# EMA starts review of cancer medicine Rubraca (rucaparib camsylate)

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**Information on Rubraca (rucaparib camsylate)**

- Rubraca is a cancer medicine that has been authorised to treat high-grade cancers of the ovary, fallopian tubes (the tubes connecting ovaries to the uterus), and the peritoneum (the membrane lining the abdomen).

- It can be used as maintenance treatment in patients whose recurring cancer has cleared (partially or completely) after treatment with platinum-based cancer medicines. It is also for use if the patient's cancer has a BRCA mutation and has returned or worsened after two treatments with platinum-based medicines and the patient can no longer have these medicines (third-line treatment).

- Rubraca was granted a 'conditional approval' on 24 May 2018. At the time of its approval, data on the size of the effect of Rubraca were limited. The medicine was therefore granted a marketing authorisation on condition that the company provided additional data from the ARIEL4 study to confirm the safety and effectiveness of the medicine. More information about the medicine can be found on the EMA website: https://www.ema.europa.eu/en/medicines/human/EPAR/rubraca.

The following product is authorised via centralised procedure.

| Active Ingredients | Product Name | Pharmaceutical Form | Classif -cation | Authorisation Number | MAH/license holder |
|---|---|---|---|---|---|
| Rucaparib camsylate | Rubraca | Film-coated tablet | POM | EMEA/H/C/004272 | Clovis Oncology Ireland Limited |

**Information from the EMA about the safety concern**

- EMA has started a review of the cancer medicine Rubraca (rucaparib camsylate) when it is used to treat cancer of the ovary, fallopian tubes, or peritoneum with a BRCA mutation in patients whose cancer has come back after platinum-based chemotherapy and who can no longer have these medicines. The review of Rubraca has been initiated at the request of the European Commission, under Article 20 of Regulation (EC) No 726/2004.

- The review follows preliminary results indicating that overall survival was shorter in these patients than in those receiving chemotherapy. These results come from the ongoing ARIEL4 study[1] comparing Rubraca with chemotherapy in patients with high-grade cancer

[1] https://www.clinicaltrialsregister.eu/ctr-search/search?query=ARIEL4

of the ovary, fallopian tubes or peritoneum with a BRCA mutation whose cancer has come back after chemotherapy.

- While the review is ongoing, EMA is recommending that doctors do not start treatment in new patients whose cancer has a BRCA mutation and has come back after at least two platinum-based chemotherapies and who cannot have further platinum-based therapy (third-line treatment). This recommendation does not affect the use of Rubraca as maintenance treatment following chemotherapy. Healthcare professionals will be informed in writing of the updated treatment recommendations.

- EMA will now assess all available information on the use of Rubraca as third-line treatment and recommend whether Rubraca's marketing authorisation in the EU should be maintained or varied.

- The review is being carried out by the Committee for Medicinal Products for Human Use (CHMP), responsible for questions concerning medicines for human use. While the review is ongoing, the CHMP has issued temporary recommendations to restrict the use of Rubraca in certain new patients as an interim measure to protect public health. The recommendation has been forwarded to the European Commission (EC), which will issue a temporary legally binding decision applicable in all EU Members States.

- Once the CHMP review is concluded, the final opinion will then be forwarded to the EC, which will issue a final legally binding decision applicable in all EU Member States.

**For Healthcare Professionals**

- The ongoing phase 3 study ARIEL4 compared Rubraca with chemotherapy in patients with relapsed, BRCA mutated, high-grade epithelial ovarian, fallopian tube, or primary peritoneal cancer.

- An interim analysis of ARIEL4 found that overall survival for Rubraca was lower than that seen in the chemotherapy control arm (19.6 months and 27.1 months, respectively, with a hazard ratio (HR) of 1.550 (95% CI: 1.085, 2.214)). Patients included in the study were stratified at the time of randomisation according to platinum sensitivity (platinum sensitive vs. partially platinum sensitive vs. platinum resistant). The HRs for overall survival in these subgroups were 1.12 (95% CI: 0.44-2.88), 1.15 (95% CI: 0.62-2.11) and 1.72 (95% CI: 1.13-2.64), respectively.

- In the efficacy population of the ARIEL4 study, a difference in favour of Rubraca was observed for the primary endpoint of progression free survival by investigator (invPFS), with a reported median invPFS of 7.4 months for the Rubraca group compared with 5.7 months for the chemotherapy group (HR=0.639; p=0.0010).

- EMA is performing a review of the findings of the study in the context of all available information to assess their impact on the use of Rubraca.

- While the review is ongoing, physicians are recommended not to start treatment with Rubraca in patients with platinum-sensitive, relapsed or progressive, BRCA mutated,

high-grade epithelial ovarian, fallopian tube, or primary peritoneal cancer, who have been treated with two or more prior lines of platinum-based chemotherapy, and who are unable to tolerate further platinum-based chemotherapy.

- There are no new safety concerns with the medicine. This recommendation does not affect the use of Rubraca as maintenance treatment following chemotherapy.

**Advice for Patients**

**Treatment with Rubraca**

- New study results suggest that, in patients with high-grade cancer of the ovary, fallopian tubes or peritoneum whose cancer has a genetic mutation (BRCA mutation) and has come back after chemotherapy treatment, overall survival (how long patients live) was shorter in patients receiving Rubraca than in those receiving chemotherapy.

- New patients with a BRCA mutation whose cancer has come back after platinum-based chemotherapy and who can no longer have these medicines should not start treatment with Rubraca.

- There are no new safety concerns with the medicine. If you have any concerns about your treatment, speak with your doctor.

For more information, please see the European Medicines Agency's press release.

**Reporting Adverse Drug Reactions**

Healthcare professionals and patients are encouraged to maintain vigilance with Rubraca (rucaparib camsylate). Suspected Adverse Drug Reactions (side effects) may be reported using the Medicines Authority Form and sending it to: Sir Temi Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN 3000 **or** online to http://www.medicinesauthority.gov.mt/adrportal or to the marketing authorisation holder or their local representatives.

**Post-Licensing Directorate**

**Medicines Authority**

***Healthcare professionals and patients are encouraged to regularly check the Medicines Authority website for product safety updates as these are issued on an ongoing basis.***

**Feedback Form**

The Medicines Authority thanks you for the time taken to read this safety circular. The dissemination of safety circulars is an important process whereby Regulatory Authorities can communicate important issues with respect to the safety of medicines, in order to protect and enhance public health.

The Medicines Authority kindly invites your anonymous feedback about the regulatory action being communicated. This may be returned by folding this form (address side up), stapling the ends and then posting (no stamp required).

**Feedback:**

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