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Authorised uses of cancer medicine Yondelis unchanged following review of new data

On 23 July 2020, EMA recommended that the use of Yondelis (trabectedin) in treating ovarian cancer remain unchanged following a review of a study that investigated Yondelis as a third-line treatment in patients with ovarian cancer. However, the study results will be included in the medicine's product information to provide healthcare professionals with the most up-to-date information on the effects of Yondelis in patients with ovarian cancer.

An analysis of study OVC-3006 investigating the use of Yondelis plus pegylated liposomal doxorubicin (PLD, another cancer medicine) in patients with ovarian cancer was carried out while the study was still ongoing and showed that, overall, patients treated with Yondelis plus PLD did not live longer than patients given PLD alone. As a result, the study was terminated ahead of time.

EMA's human medicines committee (CHMP) assessed the data and concluded that the results available are not robust enough to draw firm conclusions. Available evidence from the study does not put into question the benefits and risks of Yondelis in its currently authorised uses. Further, there are key differences between OVC-3006 and the study that supported the authorisation of Yondelis (OVA-301). The main difference is that patients in study OVC-3006 had a more advanced disease and had been more heavily treated than those included in OVA-301. In addition, a significant proportion of patients in study OVC-3006 had ovarian cancer that was resistant to medicines containing platinum, while Yondelis is currently authorised for platinum-sensitive ovarian cancer.

When considering Yondelis' safety, the CHMP noted that in the OVC-3006 study patients treated with Yondelis and PLD had more side effects and more severe ones than those treated with PLD only; however, the committee considered that a higher occurrence of side effects is not unexpected with combination treatments compared to treatments used alone.

The CHMP recommended that the results of the study be included in the summary of product characteristics of Yondelis so that healthcare professionals have the most up-to-date information when prescribing the medicine.

Information for patients

- EMA had looked at results from a study with Yondelis in ovarian cancer because of concerns that the medicine could be less effective than previously thought.
- EMA's review found that results did not impact the authorised uses of the medicine. Yondelis can therefore continue to be as used as normal.

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

- Yondelis is authorised for treating ovarian cancer that has relapsed (come back after previous treatment) and is sensitive to medicines containing platinum.
- If you have any concerns or questions about your treatment, please talk to your doctor.

Information for healthcare professionals

- OVC-3006 was a phase 3 study evaluating the efficacy and safety of Yondelis plus PLD compared with PLD alone in women with recurrent ovarian cancer after failure of two platinum-containing regimens. The study was discontinued because an unplanned interim analysis of the primary endpoint (overall survival) suggested that the study would not meet its primary objective and because the occurrence of side effects was higher in the Yondelis group.
- There was no significant difference between the median overall survival in the Yondelis plus PLD arm (23.8 months) and the PLD arm (22.2 months) (HR=0.93, 95% CI: 0.73-1.18; p=0.52) when the unscheduled futility analysis was performed at 45% of the planned events required for final analysis (232/514 deaths).
- The CHMP concluded that these data do not change the benefit-risk balance of Yondelis in the currently authorised indications as there are a number of differences between OVC-3006 and the study that supported the authorisation of Yondelis (OVA-301).
- Study OVA-301 included patients who had been previously treated for ovarian carcinoma (80% previously received taxanes) but had only one platinum-based chemotherapy regimen and had experienced either recurrence or progression after the platinum-based chemotherapy. The primary endpoint was progression-free survival.
- The CHMP noted that patients in OVA-301 were in second-line treatment while those included in OVC-3006 were in third-line treatment. In addition, a post hoc analysis determined that 42% of enrolled patients in OVC-3006 were platinum-resistant following their last platinum-containing regimen while Yondelis is currently authorised for treatment of women with relapsed platinum-sensitive ovarian cancer.
- The committee also noted that because the study was terminated early, the results do not provide sufficiently robust clinical evidence to call into question the results of the study OVA-301 which showed favourable effects of Yondelis plus PLD in terms of progression-free survival in patients with relapsed platinum-sensitive ovarian cancer.
- With regard to safety, there was a considerable difference between the two treatment arms in OVC-3006 in terms of numbers and severity of adverse events. Approximately 85% of patients in the Yondelis plus PLD arm had severe adverse events compared with 64% in the control arm. However, such a difference is not unexpected with combination treatments compared with monotherapy.
- Yondelis' summary of product characteristics will be amended to include these study results.

More about the medicine

Yondelis is used with pegylated liposomal doxorubicin to treat ovarian cancer that has relapsed (come back after previous treatment) and is sensitive to medicines containing platinum.

Yondelis is also used to treat adults with advanced soft-tissue sarcoma. It is used when the cancer had started to spread and treatment with anthracyclines and ifosfamide (other cancer medicines) have stopped working, or in patients who cannot be given these medicines.

More information about Yondelis is available: ema.europa.eu/medicines/human/EPAR/yondelis.

More about the procedure

The review of Yondelis was initiated at the request of the European Commission, under Article 20 of Regulation (EC) No 726/2004.

The review has been carried out by the Committee for Medicinal Products for Human Use (CHMP), responsible for questions concerning medicines for human use, which has adopted the Agency's opinion. The CHMP opinion was forwarded to the European Commission, which issued a final legally binding decision applicable in all EU Member States on 24 September 2020.