Sent Express Post 30/8/11

SENDER TO KEEP
085934756094
DOCUMENT 73

150

Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

File Reference 2011/011177

Attention: [redacted]
Eska Australia
Unit 32 A&B of 2-6 Chaplin Drive
LANE COVE NSW 2066

31 OCT 2011

Dear [redacted]

**Proposal to cancel the entry of a medical device from the Australian Register of Therapeutic Goods under Section 41GN of the Therapeutic Goods Act.**

| | |
|---|---|
| **Device Name:** | Eska Adapter Femoral Stem Prosthesis |
| **ARTG Number - Name:** | 118441 - Eska Australia - Prosthesis, internal, joint, hip, femoral component |
| **Sponsor:** | Eska Australia |
| **Manufacturer:** | Eska Implants GmbH and Co |

1. As a delegate of the Secretary to the Department of Health and Ageing for the purposes of Section 41GN of the Therapeutic Goods Act 1989 (the Act), I am writing to inform you that I propose to cancel the entry of the Eska Adapter Femoral Stem Prosthesis (the Device) from the Australian Register of Therapeutic Goods (the Register).

## Decision

2. I am proposing to cancel the entry of the Device because I am satisfied that it's safety and performance is unacceptable.

## Background

3. The TGA has reviewed orthopaedic implants that were identified in the 2010 Annual Report of the Australian National Joint Replacement Registry (NJRR) as having higher than expected revision rates. The Report and detailed information about implants that were identified as having higher than expected revision rates are available at http://www.dmac.adelaide.edu.au/aoanjrr/publications.jsp
4. The Device was one of the implants identified in the report as having higher than expected revision rates identified in 2010 Annual Report of the NJRR (Text, Tables and Diagrams in pages 147-152 of the report). Both the cementless and the cemented versions of the Device are identified as having higher than expected revision rates.

5. On 29 September 2010, the TGA wrote to Eska Australia about the fact that the Device had been identified in the NJRR report. The TGA letter included a comprehensive Implant Analysis Report from the NJRR about the performance of the Device in Australia and asked questions about complaint and adverse event reports, clinical trial results and other clinical evidence and for a statement from Eska Australia or the manufacturer in relation to any benefits afforded by the use of the Device that may compensate for the seemingly higher revision rates. The TGA received a response from Eska Australia on 29 October 2010.
6. The NJRR Implant Analysis Report for the Device, the complete response from Eska Australia and a case summary prepared by the TGA were presented to the Orthopaedic Expert Working Group (OEWG) for consideration at a meeting that took place on 24 November 2010. The OEWG is a group of orthopaedic surgeons, nominated by the Australian Orthopaedic Association, who advise the TGA on matters relating to the safety and performance of orthopaedic implants.
7. The OEWG expressed concern about the high revision rates being experienced with the Device in Australia and advised that Eska Australia had not made a convincing argument in favour of the safety and performance of the Device. On 17 January 2011, the TGA notified Eska Australia about the advice of the OEWG and that the TGA would have to make a decision about the ongoing availability of the Device in Australia. The letter also advised Eska Australia to review their previous submission and resubmit. The TGA received a further submission from the manufacturer of the Device – Orthodynamics – on 25 February 2011.
8. The OEWG considered all of the available information about the Device, including the Orthodynamics submission mentioned in 7 above once again at a meeting that took place on 25 May 2011. The submission from Orthodynamics failed to abate the OEWG's concern about the revision rates associated with the use of the Device.
9. After considering the information before me and the advice provided by the OEWG and the TGA's own experts, I am satisfied that the safety and performance of the Adapter Femoral Stem Prosthesis is unacceptable and propose to cancel the product from the Australian Register of Therapeutic Goods.

## Legislative Overview

10. Under Subsection 41GN(1)(e) of the Therapeutic Goods Act, the Secretary of the Department of Health and Aging has the power to cancel the entry of a medical device from the Register if she is satisfied that the safety or performance of the medical device is unacceptable.
11. Before cancelling the medical device from the Register, the Secretary must inform the person in relation to whom the medical device is included in the Register (the Sponsor) that she proposes the cancellation, setting out the reasons for it; and give the Sponsor reasonable opportunity to make submissions in relation to the proposed cancellation.

