PIGMANORM® FOR THE TREATMENT OF MELASMA (HYPERPIGMENTATION)

DOUBLE RED:

NOT RECOMMENDED FOR PRESCRIBING IN PRIMARY OR SECONDARY CARE

Name	What it is	Indication	Date Decision last revised	Decision Status	Guidance
Hydroquinone 5% w/w, hydrocortisone 1% w/w and tretinoin 0.1% w/w (Pigmanorm®)	Unlicensed cream preparation	Topical treatment for melasma (hyperpigmentation)	October 2018 – HMMC November 2018 - WEMOPB	Final	NICE- none

RECOMMENDATION:

NOT RECOMMENDED for prescribing within Hertfordshire and west Essex in primary or secondary care.

Key points

- The exact incidence of melasma is unknown but it is a common condition in adults.
- Melasma are flat, blotchy, brown patches which present in 3 different types: dermal, epidermal and mixed melasma. It is usually symmetrical on the cheekbones, forehead and chin and sometimes appears on the upper lip, neck and forearms.
- Melasma patches are neither itchy nor painful and so does not have a physical impact. However the condition often presents on exposed skin such as the face. It is the cosmetic aspect of melasma that affects people.
- Locally, treatments for melasma are considered cosmetic and therefore not recommended for prescribing on the NHS.
- There is no universally effective therapy for hyperpigmentation. No evidence was found showing the efficacy of Pigmanorm® cream itself or its specific combination of ingredients.
- Recurrences of melasma are common especially after re-exposure to the sun.
- There is no data on the cost- effectiveness of this treatment.
- There is insufficient evidence in relation to short and long term efficacy and safety.
- Pigmanorm® is a product that is unlicensed in the UK but licensed in Germany for treating melasma.

ASSESSMENT AGAINST ETHICAL FRAMEWORK

Evidence of Clinical Effectiveness

- There was no evidence found showing the efficacy of Pigmanorm® cream itself or its specific combination of ingredients.
- A 2010 Cochrane review [1] assessing interventions of all types of melasma looked at 20 studies with a total of 2125 participants covering 23 treatments. Statistical pooling of the data was not possible due to heterogeneity of treatments. Each study involved a different set of interventions. The studies were grouped into those including a bleaching agent such as hydroquinone, triple-combination creams (hydroquinone, tretinoin, and fluocinolone acetonide), and combination therapies (hydroquinone cream and glycolic acid peels), as well as less conventional therapies including rucinol, vitamin C iontophoresis, and skin-lightening complexes like Thiospot and Gigawhite.
    - Triple-combination cream was significantly more effective at lightening melasma than hydroquinone alone (RR 1.58, 95% CI 1.26 to 1.97) or when compared to the dual combinations of tretinoin and hydroquinone (RR 2.75, 95% CI 1.59 to 4.74), tretinoin and fluocinolone acetonide (RR 14.00, 95% CI 4.43 to 44.25), or hydroquinone and fluocinolone acetonide (RR 10.50, 95% CI 3.85 to 28.60).
    - Azelaic acid (20%) was significantly more effective than 2% hydroquinone (RR 1.25, 95% CI 1.06 to 1.48) at lightening melasma but not when compared to 4% hydroquinone (RR 1.11, 95% CI

0.94 to 1.32).
  - In two studies where tretinoin was compared to placebo, participants rated their melasma as significantly improved in one (RR 13, 95% CI 1.88 to 89.74) but not the other. In both studies by other objective measures tretinoin treatment significantly reduced the severity of melasma.
  - Thiospot was more effective than placebo (SMD -2.61, 95% CI -3.76 to -1.47).

Overall the authors of the Cochrane review concluded that the quality of the studies evaluating melasma treatments was generally poor and available treatments inadequate. High-quality randomised controlled trials on well-defined participants with long-term outcomes to determine the duration of response are needed.

- The British Association of Dermatologists for Skin Disease (BAD) [2] have produced a list of specials to consider where the range of licensed medicines are limited. The list includes hydroquinone 5% w/w, hydrocortisone 1% w/w and tretinoin 0.1% w/w in a non-aqueous gel 0.3% w/v – use to treat melasma in conjunction with a strong sunblock. The guidance from BAD advises - Do not use for more than 6 months due to risk of ochronosis (deposition of dark pigment).

Safety:
- A Cochrance review [1] found the adverse events most commonly reported were mild and transient such a skin irritation, itching, burning and stinging.
- Pigmanorm® should not be used longer than 6 months due to risk of ochronosis (deposition of dark pigment).

Cost of treatment and Cost Effectiveness
- There is no data on the cost- effectiveness of this treatment.
- Pigmanorm® is an unlicensed medication in the UK i.e. issued as a 'specials' product. The product when sourced by the hospital pharmacy (West Hertfordshire Hospital Trust) costs £11.90. If the product is ordered in primary care it is subject to variable pricing. Data over the period June 2017 to June 2018 showed that the costs charged in primary care in Hertfordshire and West Essex STP ranged from £50 to £155.

The needs of the population
The needs of the population appear to be low as the condition is neither itchy nor painful and so does not have a physical impact. However, as melasma often presents on exposed skin such as the face it is the cosmetic aspect of it that affected people tend to find upsetting.

The needs of the community
The impact to the health economy appears to be high as there are a large number of patients affected and the cost is both variable and high. Therefore if prescribed on the NHS this would create a cost pressure which would have an impact on the local health economy which already has to identify savings.

Policy Drivers
- NICE – no relevant NICE guidance identified

Equity: No impact anticipated

Implementability: No issues identified

References:

1. Cochrane Library and NICE evidence: Cochrane Library: Interventions for Melasma. Ratna Rajaratnam, James Halpern, Asad Salim, Charis Emmett. Published 07/07/2010 http://cochranelibrary-wiley.com/doi/10.1002/14651858.CD003583.pub2/abstract
2. British Association of Dermatology (Buckley DA, Root T, Bath S. On behalf of the BAD Specials Working Group 2014. Specials Recommended by the British Association of Dermatologists for Skin Disease. Accessed on 10th September 2018 via http://www.bad.org.uk/healthcare-professionals/clinical-standards/specials