TRANEXAMIC ACID 100MG/ML SOLUTION FOR INJECTION
PL 12762/0477

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LAY SUMMARY

The MHRA granted Mercury Pharmaceuticals Limited a Marketing Authorisation (licence) for the medicinal product Tranexamic Acid 100mg/ml Solution for Injection (PL 12762/0477) on 16 May 2013. This is a prescription-only medicine (POM) that can be used after minor surgery in people with a hereditary blood clotting disorder (haemophiliacs) and may also be used if you suffer from a serious condition called ‘disseminated intravascular coagulation’ where blood in the whole body starts to clot. Tranexamic Acid Injection can also be given to stop the bleeding after you have been treated with another medicine to break down blood clots (thrombolysis).

The active ingredient is tranexamic acid, which belongs to a group of medicines called antifibrinolytic agents, which are used to stop excessive bleeding after an operation or to assist with blood clotting. When you bleed your body forms clots as part of healing. In some people these clots do not stay in place long enough and this can cause too much bleeding.

No new or unexpected safety concerns arose from this application and it was, therefore, judged that the benefits of taking Tranexamic Acid 100mg/ml Solution for Injection outweigh the risks, hence a Marketing Authorisation has been granted.
TRANEXAMIC ACID 100MG/ML SOLUTION FOR INJECTION
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SCIENTIFIC DISCUSSION

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INTRODUCTION

The MHRA granted Mercury Pharmaceuticals Limited a Marketing Authorisation (licence) for the medicinal product Tranexamic Acid 100mg/ml Solution for Injection (PL 12762/0477) on 16 May 2013. This prescription-only medicine (POM) is indicated for the following:

Local fibrinolysis:
For short-term use in prophylaxis and treatment in patients at high risk of pre- and post-operative haemorrhage following:
- a) prostatectomy
- b) conisation of the cervix
- c) surgical procedures and dental extractions in haemophiliacs

General fibrinolysis:
- a) haemorrhagic complications in association with thrombolytic therapy
- b) haemorrhage associated with disseminated intravascular coagulation with predominant activation of the fibrinolytic system.

This application was submitted as an abridged application according to Article 10(1) of Directive 2001/83/EC, as amended, a generic application.

Tranexamic acid is an antifibrinolytic drug which is used to control bleeding by preventing clot breakdown (fibrinolysis). It is a synthetic derivative of the amino acid lysine that exerts its antifibrinolytic effect through the reversible blockade of lysine binding sites on plasminogen molecules.

No new non-clinical or clinical studies were conducted, which is acceptable given that this is a generic medicinal product for a solution for injection. Bioequivalence is confirmed through the qualitative and quantitative composition of the product.

The MHRA has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for this product type at all sites responsible for the manufacture and assembly of this product.
PHARMACEUTICAL ASSESSMENT

DRUG SUBSTANCE— Tranexamic acid
INN: Tranexamic acid
Chemical name: Trans-4-(aminomethyl) cyclohexanecarboxylic acid
Structure:

Molecular formula: C₈H₁₅NO₂
Molecular weight: 157.2
Physical form: A white or almost white crystalline powder, freely soluble in water and glacial acetic acid, practically insoluble in acetone and ethanol

Tranexamic acid is the subject of a European Pharmacopoeia monograph.

With the exception of the container-closure and retest period, all aspects of the manufacture and control of the active substance are covered by a European Directorate for the Quality of Medicines and Healthcare (EDQM) Certificate of Suitability.

Suitable specifications have been provided for all packaging used. The primary packaging has been shown to comply with current guidelines concerning contact with food.

Appropriate stability data have been generated supporting a suitable re-test period when stored in the proposed packaging.

P. Medicinal Product
Other ingredients
Other ingredients consist of the pharmaceutical excipient, water for injections, which is controlled to its European Pharmacopoeia monograph. Satisfactory Certificates of Analysis have been provided for water for injections showing compliance with its respective monograph.

None of the excipients used contain material of animal or human origin.

Pharmaceutical development
The aim of the pharmaceutical development was to create an injectable solution containing 500mg of tranexamic acid per 5ml of product that could be considered a generic medicinal product of Cyklokapron Injection 500mg/5ml (Pharmacia Limited, UK).

A satisfactory account of the pharmaceutical development has been provided.
Comparative physico-chemical characteristics have been provided for the proposed product versus the originator product, and pharmaceutical equivalence has been shown.

**Manufacture**
A description and flow-chart of the manufacturing method have been provided.

In-process controls are satisfactory based on process validation data and controls on the finished product. Process validation has been carried out on production-scale batches. The results are satisfactory.

**Finished product specification**
The finished product specification is satisfactory. Test methods have been described and have been adequately validated, as appropriate. Batch data have been provided that comply with the release specification. Certificates of Analysis have been provided for any working standards used.