## Material Considered

12. In coming to my decision I have considered the following material:
    a. Section 41GN of the Therapeutic Goods Act 1989 (see **Attachment A**).
    b. The 2010 Annual Report of the Australian National Joint Replacement Registry (NJRR); and detailed individual reports from the NJRR regarding the safety and performance of the Device;

c. A letter from the TGA to Eska Australia dated 29 September 2010, and Eska Australia's response dated 29 October 2010.

d. The advice of the OEWG after they considered the NJRR Implant Analysis Report for the Device, the complete response from Eska Australia and a case summary prepared by the TGA during a meeting that took place on 24 November 2010.

e. A letter from the TGA to Eska Australia dated January 2011 advising Eska of the OEWG's recommendations and seeking further information; and the response to that letter provided by Orthodynamics GmbH on 25 February 2011.

f. The further advice of the OEWG after they considered the Orthodynamics mentioned in (e) above at a meeting that took place on 25 May 2011.

**Findings in relation to facts**

13. The 2010 Annual Report of the NJRR identifies both the cemented and cementless versions of the Device as implants that are experiencing higher than anticipated rates of revision. The revision rates are 2.11 and 4.04 revisions per 100 observed years for the cementless and the cemented versions of the Device respectively. Compared to the average performance of all other similar implants used in Australia, the adjusted hazard ratios are 6.10 and 1.99 for the cemented and the cementless version of the Device respectively. This means that compared to the average for all other similar prostheses, the risk of revision for a person who has received the cemented version of the Device is 6.10 times higher; and the risk of revision for a person who has received the cementless version of the Device is 1.99 times higher. These findings are statistically significant at the 0.1% level. Therefore, I find that the revision rate of the device is significantly higher than that of other implants of the same type. This is a concern because revision surgery is associated with significant morbidity and mortality.

14. The implant analysis report from the NJRR for the cementless version of the Device indicates that the 23 recorded revisions are evenly distributed among implanting hospitals. This means that the high rate of revisions is not related to the surgical technique of individual surgeons. The cumulative revision rate for the Device is rising steadily and the rate of revisions for the Device relative to the rate of revisions for all other similar devices (the hazard ratio) is also increasing with time. The proportion of revisions due to pain, leg length discrepancy, metal sensitivity, wear and implant breakage are all higher than the proportion of revisions for similar reasons in similar implants. Therefore, I find that the difference in risk of revision between the Device and similar implants increases with time since original implantation and that the pattern of usage does not explain the seemingly poor performance of the Device in Australia. Finally I find that the reasons for revision, particularly the relatively high number of revisions due to wear and implant breakage support a view that there are problems with the design of the implant that are leading to a high revision rate.

15. The implant analysis report from the NJRR for the cemented version of the Device indicates that the implanting hospitals that have used the Device the most are those hospitals that have recorded the most number of revisions. This is to be expected, and indicates again that the high rate of revisions is not related to the surgical technique of individual surgeons. The cumulative revision rate of the device even at two years is very high relative to similar implants, has risen at an unacceptable rate and analysis of the trend in the cumulative revision graph for the Device would indicate that the revision rate is likely to continue to rise rapidly in the future. The relative number of revisions due to loosening, pain and dislocation are much higher than that of all other similar implants and supports the view that there are problems with the implant itself that are leading to high revision rates.

16. The approach used in your response dated 29 October 2010 was to explain, on a case by case basis why the implants have been revised, and then to provide published literature that suggests that this femoral stem prosthesis has had good results elsewhere in the world. You have claimed that all of the revisions in the "Type of Revision" table that were provided to you by the TGA on 29 September 2010 were due to surgical error or inexperience, but you have not provided any supporting evidence (eg a cross reference to investigation reports, implant retrieval analysis etc) for the assertions. For the reasons given in paragraphs 14 and 15 I do not believe that surgical technique is responsible for the high revision rates attributed to the use of the Device.

