**ANNEX I**

**LIST OF THE NAMES, PHARMACEUTICAL FORM, STRENGTHS OF THE MEDICINAL PRODUCTS, ROUTES OF ADMINISTRATION, APPLICANTS IN THE MEMBER STATES**

| **Member State EU/EEA** | **Marketing Authorisation Holder** | **Applicant** | **(Invented) Name** | **Strength** | **Pharmaceutical Form** | **Route of administration** | **Content (concentration)** |
|---|---|---|---|---|---|---|---|
| Austria | | Hospira UK Limited, Queensway, Royal Leamington Spa, Warwickshire, CV31 3RW, United Kingdom | Teicoplanin Hospira 200 mg Pulver und Lösungsmittel zur Herstellung einer Injektionslösung oder Infusionslösung | 200 mg | Powder and solvent for solution for injection or infusion | Intravenous use (injection or infusion) Intramuscular use | 200 mg/vial (66,7 mg/ml) |
| Austria | | Hospira UK Limited, Queensway, Royal Leamington Spa, Warwickshire, CV31 3RW, United Kingdom | Teicoplanin Hospira 400 mg Pulver und Lösungsmittel zur Herstellung einer Injektionslösung oder Infusionslösung | 400 mg | Powder and solvent for solution for injection or infusion | Intravenous use (injection or infusion) Intramuscular use | 400 mg/vial (133,4 mg/ml) |
| Germany | | Hospira UK Limited, Queensway, Royal Leamington Spa, Warwickshire, CV31 3RW, United Kingdom | Teicoplanin Mayne Hospira 200 mg Trockensubstanz | 200 mg | Powder and Solvent for Solution for Injection or Infusion | Intravenous use (injection or infusion) Intramuscular use | 200 mg/vial |
| Germany | | Hospira UK Limited, Queensway, Royal Leamington Spa, Warwickshire, CV31 3RW, United Kingdom | Teicoplanin Mayne Hospira 400 mg Trockensubstanz | 400 mg | Powder and Solvent for Solution for Injection or Infusion | Intravenous use (injection or infusion) Intramuscular use | 400 mg/vial |
| Ireland | | Hospira UK Limited, Queensway, Royal Leamington Spa, Warwickshire, CV31 3RW, United Kingdom | Teicoplanin 200 mg Powder and Solvent for Solution for Injection or Infusion | 200 mg | Powder and Solvent for Solution for Injection or Infusion | Intravenous use (injection or infusion) Intramuscular use | 200 mg/vial |

| **Member State EU/EEA** | **Marketing Authorisation Holder** | **Applicant** | **(Invented) Name** | **Strength** | **Pharmaceutical Form** | **Route of administration** | **Content (concentration)** |
|---|---|---|---|---|---|---|---|
| Ireland | | Hospira UK Limited, Queensway, Royal Leamington Spa, Warwickshire, CV31 3RW, United Kingdom | Teicoplanin 400 mg Powder and Solvent for Solution for Injection or Infusion | 400 mg | Powder and Solvent for Solution for Injection or Infusion | Intravenous use (injection or infusion) Intramuscular use | 400 mg/vial |
| Italy | | Hospira UK Limited, Queensway, Royal Leamington Spa, Warwickshire, CV31 3RW, United Kingdom | Teicoplanina Hospira | 200 mg | Powder and Solvent for Solution for Injection or Infusion | Intravenous use (injection or infusion) Intramuscular use | 200 mg/vial |
| Italy | | Hospira UK Limited, Queensway, Royal Leamington Spa, Warwickshire, CV31 3RW, United Kingdom | Teicoplanina Hospira | 400 mg | Powder and Solvent for Solution for Injection or Infusion | Intravenous use (injection or infusion) Intramuscular use | 400 mg/vial |
| Portugal | | Hospira UK Limited, Queensway, Royal Leamington Spa, Warwickshire, CV31 3RW, United Kingdom | Teicoplanina Hospira 200 mg Pó e solvente para solução injectável ou solução para perfusão | 200 mg | Powder and Solvent for Solution for Injection or Infusion | Intravenous use (injection or infusion) Intramuscular use | 200 mg/vial |
| Portugal | | Hospira UK Limited, Queensway, Royal Leamington Spa, Warwickshire, CV31 3RW, United Kingdom | Teicoplanina Hospira 400 mg Pó e solvente para solução injectável ou solução para perfusão | 400 mg | Powder and Solvent for Solution for Injection or Infusion | Intravenous use (injection or infusion) Intramuscular use | 400 mg/vial |
| Spain | | Hospira UK Limited, Queensway, Royal Leamington Spa, Warwickshire, CV31 3RW, United Kingdom | Teicoplanina Hospira 200 mg Polvo y disolvente para solución inyectable o para perfusión | 200 mg | Powder and Solvent for Solution for Injection or Infusion | Intravenous use (injection or infusion) Intramuscular use | 200 mg/vial |

