



Australian Government

Repatriation Medical Authority

REPATRIATION MEDICAL AUTHORITY

STATEMENT OF REASONS

SUBSECTION 196B(9), *VETERANS' ENTITLEMENTS ACT 1986*

**DECISION NOT TO AMEND THE STATEMENTS OF PRINCIPLES CONCERNING
MALIGNANT NEOPLASM OF THE BREAST**

Instrument Nos. 96 and 97 of 2014

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PART I INTRODUCTION

1. The Repatriation Medical Authority (the Authority) received a request from the applicant, a person eligible to make a claim for compensation under section 319 of the *Military Rehabilitation and Compensation Act 2004* (MRCA), on 29 November 2020. The applicant requested a review, by way of an investigation, of the contents of the Statements of Principles (SOPs) concerning malignant neoplasm of the breast (Instrument Nos. 96 and 97 of 2014).
2. At its meeting on 16 February 2021, the Authority decided to conduct a review of the SOPs concerning malignant neoplasm of the breast, to determine whether the sound medical-scientific evidence (SMSE) provided a sufficient justification to amend these instruments in accordance with the applicant's request. A Notice of Investigation was published in the Government Notices Gazette of 9 March 2021, advertising a focussed review into 'taking combined hormonal contraceptives' as a factor in malignant neoplasm of the breast. At its meeting on 7 April 2021, the Authority decided that the new SMSE, together with the SMSE it had previously considered, was not sufficient to justify the amendments to the SOPs concerning malignant neoplasm of the breast which the applicant sought.

PART II BACKGROUND TO THE REQUEST

Factual background

3. The applicant requested that the Authority consider replacing the existing factors relating to using a combined oral contraceptive pill in the SOPs concerning malignant neoplasm of the breast (Instrument Nos. 96 and 97 of 2014) with factors relating to using any combined hormonal contraceptive, irrespective of the mode of delivery.
4. In a submission which accompanied her request, the applicant noted that increasing numbers of women are undertaking service in the Australian Defence Force (ADF), and that breast cancer is the leading cause of death for women across the three services which comprise the ADF. Consequently, the applicant submitted that it was vital that the relevant SOPs reflected the current SMSE.
5. Incidentally, the applicant identified that the SOPs concerning the following 12 conditions also contained factors relating to using a combined oral contraceptive pill:
 - Inflammatory Bowel Disease
 - Malignant Neoplasm of the Cervix
 - Retinal Vascular Occlusion
 - Malignant Neoplasm of the Liver
 - Subarachnoid Haemorrhage
 - Cerebrovascular Accident
 - Depressive Disorder
 - Ischaemic Heart Disease
 - Bipolar Disorder
 - Malignant Neoplasm of the Endometrium
 - Gingivitis
 - Cholelithiasis

6. The applicant indicated that she also sought a review of the SOPs concerning these conditions, on the basis that any causal association between combined hormonal contraceptives and malignant neoplasm of the breast should be reflected, by analogy, in the other SOPs which currently have factors relating to using a combined oral contraceptive pill.
7. The Authority decided to defer its decision in relation to the request for review of the 12 conditions listed above until it had considered the current SMSE in relation to malignant neoplasm of the breast. At its meeting on 7 April 2021, the Authority decided not to proceed with focussed reviews of these conditions. The reasons for this decision are set out in a separate Statement of Reasons.

Ground upon which review was sought

8. The applicant sought a review of the SOPs concerning malignant neoplasm of the breast on the ground that alternative forms of combined hormonal contraceptives (particularly the vaginal ring) have the same contraindications, complications, side effects and interactions as the combined oral contraceptive pill. In support of this ground of review, the applicant provided references to the following material:
 - Cogliano VJ, Baan R, Straif K, Grosse Y, et al (2011). Preventable exposures associated with human cancers. *J Natl Cancer Inst*, 103(24):1827-39.
 - International Agency for Research on Cancer (2012) Pharmaceuticals. Combined estrogen-progestogen contraceptives. Retrieved 30 November 2020, from <https://publications.iarc.fr/118>.
 - Del Pup L, Codacci-Pisanelli G, Peccatori F (2019). Breast cancer risk of hormonal contraception: Counselling considering new evidence. *Crit Rev Oncol Hematol*, 137:123-130.
 - Zolfaroli I, Tarín JJ, Cano A (2018). The action of estrogens and progestogens in the young female breast. *Eur J Obstet Gynecol Reprod Biol*, 230:204-207.
 - Westhoff CL, Pike MC (2018). Hormonal contraception and breast cancer. *Contraception*, 98(3):171-173.
 - Centers for Disease Control (2020) Classifications for combined hormonal contraceptives. Retrieved 26 November 2011, from <https://www.cdc.gov/reproductivehealth/contraception/mmwr/mec/appendixd.html>.
 - Consumer Medicine Information for NuvaRing.
 - Australian Product Information for Nuvaring
 - The Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) (2019). Combined Hormonal Contraceptives.
 - Kang M, Skinner R, Foran T (2007). Sex, contraception and health. *Aust Fam Physician*, 36(8):594-600.
 - McNamee K, Harvey C, Bateson D (2013). A practical guide to contraception. Part 1: Contraceptive pills and vaginal rings. *MedicineToday*, 14(7): 18-32.
 - Family Planning Victoria (FPV) (2020). List of Combined Hormonal Contraceptives available in Australia.

