NHS PrescQIPP

DROP-List no.19: Eflornithine review

This is one of a number of bulletins providing further information on medicines contained in the PrescQIPP DROP-List (DRugs of lOw Priority). This bulletin focuses on eflornithine 11.5% cream which is a low priority treatment. Self-funded cosmetic treatments should be the primary option for facial hirsutism for the majority of women.

Further bulletins, including the DROP-List, are available on the PrescQIPP website, available at: http://www.prescqipp.info/resources/viewcategory/171-drop-list[1]

Recommendations

- The treatment of hirsutism is a cosmetic procedure which is a low priority for funding by CCGs. If hirsutism is mild and does not significantly interfere with the woman's quality of life, consider no additional treatment. Hirsutism is not usually associated with any significant medical abnormality.
- Eflornithine 11.5% cream offers very little benefit for the management of facial hirsutism in women. There is limited evidence for efficacy and patient satisfaction with eflornithine.
- Self-funded cosmetic treatments for reduction in hair growth or hair removal (e.g. shaving, plucking, laser treatment, electrolysis) should be the primary options for the majority of women with hirsutism.
- It is important that the patient is properly assessed and underlying causes addressed (such as weight reduction if obese) before pharmacological therapy is considered as hirsutism can result from serious medical conditions or from medication (e.g. ciclosporin, glucocorticoids, minoxidil, phenobarbitone, phenytoin, combined oestrogen-androgen hormone replacement therapy).
- If a local decision is taken to fund the treatment of hirsutism after failure of self-care and lifestyle measures, restrict eflornithine treatment to use in women for whom alternative therapy, e.g. co-cyprindiol, is contraindicated, ineffective, or considered inappropriate (e.g. post- menopausal women or where severe or multiple risk of venous thromboembolism may constitute a contra-indication for co-cyprindiol).
- In women with moderate or severe hirsutism test for elevated androgen levels. Eflornithine cream should only be used in patients with a raised free androgen index associated with an androgenic disease e.g. polycystic ovary syndrome.
- Prescribers are reminded that eflornithine treatment should be reviewed at 4 months and if ineffective, therapy should be discontinued at this time. Patients should also be advised that they may need to continue to use a hair removal method in conjunction with eflornithine cream.

Background

Eflornithine cream features as no.19 in the PrescQIPP DROP-List.[1] The DROP-List is an accumulation of medicines that are regarded as low priority, poor value for money or medicines for which there are safer alternatives.

In the PrescQIPP membership area (ePACT data July 2013 for 16.4million patients), £622,416 was spent on eflornithine cream over the course of 12 months. Self-funded cosmetic treatments should be the primary

option for facial hirsutism for the majority of women. As with all reviews, individual patient circumstances need to be borne in mind, however, with clearly defined review criteria, assistance from practice nurses, support from your local CCG prescribing teams and the experiences of CCGs/GPs that have already undertaken this work, it is hoped that GPs will participate in realising the cost savings.

A patient information leaflet on hirsutism is available from the British Association of Dermatologists at: www.bad.org.uk/site/826/Default.aspx

Clinical evidence

Excessive hair growth can result from serious underlying disorders (e.g. polycystic ovary syndrome, androgen secreting neoplasm) or certain drugs (e.g. ciclosporin, glucocorticoids, minoxidil, phenobarbitone, phenytoin, and combined oestrogen-androgen hormone replacement therapy). These factors should be considered in the overall medical treatment of patients who might be prescribed eflornithine.[2, 3]

Eflornithine cream is licensed only for the treatment of facial hirsutism in women.[2] Eflornithine irreversibly inhibits ornithine decarboxylase, an enzyme involved in the production of the hair shaft by the hair follicle. Patients should be advised on the dosage and administration instructions before use (i.e. to apply to the affected area at least 12 hours apart, 30g is maximum dose recommended over a month) and that they may need to continue to use a hair removal method (e.g. shaving or plucking) in conjunction with eflornithine cream.[2] In that case, the cream should be applied no sooner than five minutes after shaving or use of other hair removal methods, as increased stinging or burning may otherwise occur.

The majority of adverse events associated with eflornithine are skin related and mild in nature, with burning, tingling or stinging skin, erythema or rash more frequently reported in the eflornithine group.[2, 4] The most commonly reported adverse event in both groups was acne (very common) and pseudofolliculitis barbae (common >=1/10).[2]

There is limited evidence for efficacy and patient satisfaction with eflornithine:

- Two randomised controlled trials (RCTs)[4] of 24 weeks duration and 8 weeks follow up assessed the efficacy of eflornithine 11.5% cream compared to placebo in 596 women. The primary efficacy outcome was the change in baseline in the physician's global assessment rating scale. There was a statistically significant difference in spatial hair mass but not length at week 24 in the eflornithine group ($p<0.05$) compared to the vehicle group. There was no difference between groups at week 32 (8 weeks after cessation of treatment). Subgroup analysis showed a difference in treatment success in favour of caucasian vs. black women, 31% vs 13% in one study and 46% vs. 35% respectively in another study. Subgroup analysis also showed that 29% obese women and 43% normal weight women showed a marked or better improvement indicating a less pronounced effect in obese women.[2, 4]
- Two RCTs [5] have compared laser of the upper lip combined with either eflornithine or placebo cream. Both trials had limitations; unclear allocation in one and lack of Intention to treat (ITT) analysis in both. Both trials reported a more significant reduction in hair with the addition of eflornithine, particularly early in the trial using hair counts and subjective scoring.
- One small review[6] addressed the bother and discomfort felt by women with unwanted facial hair. The patient-related outcome measure used was ESTEEM (Exchanges of affection, Social interactions, Time spent removing facial hair, Encountering new people, Engaging in work or school, Minimizing overall bother with facial hair). There was a significant reduction in the level of overall bother caused by facial hair in women using eflornithine cream compared with placebo (estimated difference 15.8, 95% CI 10.8 to 20.8; $p < 0.01$). There was also a reduction in the level of bother due to time spent removing hair ($p < 0.05$) compared with placebo. However, it is likely that a positive outcome would have been reached by other cosmetic treatment options; this was not examined in the study.

