Medicines & Healthcare products Regulatory Agency

MHRA Regulating Medicines and Medical Devices

Public Assessment Report

Prescription Only Medicine to General Sale List Medicine Reclassification

Colourstart Test 65mcg Cutaneous Patch

Paraphenylenediamine (PPD)

PL 33784/0001

Trichocare Diagnostics Limited, UK

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1. About Colourstart Test Patch

Colourstart Test Patch is used to screen for potential allergic contact dermatitis (a reaction on the skin, usually seen as an itchy rash, redness and tiny blisters, resulting from contact with a substance to which you are allergic) to paraphenylenediamine (PPD) in people aged 16 years of age and over, prior to applying hair colourant. This medicine was licensed as a Prescription Only Medicine (POM) in 2012 and is not currently marketed.

PPD is the commonest and most widely-known component of hair colourants. It has a strong capacity to produce allergic reactions when in contact with the skin and these reactions may be severe, in some people.

The Allergy Alert Test (AAT) or so called `open test' is recommended by hair colourant manufacturers to test for potential allergy to a product before use. With this test, a small amount of hair colourant, which contains PPD + other chemicals, is applied behind the ear and left for 48 hours to detect potential allergy to the product. Exposure to PPD with this method is variable depending on the product and amount applied behind the ear.

Colourstart Test Patch is a test for potential allergy to PPD only. In contrast to the AAT, it provides a controlled and defined exposure to PPD. Colourstart Test Patch may be used instead of the AAT to detect potential allergy to PPD. If there is a positive reaction to the test patch, hair colourant should not be used.

What is in Colourstart Test Patch?
Colourstart Test Patch is a self-adhesive plaster consisting of two patches, one containing 65 micrograms of PPD (active patch) and the other patch with no PPD (control patch).

Colourstart Test Patch was the first application for a product containing PPD to be available without prescription.

What is Colourstart Test Patch used for?
Colourstart Test Patch is a medicine used as a screening test for potential allergic contact dermatitis to paraphenylenediamine (PPD) in people aged 16 years of age and over. It is recommended for use before applying hair colourant.

Who has made the proposal?
The licence-holder for Colourstart Test Patch (Trichocare Diagnostics Limited) has applied to make this product available through general sales outlets, in the absence of healthcare professional advice.

What is the view of the Commission on Human Medicines?
The Commission on Human Medicines (CHM) has advised that Colourstart Test Patch can be available as a General Sale List medicine. Views on the use of this medicine as a screening test for potential allergy to PPD in people aged 16 years of age and older were also sought at a meeting of the Gastroenterology, Rheumatology, Immunology and Dermatology Expert Advisory Group (GRID EAG). The views of the GRID EAG were summarised and provided for CHM when they considered the reclassification application.

Further to public consultation and responses received, the CHM considered their initial advice in favour of availability of Colourstart Test Patch as a General Sale List medicine and advised again in favour, but, to take into consideration issues raised from the consultation, subject to additional amendments to the product information (special warnings and precautions for use, patient information leaflet (PIL) and label (outer carton) for Colourstart.

2. Proposed terms of reclassification

What are the details of this change?
Colourstart Test Patch will be available through general sales outlets for:

- topical use (application to the skin)
- as a screening test for potential allergic contact dermatitis to paraphenylenediamine (PPD) in adults and adolescents aged 16 years of age and over
- single use only, consisting of surgical tape with two polyester patches (one active patch containing 65mcg of PPD + one negative (control) patch with no PPD)

3. How was the proposal assessed for Colourstart Test Patch being available as a General Sale List medicine?

The proposal for Colourstart Test Patch is for reclassification from POM to GSL. To be reclassified from POM to GSL, a medicine must meet both the requirements of POM to P and P to GSL reclassification. Therefore, this product was assessed firstly against the criteria for a medicine to be classified as P and then against the criterion for a medicine to be classified as GSL.
For a medicine to be classified as P it must **not** meet any of the criteria for POM classification, which are set out in the Human Medicines Regulations 2012, regulation 62(3).

