## Colourstart Test 73mcg Cutaneous Patch (para-phenylenediamine)

**PL 33784/0001**

**UKPAR**

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Colourstart Test 73mcg Cutaneous Patch (para-phenylenediamine)

PL 33784/0001

LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Trichlocare Diagnostics Limited a Marketing Authorisation for the medicinal product Colourstart Test 73mcg Cutaneous Patch (PL 33784/0001) on 03 December 2012. This medicine is only available on prescription from your doctor. The product may be referred to as ‘Colourstart’ in this report.

Colourstart is used to test for allergic contact dermatitis. Contact dermatitis is a skin reaction caused by exposure to foreign substances resulting in an allergic reaction. Colourstart is a ready-to-use patch test for finding if a patient’s allergic contact dermatitis is due to para-phenylenediamine (PPD).

The test consists of surgical tape with two patches. One of the patches contains PPD and the other is a control. Colourstart works by showing if the patient is allergic to the PPD (allergen) on the patch. If a substance to which a patient is allergic comes into contact with the skin, it causes an inflammatory reaction called contact dermatitis. These substances could be an ingredient in perfume or aftershave, an ointment or cream, rubber gloves, industrial chemicals, etcetera. PPD is a well-known allergen. If a patient is allergic to PPD, then the skin under that patch will react to it, becoming red and inflamed. If the patient is not allergic to PPD, the skin under it will not react.

No new or unexpected safety concerns arose from this application and it was, therefore, judged that the benefits of using Colourstart Test 73mcg Cutaneous Patch outweigh the risks and a Marketing Authorisation was granted.
Colourstart Test 73mcg Cutaneous Patch
(para-phenylenediamine)

PL 33784/0001

SCIENTIFIC DISCUSSION

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INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the MHRA granted Trichlocare Diagnostics Limited a Marketing Authorisation for the medicinal product Colourstart Test 73mcg Cutaneous Patch (PL 33784/0001) on 03 December 2012. This product is a prescription-only medicine (POM) product. Colourstart Test 73mcg Cutaneous Patch indicated for the diagnosis of allergic contact dermatitis to PPD (para-phenylenediamine).

The active pharmaceutical ingredient in Colourstart Test 73mcg Cutaneous Patch is PPD. PPD is a well-known allergen. Patch testing is a well established procedure which leads to a type IV reaction if sensitivity is present.

This abridged application was submitted under Article 10.3 of Directive 2001/83/EC, as a hybrid application. The reference medicinal product for this application is True Test Panel 2 (Mekos Laboratories AS, Denmark) which was first authorised in the UK on 26 September 1996.

No new non-clinical or clinical data have been submitted, which is acceptable given that this is a hybrid application based on an originator product that has been in clinical use for over 10 years.

No new or unexpected safety concerns arose during review of information provided by the Marketing Authorisation Holder and it was, therefore, judged that the benefits of using Colourstart Test 73mcg Cutaneous Patch outweigh the risks and a Marketing Authorisation was granted.
PHARMACEUTICAL ASSESSMENT

ACTIVE SUBSTANCE
INN: Para-phenylenediamine (PPD)
Chemical Name: Para-phenylenediamine
Molecular Formula: C₆H₆N₂
Structure

\[
\begin{array}{c}
\text{H}_2\text{N} \\
\text{NH}_2
\end{array}
\]

Molecular weight: 108.14
Appearance: A white to slightly red crystalline solid powder.
Solubility Soluble in 100 parts of water, soluble in alcohol, chloroform and ether.

Para-phenylenediamine is not the subject of a European Pharmacopoeia monograph.

Synthesis of the active substance from the designated starting materials has been adequately described and appropriate in-process controls and intermediate specifications are applied. Satisfactory specification tests are in place for all starting materials and reagents and these are supported by relevant Certificates of Analysis. Appropriate proof-of-structure data have been supplied. All potential known impurities have been identified and characterised.

An appropriate specification is provided for the active substance. Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specifications. Batch analysis data are provided and comply with the proposed specification.

Satisfactory Certificates of Analysis have been provided for all working standards.

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

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

DRUG PRODUCT
Other Ingredients
Other ingredients consist of the pharmaceutical excipients namely polyvidone 90, and ethanol. Appropriate justifications for the inclusion of each excipient have been provided.

All excipients comply with their respective European Pharmacopoeia monographs. Satisfactory Certificates of Analysis have been provided for all excipients, showing compliance with the proposed specifications.

None of the excipients contains materials of animal or human origin. No genetically modified organisms (GMO) have been used in the preparation of these excipients.
Pharmaceutical Development
The objective of the development programme was to formulate a safe, efficacious, stable product, which was comparable in performance to the originator product, consisting of a test patch containing the same quantity of PPD as the originator product True Test (PL 19095/0004), together with a placebo (negative) control patch.

Suitable pharmaceutical development data have been provided for this application.