| **Member State EU/EEA** | **Marketing Authorisation Holder** | **Applicant** | **(Invented) Name** | **Strength** | **Pharmaceutical Form** | **Route of administration** | **Content (concentration)** |
|---|---|---|---|---|---|---|---|
| Spain | | Hospira UK Limited, Queensway, Royal Leamington Spa, Warwickshire, CV31 3RW, United Kingdom | Teicoplanina Hospira 400 mg Polvo y disolvente para solución inyectable o para perfusión | 400 mg | Powder and Solvent for Solution for Injection or Infusion | Intravenous use (injection or infusion) Intramuscular use | 400 mg/vial |
| United Kingdom | | Hospira UK Limited, Queensway, Royal Leamington Spa, Warwickshire, CV31 3RW, United Kingdom | Teicoplanin 200 mg Powder and Solvent for Solution for Injection or Infusion | 200 mg | Powder and Solvent for Solution for Injection or Infusion | Intravenous use | 200 mg/vial |
| United Kingdom | | Hospira UK Limited, Queensway, Royal Leamington Spa, Warwickshire, CV31 3RW, United Kingdom | Teicoplanin 400 mg Powder and Solvent for Solution for Injection or Infusion | 400 mg | Powder and Solvent for Solution for Injection or Infusion | Intravenous use | 400 mg/vial |

# ANNEX II

# SCIENTIFIC CONCLUSIONS AND GROUNDS FOR REFUSAL

## SCIENTIFIC CONCLUSIONS

## OVERALL SUMMARY OF THE SCIENTIFIC EVALUATION OF TEICOPLANIN HOSPIRA AND ASSOCIATED NAMES (SEE ANNEX I)

In 2005 Hospira UK submitted applications for Decentralised Procedure for Teicoplanin Hospira 200 mg & 400 mg powder and solvent for solution for injection in the framework of Article 28 of Directive 2001/83/EC, as amended. The originator product Targocid 400mg is registered in Germany since 10th March 1992. The Applicant claimed essential similarity to the innovator product Targocid, despite acknowledging differences in the profile of glycopeptides. The Applicant therefore conducted a series of preclinical studies and reviewed the published literature on the biological activity of the individual subcomponents of teicoplanin. The results of the phase I study failed to demonstrate PK equivalence for total drug exposure. In addition, the evaluation of free drug AUC also failed to demonstrate equivalence. The Applicant conducted a bioequivalence study to provide further information on the PK/PD and to demonstrate similar safety and efficacy. It was considered that Teicoplanin Hospira and Targocid are comparable in terms of overall active drug content, but differ in the composition of the TA-2 subcomponents, resulting in major objections. The procedure was therefore referred to the CHMP. The main issue for consideration was the failure to demonstrate that Teicoplanin Hospira is a generic of Targocid. The CHMP adopted a list of questions to be addressed by the Applicant.

***Question 1*** *- The differences in composition between the two products and the resulting differences between the AUC values do not clearly demonstrate that Teicoplanin Hospira and the reference product Targocid are essentially similar. The Applicant is, therefore, requested to fully justify whether or not additional clinical data is required in the form of a comparative safety and efficacy study with the innovator product in advance of the product being granted a Marketing Authorisation.*