These criteria are as follows:

Prescription only (POM) status will apply where:

1. A direct or indirect danger exists to human health, even when used correctly, if used without medical supervision
2. There is frequently incorrect use which could lead to direct or indirect danger to human health
3. Further investigation of activity and/or side effects is required
4. The product is normally prescribed for parenteral administration (by injection)

In addition, for a medicine to be classified as GSL it must also be demonstrated that it **does** meet the GSL criterion, which is set out in the Human Medicines regulations 2012, regulation 62(5). This criterion is as follows:

`GSL may be appropriate for medicines which can, with reasonable safety, be sold or supplied otherwise by or under supervision of a pharmacist.'

`Reasonable safety' is defined as `where the hazard to health and risk of misuse and need for special precautions in handling are small, and wider sale would be a convenience to the purchaser.'

Assessment of suitability for Pharmacy availability

The MHRA assessed the application against the criteria stated above.
The key aspects of the assessment of reclassification are summarised below.

Criterion 1 - `It is likely to present a direct or indirect danger to human health, even when used correctly, if used without medical supervision.

The main criterion that needed to be considered in the reclassification of Colourstart Test Patch to P was that it does not present a direct danger to human health if used, even correctly, without supervision of a doctor. A direct danger may be present if the product causes adverse reactions that are important because of their seriousness, severity, or frequency. A danger may also be present if the reaction is one for which there is no suitable preventative action such as being able to identify the group of patients who are at risk if they use the product without medical supervision so that they may be excluded from using the product. Direct danger may also arise from drug interactions with commonly used medicines. For the product to be used without prescription, the drug interactions would need to be preventable.

Direct danger to human health

The purpose of using an allergy screening product such as Colourstart Test Patch is to determine whether a person is sensitive to PPD by using a small controlled amount of PPD, rather than using an uncontrolled amount, for example with the Allergy Alert Test (AAT), or using nothing at all.

The amount of PPD in Colourstart Test Patch (65 micrograms) is very much lower than found in hair colourants which may be up to 2% (the maximum permitted for hair colourants in line with EU Directive 2009/130/EC). As an example, a total quantity of 50mL of hair colourant mixed and ready to use may contain up to 1g of PPD.

Colourstart Test Patch has not to date been marketed. Safety of the product is based on that of a reference product (with test strip consisting of a series of 12 different allergen patches, one of which contains 65 micrograms of PPD) and a clinical study. The main adverse events for the product are irritation caused by the surgical tape adhesive and local itching where the patch is applied. These effects are usually mild and disappear in one to two days. In the case of an individual who is sensitive to PPD, a positive reaction on the skin under the active patch (containing PPD) will occur. This will be usually show as a rash, redness and tiny blisters. The skin under the patch may also itch and feel warm. This reaction to the product is as would be expected in individuals who are sensitive to PPD and therefore, should not use hair colourant. A positive reaction usually disappears within 1 to 2 weeks, but on occasion may persist for weeks or months and may leave a temporary area of pale-coloured or darker coloured skin. A test reaction which appears more than 10 days after application of the patch may be a sign of contact sensitisation (allergy the ingredients in the patch, including PPD), which may occur with patch testing.

Individuals who experience a positive test reaction should not use hair colourant and are advised to seek medical advice. In the case of a severe patch test reaction, for example, intense redness of the skin with large fluid filled blisters, the individual should seek medical advice immediately.

Direct danger with Colourstart Test Patch may potentially arise in the following situations:

- with incorrect reading of the patch test result
- when used by individuals taking certain medicines
- when used by individuals for whom the product is contraindicated (should not be used)

The main direct danger of using Colourstart Test Patch without medical supervision is that of incorrect reading of the test patch result, leading to use of hair colourant when sensitive to PPD and, consequently, experiencing an allergic reaction.

As part of the application to reclassify this product from POM to GSL and on the recommendation of the Commission on Human Medicines (CHM), the applicant has provided results of a clinical study comparing Colourstart Test Patch with the Finn Chamber (a skin patch test chamber used for patch testing) in detection of PPD allergy in subjects with known or suspected allergy and those with no known allergy to PPD. There were recruitment difficulties with this study, in part possibly due to increased media attention alerting potential participants to the risk of severe allergic reaction to ingredients in hair colourants.