17. In the same response ESKA supplied a table summarising the available literature and copies of key publications. The relationship between the implants used in the papers provided and Device is not clear in many of cases. Even so, the paper by Sielewicz et al reveals that the studies described were not without their complications (eg loosening, intraoperative stem fracture, pain). Götze et al report a cumulative survival rate of 90 ± 8 % for the acetabular component and 86 ± 5 % for the femoral component at 14.9 years. 137 patients were followed in this study and the authors state that four prostheses were revised due to implant fracture. These results call into question the performance of the Device. Further, the authors conclude that:

    *"The long term results of the spongy metal cup are good, whereas the high loosening and fracture rate of fully coated stem are a source of concern especially with regard to the difficult revision scenario with frequent massive bone loss."*

18. On 25 January 2011 Orthodynamics GmbH, the current German manufacturer of the implant, provided a further, more comprehensive response addressing the comparatively high revision rate of the Eska Adapter femoral stem prosthesis. In that submission Orthodynamics argues that the poor performance of the implant in Australia may be related to the high use of Metal on Metal bearings. Adapter femoral stems have been used in conjunction with Bionik metal femoral head in combination with Eska metal acetabular components. It is claimed that the Bionik femoral head had problems which have now been addressed through design changes, and that the Device has been "unfairly blamed" for the poor performance of the Bionik femoral head component. The main points are that the manufacturer concedes that the results are poor and that these needed addressing by changing the design of the Device and the components that are used in conjunction with the Device.

19. The OEWG made several observations about the NJRR data, and the submission made by Eska Australia and Orthodynamics:

    a. Orthodynamics had recognised several design issues with various components and made modifications in July 2007, September 2008 and most recently in February 2009. However, the cumulative revision rate appears to be getting steadily worse and diverging from the cumulative revision rate of all other similar implants. Revisions due to pain, leg length discrepancy, metal sensitivity, wear and implant breakage are occurring in relatively higher proportions compared to similar implants.

    b. Mechanical testing commissioned by Orthodynamics has revealed that the stem/adaptor interface is prone to fretting and this appears to be confirmed by the data from the Australian Registry which reports relatively large numbers of revisions due to neck failure and problems with the Adapter stem rather than a particular femoral head in combination with the stem. Therefore, the explanation given by Orthodynamics that the poor performance of the Bionik head was unfairly attributed to poor performance of the Adapter Stem was not regarded to be convincing.

The OEWG concluded that the information provided by Eska Australia and Orthodynamics did not allay their concerns about the number of revisions of Adapter Femoral Stems reported by the NJRR.

20. As a result of the facts outlined in paragraphs 13-19 above I am satisfied that:
    a. The revision rate of both the cemented and cementless versions the Adapter Femoral Stem Prosthesis is unacceptably high.
    b. Eska Australia and Orthodymics were provided with ample time and opportunity to make submissions in relation to the revision rate of the implant, both in relation to the revision rate itself and in relation to unique design features that may compensate for the higher risk of revision.
    c. Both the TGA and the Orthopaedic Expert Working Group that advises the TGA considered all the evidence, including the Eska Australia and Orthodynamics submissions carefully, and that after these considerations the revision rates of the Adapter Femoral Stem Prosthesis is regarded to be unacceptable and that the arguments in favour of continuing to use the implant are not convincing.
    d. Since revision surgery is associated with considerable morbidity and a low but not insignificant mortality rate, the high rate of revision of the Adapter Femoral Stem indicates that both the performance and the safety of the implant are unacceptable.

**Reasons for decision**

21. Section 41GN(1)(e) of the Act provides the Secretary of the Department of Health and Ageing the authority to cancel the entry of a medical device from the Australian Register of Therapeutic Goods if "the Secretary is satisfied that the safety or performance of the kind of device is unacceptable".
22. As outlined in paragraph 20 of this letter, I am satisfied that the safety and performance of the Adapter Femoral Stem Prosthesis is not acceptable, and therefore Section 41GN(1)(e) applies.

**Conclusion**

23. I am proposing to cancel the entry of the Eska Adapter Femoral Stem Prosthesis from the Australian Register of Therapeutic Goods because, for the reasons set out in paragraphs 13-20 of this letter, I am satisfied that the safety and performance of this implant is unacceptable.

**Actions Required**

24. Before cancelling the entry of a medical device under Section 41GN, the Secretary must inform the Sponsor in writing about the proposal to cancel and set out the reasons for it. The Secretary must also give the Sponsor a reasonable opportunity to make submissions in relation to the proposed cancellation.

