

New Medicine Assessment

Spironolactone

in the treatment of acne vulgaris

Recommendation:

RAG status: **RED**

Spironolactone is recommended to treat refractory adult (post teenage) female acne vulgaris resistant to multiple oral antibiotics and isotretinoin and where there are clinical signs of hyperandrogenism [unlicensed indication]. It should be noted that the evidence to support its use is in a limited number of patients and is of low quality.

This preparation should only be prescribed by a Consultant Dermatologist

Summary of supporting evidence:

- A double blind placebo controlled crossover randomised controlled trial (RCT) in 29 women reported an improvement in acne symptoms (defined as 50% reduction in number of lesions) in 58% of people taking 200 mg of spironolactone, when assessed double blind by the investigators using photographic means, compared to 21% improvement in the placebo group.
- The results from the two groups were pooled and reported a reduction in lesion counts from 37.8 ± 5.8 to 12.9 ± 3.3 in the spironolactone group and 23.5 ± 3.2 to 24.7 ± 3.9 in the placebo group.
- 86% of patients subjectively reported an improvement in acne symptoms whilst taking spironolactone in the same trial.
- Some people were permitted to take an oral contraceptive during the trial and so we cannot be confident the results seen were from the spironolactone alone.
- A placebo controlled trial in 17 male and 19 female patients found for doses ranging from 50 mg to 200 mg daily that the acne symptoms were better in 60 to 83% of people when assessed by photographic means, compared to 15% of those in the placebo group.
- 40 to 100% of patients (depending on the dose of spironolactone) reported their acne was better in the same trial, compared to 17% of those in the placebo group. No additional acne therapy was permitted during the trial.
- The trials were insufficiently powered to demonstrate whether the results found are statistically significant.
- In a retrospective analysis of 85 women, treated for 2 - 24 months with either spironolactone alone, spironolactone plus oral antibiotics, spironolactone plus oral contraceptives or spironolactone plus oral antibiotics and oral contraceptives, 66% of women had either a complete clearing or marked improvement of acne.
- All three trials report a high dropout rate; 38%, 28% and 14% respectively failed to complete the studies. Reasons reported were; adverse events and lack of improvement.
- The most commonly reported adverse events (AEs) were; menstrual irregularities, nausea, dizziness/headaches, diuresis and breast tenderness. These AEs did not always cause discontinuation of the study drug.

- A Cochrane review concluded that there is insufficient evidence of effectiveness of spironolactone in the management of acne vulgaris. It should be noted that the review only considered one trial paper [Muhlemann].
- Spironolactone is an inexpensive drug and would be used in a very small number of patients. It is estimated that the total annual cost could range from £247 to £1,080. However, due to the high dropout rates, it is unlikely that that the cost would be as high as £1,080 as many patients would fail to complete the treatment course.

Details of Review

Name of medicine (generic & brand name): Spironolactone
Strength(s) and form(s): 25 mg, 50 mg and 100 mg tablets
Dose and administration: Oral
BNF therapeutic class / mode of action 2.2.3 Potassium-sparing diuretics and aldosterone antagonists ¹
Licensed indication(s): Oedema and ascites in cirrhosis of the liver, malignant ascites, nephrotic syndrome, oedema in congestive heart failure, moderate to severe heart failure, treatment of primary hyperaldosteronism. ¹
Proposed use (if different from, or in addition to, licensed indication above): To treat refractory adult (post teenage) female acne vulgaris resistant to multiple oral antibiotics and isotretinoin and where there are clinical signs of hyperandrogenism [unlicensed indication].
Course and cost: Oral Spironolactone 25 - 200 mg daily. 12 week initial courses of treatment with clinic reviews until the desired endpoint of acne clearance. Often after this is achieved with a low dose maintenance therapy, as needed. £20 - £64 / year (25mg – 200mg daily) ²
Current standard of care/comparator therapies: Oral antibiotics usually considered in the management of acne are oxytetracycline or tetracycline; if there is no improvement in 3 months, another antibacterial should be used. Doxycycline and lymecycline are alternatives to tetracycline. Other oral antibacterials that can be considered but have some drawbacks are; minocycline, erythromycin and trimethoprim [unlicensed indication]. The oral contraceptive pill co-cyprindiol, which contains an antiandrogen, is also used for moderate to severe acne in women. Isotretinoin is useful for women who develop acne in third or fourth decades of life as it is usually unresponsive to oral antibiotics. ¹
Relevant NICE guidance: No relevant NICE guidance.

