Public Assessment Report

Decentralised Procedure

Teicoplanin 200 mg Powder and Solvent for Solution for injection/infusion or oral solution

Teicoplanin 400 mg Powder and Solvent for Solution for injection/infusion or oral solution

Procedure No: UK/H/2096/001-002/DC

UK Licence No: PL 24598/0017-0018

Noridem Enterprises Ltd
LAY SUMMARY

Teicoplanin 200 mg Powder and Solvent for Solution for injection/infusion or oral solution

Teicoplanin 400 mg Powder and Solvent for Solution for injection/infusion or oral solution

This is a summary of the Public Assessment Report (PAR) for Teicoplanin 200 mg and 400 mg Powder and Solvent for Solution for injection/infusion or oral solution. It explains how the applications for Teicoplanin 200 mg and 400 mg were assessed and their authorisation recommended, as well as their conditions of use. It is not intended to provide practical advice on how to use Teicoplanin 200 mg and 400 mg.

For practical information about using Teicoplanin 200 mg and 400 mg, patients should read the package leaflet or contact their doctor or pharmacist.

What are Teicoplanin 200 mg and 400 mg and what are they used for?
Teicoplanin 200 mg and 400 mg are ‘generic medicines’. This means that they are similar to ‘reference medicines’ already authorised in the European Union (EU) called Targocid 200 mg powder and solvent for solution for injection and Targocid 400 mg powder and solvent for solution for injection, which have been authorised since 2 August 1989.

Teicoplanin is used in adults and children (including newborn babies) to treat bacterial infections of the skin and underneath the skin (sometimes called ‘soft tissue’), the bones and joints, the lung, the urinary tract, the heart (sometimes called ‘endocarditis’), the abdominal wall (peritonitis) and the blood (when caused by any of the conditions listed above). Teicoplanin can be used to treat some infections caused by *Clostridium difficile* bacteria in the gut. When teicoplanin is used for this the solution is taken by mouth.

How do Teicoplanin 200 mg and 400 mg work?
Teicoplanin is an antibiotic that belongs to a group of medicines called the glycopeptides. It works by stopping bacteria making their cell walls and by disrupting their cell membranes. Together, the cell wall and membrane form a barrier between the bacterial cell contents and the external environment. By disrupting this barrier, teicoplanin kills the bacteria that are causing the infection.

How are Teicoplanin 200 mg and 400 mg used?
Teicoplanin is normally given by a doctor or nurse. It may be given by injection into a vein (intravenous use) or muscle (intramuscular use). It can also be given as an infusion through a drip into a vein. Only the infusion method should be used to treat babies from birth to the age of 2 months. To treat certain infections, the solution may be taken by mouth.

The amount of teicoplanin taken will depend upon the age of the patient and the type of infection that it is being used to treat.

To treat skin and soft tissue, lung and urinary tract infections in adults and children (12 years and over) with no kidney problems the recommended starting dose (for the first three doses) is 400 mg given every 12 hours followed by a maintenance dose of 400 mg given once a day by injection into a vein or muscle.

To treat bone and joint infections and heart infections in adults and children (12 years and over) with no kidney problems the recommended starting dose (for the first three to five doses) is 800 mg given every 12 hours followed by a maintenance dose of 800 mg given once a day by injection into a vein or muscle.
Teicoplanin 200 mg and 400 mg Powder and Solvent for Solution for injection/infusion or oral solution

To treat infections caused by *Clostridium difficile* bacteria in adults and children (12 years and over) with no kidney problems the recommended dose is 100 to 200 mg by mouth, twice a day for 7 to 14 days.

In adults and elderly patients with kidney problems the dose will usually need to be lowered after the fourth day of treatment. For people with mild and moderate kidney problems the maintenance dose will be given every two days, or half of the maintenance dose will be given once a day. For people with severe kidney problems or on haemodialysis the maintenance dose will be given every three days, or one-third of the maintenance dose will be given once a day.

To treat peritonitis in patients on peritoneal dialysis the starting dose is 6 mg for every kilogram of body weight as a single injection into a vein, followed by 20 mg/L in each dialysis bag in week one, 20 mg/L in every other dialysis bag in week two and 20 mg/L in the overnight dialysis bag in week three.

In babies (from birth to the age of 2 months) the starting dose (on the first day) is 16 mg for every kilogram of body weight followed by a maintenance dose of 8 mg for every kilogram of body weight given once a day as an infusion through a drip into a vein.