Phase 1 Clinical PK/PD

The Applicant acknowledged that AUC 0-tlast and AUC 0-inf were below the accepted range, indicating that the two preparations were not PK equivalent for total drug exposure. The half- lives of the TA2 components correlates to their lipophilicity, and because Teicoplanin Hospira has a lower proportional content of subcomponents with a longer half-life and a higher proportion with a shorter half-life, the overall elimination of total teicoplanin is faster, and the resulting AUC is lower. Protein binding was assessed, showing that the unbound fraction for each sub-component was essentially similar for Targocid and Teicoplanin Hospira and confirming that the individual protein binding values for the subcomponents did not vary with the different component composition. It is agreed that bound drug is not available to exert its therapeutic effect and that for antimicrobial agents, only free drug treats infections. Therefore, PK/PD relationships for antimicrobials are based on free drug. The Applicant examined both available active drug (free AUC) and whole drug and free AUC/MIC, concluding that Teicoplanin Hospira is at least as efficacious as Targocid. The effect of variability in PK on the expected outcome (AUC/MIC) was assessed and even with differences in distributions for the subcomponents, the overall AUC/MIC values are similar for the two products. According to the Applicant, this indicates essentially similar therapeutic outcome. The Applicant discussed the compliance of Teicoplanin Hospira to the monographs, stating that the tighter controls over the individual components proposed signify that the active pharmaceutical ingredient used in Teicoplanin Hospira meets the requirements of both monographs and that the individual components are controlled to a far greater extent. The variability seen in the subcomponent composition is inherent to a fermentation product, and both products show variability for all individual components, although remaining well within the JP and European specifications. On this basis, the Applicant concluded that small variations in the composition of the active fractions are unlikely to affect the safety and efficacy of the drug in vivo.

Non-clinical study results

The Applicant undertook an extensive testing program to characterise the activity of Teicoplanin Hospira versus Targocid against a series of clinically relevant species and demonstrated essential similarity between Teicoplanin Hospira and Targocid for all individual strains and species. Most MIC values were identical for the two preparations, and the remaining 10.2% of the results were within one twofold dilution. The study

concluded that the biological activity of Teicoplanin Hospira is equivalent to that of Targocid and therefore confirmed that the minor differences in the composition of individual active components of teicoplanin do not affect the biological activity. The Applicant also discussed the data from the neutropenic mouse thigh infection study, arguing that the results clearly show that Teicoplanin Hospira and Targocid were equally effective in reducing bacterial count, confirming that the differences in relative composition of individual components do not affect the biological activity of the product.

Safety data obtained from clinical study and non-clinical toxicity study

The Applicant stated that the dosing regimen of teicoplanin is predictable, therefore dose-dependent toxicity is not of concern under standard clinical use. Accidental overdosing showed no adverse events or abnormalities. The related substances resulting from the fermentation process are well documented and the Applicant undertook a toxicity study program to demonstrate a similar safety profile to that of the originator. Overall the total numbers of adverse events observed were similar for both treatments. The majority of the adverse events observed were mild in intensity and not considered related to drug administration. The Applicant concluded that no additional clinical data are required.

The CHMP considered that similarity with regards to the free drug is important and that with regards to free AUC, the sum of all free TA2 subcomponents is 13% higher for Teicoplanin Hospira. These differences are indicative that Teicoplanin Hospira is not a generic of Targocid and the potential impact on the safety of the drug is still not clear. The CHMP noted that the proposed specifications result in a considerably greater control of the individual subcomponents than if they had simply been in line with the monographs; however this does not establish that Teicoplanin Hospira is a generic of Targocid. The CHMP noted the neutropenic mouse study demonstrating efficacy in reducing bacterial count and demonstrating biological equivalence. Regarding safety, the data from study TEC062 showed no differences between Teicoplanin Hospira and Targocid, however, the premature termination of the study does not allow solid conclusions to be drawn, although there were no suggestions of any differential safety profile between the two products. In conclusion, the CHMP considers that the difference in concentration of the glycopeptide subcomponents precludes Teicoplanin Hospira being a considered a generic of Targocid, despite the composition being in line with the JP monograph and the draft Ph.Eur monograph. The CHMP requested the Applicant to further discuss their claim that Teicoplanin Hospira is a generic of Targocid.

***Question 2*** *- The Applicant is requested to fully justify why the Phase I study submitted should not be considered a failed study.*

The Applicant responded that the Phase I study (TEC062) provided in support of this application, should not be considered as a failed study, as it was conducted in accordance with the relevant guidelines and that an inspection identified no major findings specifically related to the conduct of the study. The Applicant also provided a briefing document stating that other endpoints, including pharmacodynamics, protein binding and analysis of the PK and PD of the principal sub-components, were measured in the study as it is believed that only free drug (non-protein bound teicoplanin) contributes to pharmacodynamic activity. Although the EMEA guideline for bioequivalence states that a bioequivalence study is not required for IV products, this study provided useful additional information. The study was stopped early due to safety reasons, but the available pharmacokinetics data of teicoplanin was still assessed to the extent the data would allow. From a GCP perspective and in terms of the data generated which support the CMC and non-clinical data, TEC062 cannot be considered a failed study. The CHMP considers that with respect to pharmacodynamics, the study demonstrated that serum bactericidal activity was similar for both the Teicoplanin Hospira and Targocid and that the free drug proportion for each sub-component was similar for the two products. However, these results are not considered to demonstrate that Teicoplanin Hospira is a generic of Targocid, with regards to overall similarity. The issue was considered unresolved and needs further discussion.