9. As indicated above, the Authority concluded that this ground when considered in light of the supporting material, provided a basis for it to carry out an investigation into 'taking combined hormonal contraceptives' as a factor in malignant neoplasm of the breast.

PART III EVIDENCE PREVIOUSLY CONSIDERED BY THE AUTHORITY

10. At the time that the SOPs concerning malignant neoplasm of the breast (Instrument Nos. 96 and 97 of 2014) were determined, the Authority had before it information including:
- briefing papers prepared in October 2014 by a Repatriation Medical Authority medical researcher; and
 - an extensive number of articles published in the peer-reviewed literature.

PART IV NEW INFORMATION CONSIDERED BY THE AUTHORITY

11. The information provided by the applicant, identified above, was considered. A discussion paper that considered the information supplied by the applicant and other available relevant sound medical-scientific evidence (SMSE) was prepared by a medical researcher for the Authority's meeting held on 16 February 2021.
12. A briefing paper providing a more detailed analysis of the current SMSE was prepared by a medical researcher for the Authority's meeting held on 7 April 2021, as part of the focussed review into 'taking combined hormonal contraceptives' as a factor in malignant neoplasm of the breast.

PART V SUMMARY OF NEW AND EXISTING EVIDENCE

13. While there is some biological plausibility in favour of causation based on the similarity of the hormones in oral and non-oral forms of hormonal contraception, it is possible that the lower doses of these hormones delivered by the vaginal ring (MIMS 2021, Van den Heuvel et al 2005) compared with oral contraceptives may have a lower risk of adverse outcomes.
14. In evaluating exposure to hormones from using contraceptives, parameters that need to be considered include peak values, mean values and timing and duration of exposure. Relevantly,
- The maximum serum values for the vaginal ring components (etonogestrel and ethinylestradiol) are approximately 40% and 30% respectively of comparator combined oral contraceptive (30 microgram ethinylestradiol/150 microgram desogestrel).
 - The mean etonogestrel serum levels are in the same order of magnitude as those obtained for the combined oral contraceptive, whereas the mean ethinylestradiol serum levels are approximately 50%.
 - As the vaginal ring is used continuously for three weeks, the exposure to maximum doses from the vaginal ring occurs only once per cycle (about 3 to 7 days after insertion), whereas the oral form contraceptive causes a peak value with each daily dose. Vaginal administration avoids daily peak concentrations (MIMS 2021).

This suggests a reasonable basis for the view that the risks from exposure to hormones from using contraceptives are likely to be lower with the use of the vaginal ring method.

15. There is in any case some uncertainty whether the small and transient increased risk of breast cancer observed with combined oral contraceptives is truly causal. This small excess risk may be real or may, at least in part, be explained by an advance in the timing of diagnosis in pill users, since diagnosed cancers are less advanced (Westoff and Pike 2018).
16. The one available epidemiological study showed no increase in risk of breast cancer in users of the vaginal ring or transdermal patches (Morch et al 2017). Further epidemiological studies of risks associated with non-oral forms of combined hormonal contraception are needed to assess whether or not there is a reasonable hypothesis of a causal association with breast cancer.

PART VI FINDINGS OF FACT

17. In light of the material discussed above, the Authority made the following finding of fact:
 - The body of available SMSE does not support the existence of a causal association between taking non-oral combined hormonal contraceptives and the clinical onset or clinical worsening of malignant neoplasm of the breast. Consequently, the Authority is not satisfied that there is at least a reasonable hypothesis that taking a non-oral combined hormonal contraceptive is a factor which causes, or contributes to, the clinical onset or clinical worsening of malignant neoplasm of the breast.

PART VII REASONS FOR THE DECISION

18. The Authority was cognisant of the provisions of the VEA, and had particular regard to subsection 5AB(2) SMSE, s 5D injury/disease, and Part XIA.

SMSE is defined as follows:

*"Information about a particular kind of injury, disease or death is taken to be **sound medical-scientific evidence** if:*

(a) *the information:*

(i) *is consistent with material relating to medical science that has been published in a medical or scientific publication and has been, in the opinion of the Repatriation Medical Authority, subjected to a peer review process; or*

(ii) *in accordance with generally accepted medical practice, would serve as the basis for the diagnosis and management of a medical condition; and*

(b) *in the case of information about how that kind of injury, disease or death may be caused - meets the applicable criteria for assessing causation currently applied in the field of epidemiology."*

19. The Authority noted sub-sections 196B(7), 196B(8) and 196B(9) and section 196E, which relevantly provide:

196B(7)

If the Authority:

(a) *is asked under section 196E to review:*

(i) *some or all of the contents of a Statement of Principles;*

[...]