In children (from 2 months to 12 years) the starting dose (for the first three doses) is 10 mg for every kilogram of body weight given every 12 hours followed by a maintenance dose of 6 to 10 mg for every kilogram of body weight given once a day by injection into a vein.

Teicoplanin 200 mg and 400 mg can only be obtained with a prescription.

**What benefits of Teicoplanin 200 mg and 400 mg have been shown in studies?**

No studies were needed because Teicoplanin 200 mg and 400 mg are generic medicines that are taken as solutions for injection or infusion or as oral solutions and contain the same active substances as their respective reference medicines, Targocid 200 mg powder and solvent for solution for injection and Targocid 400 mg powder and solvent for solution for injection.

**What are the possible side effects of Teicoplanin 200 mg and 400 mg?**

Because Teicoplanin 200 mg and 400 mg are generic medicines their possible side effects are taken as being the same as those of the reference medicines.

For the full list of all side effects reported with Teicoplanin 200 mg and 400 mg, see section 4 of the package leaflet.

For the full list of restrictions, see the package leaflet.

**Why are Teicoplanin 200 mg and 400 mg approved?**

It was concluded that, in accordance with EU requirements, Teicoplanin 200 mg and 400 mg have been shown to be comparable to Targocid 200 mg and 400 mg powder and solvent for solution for injection. Therefore, the MHRA decided that, as for Targocid 200 mg and 400 mg powder and solvent for solution for injection, the benefits outweigh the identified risks and recommended that Teicoplanin 200 mg and 400 mg can be approved for use.

**What measures are being taken to ensure the safe and effective use of Teicoplanin 200 mg and 400 mg?**

Safety information has been included in the Summaries of Product Characteristics and the package leaflet for Teicoplanin 200 mg and 400 mg, including the appropriate precautions to be followed by healthcare professionals and patients.

Known side effects are continuously monitored. Furthermore new safety signals reported by patients/healthcare professionals will be monitored and reviewed continuously.
Other information about Teicoplanin 200 mg and 400 mg
Marketing Authorisations were granted in the UK for Teicoplanin 200 mg and 400 mg on 13 April 2015.

The full PAR for Teicoplanin 200 mg and 400 mg follows this summary.

For more information about treatment with Teicoplanin 200 mg and 400 mg, read the package leaflet or contact your doctor or pharmacist.

This summary was last updated in June 2015.
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UK/H/2096/001-002/DC

Scientific discussion

I INTRODUCTION
Based on the review of the data on quality, safety and efficacy, the Competent Authorities of Austria, Germany, Greece, Spain, Ireland and the UK considered that the applications for Teicoplanin 200 mg and 400 mg Powder and Solvent for Solution for injection/infusion or oral solution (PL 24598/0017-0018; UK/H/2096/001-002/DC) could be approved. These are prescription-only medicines (POMs).

Teicoplanin is indicated in adults and in children from birth for the parenteral treatment of the following infections:

- complicated skin and soft tissue infections,
- bone and joint infections,
- hospital acquired pneumonia,
- community acquired pneumonia,
- complicated urinary tract infections,
- infective endocarditis,
- peritonitis associated with continuous ambulatory peritoneal dialysis (CAPD)
- bacteraemia that occurs in association with any of the indications listed above.

Teicoplanin is also indicated as an alternative oral treatment for *Clostridium difficile* infection-associated diarrhoea and colitis.

Where appropriate, teicoplanin should be administered in combination with other antibacterial agents.

These applications were submitted using the Decentralised Procedure (DCP), with the UK as Reference Member State (RMS), and Austria, Germany, Greece, Spain and Ireland as Concerned Member States (CMS). The applications for Teicoplanin 200 mg and 400 mg Powder and Solvent for Solution for injection/infusion or oral solution were submitted under Article 10(1) of Directive 2001/83/EC, as amended, as generic applications. Teicoplanin 200 mg and 400 mg Powder and Solvent for Solution for injection/infusion or oral solution cross-refer to the reference medicinal products Targocid 200 mg powder and solvent for solution for injection (PL 04425/0088) and Targocid 400 mg powder and solvent for solution for injection (PL 04425/0089), which were authorised to Sanofi Aventis in the UK on 2 August 1989.

Teicoplanin inhibits the growth of susceptible organisms by interfering with cell-wall biosynthesis at a site different from that affected by beta-lactams. Peptidoglycan synthesis is blocked by specific binding to D-alanyl-D-alanine residues.

No new non-clinical or clinical data were submitted, which is acceptable given that the applications are for solution for injection/infusion and oral solutions which are generic medicinal products of originator products that have been in clinical use for over 10 years.

