CHMP confirms that patients on Zydelig should be monitored for infection and given antibiotics during and after treatment

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Information on Zydelig

Zydelig is a cancer medicine containing the active substance idelalisib. In the EU, Zydelig is authorised for the treatment of two cancers of white blood cells, chronic lymphocytic leukaemia and follicular lymphoma (one of a group of cancers called non-Hodgkin's lymphomas).

- In chronic lymphocytic leukaemia, Zydelig is used in combination with another medicine (rituximab) in patients who have received at least one previous treatment and in previously untreated patients who have genetic mutations in their cancer cells called 17p deletion or TP53 mutation and who are not eligible for other therapies.
- In follicular lymphoma, Zydelig is used on its own in patients whose disease has not responded to two previous treatments.

In Malta Zydelig is available on a named patient program basis and is dispensed from Sir Anthony Mamo Oncology Centre (SAMOC) pharmacy. More information on Zydelig can be found here.

CHMP confirms recommendations for use of Zydelig - Patients should be monitored for infection and given antibiotics during and after treatment

The CHMP (EMA's Committee for Medicinal Products for Human Use) has confirmed that the benefits of Zydelig (idelalisib) in the treatment of the blood cancers chronic lymphocytic leukaemia (CLL) and follicular lymphoma outweigh the risk of side effects.

The review was carried out by EMA's Pharmacovigilance Risk Assessment Committee (PRAC) and the CHMP has confirmed the recommendations issued. The CHMP's opinion will now be sent to the European Commission for a final legally binding decision and the recommendations to minimise the risk of serious infections in patients treated with Zydelig will be updated in due course. Below is a summary of the recommendations.

In Malta

Information for patients

- There have been reports of serious infections in clinical studies with the cancer medicine Zydelig. Some changes have now been made in how the medicine is used to ensure it is given as safely as possible.
- If you are taking Zydelig, you will receive antibiotics to prevent a type of lung infection (*Pneumocystis jirovecii* pneumonia). Because some infections have occurred after patients had finished their cancer treatment, you will have to keep taking these antibiotics for 2 to 6 months after stopping Zydelig.
- Your doctor will regularly check you for signs of infections. If you develop fever, cough or difficulty breathing you should contact your doctor straight away.
- You will have regular blood tests to check if you have a low white blood cell count, as a low count can put you at more risk of developing an infection. Your doctor may stop your treatment with Zydelig if your white blood cell count is too low.
- You should not stop Zydelig without speaking to your doctor. If you are taking Zydelig and have any questions or concerns speak to your doctor, nurse or pharmacist.

Information for healthcare professionals

- Increased rates of serious adverse effects including deaths were seen in the treatment arm of 3 clinical trials evaluating the addition of Zydelig to standard therapy in first-line treatment of chronic lymphocytic leukaemia (CLL) and relapsed indolent non-Hodgkin lymphoma. The percentage of deaths in the treatment arms was 8% in the CLL study and 8% and 5% in the lymphoma studies, compared with 3%, 6% and 1% respectively in the placebo arms. The additional deaths were mainly caused by infections, including *Pneumocystis jirovecii* pneumonia and cytomegalovirus infections.
- These studies included patients with disease characteristics that were different from those covered by the currently approved indications for Zydelig and investigated use with treatment combinations that are not currently licensed and which may have influenced the infection rate. The relevance of these results to the authorised use of Zydelig is therefore limited, but suggests a need to strengthen measures to minimise the risk of infection.
- Provided that strengthened measures are followed to minimise the risk of infection (see below), Zydelig can continue to be used in combination with rituximab in CLL

patients who have received at least one prior therapy, and as monotherapy in patients with follicular lymphoma that is refractory to two lines of treatment.

- Zydelig may also be used in combination with rituximab, as first line treatment in CLL in the presence of 17p deletion or *TP53* mutation provided patients cannot take any alternative treatment and provided again that the below measures are followed to reduce the risk of infection.
- Patients should be informed about the risk of serious infections with Zydelig and must not be started in patients with any evidence of ongoing systemic infection.
- All patients should receive prophylaxis for *P. jirovecii* pneumonia during Zydelig treatment and for 2 to 6 months after stopping treatment. Patients should be monitored for respiratory signs and symptoms. Regular clinical and laboratory monitoring for cytomegalovirus infection is also recommended and specific guidance is included in the updated summary of product characteristics (SmPC).
- Patients should also have regular checks of their blood counts to detect neutropenia. If the patient develops severe neutropenia, treatment with Zydelig may have to be interrupted, in line with the updated SmPC.

A letter (DHPC) will be sent to healthcare professionals, advising them of these changes.

Reporting Adverse Drug Reactions

Healthcare professionals and patients are encouraged to maintain vigilance on Zydelig. Suspected Adverse Drug Reactions (side effects) or medication errors may be reported using the Medicines Authority ADR reporting form or online at 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.

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