

Yondelis
trabectedin

EPAR summary for the public

This document is a summary of the European Public Assessment Report (EPAR). It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the studies performed, to reach their recommendations on how to use the medicine.

If you need more information about your medical condition or your treatment, read the Package Leaflet (also part of the EPAR) or contact your doctor or pharmacist. If you want more information on the basis for the CHMP recommendations, read the Scientific Discussion (also part of the EPAR).

What is Yondelis?

Yondelis is a powder that is made up into a solution for infusion (drip into a vein). It contains the active substance trabectedin.

What is Yondelis used for?

Yondelis is used to treat adults with two types of cancer:

- advanced soft-tissue sarcoma, a type of cancer that develops from the soft, supporting tissues of the body. ‘Advanced’ means that the cancer has started to spread. Yondelis is used when treatment with anthracyclines and ifosfamide (other anticancer medicines) have stopped working, or in patients who cannot be given these medicines;
- ovarian cancer (cancer of the ovaries) that has relapsed (come back after previous treatment) and is sensitive to medicines containing platinum. Yondelis is used in combination with pegylated liposomal doxorubicin (PLD, another anticancer medicine).

Because the numbers of patients with soft-tissue sarcoma and ovarian cancer are low, the diseases are considered ‘rare’, and Yondelis was designated an ‘orphan medicine’ (a medicine used in rare diseases) on 30 May 2001 (for soft-tissue sarcoma) and on 17 October 2003 (for ovarian cancer).

The medicine can only be obtained with a prescription.

How is Yondelis used?

Yondelis must be given under the supervision of a doctor who is experienced in the use of chemotherapy (medicines to treat cancer). It should only be used by qualified oncologists (cancer specialists) or other health professionals who are specialised in giving cytotoxic (cell-killing) medicines.

For soft-tissue sarcoma, the recommended dose of Yondelis is 1.5 mg per square metre of body surface area (calculated using the patient’s height and weight), given as a single infusion lasting 24 hours every three weeks. For ovarian cancer, it is given at a dose of 1.1 mg/m² every three weeks as an infusion lasting three hours, immediately after the PLD infusion.

Treatment carries on for as long as the patient shows a benefit. It is recommended that Yondelis be given through a central venous line (a thin tube leading from the skin into the large veins just above the heart). To prevent vomiting and to protect the liver, patients must receive an infusion of corticosteroids such as dexamethasone before treatment. If the patient’s blood counts are abnormal, infusion with Yondelis should be delayed, the dose of Yondelis should be reduced or other medicines

can be used to treat the blood problems. For more information, see the Summary of Product Characteristics (also part of the EPAR).

How does Yondelis work?

The active substance in Yondelis, trabectedin, is an anticancer medicine. It is a synthetic version of a substance that was originally extracted from a species of tunicate or 'sea squirt' (a marine animal). Cancer is a disease where cells divide too quickly, usually because the way their genes work is faulty. Trabectedin works by attaching to the DNA, the chemical molecule that makes up genes, and preventing some genes in human cells from increasing their activity. This can prevent the cells from dividing too quickly, slowing down the growth of various types of cancer.

How has Yondelis been studied?

For soft-tissue sarcoma, Yondelis has been studied in one main study involving 266 patients with liposarcoma (a sarcoma originating in fat cells) or leiomyosarcoma (a sarcoma originating in 'smooth' or involuntary muscle cells) that was advanced or metastatic (had spread to other parts of the body). All of the patients had been treated previously with an anthracycline and ifosfamide but this treatment had stopped working. The study compared two different dosing schedules of Yondelis: three times per month, or once every three weeks.

For ovarian cancer, Yondelis in combination with PLD was compared with PLD alone in one main study involving 672 women whose disease had come back or got worse after previous treatment. Around two-thirds of the patients had cancer that was sensitive to platinum-containing medicines. In both studies, the main measure of effectiveness was how long the patients lived without their disease getting worse.

What benefit has Yondelis shown during the studies?

For soft-tissue sarcoma, Yondelis was more effective when it was given once every three weeks than when it was given with the alternative dosing schedule. Patients receiving it once every three weeks lived for an average of 3.8 months without their disease getting worse, compared with 2.1 months in those receiving Yondelis three times per month.

For ovarian cancer, the combination of Yondelis and PLD was more effective than PLD alone: the patients receiving the combination treatment lived for an average of 7.3 months without their disease getting worse, compared with 5.8 months in those receiving PLD alone. The effect of Yondelis was more pronounced in the women whose cancer was sensitive to platinum-containing medicines.

What is the risk associated with Yondelis?

The most common side effects with Yondelis when used on its own for soft-tissue sarcoma (seen in more than 1 patient in 10) are increased blood levels of creatine phosphokinase (a marker of muscle breakdown) and of creatinine (a marker of kidney problems), decreased blood levels of albumin (a marker of liver problems), neutropenia (low levels of neutrophils, a type of white blood cell), thrombocytopenia (low blood platelet counts), anaemia (low red blood cell counts), leucopenia (low white blood cell counts), headache, vomiting, nausea (feeling sick), constipation, loss of appetite, fatigue (tiredness), asthenia (weakness), hyperbilirubinaemia (high levels of bilirubin in the blood) and increased levels of liver enzymes in the blood. Side effects were similar when Yondelis was used together with PLD for ovarian cancer, although palmar-plantar erythrodysesthesia syndrome (rash and numbness on the palms and soles) and mucosal inflammation (inflammation of the moist body surfaces) seemed to be more common. For the full list of all side effects reported with Yondelis, see the Package Leaflet.

Yondelis should not be used in people who may be hypersensitive (allergic) to trabectedin or any of the other ingredients. It must not be used in patients who have any serious or uncontrolled infection, in combination with the vaccine for yellow fever, or in breast-feeding women.

Why has Yondelis been approved?

The Committee for Medicinal Products for Human Use (CHMP) concluded that Yondelis's benefits are greater than its risks and recommended that it be given marketing authorisation. Yondelis has been authorised under 'Exceptional Circumstances'. This means that because soft tissue sarcoma is rare, it has not been possible to obtain complete information about Yondelis. Every year,

the European Medicines Agency will review any new information that may become available and this summary will be updated as necessary.

What information is still awaited for Yondelis?

The company that makes Yondelis will continue to assess which patients with soft tissue sarcoma are more likely to respond to the medicine.

Other information about Yondelis:

The European Commission granted a marketing authorisation valid throughout the European Union for Yondelis to Pharma Mar, S.A. on 17 September 2007. The marketing authorisation is valid for five years, after which it can be renewed.

The summaries of opinion of the Committee for Orphan Medicinal Products are available [here](#) (soft-tissue sarcoma) and [here](#) (ovarian cancer).

The full EPAR for Yondelis can be found [here](#).

This summary was last updated in 10-2009.