25. If you wish to make a submission in relation to this proposal to cancel I request that you do so **in writing** and submit it **within 20 working days of the date of this letter** to:

Dr Jorge Garcia
Director, Biomaterials and Engineering Section
Therapeutic Goods Administration
PO Box 100, Woden, ACT 2606
e-mail: jorge.garcia@tga.gov.au
Telephone : +61 2 6232 8432

26. I believe that the 20 working day deadline is reasonable because Eska Australia and the manufacturer were provided the opportunity to make submissions in relation to the implant on two previous occasions. I also wish to stress that your previous submissions have already been given careful consideration by the TGA and the Orthopaedic Expert Working Group. Therefore any further submission should provide new evidence and/or highlight facts that you believe have been overlooked. It is not necessary to repeat your previous submissions.

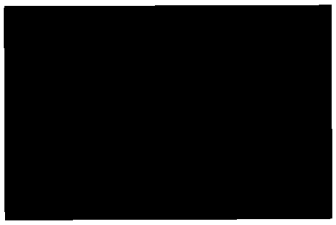
**Date of effect**

27. The cancellation will NOT take effect until any submission that you wish to make in relation to this proposal has been considered. If the TGA does not receive a submission within 20 working days of the date of this letter, then the TGA will consider moving to cancel the Device from the Register.

**Other Matters**

28. If you require further information regarding this matter, please contact Dr Garcia on the telephone or e-mail provided in paragraph 25.

Yours sincerely



Head, Monitoring and Compliance Group
Therapeutic Goods Administration
(Delegate of the Secretary to the Department of Health and Ageing for the purposes of Section 41GN of the Therapeutic Goods Act 1989)

Date:30th August, 2011.

# ATTACHMENT A

**41GN Cancellation of entries of kinds of medical devices from the Register after notice of proposed cancellation**

(1) The Secretary may, by written notice given to the person in relation to whom a kind of medical device is included in the Register, cancel the entry of the kind of device from the Register if:

(a) medical devices that were devices of that kind when the kind of device was included in the Register have changed so those medical devices are no longer devices of that kind; or

(b) the person in relation to whom the kind of medical device is included in the Register refuses or fails to comply with a condition to which that inclusion is subject; or

(c) the Secretary gives to the person a notice under section 41JA:

(i) that requires the person to give to the Secretary information or documents relating to the kind of device; and

(ii) in respect of which section 41GM does not apply;

and the person fails to comply with that notice within a further 10 working days from the day specified in that notice; or

(d) the person contravenes subsection 41MP(1) or 41MPA(1) in relation to the kind of device; or

(e) the Secretary is satisfied that the safety or performance of the kind of device is unacceptable; or

(f) the Secretary is satisfied that any certification, or part of a certification, under section 41FD in relation to the application for inclusion of the kind of device in the Register is incorrect, or is no longer correct, in a material particular.

Note: The matters that must be certified under section 41FD include compliance with the essential principles and the application of conformity assessment procedures, being able to substantiate the compliance and application, and compliance with advertising requirements.

(2) However, before cancelling the entry of the kind of device from the Register, the Secretary must:

(a) inform the person in writing that the Secretary proposes the cancellation and set out the reasons for it; and

(b) give the person a reasonable opportunity to make submissions to the Secretary in relation to the proposed cancellation.

(3) The Secretary is not to make a decision relating to the proposed cancellation until the Secretary has had regard to any submissions the person makes under paragraph (2)(b).

**41GO Limiting cancellation of entries from Register to some medical devices of a particular kind**

(1) If the Secretary is satisfied that the ground for cancelling the entry of a kind of medical device from the Register applies only to some medical devices of that kind, the Secretary must limit the cancellation to the medical devices to which that ground or any other ground for cancellation applies.

(2) If the cancellation of the entry of a kind of medical device from the Register is limited to some medical devices of that kind, the Secretary:

(a) must vary the entry in the Register accordingly; and

(b) must not delete the entry from the Register because of the cancellation.

**41GP Publication of cancellation of entry from Register**

The Secretary must cause to be published in the Gazette, as soon as practicable after cancelling an entry from the Register of a kind of medical device, or of some devices of a particular kind, a notice setting out particulars of the cancellation.

**41GQ Date of effect of cancellation of entries from Register**

If the Secretary cancels an entry of a kind of medical device, or some devices of a particular kind, from the Register, the cancellation has effect:

(a) if the cancellation is under section 41GK or 41GL—on the day on which the notice of cancellation is given to the person in relation to whom the kind of device was included in the Register; or

(b) in any other case—on such later day as is specified in the notice, being a day not earlier than 20 working days after the notice is given to the person.