- There are no trials comparing eflornithine with other hirsutism treatments. In addition, the efficacy and safety of eflornithine cream has not been specifically investigated in women who are not able to receive co-cyprindiol due to contra-indications. When eflornithine cream is discontinued, hair treatment returns to pretreatment levels within about 8 weeks. Other cosmetic treatment options e.g. electrolysis, laser treatment may offer long term treatment solutions; continued treatment is necessary with eflornithine cream to maintain the benefits.

National guidance

The Scottish Medicines consortium (SMC)[7] has restricted use of eflornithine cream within NHS Scotland for the treatment of facial hirsutism in women for whom alternative drug therapy is ineffective, contra-indicated or considered inappropriate. As a topical treatment, eflornithine cream may offer advantages over existing therapy for some women as it avoids the risks associated with systemic therapies.

The Midlands Therapeutic Review and Advisory Committee (MTRAC),[8] states that the evidence for the safety and efficacy of eflornithine was considered to be weak. Although eflornithine is the only topical treatment available for hirsutism, it was considered to have a low place in therpay, as the long term safety of the drug has not been evaluated and has not been compared with the only other licensed therapy, co-cyprindiol. The verdict also states that it is important that the patient is properly assessed before eflornithine is prescribed, because hirsutism can result from serious medical conditions.

The Endocrine Society guidelines[3] recommend the following measures for women with 'patient-important' hirsutism despite cosmetic measures:

- Test for elevated androgen levels in women with moderate or severe hirsutism or hirsutism of any degree when it is sudden in onset, rapidly progressive, or associated with other abnormalities such as menstrual dysfunction, obesity, or clitoromegaly.
- For women who choose hair removal therapy, the guidelines recommend laser treatment or electrolysis.
- For pharmacological therapy, consider:
  - Oral contraceptives for the majority of women, adding an antiandrogen after 6 months if the response is suboptimal.
  - The guidelines recommend against antiandrogen monotherapy unless adequate contraception is used and also against using insulin-lowering drugs.

Clinical Knowledge Summary (CKS)[9] provides guidance on the management of hirsutism in premenopausal and postmenopausal women:

Premenopausal women (with or without polycystic ovary syndrome)

- Encourage weight loss in women who are overweight or obese.
- Discuss cosmetic methods of hair reduction and removal as these will remain an important part of management.
- If hirsutism is mild and does not significantly interfere on the women's quality of life, consider no additional treatment. The NICE CKS also states that a subjective approach is generally appropriate in primary care to assess severity of hirsutism, using the woman's own perception of her condition and the extent it impacts on her quality of life. Hirsutism can be more formally evaluated using the Ferriman–Gallwey[3] scoring system; however, this scoring system has several limitations, and is impractical for routine use in clinical practice.
- If additional treatment is required, offer co-cyprindiol. Co-cyprindiol[10] is licensed for the treatment of moderately severe hirsutism but should be stopped after three or four menstrual cycles after the woman's hirsutism has completely resolved because of an increased risk of venous thromboembolism
- Advise women that treatment may take at least 6 months to work
- If combined oral contraceptives (COCs) are contraindicated or have not worked offer women topical eflornithine.

Postmenopausal women

- Discuss cosmetic methods of hair reduction and removal.
- If hirsutism is mild and does not significantly interfere on the women's quality of life, consider no additional treatment.
- If additional treatment is required, consider topical eflornithine.
- Benefit should be noted in 6-8 weeks and eflornithine should be discontinued if no benefit is seen within 4 months of starting treatment.
- If improvement is seen, continued treatment is necessary to maintain the benefits. Once the cream is discontinued, hair growth returns to pretreatment levels within about 8 weeks.

Costs

There is a significant difference in cost between eflornithine and the COCs. Table 1 below illustrates the cost differences.

Table 1: Eflornithine product and price comparison – Drug Tariff November 2013[11]

Product	Dose per month	Cost per 28 days
Eflornithine 11.5% cream	Max 30g	£28.44
Co-cyprindiol	1 daily for 21 days	£1.76

Savings

In the PrescQIPP membership area of 16.4 million patients, there is a strong variation in prescribing with around £622,416 being spent on eflornithine over the course of 12 months. Reviewing the appropriateness of current eflornithine therapy and discontinuing treatment if not a funding priority locally for CCG or ineffective could reduce this spend. **This equates to total savings across the PrescQIPP membership per 100,000 patients of £3795.**

80% discontinuation of eflornithine could reduce this spend by £497,932. This equates to total savings across PrescQIPP membership per 100,000 patients of £3036.

References

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11. Drug Tariff, November 2013

Additional PrescQIPP resources

 Briefing

 Data pack

 Audit and patient letters

Available for download here: http://www.prescqipp.info/-eflornithine/viewcategory/198

Information prepared by Anita Hunjan, NHS PrescQIPP Programme, November 2013 and reviewed by Katie Smith, East Anglia Medicines Information Service, December 2013.

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