However, the study demonstrated that participants were able to identify allergy if present, and in general took a more conservative approach to interpreting the patch test result than the study investigators. Adverse events were mainly mild in nature and, in most cases, resolved without treatment.

The applicant also provided details of a Patient Group Direction (PGD) which was undertaken with Colourstart Test Patch. A PGD is a written protocol by which a pharmacist can provide prescription only medicines to the public without the need of a prescription from a doctor. The PGD carried out was a means of allowing easier access to Colourstart Test Patch while ensuring that a pharmacist would be involved with the supply and advising on the use of the medicine in each individual participant. The PGD was not completed as planned and as with the clinical study, there were recruitment difficulties. However, the PGD did not raise any safety concerns with Colourstart Test Patch.

Incorrect interpretation of the patch test result may occur if an individual is taking medicines such as corticosteroids or immunosuppressants. These medicines may supress a positive test reaction, resulting in a false negative test result. Colourstart Test Patch is contraindicated, and therefore should not be used, by individuals taking such medicines. The patient information leaflet states `Do not use Colourstart if you are taking oral or topical steroids (such as prednisolone, betamethasone, fluticasone, hydrocortisone) or immunosuppressant medicines (such as tacrolimus, cyclosporine, mycophenolate, azathioprine, sirolimus), as they may supress a positive reaction.' Similarly, the outer carton label states not to use Colourstart `if you are taking steroid medicines, using steroid ointment/creams, or taking immunosuppressant medicines'.

Following responses received to public consultation and further advice from the CHM, the patient information leaflet was revised to include additional examples of commonly used oral corticosteroids (dexamethasone, fludrocortisone) and advice to the consumer to consult their pharmacist if necessary as follows: `If you are unsure if any medicines you may be taking will interfere with Colourstart, you should speak to your pharmacist.'

Colourstart Test Patch is contraindicated and therefore should not be used in the following situations:

- in individuals with a history of a reaction to black henna tattoo or presence of a current black henna tattoo (This is because there may be cross-sensitivity to PPD and black henna tattoo)
- pregnant or breast-feeding women
- individuals with acute dermatitis (This is because flare up of dermatitis may occur)
- use of the allergy alert test (AAT) at the same time as/in addition to Colourstart Test Patch (This is because there is potential for sensitisation to PPD with repeated exposure over time)

Repeated use leading to sensitisation to PPD, may potentially occur with use of Colourstart Test Patch. This may also occur for example with repeated use of the Allergy Alert Test

(AAT) method and with the use of hair colourants themselves. With Colourstart Test Patch an individual is exposed to a small controlled amount of PPD.

The applicant has provided references from the literature and report written by a consultant toxicologist which confirms that risk of sensitisation with use of Colourstart Test Patch is low. Nonetheless, to minimise this potential risk, individuals should not perform the AAT at the same time as/or in addition to using Colourstart Test Patch. The patient leaflet for the product includes information regarding sensitisation to PPD, a warning not to perform the AAT in addition to using Colourstart Test Patch and advice to the individual to consult their doctor if sensitisation does occur.

Following responses received to public consultation and further advice from the CHM the product information for Colourstart was revised as follows:

i. the warning concerning sensitisation (section 4.4 of the SmPC) was strengthened to limit frequency of use of the test. As there is a lack of evidence concerning safe frequency of exposure to PPD, as a risk minimisation measure to enable the product to be used safely in the GSL setting, the warning, limiting frequency of use of the Colourstart test was considered necessary
(see section 5.2.2 a) for revised SmPC wording).

ii. the patient information leaflet (PIL) was amended to provide further information regarding potential sensitisation with repeated exposure to PPD, including advice on frequency of use of the test, and clarification of why the `Allergy Alert Test' (AAT) should not be performed in addition to using the Colourstart test.
(see section 5.2.2 a) for revised PIL wording).

Use of Colourstart Test Patch without medical (or other healthcare professional) supervision is unlikely to result in direct danger. The product is supported by appropriate information for the user (patient information leaflet and labelling) to minimise risks associated with use in the absence of healthcare professional supervision. The patient information leaflet gives clear directions to the user on how to apply the patch and interpret the patch test result.

