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## Questions and answers on the review of Tygacil (tigecycline)

### Outcome of a renewal procedure

The European Medicines Agency has completed a review of the benefit-risk balance for Tygacil, as part of the procedure for the marketing authorisation renewal, five years after the medicine was first authorised. The Agency's Committee for Medicinal Products for Human Use (CHMP) concluded that the benefits of Tygacil continue to outweigh its risks but recommended changes to the product information to ensure that it is used appropriately, by making prescribers aware that the medicine has been associated with an increased mortality in clinical studies.

### What is Tygacil?

Tygacil is an antibiotic used as an infusion (drip into a vein) to treat complicated infections of the skin and soft tissue (the tissue below the skin) and complicated infections in the abdomen. 'Complicated' means that the infection is difficult to treat.

Tygacil contains the active substance tigecycline, an antibiotic that belongs to the group 'glycylcyclines'. It works by blocking the bacteria's ribosomes, the parts of the cell where new proteins are made. Tigecycline is known to be a broad spectrum antibiotic, because it works against a wide range of bacteria, including 'Gram-positive' bacteria (such as *Enterococcus*, *Staphylococcus aureus*, *S. epidermidis*, *S. haemolyticus*, *S. agalactiae*, *S. anginosus* and *S. pyogenes* and viridans group streptococci), 'Gram-negative' bacteria (such as *Citrobacter freundii*, *C. koseri*, *Escherichia coli* and *Klebsiella oxytoca*) and 'anaerobes' (*Clostridium perfringens*, *Peptostreptococcus* and *Prevotella*).

Tygacil was first authorised on 24 April 2006. It is marketed by Wyeth in all European Union Member States, and in Iceland, Liechtenstein and Norway.

### Why was Tygacil reviewed?

Initial marketing authorisations granted by the European Commission are granted for a five-year period. At the end of these five years, the CHMP re-evaluate the benefit-risk balance of the medicine to decide whether the validity should be extended for a further five years or become unlimited. The marketing authorisation for Tygacil had reached the limit of its first five-year validity period, and was



due for renewal by 23 April 2011. Therefore, the company for Tygacil submitted an application for renewal in October 2010.

### **Which data has the CHMP reviewed?**

The Committee looked at the results of all clinical studies carried out with Tygacil since its first authorisation, both in the treatment of diseases for which the medicine is already authorised and in the treatment of diseases for which the medicine is not yet approved. The clinical studies taken into consideration by the CHMP were carried out to support the use of Tygacil in complicated skin and soft tissue infections and complicated intra-abdominal infection as well as to support the possible use of Tygacil to treat diseases such as community- or hospital-acquired pneumonia, diabetic foot infections and its use in subjects with resistant pathogens. The Committee also looked at all the periodic safety reports for Tygacil since first authorisation. The CHMP also convened a meeting of infections specialists to provide advice on the benefits and risks of Tygacil.

### **What are the conclusions of the CHMP?**

When looking at all the clinical studies where Tygacil was compared with other antibiotics, the Committee noted that in 12 out of the 13 studies, more deaths occurred among patients receiving Tygacil than among patients receiving the comparator antibiotics. The increase was small but consistent across the 12 studies. When the results of all studies were pooled together, there were 3.9% (147/3,788) deaths in patients receiving tigecycline compared with 2.9% (105/3,646) in patients receiving a comparator. The CHMP acknowledged that it was difficult to identify the exact reason for the increase, and that factors such as the health of the patient or Tygacil's failure to treat the infection could contribute.

Based on the evaluation of the currently available data and the scientific discussion within the Committee, the CHMP concluded that the benefits of Tygacil continue to outweigh its risks, but that measures were necessary to ensure that doctors are made aware of the risk, and warned that the medicine should only be used for its approved uses, in the treatment of complicated skin and soft tissue infections and complicated intra-abdominal infections, and only when other antibiotics are not suitable.

The full changes made to the information to doctors and patients are detailed [here](#).

### **What are the recommendations for prescribers?**

- Doctors are reminded that Tygacil is only indicated in the treatment of patients with complicated skin and soft tissue infections and complicated intra-abdominal infections.
- They should only use Tygacil when other antibiotics are not suitable.
- Patients on Tygacil should be monitored closely, especially to detect the possible development of superinfections. Superinfection, in particular pneumonia, can be associated with poor patient survival. If a superinfection occurs, treatment should be switched to another antibiotic.

This medicine is used only in hospitals. There are no recommendations for patients, but patients who are or have been treated with Tygacil and have any questions should speak to their doctors to discuss their treatment.

A European Commission decision on this opinion will be issued in due course.