Background and context

Acne is the most common skin disease of adolescence, and in most cases it clears spontaneously. Nearly 90% of teenagers have acne, and half of them continue to experience symptoms as adults. By age 40 years, 1% of men and 5% of women still have lesions.³

Acne is an inflammatory disease of the pilosebaceous duct that results from four primary pathophysiologic processes. Increased androgen production causes abnormal epithelial desquamation and follicular obstruction, which lead to the primary precursor lesion in acne—the microcomedone. Microcomedones are pathological structures not visible to the naked eye that evolve into visible lesions. An increase in circulating androgens also promotes sebum production, causing these obstructed follicles to fill with lipid rich material and form visible open and closed comedones. Sebum serves as a substrate for bacterial growth, leading to proliferation of *P. acnes*. Finally, *P. acnes* releases chemical mediators that promote inflammation, which is propagated by traumatic rupture of comedones into the surrounding dermis. This inflammation manifests through the development of inflammatory papules, pustules, nodules, and cysts.³

Mild to moderate acne is generally treated with topical preparations, which include benzoyl peroxide, azelaic acid, antibacterials or retinoids. Systemic treatment with oral antibacterials is usually used for moderate to severe acne or where topical treatments are not tolerated or are ineffective, or where application to the affected site is difficult. The antibacterials that are used are; oxytetracycline, tetracycline, doxycycline, lymecycline, erythromycin, minocycline and trimethoprim [unlicensed indication]. Another oral preparation used in the management of acne in women is the hormonal treatment co-cyprindiol (cyproterone acetate with ethinylestradiol). Severe acne unresponsive to prolonged courses of oral antibacterials, scarring, or acne associated with psychological problems requires referral to a dermatologist for consideration of oral isotretinoin. Isotretinoin is particularly useful for those patients who develop acne in the third or fourth decades of life as late onset acne tends to be unresponsive to antibacterials.¹

Spirolactone is widely used for oedema and ascites in cirrhosis of the liver, hypertension [unlicensed indication] and in heart failure. The antiandrogenic effects of spironolactone were first discovered when it was being used to treat hypertension in women with concurrent polycystic ovary syndrome (PCOS) and hirsutism. It has been used frequently in the dermatology clinic for women with hormonal-pattern AV.⁴

Spirolactone has a number of effects which may be beneficial in acne vulgaris. Spirolactone is an antiandrogen in addition to being an aldosterone antagonist. It has been shown to inhibit sebaceous gland activity in hamsters (increased sebaceous glands and increased sebum secretion are essential components in the development of acne vulgaris lesions).⁴ Spirolactone has been shown *in vitro* to decrease androgen-stimulated sebocyte proliferation. Women with high androgenic states will also have increased sebum production which in turn can cause worsening of acne vulgaris. It has been noted that acne prone skin has a greater activity of type-1 5-alpha-reductase activity and spironolactone decreases 5-alpha reductase activity via increased clearance of testosterone, secondary to augmented liver hydroxylase activity. Spirolactone is thought to increase the level of steroid hormone binding globulin (SHBG) which provides a sink that reduces circulating free testosterone. Spirolactone is also thought to have a direct peripheral effect on the cutaneous androgen receptors, competing with dihydrotestosterone, hence reducing sebum production and comedone formation.⁴

Summary of evidence

Summary of efficacy data in proposed use:

Published evidence in support of spironolactone in the treatment of acne is limited to two small double blind placebo controlled trials and one retrospective analysis. Further supporting information is provided from two papers (available only as abstracts) one of which was performed in patients of Japanese origin.