Following responses received to public consultation and further advice from the CHM, the PIL for Colourstart was amended to include additional information concerning interpretation of the patch test result, specifically clarification of the need to test at least 5 days before using hair colourant in order to detect any possible late reaction to PPD and to minimise false negative interpretation and use of hair colourant before the 5-day period, which may give rise to an allergic reaction.

The MHRA considers that the direct risks associated with Colourstart Test Patch can be minimised to an acceptable level to be used without medical supervision.

Indirect danger to human health

Medicines may present an indirect danger when symptoms to be treated are caused by a range of different conditions. If the patient cannot easily self-diagnose the cause of such symptoms, it may be inappropriate to provide a product to treat symptoms without treating the underlying disease.

An important example of an indirect danger is when treating symptoms might mask an underlying condition requiring medical attention. Use of the medicine might delay diagnosis and definitive treatment and jeopardise the chance of more successful therapy. Consideration should be given to whether an indirect danger might exist and if so, whether the risk, its frequency and seriousness of the consequences would make reclassification unacceptable. Additional warnings such as a recommendation to seek medical advice if symptoms continue beyond a stated time period, may be necessary in such instances.

Individuals purchasing and intending to use Colourstart Test Patch will be aware of the risks associated with use of hair colourants. In using Colourstart Test Patch, individuals will be screening for potential allergy to the ingredient PPD. If they react positively to the patch test, they are instructed not to apply hair colourant, therefore preventing a potentially serious allergic reaction.

The MHRA considers that the indirect risk associated with use of Colourstart Test Patch is low.

Criterion 2 - `It is frequently and to a very wide extent used incorrectly, and as a result is likely to present a direct or indirect danger to human health.

Addiction, dependence, recreational use, and misuse are considered as incorrect use in relation to this criterion.

Colourstart Test Patch has not been marketed as a prescription product. Data are available for the reference product and from a clinical study performed with Colourstart Test Patch. From data available, there is no evidence to suggest that Colourstart Test Patch will be frequently and to a very wide extent used incorrectly. PPD is not considered to be a compound associated with abuse or addiction potential and there is no known illicit use of the compound.
Incorrect use of Colourstart Test Patch, frequently and to a very wide extent would therefore not be expected, nor would abuse of the product.

Criterion 3 - `It contains substances or preparations of substances of which the activity requires, or the side effects require, further investigation.'

PPD is the commonest and most widely-known component of hair colourants and it has a strong capacity to produce allergic reactions when in contact with the skin. The purpose of using Colourstart Test Patch is to screen for potential allergy to this compound prior to using hair colourant.

There is limited experience of PPD as an ingredient in a medicinal product. From the clinical study conducted, no major safety issues were identified. The most common adverse events were irritation caused by the surgical tape adhesive and local itching where the patch is applied, and these were likely to resolve spontaneously after removal of the patch. Sensitisation to PPD may occur with patch testing. This may also occur with use of the AAT method to detect potential allergy to hair colourant products and with use of hair colourants themselves.

Following responses received to public consultation and further advice from the CHM, the product information for Colourstart was amended to address concerns raised regarding sensitisation to PPD. (see section 5.2.2 a))

Criterion 4 - `It is normally prescribed by a doctor for parenteral administration (by injection).'

Colourstart Test Patch is for application to the skin only, so this criterion does not apply.

Assessment of suitability for availability in general sales outlets

A GSL medicine may be sold in general sales outlets in the absence of healthcare professional advice. It is important therefore, that a GSL medicine may be safely sold or supplied without need of a consultation with a doctor or pharmacist.

Hazard to health

This is addressed under POM criterion 1 (page 4)

Risk of misuse

This is addressed under POM criterion 2 (page 7)

Special precautions in handling

There are no special handling requirements for Colourstart Test Patch that would prevent its availability as a GSL medicine.

Role of the pharmacist

Individuals purchasing and intending to use Colourstart Test Patch will be aware of the risks associated with the use of hair colourants and the need to test for potential allergy to hair colourants prior to use. Advice of a pharmacist is not considered necessary for the consumer to purchase Colourstart Test Patch for its intended use.

