Yondelis: unchanged use for the cancer medicine following review of new data

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Information on Yondelis

- Yondelis (trabectedin) is a cancer medicine which is used together 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 used to treat adults with advanced soft-tissue sarcoma when it starts spreading and treatment with anthracyclines and ifosfamide (other cancer medicines) have stopped working or when treatment with these medicines cannot be given.

In Malta Yondelis is authorised through a centralised procedure

Information from the EMA about the use of Yondelis

The Committee for Medicinal Products for Human Use (CHMP) carried out a review on Yondelis following a request from the European Commission. During the review, study OVC-3006, investigating the use of Yondelis plus pegylated liposomal doxorubicin (PLD) in patients with ovarian cancer, was analysed. At the time, study OVC-3006 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.

Following the assessment of data, the CHMP has concluded that the results available are not robust enough to draw conclusions. The risk/benefit balance of Yondelis in its currently authorised indications has been further demonstrated to be positive. Also, key differences between OVC-3006 and the study that supported the authorisation of Yondelis (OVA-301), are present. Patients in study OVC-3006 had a more advanced diseases and had been more heavily treated than those included in OVA-301. Moreover, 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.

From a safety perspective, the CHMP observed that in study OVC-3006, patients treated with Yondelis and PLD had more and more serious side effects 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 EMA has recommended the following:

- The use of Yondelis 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

- 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

The CHMP opinion will now be forwarded to the European Commission, which will issue a final legally binding decision applicable in all EU Member States.

In Malta

For Healthcare Professionals

- Study OVC-3006 was a phase III study, evaluating safety and efficacy of Yondelis used in association with PLD compared with PLD alone in women with recurrent ovarian cancer after failure of two platinum-containing regimens. Following an unplanned interim analysis of the primary endpoint (overall survival), which suggested that the study would have not met its primary objective and the higher rate of side effects in the Yondelis group, the study was discontinued
- No significant difference was observed 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% Cl: 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 conclude that no change in the risk/benefit balance of Yondelis in the authorised indications is shown by current data. Furthermore a number of differences between OVC-3006 and the study that supported the authorisation of Yondelis (OVA-301) have been observed:
    - In study OVA-301, patients previously treated for ovarian carcinoma (80% previously received taxanes) with only one platinum-based chemotherapy regimen and had experienced either recurrence or progression after the platinum-based chemotherapy were included. The primary endpoint was progression-free survival
    - 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 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

Advice 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.
- 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.

For more information, visit the European Medicines Agency's Yondelis referral page

Reporting Adverse Drug Reactions

Healthcare professionals and patients are encouraged to maintain vigilance on Yondelis. 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 formt (address side up), stapling the ends and then posting (no stamp required)

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