In 1986 a double-blind placebo-controlled crossover trial assessed spironolactone 200 mg daily in 29 women with moderate to severe acne.⁵ No antibiotics were administered during the month preceding the trial and no topical agents were used during the study period. Six women continued to take an oral contraceptive pill during the trial. Patients were randomised to either 200 mg daily of spironolactone or placebo in a double-blind fashion. After 3 months, all patients were given one month of placebo and then crossed over to receive either placebo or 200 mg daily of spironolactone for a further 3 months.

Of the original 29 patients, 21 patients completed the trial; 2 withdrew due to adverse events (AE) and 6 failed to return after the initial interview. The patients were asked at each interview to grade their acne on a 5 point scale (much worse, worse, unchanged, better, much better). All patients were seen by the same observer. At each visit only the inflamed lesions were counted – papules, pustules and nodules. Improvement was defined as a greater than 50% reduction in the number of lesions and worsening as a greater than 50% increase. Photographs were also taken at each visit which were then assessed double blind by the three co-authors. The patients were evaluated objectively and subjectively and were recorded as worse, unchanged or improved. The results from both groups were pooled and reported that the mean lesion count fell from 37.8 ± 5.8 to 12.9 ± 3.3 on spironolactone ($p < 0.001$) and 23.5 ± 3.2 to 24.7 ± 3.9 ($p > 0.1$) for placebo. 18 (86%) of the patients reported improvement whilst taking spironolactone, compared to 5 (24%) whilst taking placebo ($P < 0.001$). For change in lesion counts 15 patients (75%) improved on spironolactone and 4 (20%) for those taking placebo ($P < 0.001$). Using the photographic method 11 patients (58%) improved on spironolactone compared to 4 (21%) on placebo ($P < 0.02$). Plasma testosterone and sex hormone binding globulin (SHBG) assays were also taken at each visit. In response to spironolactone the SHBG fell from a mean of 48 ± 4.6 to 39 ± 3.4 nmols DHT bound/l ($P < 0.001$). The plasma testosterone levels did not change significantly 2.0 ± 0.1 and 2.0 ± 0.3 nmols/l ($P > 0.1$) and no significant changes were observed for placebo.⁵

In 1984, another double-blind study which took place over three months, recruited 17 male and 19 female patients aged between 18 and 38 with severe acne vulgaris.⁶ All patients discontinued acne therapy prior to commencement of the trial and were only allowed to use their normal soap. No patients were permitted to use the oral contraceptive pill for the duration of the study. Patients were randomly allocated to placebo, spironolactone 50 mg, 100 mg, 150 mg or 200 mg. Patients' sebum secretion rate was measured before treatment and at 6 and 12 weeks. The acne severity was assessed by three methods. The appearance was assessed objectively and noted by the same observer at each visit. The clinical response noted subjectively by the patients was also recorded. Photographs were taken of the affected areas before treatment and at 12 weeks and assessed blind by 2 observers unconnected with the study and the author of the paper. Plasma testosterone, SHBG, electrolytes, urea and creatinine were all measured prior to commencement of spironolactone and on completion of the study.⁶

Of the original 36, 26 patients completed the trial. One patient discontinued treatment due to no improvement in her skin, one was withdrawn from the trial by her GP, and the remaining 8 did not return after initial baseline studies had been performed. The table below shows the number of patients in each treatment group with worse, unchanged or better acne reported by patients,

investigator and photographic review (carried out by 3 investigators).⁶

	Placebo (n=6)	Spironolactone 50 mg (n=5)	Spironolactone 100 mg (n=5)	Spironolactone 150 mg (n=6)	Spironolactone 200 mg (n=4)
Photographic	Worse = 3 (50%) Unchanged = 2 (35%) Better = 1 (15%)	Worse = 1 (20%) Unchanged = 1 (20%) Better = 3 (60%)	Worse = 1 (20%) Unchanged = 1 (20%) Better = 3 (60%)	Worse = 0 Unchanged = 1 (17%) Better = 5 (83%)	Worse = 1 (25%) Unchanged = 1 (25%) Better = 3 (75%)
Objective	Worse = 1 (17%) Unchanged = 4 (66%) Better = 1 (17%)	Worse = 0 Unchanged = 4 (80%) Better = 1 (20%)	Worse = 0 Unchanged = 3 (60%) Better = 2 (40%)	Worse = 0 Unchanged = 2 (33%) Better = 4 (67%)	Worse = 0 Unchanged = 1 (25%) Better = 3 (75%)
Subjective	Worse = 1 (17%) Unchanged = 4 (66%) Better = 1 (17%)	Worse = 1 (20%) Unchanged = 2 (40%) Better = 2 (40%)	Worse = 0 Unchanged = 1 (20%) Better = 4 (80%)	Worse = 0 Unchanged = 1 (17%) Better = 5 (83%)	Worse = 0 Unchanged = 1 (25%) Better = 4 (100%)