Convenience to the purchaser

Availability of Colourstart Test Patch in hair dressing salons or other outlets where hair colourants are sold is considered appropriate. Most hair colourants are purchased outside pharmacies and the ATT test is undertaken without advice from a pharmacist. Limiting Colourstart Test Patch to pharmacy (P) legal status would unnecessarily limit the availability of the test.

4. Further details on the application

Risk Management Plan
The application contains a risk management plan (RMP) which was required when the product was first authorised. The RMP documents the following:

- the known safety profile of the medicine, including any important identified and potential risks
- what is not known about the safety profile (`missing information')
- how the safety profile will be monitored after the medicine is licensed, including any plans for further studies to actively gain more knowledge about the safety of the medicine (`additional pharmacovigilance activities')
- how any important risks will be prevented or minimised in patients (`risk minimisation measures') and how the usefulness and effectiveness of the risk minimisation measures will be assessed

The RMP for Colourstart Test Patch has identified the main risks associated with the product and proposes how these will be managed through routine pharmacovigilance (monitoring and reporting of adverse events for a medicine, for which there are no special

safety concerns) and via the product information (SmPC, labelling and patient information leaflet). No additional risk minimisation measures are proposed for the product.

5. Consultation on GSL availability

Consultation document ARM[1] 97, which summarises the proposal for prescription only to general sale list (POM to GSL) reclassification of Colourstart Test Patch was posted on the GOV.UK website on 17 October 2018. The deadline for comments was given as 7 November 2018.

ARM 97 can be accessed at the following link:

https://www.gov.uk/government/consultations/proposal-to-make-colourstart-test-65mcg-cutaneous-patch-available-from-general-sales-outlets-without-prescription

5 responses were received. 2 responses supported the proposal and 3 did not support the proposal. The 5 responses received were from professional bodies/associations and a trade body.

5.1 Responses agreeing with the proposal to reclassify Colourstart Test Patch as a General Sale List (GSL) medicine

One professional body and one trade association supported reclassification of Colourstart Test patch to GSL noting that hair colourants are widely available and therefore, a test to check for potential allergy to a common ingredient (PPD) in these products would be welcomed. It was also noted that since pharmacies also sell hair colourants, they should be included on the list of retailers able to supply Colourstart, where pharmacists would be well placed to provide additional advice to the consumer where required.

Points were also made regarding the patient information leaflet (PIL) as follows:

1. leaflet is comprehensive
2. print size looks small, so may be difficult to read
3. need to clarify warning statement `Talk to your doctor or pharmacist before using Colourstart if any of these factors apply to you'
4. need to include more examples of oral corticosteroids in section on taking other medicines

Concerning point 2 above, the patient information leaflet was user tested, as required to ensure that it met necessary requirements, including those of legibility. Following responses received to public consultation and further advice from the CHM points 3 and 4 above have been addressed by further amendments to the PIL.

[1] ARM stands for Application to Reclassify a Medicine. An ARM consultation is a public consultation inviting views from all stakeholders on a proposal to reclassify a medicine from POM to P or P to GSL.

5.2 Responses disagreeing with the proposal to reclassify Colourstart Test Patch as a General Sale List (GSL) medicine

5.2.1 One professional association noted that the patient information leaflet (PIL) was comprehensive with respect to the uses and contraindications (reasons why the product should not be used) of the product. It also commented that availability of the Colourstart Test Patch should be limited to pharmacies as a Pharmacy (P) medicine, since pharmacists are well positioned to provide advice and support to the customer for example on side effects, drug interactions, false positive results and persistence of positive reactions. The provision of the patch through the pharmacy may also lead to an increase in and/or earlier diagnosis of potential undiagnosed skin conditions, leading to immediate advice and treatment.

The CHM has advised in favour of GSL availability of Colourstart Test Patch. Most hair colourants are purchased in non-pharmacy outlets; limiting the supply of Colourstart Test Patch to pharmacies only would unnecessarily limit availability of the product when it is considered safe for use in the GSL setting. The advice of a pharmacist is not considered necessary for the consumer to purchase the product for its intended use. The product outer carton clearly states what the product is for and when it should not be used. The PIL clearly advises the consumer to seek advice from their doctor or pharmacist as needed for example concerning side effects, drug interactions, interpretation of test results, including late and persistent reactions to the patch. In cases of severe reaction to the patch, the consumer is advised to seek immediate advice from a doctor and with any reaction to the patch test, the consumer is advised not to apply hair colourant.