Comparative in-vitro dissolution and impurity profiles have been provided for this product and the reference product.

Manufacturing Process
A satisfactory batch formula has been provided for the manufacture of the product, along with an appropriate account of the manufacturing process. Based on production-scale batches, the manufacturing process has been validated and has shown satisfactory results.

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

Container Closure System
The product is packaged as a single patch test into a sachet of packaging laminate together with a desiccant paper. The allergen-coated polyester patch is placed on a self-adhesive plaster and covered by a protective sheet of silicone-treated polyethylene. The product is packed into cardboard cartons with Patient Information Leaflets, in a pack size of one sachet.

Satisfactory specifications and Certificates of Analysis have been provided for all packaging components. All primary packaging complies with the current European regulations concerning materials in contact with food.

Stability
Finished product stability studies were performed in accordance with current guidelines on batches of finished product packed in the packaging proposed for marketing. The data from these studies support a shelf-life of 24 months, with the storage conditions ‘Store at 2°C to 8°C.’

Bioequivalence
As the product provides local diagnostic activity (that is, not systemic), investigation of bioequivalence is not appropriate for this product.

Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and Labelling
The SmPC, PIL and labelling are satisfactory from a pharmaceutical perspective.

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.

**MAA (Marketing Authorisation Application) Form**
The MAA form is satisfactory from a pharmaceutical perspective.

**Expert Report (Quality Overall Summary)**
The quality overall summary is written by an appropriately qualified person and is a suitable summary of the pharmaceutical aspects of the dossier.

**Conclusion**
The grant of a Marketing Authorisation is recommended.
NON-CLINICAL ASSESSMENT

PHARMACODYNAMICS, PHARMACOKINETICS, TOXICOLOGY
No new non-clinical data has been submitted in support of this application, which is acceptable given that PPD is a well established substance that has been in use for over 100 years in a number of different industries.

NON-CLINICAL EXPERT REPORT (NON-CLINICAL OVERVIEW)
The applicant’s 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.

ENVIRONMENTAL RISK ASSESSMENT
Suitable justification has been provided for non-submission of an Environmental Risk Assessment. As this product is intended for substitution with a product that is already marketed, no increase in environmental burden is anticipated. Thus, the justification for non-submission of an Environmental Risk Assessment is accepted.

CONCLUSION
The grant of a Marketing Authorisation is recommended.
CLINICAL ASSESSMENT

CLINICAL PHARMACOLOGY
The clinical pharmacology of PPD is well-known.

No clinical studies have been conducted to support the application. Essential similarity with the originator product is based on the comparative quality attributes of the product. This application is being made under Article 10.3 (hybrid) of Directive 2001/83/EC, which states that bioequivalence cannot be demonstrated through bioavailability studies for products for local use intended to act without systemic absorption - in this case – after topical administration.

Efficacy
The efficacy profile of PPD is well-known. Efficacy is reviewed in the clinical overview. No new efficacy data have been submitted and none are required for this application.

Safety
The safety profile of PPD is well-known. The safety profile PPD is reviewed in the clinical overview. No new safety data have been submitted with this application and none are required.

Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and Labelling
The SmPC, PIL and labelling are satisfactory from a clinical perspective. The SmPC is consistent with that for the originator product. The PIL is consistent with the details in the SmPC and in-line with the current guidelines. The labelling is in-line with the current guidelines.

Clinical Expert Report
The clinical overview has been written by an appropriately qualified physician and is a suitable summary of the clinical aspects of the dossier.

Pharmacovigilance System and Risk Management Plan
The Pharmacovigilance System, as described by the applicant, fulfils the requirements and provides adequate evidence that the applicant has the services of a qualified person responsible for pharmacovigilance, and has the necessary means for the notification of any adverse reaction suspected of occurring either in the Community or in a third country.

Suitable justification has been provided for not submitting a Risk Management Plan for this product.

Conclusion
The grant of a Marketing Authorisation is recommended.
OVERALL CONCLUSION AND BENEFIT/RISK ASSESSMENT

QUALITY
The important quality characteristics of Colourstart Test 73mcg Cutaneous Patch 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. As the pharmacokinetics, pharmacodynamics and toxicology of PDD are well-known, no additional data were required.

EFFICACY
No clinical studies have been conducted to support the application. Essential similarity with the originator product is based on the comparative quality attributes of the product. This application is made under Article 10.3 (hybrid) of Directive 2001/83/EC, which states that bioequivalence cannot be demonstrated through bioavailability studies for products for local use intended to act without systemic absorption – in this case – after topical administration.

SAFETY
The safety profile of PDD is well-known. No new safety data were submitted and none were required for this application.

PRODUCT LITERATURE
The SmPC, PIL and labelling are acceptable. The SmPC is consistent with that for the reference product. The PIL is consistent with the details in the SmPC and in line with the current guidelines. The labelling is in line with current guidance.