(b) *thinks that there are grounds for such a review; [...]*

the Authority must, subject to subsection 196C(4) and section 196CA in a case where paragraph (a) applies, carry out an investigation to find out if there is new information available about:

- (d) how the injury may be suffered, the disease may be contracted or the death may occur; or*
- (e) the extent to which the disease, injury or death may be war-caused or defence-caused.*

196B(8)

If, after carrying out the investigation, the Authority is of the view that there is a new body of sound medical-scientific evidence available that, together with the sound medical-scientific evidence previously considered by the Authority, justifies the making of a Statement of Principles, or an amendment of the Statement of Principles already determined, in respect of that kind of injury, disease or death, the Authority must:

- (a) [...]; or*
- (b) make a determination amending the Statement of Principles determined under subsection (2) or (3) in respect of that kind of injury, disease or death; or*
- (c) [...];*

as the case requires.

196B(9)

If, after carrying out the investigation, the Authority is of the view:

- (a) that there is no new sound medical-scientific evidence about that kind of injury, disease or death; or*
- (b) that the new sound medical-scientific evidence available is not sufficient to justify the making of a Statement of Principles, or an amendment of the Statement of Principles already determined in respect of that kind of injury, disease or death;*

the Authority must make a declaration in writing:

- (c) stating that it does not propose to make a Statement of Principles, or amend the Statement of Principles already determined (as the case may be); and*
- (d) giving the reasons for its decision.*

196E

- (1) Any of the following:*
 - (b) a person eligible to make a claim for a pension under Part II or IV;*
 - (ba) a person eligible to make a claim for compensation under section 319 of the MRCA;*
 - (c) an organisation representing veterans*
- may ask the Repatriation Medical Authority:*
- (f) to review the contents of a Statement of Principles in force under this Part.*

Basis for commencing review of an existing SOP

20. It is the applicant's request which prompted the Authority to commence an investigation into this particular factor under s 196B(7)(a) of the VEA.¹

Basis for amending an existing SOP

21. In forming any view during an investigation, the Authority may rely only on SMSE. Subsection 196B(8) provides that where there is a new body of sound medical-scientific evidence available that, together with the sound medical-scientific evidence previously

¹ It not otherwise being an application within either subsection 196C(4) or section 196CA of the VEA.

considered by the Authority, justifies the amendment of a SOP the Authority is required to do so. On the other hand where there is no new SMSE or the new SMSE is insufficient to justify an amendment subsection 196B(9) provides that the Authority *must* make a declaration stating that it does not propose to amend the SOP and give reasons for that decision.

Reasons for deciding not to amend an existing SOP

22. Together with its own expert knowledge, the Authority took into consideration:
- the information provided by the applicant;
 - the information held by the Authority and obtained during its previous investigations leading up to the determination of the SOPs concerning malignant neoplasm of the breast (Instrument Nos. 96 and 97 of 2014); and
 - the discussion paper prepared by a medical researcher for the February 2021 meeting;
 - the briefing paper prepared by a medical researcher for the April 2021 meeting.
23. As noted above, the applicant relied on the following ground for seeking a review of the contents of the SOPs concerning malignant neoplasm of the breast:
- alternative forms of combined hormonal contraceptives (particularly the vaginal ring) have the same contraindications, complications, side effects and interactions as the combined oral contraceptive pill.

Is there new sound medical-scientific evidence?

24. Since its previous consideration of the SMSE in relation to using oral contraceptive pills, new SMSE concerning the use of contraceptives has been published (some of which was identified by the applicant in her request).

Is the available sound medical-scientific evidence sufficient to justify amendment?

25. The Authority is of the view that the currently available SMSE including the new SMSE was not sufficient to justify the amendment which the applicant sought. The limited epidemiological data, being one study which did not find an increased risk, meant that inclusion of non-oral forms of hormonal contraception in the SOPs would largely be based on analogy. Other bodies treat oral and non-oral methods as equivalent in terms of safety, based on the precautionary principle rather than evidence. However, the Authority is obliged to only rely on the evidence in assessing how a disease may be caused.
26. Here, the vaginal ring delivers lower overall and maximal doses of the estrogen and progesterone components than combined oral contraceptives with less fluctuation, as well as lower mean doses of the estrogen component. In general, adverse outcomes associated with oral contraceptive pills have reduced as lower doses of estrogen have been introduced over the last few decades. Nonetheless, the evidence is too equivocal to say with any certainty whether the risks of using non-oral forms of combined hormonal contraception are similar, higher or lower than the risks of using combined oral contraceptive pills.

PART VIII CONCLUSIONS

27. Overall, for the reasons set out above, the available SMSE is not sufficient to justify the amendment of the SOPs concerning malignant neoplasm of the breast by including factors for the use of non-oral forms of combined hormonal contraception.

PART IX DECISION

28. The Authority decided at its meeting on 7 April 2021 not to amend the SOPs concerning malignant neoplasm of the breast (Instrument Nos. 96 and 97 of 2014) as it considered that the SMSE was not sufficient to justify the amendment sought in the application.

Professor Nicholas Saunders AO
Chairperson
Repatriation Medical Authority

23 April 2021