5.2.2 One professional association and one professional society have communicated concerns over the use of Colourstart Test Patch in a GSL setting from the following key perspectives:

a) Risk to human health of inducing sensitisation to PPD from frequent and inappropriate use, thereby causing co-sensitisation (development of allergy to substances with similar chemical structure) to other drugs such as local anaesthetics

b) Risk to human health arising from failure to detect PPD and other hair colourant allergens (false negative reactions)

c) Risk to human health from members of the public failing to properly use a diagnostic device intended by its manufacturer for use by trained clinicians

5.2.2 a) Induction of sensitisation to PPD from frequent and inappropriate use

Concern was raised that there is no mention for the consumer of how frequently the Colourstart Test Patch should be used, thereby having the potential risk of sensitisation (development of allergy due to repeated exposure) to PPD.

Sensitisation with repeated use is a concern not only with the Colourstart Test Patch, but also in performing the Allergy Alert test (AAT) recommended on packaging of hair colourants containing potent sensitisers such as PPD and with the use of hair colourants themselves. The applicant provided an expert report written by a toxicologist in which it was concluded that the risk of sensitisation with use of Colourstart based on estimate linked to hair colourant use, was low. In addition, in order to limit exposure to PPD, the initial proposed patient information leaflet was amended to advise the consumer not to perform the AAT in addition to using Colourstart. This advice was also provided on the outer packaging of the product. The PIL states that a reaction which occurs at the site where the

patch was applied, approximately 10 days later, may be a sign of sensitisation and clearly advises the consumer to seek advice from their doctor and not to apply hair colourant if this happens.

To address concern regarding frequency of use of the test patch and potential for sensitisation, following advice from the CHM, the product information for Colourstart was further amended as follows:

SmPC section 4.4 (Special warnings and precautions for use) – the warning concerning sensitisation strengthened to limit frequency of use of Colourstart and therefore state `*Sensitisation to PPD may occur with patch testing. The test need not be repeated more than once if the individual is using the same hair colouring product, but may be repeated if they switch to a new hair colour product. A test reaction that appears on day 10 or later may be a sign of contact sensitisation. If this happens, advice should be sought from a doctor or pharmacist.'*

Patient information leaflet (PIL) – providing further information regarding potential sensitisation with repeated exposure to PPD, clarification of why the `Allergy Alert test' should not be used in addition to using the Colourstart test and providing advice on frequency of use of the test consistent with the revised SmPC section 4.4. The revised PIL (section 2) includes the following text:

`DO NOT perform the `Allergy Alert Test' as instructed on hair colorants in addition to using this medicine. This is because repeated exposure of the skin to PPD whether in applying hair colorant, performing the `Allergy Alert Test' or in using Colourstart, may cause sensitisation (development of allergy) in some individuals. For this reason, Colourstart Test Patch should not be used more than once if you are using the same hair colour product, but may be repeated if you switch to a new hair colour product. (See 'Warnings and precautions: sensitisation).'

`Sensitisation: In rare instances, you may become allergic to the PPD present on the Colourstart patch. This is also a risk with exposure to hair colorants containing PPD. Any reaction which occurs at the site of where the patch was applied, approximately 10 days later, may be a sign of contact sensitisation. If this happens talk to your doctor or pharmacist and DO NOT use hair colorants if this happens.'

Concerning co-sensitisation (development of allergy to substances with similar chemical structure) to drugs such as local anaesthetics, for example, benzocaine, the applicant provided additional expert commentary from a toxicologist which concluded that the risk of clinically relevant cross reaction to local anaesthetic agents is low. The CHM considered this evidence and were reassured concerning their initial advice in favour of GSL availability of Colourstart Test Patch.