BENEFIT/RISK ASSESSMENT
The quality of the product is acceptable, and no new non-clinical or clinical safety concerns have been identified. Extensive clinical experience with PDD is considered to have demonstrated the therapeutic value of the product. The benefit/risk balance is, therefore, considered to be positive.
**Colourstart Test 73mcg Cutaneous Patch (para-phenylenediamine)**

**PL 33784/0001**

**STEPS TAKEN FOR ASSESSMENT**

1. The MHRA received the Marketing Authorisation application on 07 July 2010.

2. Following standard checks and communication with the applicant the MHRA considered the application valid on 28 July 2010.

3. Following assessment of the application the MHRA requested further information relating to the clinical dossier on 06 December 2010, 26 September 2011, and on the quality dossier on 20 December 2010 and 26 September 2011.

4. The applicant responded to the MHRA’s requests, providing further information on the clinical dossier on 30 March 2011, 08 December 2011 and 30 May 2012, and on the quality dossier on 30 March 2011 and 02 July 2012 and 20 September 2012.

5. The application was granted on 03 December 2012.
SUMMARY OF PRODUCT CHARACTERISTICS

In accordance with Directive 2010/84/EU, the Summaries of Product Characteristics (SmPCs) for products granted Marketing Authorisations at a national level are available on the MHRA website.
PATIENT INFORMATION LEAFLET

In accordance with Directive 2010/84/EU, the Patient Information Leaflets (PILs) for products granted Marketing Authorisations at a national level are available on the MHRA website.
LABELLING

The labelling text below is that agreed. The Marketing Authorisation Holder has committed to submit the UK labelling for review to the competent authority before marketing any pack size.

<table>
<thead>
<tr>
<th>PARTICULARS TO APPEAR ON CARTON BOX AND FOIL PACKAGING</th>
</tr>
</thead>
<tbody>
<tr>
<td>(NATURE/TYPE)</td>
</tr>
</tbody>
</table>

1. **NAME OF THE MEDICINAL PRODUCT**

Colourstart® Test 73 mcg Cutaneous Patch

2. **STATEMENT OF ACTIVE SUBSTANCE(S)**

Each patch contains 73 micrograms PPD in a patch size of 0.9 cm x 0.9 cm (0.81 cm²), which is equivalent to 90 micrograms/cm²

3. **LIST OF EXCIPIENTS**

<table>
<thead>
<tr>
<th>Excipient</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethanol 99.5%</td>
<td>Solvent</td>
</tr>
<tr>
<td>Polyvidone 90</td>
<td>Vehicle</td>
</tr>
</tbody>
</table>

4. **PHARMACEUTICAL FORM AND CONTENTS**

Plaster: self-adhesive plaster for cutaneous use.

Colourstart is a self adhesive patch consisting of a piece of surgical tape with two polyester patches, one with P-Phenylenediamine (PPD) ('active patch') and one control patch ('negative patch').

**Active patch (A+)**
Each patch contains 73 micrograms PPD in a patch size of 0.9 cm x 0.9 cm (0.81 cm²), which is equivalent to 90 micrograms/cm².

**Negative patch (A-)**
Each patch contains 0 micrograms PPD in a patch size of 0.9 cm x 0.9 cm (0.81 cm²), which is equivalent to 0 micrograms/cm².

5. **METHOD AND ROUTE(S) OF ADMINISTRATION**

Read the package leaflet before use.

6. **SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN**

Keep out of the sight and reach of children.

7. **OTHER SPECIAL WARNING(S), IF NECESSARY**
8. **EXPIRY DATE**

Expiry date:

9. **SPECIAL STORAGE CONDITIONS**

Store between 2°C and 8°C.

10. **SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**

11. **NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Trichocare Diagnostics Ltd,
Berry End Farm House
Berry End
Eversholt
Bedfordshire MK17 9EB
United Kingdom.

12. **MARKETING AUTHORISATION NUMBER(S)**

PL 33784/0001

13. **BATCH NUMBER**

Batch No:

14. **GENERAL CLASSIFICATION FOR SUPPLY**

POM

15. **INSTRUCTIONS ON USE**

1) Peel open the package and remove the test panel.
2) First remove the perforated top part of protective plastic backing then carefully peel the rest of the backing from the test surface of the panel. Be careful not to touch the test substances.
3) Position the test on the patient's upper arm. From the centre of the panel, smooth outward toward the edges, making sure each patch makes adequate contact with the skin.

The test should be applied to healthy skin that is free from acne, scars, dermatitis or any other condition that might interfere with interpretation of results (see Precautions).

The test is best applied on the upper part of the back approximately 5 cm from the midline. However, the outer part of the upper arms is also acceptable.
The patient should wear Colourstart for a minimum of 48 hours without removing it and being careful not to get the test area wet. Following this period, the test is removed, either by the physician or the patient.

16. INFORMATION IN BRAILLE

N.A.