The RMS has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place at all sites responsible for the manufacture, assembly and batch release of the product.

For manufacturing sites within the Community, the RMS has accepted copies of current manufacturing authorisations issued by inspection services of the competent authorities as certification that acceptable standards of GMP are in place at those sites.
The UK, Austria, Germany, Greece, Spain and Ireland considered that the applications could be approved at the end of procedure (Day 210) on 19 March 2015. After a subsequent national phase, Marketing Authorisations were granted to Noridem Enterprises Ltd in the UK on 13 April 2015.

II QUALITY ASPECTS

II.1 Introduction
The powder is presented in Type I, colourless glass vials closed with a rubber (Type I) stopper and sealed with aluminium flip-off cap. The vials for Teicoplanin 200 mg and 400 mg have a useful volume of 10 mL and 22 mL, respectively. The water for injections is packed in polypropylene blow-fill-sealed ampoules.

II.2 DRUG SUBSTANCE – TEICOPLANIN
INN: Teicoplanin
Chemical name: \((2RS)-N,N,2\text{-Trimethyl-3-}(10\text{H}-\text{phenothiazin-10-yl})\text{propan-1-amine}\)
\[\text{hemi}[(2R,3R)-2,3\text{-dihydroxybutanedioate}].\]

With the exception of stability studies undertaken by the drug substance manufacturer, all aspects of the manufacture and control of teicoplanin are covered by a European Directorate for the Quality of Medicines and Healthcare (EDQM) Certificate of Suitability.

Appropriate stability data have been generated to support a suitable retest period when stored in the proposed packaging.
II.3 MEDICINAL PRODUCTS

Pharmaceutical Development
The aim of the pharmaceutical development of Teicoplanin 200 mg and 400 mg was to develop generic versions of the innovator products, Targocid 200 mg and Targocid 400 mg powder and solvent for solution for injection.

All the excipients comply with their respective European Pharmacopoeia monographs. Satisfactory Certificates of Analysis have been provided for all excipients. None of the excipients contain materials of animal or human origin.

Manufacturing Process
Satisfactory batch formulae have been provided for the manufacture of the products, along with an appropriate description of the manufacturing process. Based on full-scale batches, the manufacturing process has been validated and has shown satisfactory results.

Control of Finished Products
The finished product specifications are acceptable. Test methods have been described and have been validated adequately. Batch data have been provided that comply with the release specifications. Certificates of Analysis have been provided for all working standards used.

Stability of the Products
Finished product stability studies were performed in accordance with current guidelines on batches of finished product in the packaging proposed for marketing. Based on the results, a shelf-life 24 months has been approved. The storage precautions for the powder as packaged for sale are ‘Store below 25°C’ and ‘Keep the container in the outer carton in order to protect from light’.

II.4 Discussion on chemical, pharmaceutical and biological aspects
It is recommended that Marketing Authorisations are granted for Teicoplanin 200 mg and 400 mg Powder and Solvent for Solution for injection/infusion or oral solution.

II.5 Summaries of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and Labels
The SmPCs, PIL and labelling are satisfactory and, where appropriate, in line with current guidance.

In accordance with Directive 2010/84/EU, the current version of the SmPCs and PIL are available on the MHRA website. The current labelling is presented below:
Teicoplanin 200 mg and 400 mg Powder and Solvent for Solution for injection/infusion or oral solution

Labels:

Carton:

Each vial contains 200 mg teicoplanin equivalent to not less than 200,000 IU. After reconstitution, the solution will contain 200 mg teicoplanin in 3 ml. Powder for solution for injection/infusion or oral solution also contains: sodium chloride, sodium hydrogen carbonate. Solvent: water for injections. The concentration of sodium per vial is 0.41 mmol. See package leaflet for further information. Read the package leaflet before use. Read the leaflet for the shelf-life of the reconstituted medicine. Store below 25°C. Keep the container in the outer carton in order to protect from light. For storage conditions and in use shelf life of the reconstituted solution see package leaflet. Keep out of the sight and reach of children.
Teicoplanin 200 mg and 400 mg Powder and Solvent for Solution for injection/infusion or oral solution

Teicoplanin 400 mg Powder and Solvent for Solution for injection/infusion or oral solution:

Labels:

Carton:

Each vial contains 400 mg teicoplanin equivalent to not less than 400,000 IU. After reconstitution, the solution will contain 400 mg teicoplanin in 3 ml.

Powder for solution for injection/infusion or oral solution also contains: sodium chloride, sodium hydroxide. Solvent: water for injections. The content of sodium per vial is 0.41 mmol. See leaflet for further information. Read the package leaflet before use. Read the leaflet for the shelf-life of the reconstituted medicine.

