NICE National Institute for Health and Care Excellence

**DIAGNOSTICS ASSESSMENT PROGRAMME**

**Tests in secondary care to identify people at high risk of ovarian cancer**

**Diagnostics Consultation Document – Comments**

**Diagnostics Advisory Committee date: 22 August 2017**

**THEME: Interventions and comparator**

| Comment number | Name and organisation | Section number | Comment | NICE considerations |
|---|---|---|---|---|
| 1 | Fujirebio | 3 | **Diagnostic tests (comparator RMI 1)**<br>Surveillance report 2016 – Which tumor markers used ?<br>Surveillance project team selected a systematic review by Zhen et al (2014) evidence that the measurement of HE4 may be superior to CA125 regarding diagnostic performance in OC (25 studies included – 4729 women).<br>This information is missing. HE4 could be beneficial as alternative to CA125.<br>It could be interesting to know the committee opinion. Use of HE4 vs. CA125 is a common question from healthcare professionals | Thank you for your comment which the committee considered.<br><br>The committee heard from the EAG that the systematic review by Zhen et al. (2014) is out of scope for this assessment because it uses CA125 as a comparator.<br><br>CA125 alone was not included as a comparator in the diagnostics assessment scope. This is because CA125 is not recommended for use as stand-alone marker for making decisions in secondary care. |
| 2 | Fujirebio | 4.33 | **Costs**<br>Cost effectiveness using TV Ultrasound + HE4 was not included (could be relevant for secondary care) | Thank you for your comment which the committee considered.<br><br>The HE4 test with transvaginal ultrasound was out of scope for this assessment, because HE4 assays are indicated for use in conjunction with CA125 assays, using the Risk of Ovarian Malignancy Algorithm (ROMA). |

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**THEME: Diagnostic pathway**

| Comment number | Name and organisation | Section number | Comment | NICE considerations |
|---|---|---|---|---|
| 3 | Fujirebio | 4.33 | If CA125 is applied in primary care, what is the benefit to re-test CA125? | Thank you for your comment which the committee considered.<br><br>The committee heard from the EAG that the economic model assumed that all patients receive a CA125 test in secondary care, even if they previously had one in primary care (except for IOTA simple rules, which does not use CA125 level). The committee heard from clinical experts that the reasons patients receive another CA125 test in secondary care are: CA125 levels may have changed since the first test was carried out; some risk scores are only compatible with a specific brand of CA125 test; and some tests include CA125 as part of an array. The committee concluded that the assumption in the economic model was valid.<br><br>The EAG did a scenario analysis which removed the cost of re-testing CA125 from all interventions. This did not have a large impact on the results: ROMA, RMI 1 (threshold 200) and Ova2 remain dominated and IOTA simple rules and the IOTA ADNEX model remain cost effective. |

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**THEME: Diagnostic pathway**

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|---|---|---|---|---|
| | | | | The committee decided to add it's considerations on CA125 testing into the diagnostics guidance (section 5.12). |

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**THEME: Use of tests in combination**

| Comment number | Name and organisation | Section number | Comment | NICE considerations |
|---|---|---|---|---|
| 4 | Fujirebio | 5.16 & 6.3 | **Use of tests in sequence**<br>There is evidence of adding HE4 after first triage using RMI 1 or TV Ultrasound could increase the diagnostic accuracy<br>The committee considered that the use of tests in sequence could be cost effective, but no estimation for accuracy and cost effectiveness in the EAG model.<br><br>*Reference: A predictive model combining human epididymal protein 4 and radiologic features for the diagnosis of ovarian cancer. Stiekema A, Lok CA, Kenter GG, van Driel WJ, Vincent AD, Korse CM.*<br>*Gynecol Oncol. 2014 Mar;132(3):573-7* | Thank you for your comment which the committee considered.<br><br>The committee heard from the EAG that the study by Stiekema et al. (2014) uses HE4 alone or as part of risk scores other than those specified in the scope. Therefore this study was out of scope for this assessment. |

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**THEME: Benefits to patients**

| Comment number | Name and organisation | Section number | Comment | NICE considerations |
|---|---|---|---|---|
| 5 | Target Ovarian Cancer | - | It is disappointing that the evidence is insufficient to support adoption of IOTA Simple Rules, or IOTA ADNEX model in the secondary care setting. The data presented suggests that for a relatively small difference in cost these models offer increased sensitivity over RMI 1 at the 250 threshold.<br><br>Women with ovarian cancer often face a protracted diagnosis. Increasing the sensitivity of tests and risk scores, at relatively low cost, is imperative in ensuring that women with ovarian cancer are referred to an appropriate multidisciplinary team. Women who are diagnosed by a specialist multidisciplinary team are more likely to benefit from improved outcomes. | Thank you for your comment which the committee considered.<br><br>The committee heard from lay experts that there was wide variation in access to tests in primary care for those presenting with symptoms of ovarian cancer, and that getting a referral to secondary care may take a long time. It agreed that differences in initial assessment may lead to variation in patient outcomes. The committee decided to add these considerations into the diagnostics guidance (section 5.17). |

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**Diagnostics Consultation Document – Comments**

**Diagnostics Advisory Committee date: 22 August 2017**

**THEME: General**

| Comment number | Name and organisation | Section number | Comment | NICE considerations |
|---|---|---|---|---|
| 6 | Roche Diagnostics Ltd | - | We have no further comments to make on this consultation. | Thank you for your comment which the committee considered. |
| 7 | Target Ovarian Cancer | - | We welcome recommendations for further research which may lead to improve diagnostic accuracy of the tests and risk scores. | Thank you for your comment which the committee considered. |