5.2.2 b) *Risk from failure to detect PPD and other hair colourant allergens (false negative reactions)*

Concern was raised that consumers purchasing Colourstart for its intended purpose be clearly advised that it may not detect all adverse (allergic) reactions to hair dyes, particularly if products to which they are being exposed to do not contain PPD. The limitations of the Colourstart test should be fairly explained to consumers. In a reference provided by this respondent in response to consultation, the following statement concerning cross-reactivity (ability to detect allergy to other similarly structured compounds) of PPD is provided:

*`Indeed, the present evidence suggests that although PPD might not be responsible for all cases of hair dye allergy, the fact that it cross-reacts so well with other commonly used hair dye allergens (eg. toluene-2,5-diamine (PTD) and the aminophenols), makes it an effective marker of the majority of hair dye allergy problems.' **

* Orton D and Basketter DA (2012) Hair dye sensitivity testing: a critical commentary. *Contact Dermatitis*, 66, 312-316

While reference in the literature to cross-reactivity of PPD has been noted, it was recognised that not all hair dye products contain PPD or closely related (cross-reactive) ingredients. To address concerns raised by the respondent and further to advice from the CHM, the PIL for Colourstart was further amended to:

i. provide information on the proportion of hair dye products containing PPD
ii. clarify that the product was for screening for potential allergy to PPD only and not other ingredients in hair colourants, thereby providing information for the consumer regarding limitations of the test

as follows:

`*Colourstart is a ready-to-use patch test for finding out if you may be allergic to one of the ingredients (PPD) in hair colorants. PPD is present in more than two out of three hair colorants. PPD is known to cause allergic reactions, which may be severe, in some individuals.'*

`*If your hair colorant recommends that you carry out an allergy alert test prior to application, Colourstart can be used instead of this test to test for allergy to PPD. Colourstart works by showing if you are likely to be allergic to PPD only and will not detect if you might be allergic to other components in hair colorants. The absence of a reaction following use of Colourstart does not guarantee a safe hair colour treatment, but by using this product correctly, you can minimise the risk of reaction to hair colorant.'*

In addition, on advice of the CHM, the statement of indication (what the product is used for) on the label (outer carton) for Colourstart was revised to clarify that the product is to test for potential allergy to PPD.

Concern was raised that false negative results from consumer `self-testing' may cause harm to consumers, as they may lead to severe allergic reactions due to hair dyeing with substances to which the consumer is allergic. Incorrect interpretation of the patch test result may occur if an individual is taking medicines such as corticosteroids or immunosuppressants.

Concern was also raised regarding the strength (amount of) of PPD in the patch test. The preferred test concentration of PPD to be used has varied over time and between experts on the subject, considering a risk of inducing allergy (if concentration of PPD is too high) verses risk of a false-negative result (if concentration of PPD is too low).

False negative results from `self-testing' was considered in the submitted clinical study (see page 5) where the interpretation of the patch test result by the consumer showed good concordance (agreement or consistency) with those of skilled investigators. Consumers also appeared to take a more conservative approach when interpreting the test results, which was considered beneficial from a safety perspective.

With respect to the strength (amount of PPD) in the Colourstart test patch, for the POM and the proposed GSL product, this was based on and identical to the reference product for which efficacy has been demonstrated.

Concerning incorrect interpretation of the patch test result if an individual is taking corticosteroids or immunosuppressants, on the advice of the CHM, further information has

been provided in the PIL regarding `Other medicines and Colourstart' to include:

i. additional examples of commonly used oral corticosteroid medicines (ie. dexamethasone, fludrocortisone)
ii. advice to the consumer to consult their pharmacist if they are unsure if any medicines they may be taking could interfere with the Colourstart test *(`If you are unsure if any medicines you may be taking will interfere with Colourstart, you should speak to your pharmacist.'*

5.2.2 c) *Risk to human health from members of the public failing to properly use a diagnostic device intended by its manufacturer for use by trained clinicians*

Concern was raised that to make any form of clinical diagnosis, a trained clinician should be involved, and not a member of the public or hairdresser. Concern was also raised that the PIL for Colourstart confused the issue of when to apply the test patch before considering a colouring process, and when to take readings looking for a positive patch test reaction. Information on when to apply the patch was also considered too ambiguous. The information *`Always apply the self-adhesive patch at least 48 hours (2 days) or ideally 5 days before any colouring process'* contradicts standardised diagnostic patch testing techniques where recommended readings take place between 48 hours, 72 hours and 7 days in order to give the greatest chance of detecting contact allergy.

