence of harm. Does the Working Group agree with the conclusion? Why and/or why not?

Having regard for the need to consider different types of procedures for the treatment of different conditions (as detailed above), the Working Group did not agree with the generalised, overarching statement that *"there does not appear to be evidence of benefit, but there is evidence of harm"* resulting from the use of mesh as it is inaccurate to apply such a statement to both POP and SUI mesh repairs.

The Working Group noted that the use of full-length synthetic slings for SUI had adequate support in the literature – including long term data. The Working Group noted that there was a lack of long term clinical evidence for the use of short or mini-slings.

With regard to the use of mesh for POP repair the Working Group stated that the data indicated there is some evidence of benefit in using mesh via an abdominal approach for apical compartment repairs.

The Working Group also advised there is very minimal data available to draw any clear conclusions regarding the use of transvaginal polypropylene mesh in the anterior compartment. Anterior compartment repairs are usually performed trans-vaginally, although there may be some cases where the abdominal approach could be considered. However, the Working Group agreed that with insufficient evidence of benefit and with some suggestion of increased harm, there was no current evidence to support the use of mesh in the anterior compartment when inserted trans-vaginally, unless determined to be appropriate on a case-by-case basis.

It was also noted there is a three-fold increased rate of reoperation rates to treat complications such as pain, and erosion when compared with complications and reoperations for NT repair. The Working Group also agreed that while there is some evidence of potential harm following the use of mesh in the posterior and apical compartments, the current evidence was that there was also no benefit in using mesh in the posterior compartment. The Working Group also advised that there was insufficient evidence to determine the role of mesh in the apical compartment when inserted transvaginally.

Can the Working Group provide additional comments on the review, including about the robustness of the evidence considered?

The Working Group agreed there is a lack of good evidence to demonstrate a clear benefit in the overall use of mesh compared to non-mesh procedures. In relation to whether there is sufficient evidence that the use of mesh causes clear patient harm, members pointed to conflicting advice in the literature.

Against this background, the Working Group agreed that there is some long term data in the literature which supports the use of full length sling meshes for the treatment SUI and in these cases the devices have demonstrated satisfactory safety and performance. Members noted that the use of mesh for transvaginal repairs is the main problem area. The committee therefore agreed that consideration of the remaining questions would be in the context of meshes used for transvaginal repair and there was no need for further consideration of meshes used in the treatment of SUI.

From the evidence considered, can the Working Group identify any patient groups where the use of urogynaecological mesh would be particularly advantageous?

Members noted the statement from the Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) that "very little robust information is available on the efficacy and long term safety of polypropylene mesh kits marketed for use in the surgical management of pelvic organ prolapse".

Members also noted the RANZCOG advice that it is not easy to identify who would benefit from a transvaginal mesh implant "since clear evidence is lacking and no guidance can be given regarding which specific mesh implant should be used since there is simply no robust comparative data available".

A recent useful consensus statement has been published in the International Urogynaecology Journal and a broad summary of the recommendations are:

> *"Exercise caution in using transvaginal mesh implants in:*
> *1. Primary prolapse cases;*
> *2. Patients younger than 50;*
> *3. Lesser grades of prolapse (POP-Q ordinal grade 2 or less);*
> *4. Posterior compartment prolapse without significant apical descent;*
> *5. Patients with chronic pelvic pain; and*
> *6. Postmenopausal patients who are unable to use vaginal oestrogen therapy since this will be first line therapy for erosion".*

It was also noted that "these suggestions on patient selection are not intended to be exclusive or all encompassing, and do not preclude the necessity of a broad based wide ranging discussion with the patient regarding her specific situation".

The Working Group agreed that the evidence of benefit in higher risk groups (eg obese patients, smokers, the elderly, those with failed primary repairs) is limited and the overall body of evidence shows no clear benefit for any patient group. They noted that although there was no evidence available, there may however, be a theoretical benefit in some cases, for example –

- where there has been a failed previous repair in the anterior compartment (which is traditionally performed by the vaginal approach); or
- in groups where there is a potential for higher rates of recurrence eg patients with higher grades of prolapse, or poor connective tissue, failed previous surgery in any compartment, obese patients and patients with raised intra-abdominal pressure (such as a chronic cough in smokers).

It was noted that the identified risk groups are those who experience higher rates of prolapse as well as a higher comparative rate of complications. Members emphasised that it is not possible to set parameters which would adequately define an appropriate patient population for the use of these devices. The role of clinicians in determining patient suitability on a case by case basis will continue to be very important.