There was a mean reduction in the sebum excretion rate for men of 2.8 ± 0.7 to $1.8 \pm 0.3 \mu\text{g}/\text{cm}^2/\text{min}$ ($P < 0.01$) and women 4.7 ± 1.7 to $1.0 \pm 0.2 \mu\text{g}/\text{cm}^2/\text{min}$ ($P < 0.025$) for the combined treatment groups. The change was not reported numerically in the paper for the women in the placebo group; the change in men for the placebo group was 2.5 ± 0.6 to $1.3 \pm 0.5 \mu\text{g}/\text{cm}^2/\text{min}$ ($t = 1.5$; $P > 0.05$). For the male patients there were no significant changes in endocrine values: serum testosterone 25.0 ± 6.3 compared to $23.8 \pm 3.0 \text{ nmol/l}$ ($P > 0.1$), SHBG 33.5 ± 5.1 compared to $29.0 \pm 3.2 \text{ nmol/l}$ DHT bound/l ($P > 0.1$). For the female subjects there was a mean rise in plasma testosterone from 1.3 ± 0.1 to $1.9 \pm 0.1 \text{ nmol/l}$ ($P < 0.01$) and the SHBG fell from 55.0 ± 9.6 to $45.3 \pm 5.7 \text{ nmol/l}$ DHT bound/l ($P > 0.1$).⁶

A third paper, published in 2000, was a retrospective analysis of 85 women aged between 18 and 52 years of age who were treated with 50mg or 100mg of spironolactone either alone or adjunctive to other systemic treatments.⁷ Patients had either failed previous systemic acne therapy including antibiotics, isotretinoin, or oral contraceptives and/or had a clinical presentation demonstrating hormonal influences; 58 of the women had both. All had moderate or severe inflammatory papular or nodular facial acne. All patients were monitored monthly or bi-monthly and assessed by interim patient history and physician examination. 67 (79%) of the patients had failed to respond to one or more courses of systemic antibiotics (minocycline, tetracycline and erythromycin), either due to inadequate responses ($n = 53$) or side effects ($n = 14$). 14 patients had previously used oral contraceptives to clear their acne without success. 12 patients had tried at least one course of isotretinoin which had failed to improve the symptoms.⁷

Patients were prescribed 50 mg or 100 mg daily of spironolactone either alone or in combination with systemic antibiotics and/or oral contraceptives (ethinylestradiol 35 micrograms and norethindrone 1 mg). 17 were treated with spironolactone alone, 46 were given a combination of spironolactone and systemic antibiotics, 10 received oral contraceptives in addition to spironolactone and finally 12 patients were prescribed spironolactone, antibiotics and an oral contraceptive. Treatment duration ranged from 2 to 24 months.⁷

Of the 85 who started treatment, 73 were available for evaluation of their acne; 7 stopped the spironolactone (6 of these due to AEs) and 5 were lost to follow up before the minimum of 2 months of treatment. 24 of the remaining 73 patients (33%) demonstrated clearing of their acne, defined as no lesions or occasional isolated lesions. 24 patients (33%) demonstrated marked improvement which was defined as 50% improvement. 5 patients demonstrated no improvement and the remaining 20 patients demonstrated partial improvement ($< 50\%$).⁷

Of those who had complete clearing, 5 were prescribed spironolactone alone, 10 were taking spironolactone plus oral antibiotics, 4 were prescribed spironolactone plus oral contraceptives and the remaining 5 were taking; spironolactone plus oral antibiotics and oral contraceptives. The results, broken down into concomitant therapy, are shown in the table below:⁷