Store below 25°C. Keep the container in the outer carton in order to protect from light. For storage conditions and in use shelf life of the reconstituted/diluted product see package leaflet.

Keep out of the sight and reach of children.

POM
PL 24598/0018
PA1122/009/002
Teicoplanin 200 mg and 400 mg Powder and Solvent for Solution for injection/infusion or oral solution

III NON-CLINICAL ASPECTS

III.1 Introduction
The pharmacodynamic, pharmacokinetic and toxicological properties of teicoplanin are well known. No new non-clinical data have been submitted for these applications and none are required.

The applicant has provided an overview based on published literature. The non-clinical overview has been written by an appropriately qualified person and is satisfactory, providing an appropriate review of the relevant non-clinical pharmacology, pharmacokinetics and toxicology.

III.2 Pharmacology
Not applicable, see Section III.1 Introduction, above.

III.3 Pharmacokinetics
Not applicable, see Section III.1 Introduction, above.

III.4 Toxicology
Not applicable, see Section III.1 Introduction, above.

III.5 Ecotoxicity/Environmental Risk Assessment (ERA)
Suitable justification has been provided for non-submission of an Environmental Risk Assessment. As the products are intended for generic substitution with products that are already marketed, no increase in environmental exposure to teicoplanin is anticipated. Thus, the justification for non-submission of an Environmental Risk Assessment is accepted.

III.6 Discussion of the non-clinical aspects
It is recommended that Marketing Authorisations are granted for Teicoplanin 200 mg and 400 mg Powder and Solvent for Solution for injection/infusion or oral solution, from a non-clinical point of view.

IV. CLINICAL ASPECTS

IV.1 Introduction.
No new clinical data have been submitted and none are required for an application of this type. The applicant’s clinical overview has been written by an appropriately qualified person and is considered acceptable.

IV.2 Pharmacokinetics
No bioequivalence studies are required for this type of product according to ‘Note for guidance on the investigation of bioavailability and bioequivalence (CPMP/EWP/QWP/1401/98)’ and the Applicant has submitted none.

IV.3 Pharmacodynamics
The clinical pharmacodynamics properties of teicoplanin are well-known. No new pharmacodynamic data were submitted and none are required for an application of this type.

IV.4 Clinical Efficacy
The clinical efficacy of teicoplanin is well-known. No new efficacy data are presented or are required for this type of application.
IV.5  Clinical Safety
The clinical safety of teicoplanin is well-known. No new safety data were submitted and none are required for this type of application.

IV.6  Risk Management Plan (RMP)
This Marketing Authorisation Applications were submitted before the requirements for RMP were put in place, therefore the absence of an RMP is considered justified.

IV.7  Discussion of the clinical aspects
It is recommended that Marketing Authorisations are granted for Teicoplanin 200 mg and 400 mg Powder and Solvent for Solution for injection/infusion or oral solution.

V.  USER CONSULTATION
The package leaflet has been evaluated via a user consultation study in accordance with the requirements of Articles 59(3) and 61(1) of Directive 2001/83/EC. The language used for the purpose of user testing the pack leaflet was English.

The results show that the package leaflet meets the criteria for readability as set out in the Guideline on the readability of the label and package leaflet of medicinal products for human use.

VI.  OVERALL CONCLUSION AND BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

QUALITY
The important quality characteristics of Teicoplanin 200 mg and 400 mg Powder and Solvent for Solution for injection/infusion or oral solution are well-defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

NON-CLINICAL
No new non-clinical data were submitted and none are required for an application of this type. As the pharmacokinetics, pharmacodynamics and toxicology of teicoplanin are well-known, no additional data were required.

EFFICACY
No new data were submitted and none are required for this type of application.

SAFETY
No new data were submitted and none are required for this type of application.

PRODUCT LITERATURE
The SmPCs, PIL and labelling are satisfactory and, where appropriate, in line with current guidance.

BENEFIT/RISK ASSESSMENT
The quality of the products is acceptable, and no new non-clinical or clinical safety concerns have been identified. Extensive clinical experience with alimemazine tartrate is considered to have demonstrated the therapeutic value of the compound. The benefit/risk assessment is therefore considered to be positive.

RECOMMENDATION
The grant of Marketing Authorisations is recommended.
### Annex 1 - Table of content of the PAR update for MRP and DCP

**Steps Taken After The Initial Procedure With An Influence On The Public Assessment Report**  
(Type II variations, PSURs, commitments)

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