JPC 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).
Background Information

Hirsutism can arise as a result of a hormonal disorder or as a side effect of drug therapy e.g. minoxidil, corticosteroids, anabolic steroids, androgens, danazol and progestrons. In general, women should be advised about local methods of hair removal. This is often sufficient in mild cases however alternative treatments may be required.

Treatment Options

Eflornithine Cream (Vaniqa®)
Eflornithine is an antiprotozoal drug that irreversibly inhibits ornithine decarboxylase (an enzyme involved in the production of the hair shaft by the hair follicle). Eflornithine cream 11.5% (Vaniqa®) is licensed for the treatment of facial hirsutism in women.

Co-cyprindiol tablets (mixture of cyproterone acetate 2mg / ethinylestradiol 35 micrograms)
Some women with moderately severe hirsutism may benefit from treatment with co-cyprindiol because hair growth is androgen dependent. Contra-indications to co-cyprindiol include pregnancy and a pre-disposition to thrombosis. It is contra-indicated in those with a personal or close family history of venous thromboembolism. Women with severe acne or hirsutism may have an inherently increased risk of cardiovascular disease. (Source: BNF 65)

Metformin
Metformin may be considered as an alternative treatment option in women with polycystic ovary syndrome. NB: Use of metformin for this indication is unlicensed.

Laser depilation Therapy
There is local guidance on the use of laser hair depilation therapy. This is outlined in the Bedfordshire and Hertfordshire Priorities Forum Statement Number: 1 The provision of cosmetic treatments and surgery (Appendix 2 – see website link, section “Abnormally placed hair and hirsutism” page 2).

Cost of Drug Treatment Options (Drug Tariff Nov 13)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eflornithine 11.5% cream</td>
<td>£56.87 (60g)</td>
</tr>
<tr>
<td>Co-cyprindiol tablets</td>
<td>£1.76 (1 tab daily for 21 days)</td>
</tr>
</tbody>
</table>

Cost of laser depilation therapy

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>One course of treatment</td>
<td>£ 1,555</td>
</tr>
<tr>
<td>(consisting of 6 sessions)</td>
<td></td>
</tr>
</tbody>
</table>

NB: Local commissioning will fund a single course of laser depilation therapy only.

Aim of Briefing Paper
Eflornithine 11.5% cream was originally included in the PrescQIPP DROP List (Drugs of low Priority, Feb 2012, ref 1). The Drop list consists of a range of medications that
PCT’s (now CCGs) consider should be given a low priority, are poor value for money or for which there are safer alternatives. Subsequent to the publication of this list, PrescQIPP have published a review of eflornithine, Bulletin 57 – Drop List – Eflornithine Review (December 2013) to explain and support the inclusion of eflornithine in the DROP-List.

The purpose of this Briefing Paper is to discuss the place in therapy of eflornithine 11.5% cream for the treatment of hirsutism in relation to the following two points:

- The specific set of recommendations where eflornithine is now recommended for use as detailed in PrescQIPP bulletin 57 - Appendix 1.
- In relation to laser depilation therapy as detailed in local Beds & Herts Priorities statement (appendix 2)

Information relating to Eflornithine Cream:

1) Drop-List – Eflornithine Review (Extracts from Bulletin 57)
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.

Recommendations (as per PrescQIPP, Bulletin 57)

- 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.

Savings (extract from PresQIPP Bulletin 57)
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.

2) Summary of Product Characteristics (SPC)

Extract from Summary Product of Characteristics (SPC) for Eflornithine ((Vaniqa®))

Eflornithine cream should be applied to the affected area twice daily, at least eight hours apart. Efficacy has only been demonstrated for affected areas of the face and under the chin. Application should be limited to these areas. Maximal applied doses used safely in clinical trials were up to 30 grams per month.

Improvement in the condition may be noticed within eight weeks of starting treatment. Continued treatment may result in further improvement and is necessary to maintain beneficial effects. The condition may return to pre-treatment levels within eight weeks following discontinuation of treatment.

Use should be discontinued if no beneficial effects are noticed within four months of commencing therapy.

Patients may need to continue to use a hair removal method (e.g. shaving or plucking) in conjunction with Vaniqa. 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.

3) BNF Information

The BNF states that topical eflornithine can be used as an adjunct to laser therapy for facial hirsutism in women. Eflornithine should be discontinued in the absence of improvement after treatment for 4 months.

4) Scottish Medicine Consortium (SMC) Position (March 2005 and revised August 2005)

The SMC issued a recommendation in March 2005 that Eflornithine 11.5% cream (Vaniqa®) was not recommended for use within NHS Scotland for the treatment of facial hirsutism in women. The reasons given for this decision were that there was no evidence of its efficacy in comparison to existing treatments and it was substantially more expensive.

Following a re-submission, the SMC revised their advice. The current position from the SMC (August 2005), now states:

“Eflornithine 11.5% cream (Vaniqa) is accepted for restricted use within NHS Scotland for the treatment of facial hirsutism in women. It is restricted to use in women for
whom alternative drug therapy is ineffective, contraindicated or considered inappropriate. Eflornithine 11.5% cream, as a topical treatment, may offer advantages over existing Therapy for some women as it avoids the risks associated with systemic therapies.

**Local Usage Figures of eflornithine cream 11.5% (60g size)– Bedfordshire CCG**

**Dec 2012- Nov 2013**
- Total Number of tubes issued = 355
- Total cost = £ 18, 798

**Previous 12 months**
- Total Number of tubes issued = 386
- Total cost = £ 19, 923

**References**
3. BNF 65
4. Epact.net – Usage data for eflornithine for Bedfordshire ccg
DROP List: 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/10-drop-list/viewcategory/58](http://www.prescqipp.info/10-drop-list/viewcategory/58).

**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 contraindication 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. 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 review6 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) 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), 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 therapy, 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 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) 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 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 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 efloinithine.
- Benefit should be noted in 6-8 weeks and efloinithine 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 efloinithine and the COCs. Table 1 below illustrates the cost differences.

Table 1: Efloinithine product and price comparison – Drug Tariff November 2013

<table>
<thead>
<tr>
<th>Product</th>
<th>Dose per month</th>
<th>Cost per 28 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efloinithine 11.5% cream</td>
<td>Max 30g</td>
<td>£28.44</td>
</tr>
<tr>
<td>Co-cyprindiol</td>
<td>1 daily for 21 days</td>
<td>£1.76</td>
</tr>
</tbody>
</table>

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 efloinithine over the course of 12 months. Reviewing the appropriateness of current efloinithine 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 efloinithine could reduce this spend by £497,932. This equates to total savings across PrescQIPP membership per 100,000 patients of £3036.

References


11. Drug Tariff, November 2013

Additional resources to accompany this Bulletin include:

Briefing  Data pack  Implementation pack (Audit and patient letters)

Available for download here: http://www.prescqipp.info/downloads/viewcategory/129-eflornithine

Non-subscriber publication April 2014.
Bedfordshire and Hertfordshire Priorities Forum Statement
Number: 1
Subject: The provision of cosmetic treatments and surgery

See link below for current statement relating to the provision on cosmetic treatments and surgery. This document contains a section on "abnormally place hair and hirsutism" (page 2) (available on Beds and Herts Priority Forum website).

http://www.enhertsccg.nhs.uk/sites/default/files/Interim%20guidance%20cosmetic%20dec%202013.pdf