	Clearing of acne	Marked improvement	Partial improvement	No improvement	Lost to follow up
Spironolactone alone	5/17 (29%)	5/17 (29%)	3/17 (18%)	1/17 (6%)	3
Spironolactone plus oral antibiotics	10/46 (22%)	14/46 (42%)	10/46 (22%)	4/46 (9%)	8
Spironolactone plus oral contraceptives	4/10 (40%)	3/10 (30%)	3/10 (30%)*	0/10 (0%)	0
Spironolactone plus oral antibiotics and oral contraceptives	5/12 (42%)	2/12 (17%)	4/12 (33%)*	0/12 (0%)	1

*Discrepancy between the text and tables within the paper. Fig 2 implies that there should be 4 partial improvers in the spironolactone plus oral contraceptives group and 3 partial improvers in the spironolactone plus oral antibiotics and oral contraceptives group.

In this retrospective study 66% (48 patients) of women who received low dose spironolactone had either a complete clearing or a marked improvement of acne, although most were also receiving concomitant medications.

A Cochrane review published in 2009⁸ discusses the use of spironolactone in acne but the paper is predominantly assessing its use in the management of hirsutism with a note that those suffering from hirsutism often suffer from other symptoms such as acne. The paper discusses the evidence for spironolactone in acne and surmises that from studies included, there is insufficient evidence of effectiveness for the management of acne vulgaris. The paper does state that it is difficult to draw conclusions from the limited number of studies available in this review. It should be noted that the review only included one paper which is a small RCT using oral spironolactone and is the paper discussed above [Muhlemann 1986].⁸

Other efficacy data:

During the literature search two additional papers were found, but the full papers were unobtainable so the quality and outcomes of the studies cannot be fully assessed. Using the information from the abstracts only:

One paper assessed spironolactone 100 mg daily for 16 consecutive days each month for 3 months in 35 women. The study states that a clinically significant improvement was noted in 24 of those administered the study drug. Of these 24 the abstract states that the mean number of lesions decreased, and states a P value of < 0.01. It notes that no response was seen in 4 patients and 2 discontinued treatment due to side effects. It needs to be noted that this information is obtained from the abstract and therefore the quality of the study cannot be fully assessed.⁹

Another study assessed spironolactone in patients of Asian origin (139 Japanese patients) for 20 weeks and noted that due to differing responses to hormonal therapy the results cannot be

extrapolated to a white population. The paper looked at both male and female patients who were administered initially 200 mg daily of spironolactone. It evaluated the effectiveness by a photographic grading scale and noted most female patients exhibited excellent improvement. However, the exact results and what criteria had to be met for a conclusion of excellent improvement were not stated in the abstract.¹⁰

Summary of safety data:

In the first study⁵ the most commonly reported AEs were menstrual irregularity (11 of the 15 (73.3%) of women who were not on an oral contraceptive pill during the study). This did not cause discontinuation of the treatment during the study period and returned to normal after discontinuation of the spironolactone. Nausea was reported in 3 of the 21 (14.3%) women who completed the trial and dizziness in 1 of the 21 (4.8%) women. The two people who withdrew from treatment complained of nausea. Nine of the 21 (42.9%) patients reported having less greasy skin and hair and two of the 21 (9.5%) developed some breast enlargement.⁵

The second study⁶ reported that 7 of the 12 female patients (58.3%) noted minor increases in frequency of periods; this did not cause any of the patients to discontinue therapy. 2 out of 12 female patients (16.7%) noted a transient diuretic effect. No gynaecomastia was reported among the male patients; however, the study duration was short, at 3 months. No significant changes in serum electrolytes were reported.⁶