***Question 3*** *- The Applicant should discuss the scientific basis for the post hoc analysis on the free AUC instead of the total AUC.*

The Applicant discussed the results of a post hoc analysis on the free AUC, rather than on total AUC. In particular, the non-protein bound kinetics of the sub-components of teicoplanin that contribute to its activity ($TA2_{1-5}$) was examined. The pharmacokinetics of teicoplanin has been determined for both the total complex and for the individual components and analyses of the subcomponents confirmed that the pharmacokinetics of the individual TA2 subcomponents are the same for Teicoplanin Hospira and Targocid. The Applicant considers it relevant to measure free drug AUC (as the sum of the major active drug components). The CHMP endorsed the answer of the Applicant, from a pharmacodynamic point of view, free AUC is the most important PK parameter.

***Question 4 -*** *The Applicant states that in clinical practice, the dose of teicoplanin is adjusted to the clinical course and the trough serum concentrations especially in severe infections. The Applicant should provide data (e.g. guidance documents) demonstrating that adjustment of the dose to the clinical course is generally accepted and practised.*

The Applicant stated that appropriate loading doses of teicoplanin must be considered mandatory for all patients regardless of their renal function in order to achieve therapeutically relevant concentrations early in the treatment period. Subsequently, therapeutic drug monitoring is important to ensure that dose regimens are optimized and that it is recommended that teicoplanin are monitored and dosage adjusted to ensure trough levels of at least 20mg/L. A number of guidelines support monitoring. The Applicant concluded that there are many recent references recommending that the dose of teicoplanin is adjusted based on the monitoring of blood levels and that the guidance in the proposed SPC provides a solid baseline for managing patients requiring teicoplanin. The CHMP accepted the Applicant response, as the provided guidance documents supporting teicoplanin monitoring were considered relevant.

***Question 5-*** *The post hoc analysis conducted by the Applicant as a response to the concerned member state Day 145 comments was based on the individual Cmax/MIC or AUC/MIC ratios, determined for each sub-component and then summed. The Applicant should provide an analysis based on whole (total) teicoplanin plasma concentrations.*

The Applicant considered that the PK results for whole teicoplanin demonstrated that Cmax and Tmax of Teicoplanin Hospira and Targocid were essentially similar, and the 90% CI for Cmax was within the acceptance range for bioequivalence. However, AUC 0-tlast and AUC 0-inf were lower for Teicoplanin Hospira, indicating that PK equivalence was not shown for the total (bound plus unbound) drug exposure. The Applicant considered the AUC/MIC ratio individually for all 5 subcomponents, for the free drug, as teicoplanin is extensively protein bound, and the biological activity of the preparation mainly results from the free drug component. The Applicant believes that the sum of the individual ratios determined for each subcomponent is essentially the same as for the total teicoplanin. The CHMP noted the Applicant data and agreed that free drug is more important for biological activity and is thus the better parameter to demonstrate "pharmacodynamic"-equivalence.

***Question 6 -*** *The MIC values used in the calculations for each sub-component have not been approved by the EUCAST. EUCAST reported values for the whole (total) teicoplanin should be used instead*.

The Applicant stated that the antimicrobial potency of the drug is a sum of the component parts and that *In vitro* antibacterial potency is established by MIC testing. Teicoplanin Hospira has a different sub-component mix to the originator; however the Applicant considers that it is not reasonable to use total teicoplanin MICs to assess the impact of differing proportions of subcomponents. While EUCAST approved subcomponent MICs are not available for any antibacterial, this should not constitute an argument against their use. The CHMP agreed with the Applicant response and considered the issue to be resolved.

The CHMP acknowledged that safety and efficacy were established, as well as the general equivalence. However, the exact level of activity, which must be determined in order to propose the recommendations for use, has not been established. The CHMP therefore adopted the following List of Outstanding Issues to be addressed by the Applicant: "Following discussion and considering the differences in the composition and

the demonstrated PK differences, the CHMP was of the opinion that it was not sufficiently demonstrated that Teicoplanin Hospira is a generic of Targocid. Taking into consideration the legal basis of the application, a clear negative trend was observed at the CHMP. The Applicant is therefore requested to further justify that Teicoplanin Hospira is a generic of Targocid in writing and/or at an Oral Explanation in light of the CHMP opinion." The Applicant decided to address the List of Outstanding Issues during an oral explanation. The company presented no new data but reiterated the previous arguments. The CHMP was of the opinion that compliance with the specifications of the European Pharmacopoeia does not automatically imply that Teicoplanin Hospira is a generic of Targocid and maintained that demonstrating this is crucial for approval.