The Colourstart Test Patch is meant as a `screen' (means of alerting the consumer to possible allergy) and thereby preventing them from using hair colourant and possibly suffering a severe reaction. With any sign of a reaction to the patch test, the consumer is advised not to use hair colourant and to seek the advice of their doctor. This will facilitate referral to a dermatologist in cases where the doctor considers necessary. Colourstart is not intended for diagnostic use. Neither the proposed conditions for use of Colourstart in the GSL setting, nor the patient information imply that patch testing by the consumer is a substitute for professional allergy testing as carried out by a dermatologist.

Concerning information in the PIL regarding when to apply the patch test and interpretation of results, the patch should be worn without removing it, being careful not to get the test area wet, for at least 48 hours. The product information for both the prescription only (POM) Colourstart product and that proposed for the GSL setting state *`Although the response can appear as early as six hours, it is believed that the most accurate interpretation may be made between 72 and 96 hours after application since `irritant' reactions will have faded by then.'*

To provide clarity for the consumer regarding when to apply the patch test and interpretation of the results, on the advice of the CHM, the PIL was revised to:

i. instruct the patient to use the patch test at least 5 days before any colouring process
ii. to state the reason why this is necessary (to detect any possible late reactions to PPD)

as follows:

`Always apply the self-adhesive patch at least 5 days before any colouring process. This is because PPD sensitivity sometimes causes reactions which may not appear until 4 to 5 days after application.'

`It is important to continue to look at the area for at least 5 days after initial application of

the patch. This is because PPD sensitivity sometimes causes reactions which may not appear until 4 to 5 days after the application.'

Concern was also raised regarding information provided in the patient information leaflet about what a usual positive test reaction looks like, what a severe test reaction is and possible adverse effects which may occur following a positive test reaction.

Section 3 (How to use Colourstart) of the patient information leaflet states that `*A positive reaction is usually seen as a rash, redness and tiny blisters. It may also itch and feel warm. Note that the redness may not be evenly spread across the area.'* If such a reaction occurs following use of Colourstart, the patient is clearly advised not to apply hair colourant and to seek advice from their doctor.

The description of a severe test reaction was revised to include `intense redness' as follows: `*If a severe patch test reaction develops which is seen as intense redness with large fluid filled blisters, talk to your doctor immediately. DO NOT apply hair colorant.'* This information is stated in bold text.

Section 4 (Possible side effects) of the leaflet clearly describes effects on the skin which may occur following a positive test reaction as follows:

`*A positive test reaction usually disappears within 1-2 weeks. On rare occasions, a positive test reaction may last for weeks or months. Such reactions will leave a temporary area of pale coloured skin (hypopigmentation) or darker coloured skin (hyperpigmentation).'*

Information regarding positive test reactions, severe test reactions and possible side effects following a positive test reaction are clearly communicated to the patient in the leaflet.

6. Advice from the Commission on Human Medicines

CHM considered the reclassification application and the responses to the public consultation and advised in favour of GSL availability of Colourstart Test 65mcg Cutaneous Patch under the conditions outlined above – as a screening test for potential allergic contact dermatitis to paraphenylenediamine (PPD) for use by adults and adolescents aged 16 years and over.

7. Conclusion

Assessment of the responses to consultation on the application to reclassify Colourstart test to GSL legal status revealed no new issues of concern in addition to those considered initially by the CHM. In a further (post-consultation) consideration of this application by the CHM, they were reassured of the suitability of Colourstart for the GSL setting, provided additional amendments to the product information (warnings, patient information leaflet and outer carton label) for the product were made. Considering the advice from the CHM before and after consultation, the MHRA has taken the decision to approve GSL legal status for Colourstart Test 65mcg Cutaneous Patch.

8. Further information

The summary of product characteristics and patient information leaflet are available on the MHRA website:

https://www.gov.uk/pil-spc

The responses to consultation are published here:

https://www.gov.uk/government/consultations/proposal-to-make-colourstart-test-65mcg-cutaneous-patch-available-from-general-sales-outlets-without-prescription