The retrospective analysis which permitted treatment with other systemic acne treatments⁷ concomitantly reported that 46 out of 85 women (57.5%) reported no AEs. 14 out of 85 women (17.5%) reported menstrual irregularities. Lethargy, fatigue, dizziness, or headaches were reported in 13 of the 85 women (16.3%). Other AEs that were reported were breast tenderness in 4 patients, diuretic effect with increased urinary frequency in 2 of the 85 patients (2.3%), postural light-headedness in 2 of the 85 patients (2.3%), melasma (dark skin discolouration) in 2 of the 85 patients (2.3%), nausea in 1 of the 85 patients (1.2%), decreased libido in 1 of the 85 patients (1.2%) and xerosis (abnormal dryness of the skin, mucous membranes or conjunctiva) in 1 of the 85 patients (1.2%). Serum potassium levels were measured in 73 patients and 10 were hyperkalaemic (range 4.8 to 5.3 mEq/L). Blood pressure was measured before and after treatment in 19 patients and showed maximal individual reductions of 15 mm Hg systolic and 10 mm Hg diastolic, with a mean reduction of 5 mm Hg systolic and 2.6 mm Hg diastolic. The paper also listed the following as beneficial side effects; improved symptoms of premenstrual syndrome for 13 of the 85 patients (15.3%), improvement in facial seborrhoea for 9 of the 85 women (10.6%), decreased menorrhagia (uterine bleeding at irregular intervals) in 2 of the 85 patients (2.4%), increased libido for 1 of the 85 patients (1.2%) and for 1 of the 85 patients (1.2%) reduced endometriosis pain.⁷

Strengths and limitations of the evidence:

General limitations in all the studies:

- The RCTs recruited very small numbers of patients and therefore the results must be interpreted with caution as they cannot prove statistical significance of the results found.
- It should be noted that the allowance of additional therapies during the treatment period in one of the studies means that we cannot be sure that the results found are due to the spironolactone or due to the other therapies which are also effective in the management of acne.

- Most studies were short-term.

Strengths of the RCTs were:

- The patients and investigators were blinded to treatment.
- The photographs taken at each clinic visit were assessed double-blind to try and eliminate investigator bias.
- One of the papers did not allow concomitant treatment with any other topical or oral therapies used in the management of acne and therefore the results seen are more likely to be due to the spironolactone.

In the retrospective case analysis (case series):

- The patient assessments were qualitative and not blinded and could lead to patient and investigator bias.
- The length of treatment was variable; from 2 to 24 months (mean 10 months) and it is not clear whether the length of treatment influences the outcome or AEs.
- It was not placebo-controlled or randomised to accurately compare spironolactone against placebo – the patients could have improved regardless of whether they were taking spironolactone or not.
- It is unclear whether the benefits seen in the patients taking concomitant therapy were due to the spironolactone or the other therapies they were taking for their acne.
- The patient numbers were too small for accurate statistical analysis, so it cannot be known whether the results are true or down to chance.

Summary of evidence on cost effectiveness:

No cost effectiveness analysis available.

Prescribing and risk management issues:

This preparation would be being prescribed off label and this would therefore need to be discussed with the patient and documented in the medical notes.

Decreased circulating testosterone can increase oestrogenic state which can lead to gynaecomastia and decreased libido.

Spironolactone can affect a patient's potassium levels and so these would need to be monitored during treatment. If hyperkalaemia was found, the spironolactone would need discontinuing.^{1,11}

Spironolactone has teratogenic potential and therefore as many patients will be women of child bearing age, they need to be counselled on the need for adequate contraception.^{1,11}

Patients need to be counselled around the potential for changes in blood pressure and symptoms of orthostatic hypotension.^{1,11}

Commissioning considerations:

Comparative unit costs:

Drug	Example regimen	Pack cost	Cost per patient per course/ per year (ex VAT)
Spironolactone	Dose range from 25 50 to 200 mg daily	25mg tablets = £1.55/28 50 mg tablets = £1.97/28 100 mg tablets = £2.43/28	£20 - £64/year
Oxytetracycline	500 mg BD	250 mg tablets = £1.22/28	£29/year (if used for 6/12)
Tetracycline	500 mg BD	250 mg tablets = £2.61/28	£63/year (if used for 6/12)
Doxycycline	100 mg OD	50 mg capsules = £1.70/28	£20/year (if used for 6/12)
Lymecycline	408 mg OD	408 mg capsules = £7.49/28	£45/year (if used for 6/12)
Minocycline	100 mg OD	100 mg m/r capsules = £20.08/56	£60/year (if used for 6/12)
Erythromycin	500 mg BD	250 mg tablets = £1.89/28	£45/year (if used for 6/12)
Trimethoprim	300 mg BD	100 mg tablets = £1.08/28	£39/year (if for 6/12)
Co-cyprindiol	2000/35 for 21 days each month	£5.42/63	£22/year
Isotretinoin	1mg/kg for 16 to 24 weeks, can be repeated	20 mg capsules = £19.52/30	Based on 60 kg £219 - £328/course
Drug Tariff for England and Wales, NHS Prescription Services (accessed 28/11/14) This table does not imply therapeutic equivalence of drugs or doses.			