Re-examination procedure under Article 32(4) of Directive 2001/83/EC, as amended

The Applicant submitted a request for a re-examination of the CHMP opinion, responding to the grounds supporting the decision that Teicoplanin Hospira cannot be considered to be a generic of the innovator Targocid and addressed one by one the three grounds for refusal of the granting of the Marketing Authorisations.

**Ground 1: The Applicant has not sufficiently justified why the specifications of the innovator were not met.**

The CHMP noted the Applicant response, and the summary of advice received from national agencies. The Applicant stated that generic applicants do not have access to the specifications of the originator products and that it therefore attempted to develop an API containing subcomponents at levels similar to that seen in Targocid. The Applicant considers that the achieved product is in line with the published EDQM teicoplanin monograph, but stated that only the originator MAH was invited to comment on this monograph, and that comments submitted by Hospira were not accepted. The Applicant concluded that taking into account the teicoplanin subcomponents and their relative amounts, lipophilicity and MIC's, numerous experts believe that in a clinical setting, teicoplanin should be treated as a whole, regardless of the relative levels of subcomponents, due to the differences in PK characteristics being small.

The CHMP noted that for Teicoplanin Hospira to be considered as a generic product, the difference in the amounts of glycopeptides subcomponents must be acceptable and that this difference must not lead to a difference in safety and/or efficacy. Both products include the same subcomponents and despite differences in the subcomponent ratios, both comply with the European Pharmacopoeia (Ph.Eur.) monograph. However, although these monographs ensure acceptable quality, they do not establish therapeutic equivalence. It must therefore be demonstrated that the subcomponent ratio differences do not result in efficacy and/or safety differences and the CHMP is of the opinion that the clinical and non-clinical data and the bioequivalence trials provided are insufficient to demonstrate this. The CHMP acknowledges that the specifications of the innovator are confidential however, analysing innovator product batches will provide insight into the variability of innovator subcomponent levels and achieving specifications within this variability range would ensure equivalence. As the ratios observed for Teicoplanin Hospira fall outside these ranges, equivalence cannot be assumed, based on the *in vitro* data alone. Regarding the available literature concluding that Teicoplanin should be treated as a whole regardless of the relative levels of subcomponents, the CHMP is of the opinion that this would have been considered during the development of the Ph.Eur. monograph. Finally, the in vitro MIC studies performed by the Applicant are not sensitive enough to detect any differences between the two products since in vitro anti-bacterial activity is independent of lipophilicity, tissue distribution and clearance of the subcomponents.

**Ground 2: Bioequivalence was not demonstrated for each subcomponent.**

The Applicant did not further discuss the outcomes of the partially completed bioequivalence studies evaluating AUC and Cmax, as the CHMP considered that due to the nature of this drug, the whole drug (total) AUC is not appropriate to demonstrate bioequivalence. As the CHMP considered that free AUC is the most important PK parameter and that the dominant pharmacodynamic driver of microbiological and

clinical outcome is AUC/MIC, the Applicant concluded that the most important PK/PD parameter for assessing microbiological and clinical outcome is the free AUC/MIC. Accordingly, the Applicant argued that the sum of free AUC/MIC of the subcomponents is substantiating comparable activity between the generic and the innovator. The Applicant discussed the variation in subcomponent levels and stated that bioequivalence or essential similarity for Teicoplanin is best assessed by comparing the sum of free AUC/MIC for the subcomponents. The free drug AUC/MIC for the sum of TA2 subcomponents for Teicoplanin Hospira was within 2% of the Targocid value and the totality of the pre-clinical MIC studies combined with the mouse thigh study and the identical bactericidal serum titres give re-assurance that the microbiological activity of the two products is the same and that pharmacodynamically, the two products can be considered equivalent. Therefore, the Applicant considers Teicoplanin Hospira to be a generic of Targocid.