**Container Closure System**
The finished product is stored in clear Type I glass 5ml ampoules, which are packed into cardboard cartons in a pack size of five ampoules.

Specifications and Certificates of Analysis for all packaging types used have been provided. These are satisfactory.

**Stability**
Finished product stability studies have been conducted in accordance with current guidelines. Based on the results, a shelf-life of 3 years with no specific storage conditions has been set; this is satisfactory.

**Bioequivalence/bioavailability**
No bioequivalence study is submitted with this application. Generic equivalence with the reference product is shown by the qualitative and quantitative composition of the finished product.

**Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and Labels**
The SmPC, PIL and labels are pharmaceutically acceptable.

A package leaflet has been submitted to the MHRA along with results of consultations with target patient groups (‘user testing’), in accordance with Article 59 of Council Directive 2001/83/EC, as amended. The results indicate that the package leaflet is well-structured and organised, easy to understand and written in a comprehensive manner. The test shows that the patients/users are able to act upon the information that it contains.

**Marketing Authorisation Application (MAA) form**
The MAA form is pharmaceutically satisfactory.
Quality Overall Summary (Expert report)
The pharmaceutical expert report has been written by an appropriately qualified person and is a suitable summary of the pharmaceutical dossier.

Conclusion
The grant of a Marketing Authorisation is recommended.

NON-CLINICAL ASSESSMENT

This application was submitted as an abridged application according to Article 10(1) of Directive 2001/83/EC, as amended, a generic application.

No new non-clinical studies were conducted, which is acceptable given that this is a generic application containing an active substance that has been in clinical use for many years.

No environmental risk assessment has been submitted with this application. As this product is intended for generic substitution with an already marketed product, no increase in environmental burden is anticipated.

The non-clinical expert report has been written by an appropriately qualified person and is a suitable summary of the non-clinical dossier.

The grant of a marketing authorisation is recommended.

CLINICAL ASSESSMENT

CLINICAL PHARMACOLOGY AND EFFICACY
This application was submitted as an abridged application according to Article 10(1) of Directive 2001/83/EC, as amended, a generic application.

No new clinical studies were conducted, which is acceptable given that this is a generic application containing an active substance that has been in clinical use for many years.

SAFETY
No new safety concerns have been raised by this application.

EXPERT REPORTS
A clinical expert report has been written by a suitably qualified person and is satisfactory.

SUMMARY OF PRODUCT CHARACTERISTICS (SMPC)
The SmPC is satisfactory and consistent with other similar products.

PATIENT INFORMATION LEAFLET (PIL)
The PIL is satisfactory and consistent with other similar products.

LABELLING
This is satisfactory
APPLICATION FORM (MAA)
This is satisfactory.

MEDICAL CONCLUSION
The grant of a marketing authorisation is recommended.

OVERALL CONCLUSION AND BENEFIT/RISK ASSESSMENT

QUALITY
The important quality characteristics of Tranexamic Acid 100mg/ml Solution for Injection 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.

CLINICAL
No clinical studies have been conducted to support the application. Essential similarity with the originator product is based on the qualitative and quantitative composition of the product versus that of the reference product, Cyklokapron Injection 500mg/5ml solution for injection (Pharmacia Limited, UK).

No new or unexpected safety concerns arose from this application.

The SmPC, PIL and labelling are satisfactory and consistent with those for the reference product.

BENEFIT-RISK ASSESSMENT
The quality of the product is acceptable and no new non-clinical or clinical safety concerns have been identified. The qualitative and quantitative assessment supports the claim that the applicant’s product and the reference product Cyklokapron Injection 500mg/5ml solution for injection (Pharmacia Limited, UK) are interchangeable. Extensive clinical experience with tranexamic acid is considered to have demonstrated the therapeutic value of the active substance. The benefit/risk ratio is considered to be positive.
**TRANEXAMIC ACID 100MG/ML SOLUTION FOR INJECTION**  
**PL 12762/0477**

**STEPS TAKEN FOR ASSESSMENT**

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<tr>
<td>1</td>
<td>The MHRA received the marketing authorisation application on 18 July 2012</td>
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<td>2</td>
<td>Following standard checks and communication with the applicant the MHRA considered the application valid on 03 August 2012</td>
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<td>3</td>
<td>Following assessment of the application the MHRA requested further information on 02 November 2012 and 15 February 2013</td>
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<td>4</td>
<td>The applicant responded to the MHRA’s requests, providing further information on 14 January 2013 and 20 March 2013</td>
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<td>5</td>
<td>The application was determined on 16 May 2013</td>
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STEPS TAKEN AFTER AUTHORISATION - SUMMARY

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<tr>
<th>Date submitted</th>
<th>Application type</th>
<th>Scope</th>
<th>Outcome</th>
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Summary of Product Characteristics and Patient Information Leaflet

The current approved versions of the SmPC and PIL are available on the MHRA website.

Labelling