Associated additional costs or available discounts:

No associated additional costs.

No available discounts.

Productivity, service delivery, implementation:

This preparation would be an additional treatment option in the management of acne. The dermatology clinics are already in operation and therefore there would not be a requirement for an additional service.

Anticipated patient numbers and net budget impact:

It is anticipated by the requesting clinician that the patient numbers will be very small. Many of the dermatologists across the locality do not recommend spironolactone for this indication. The requesting clinician has stated that there will only be 20 patients per year. Therefore even if patients

were prescribed spironolactone continuously at the highest dose the annual cost would only be £1,080. It is more likely that patients will only be prescribed a 12 week course which would be an annual cost of £247 for all 20 patients and due to the high dropout rates in the trials it is unlikely that all 20 patients would complete the course or continue treatment.

Innovation, need, equity:

Some patients across the locality have spironolactone as an option for the management of their acne. It is not anticipated that the recommendation will change practice as feedback from dermatologists has been that some do not use spironolactone for the management of acne. The recommendation is aimed to assess the evidence available for those who are already prescribing spironolactone in acne.

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References

1. Joint Formulary Committee. British National Formulary. 68th ed. London: British Medical Association and Royal Pharmaceutical Society of Great Britain; September 2014. https://www.medicinescomplete.com/mc/bnf/current/PHP834-spirolactone.htm?q=spironolactone&t=search&ss=text&p=1#_hit accessed 24/11/14
2. National Health Service Drug Tariff for England and Wales, NHS Prescription Services. http://www.ppa.org.uk/ppa/edt_intro.htm (accessed 28/11/14).
3. Dawson AL, Dellavalle RP. Acne vulgaris - Clinical Review. *BMJ* 2013;346:f2634 <http://www.bmj.com/content/346/bmj.f2634>
4. Kim G K, Del Rosso J Q. Oral Spironolactone in Post-teenage Female Patients with Acne Vulgaris: Practical Considerations for the Clinician Based on Current Data and Clinical Experience. *Journal of Clinical Aesthetic Dermatology* 2012;5(3): 37-50.
5. Muhlemann MF, Carter GD, Cream JJ, Wise P. Oral spironolactone: an effective treatment for acne vulgaris in women. *Br J Dermatol.* 1986;115: 227–232.
6. Goodfellow A, Alaghband-Zadeh J, Carter G, *et al.* Oral spironolactone improves acne vulgaris and reduces sebum excretion. *Br J Dermatol.* 1984;111:209-214.
7. Shaw J C. Low-dose adjunctive spironolactone in the treatment of acne in women: A retrospective analysis of 85 consecutively treated patients. *J Am Acad Dermatol.* 2000; 43(3): 498-502.
8. Brown J, Farquhar C, Lee O, Toomath R, Jepson R G. Spironolactone versus placebo or in combination with steroids for hirsutism and/or acne (Review). *Cochrane Database of Systematic Reviews* 2009, issue 2. <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD000194.pub2/pdf> accessed 24/11/14
9. Yemisci A, Gorgulu A, Piskin S. Effects and side-effects of spironolactone therapy in women with acne. *J Eur Acad Dermatol Venereol.* 2005;19(2):163-6. [Abstract]
10. Sato K, Matsumoto D, Iizuka F, *et al.* Anti-androgenic therapy using oral spironolactone for acne vulgaris in Asians. *Aesthetic Plast Surg.* 2006; 30(6): 689-94. [Abstract]
11. Blair G S, Allie N D, Spironolactone Use for Women With Acne or Hirsutism. *Journal of the Dermatology Nurses' Association* 2011; 3(6): 374-376.