The CHMP noted the data comparing the PK, PDD and safety of Teicoplanin Hospira and the originator. The results show that free drug for each teicoplanin subcomponent was similar. However, the validity and sensitivity of free AUC and PK/PD parameters in the evaluation of a generic product have not been established, and this approach contravenes the CHMP guideline on the Investigation of Bioavailability and Bioequivalence. The nature of the active substance and the fermentation process used may lead to subcomponent differences, affecting the lipophilicity of the drug and as such the PK and indeed, the PK data indicates that for AUC, bioequivalence could not be shown. Comparable free AUC/MIC activity cannot waive potential PK differences or the outcome of the bioequivalence study. For generics, including this i.v. teicoplanin formulation, bioequivalence should be shown as the supporting clinical data is not sensitive enough to detect differences between formulations. In addition, the use of MIC values from 1984 published data is not supported and correlating PK/PD with clinical outcome and the probability of achieving certain targets is not accepted for abridged products. The CHMP also noted that the PK parameters of the subcomponents are unknown in children and that composition differences may lead to more pronounced PK differences in children, as literature data indicates differences in PK properties in adults and children.

**Ground 3: Furthermore the submitted additional non-clinical and serum bactericidal data are not considered sufficient to adequately demonstrate that Teicoplanin Hospira is a generic of the innovator Targocid**

The Applicant discussed the legal basis of their application, stating that it was accepted as such by the RMS and all other member states and considering that the requirements of this legal basis have been met. Therefore a bioequivalence study is not required, in line with the Note for Guidance on The Investigation of Bioavailability and Bioequivalence (CPMP/EWP/QWP/1401/98). Apart from the difference in levels of the TA2 subcomponents, there are no concerns over the manufacturing process used, particularly in terms of impurities. The Applicant then defined the active ingredient by referring to the INN and the pharmacopoeial monographs, concluding that Teicoplanin Hospira meets all of the criteria necessary to define it as a generic of the originator product. The Applicant further discussed the supporting pre-clinical data in detail, describing the studies submitted (two MIC studies using a number of organisms, a neutropenic mouse thigh infection model and a repeated dose toxicity study in rats). The Applicant concluded that all the studies support the efficacy and safety of Teicoplanin Hospira and that the results were similar to those obtained with the originator. The mouse thigh infection model study was considered to be representative of deep seated infections and provides a comparison of the tissue penetration characteristics of Teicoplanin Hospira and Targocid. In conclusion, irrespective of the legal basis, the Applicant believes that the product is developed in accordance with all appropriate specifications for teicoplanin and that no additional non-clinical studies are necessary. All subcomponents are well characterised and readily identifiable and there is no doubt that each individual subcomponent in Teicoplanin Hospira has the same characteristics as in Targocid.

The CHMP assessed the studies and concluded that the MIC results were similar between Teicoplanin Hospira and the originator and that no difference in antibacterial activity or in effectiveness was observed. It was however noted that tissue concentrations of drug components were not measured and that regarding the toxicology, it cannot be concluded whether the products are comparable as the histopathology was

investigated only for Teicoplanin Hospira. The CHMP was also of the opinion that the study conducted by the Applicant did not demonstrate bioequivalence between Teicoplanin Hospira and Targocid and that the MIC studies are not sensitive enough to detect differences between the two products in the case of teicoplanin, since in vitro anti-bacterial activity is independent of lipophilicity, tissue distribution and clearance of the subcomponents, i.e. differences in systemic exposure. Results from animal studies do not supersede comparative PK data from a clinical study in the evaluation of abridged products.

**GROUNDS FOR REFUSAL**

In conclusion, the CHMP noted that although complying with the European Pharmacopoeia monograph, the quality of Teicoplanin Hospira is different from the innovator subcomponents as Teicoplanin Hospira does not meet the originator specifications with respect to the individual glycopeptides subcomponents. Due to the differences in systemic exposure between Teicoplanin Hospira and Targocid and because the effect of the subcomponent differences on tissue drug concentrations was not measured, the CHMP concluded that bioequivalence could not be demonstrated. As the additional non-clinical and serum bactericidal data submitted are not sufficient to adequately demonstrate that Teicoplanin Hospira is a generic of Targocid, the CHMP therefore maintained its previous opinion that the current application for this product is not approvable.

Whereas

- Teicoplanin Hospira does not meet the originator specifications with respect to the individual glycopeptides subcomponents and has shown to be bio-inequivalent to the originator

- the submitted additional non-clinical and serum bactericidal data are not sufficient to adequately demonstrate that Teicoplanin Hospira is a generic of Targocid

the CHMP has recommended the refusal of the granting of the Marketing Authorisations for Teicoplanin Hospira and associated names (see Annex I).