Canadian Expert Drug Advisory Committee
Final Recommendation — Plain Language Version

AZELAIC ACID
(Finacea — Bayer Inc.)
Indication: Rosacea

Recommendation:
The Canadian Expert Drug Advisory Committee (CEDAC) recommends that Finacea, which is also called azelaic acid 15% gel, be listed by Canada's publicly funded drug plans for the treatment of rosacea (skin on the face that is red with bumps and/or cysts).

Reason for the Recommendation:
In two studies, Finacea compared with MetroGel (metronidazole, as either 0.75% or 1% gel), showed similar results for patients with mild-to-moderate papulopustular (bumpy and pus-filled) rosacea in terms of decreased number of bumps and/or cysts and overall severity, as assessed by the investigator.

Of Note
Finacea is similar in cost to MetroGel 0.75%, but more costly than MetroGel 1%, when all three products are used the recommended number of times per day (as written in the product monographs).

Background:
Health Canada has approved Finacea to treat the redness and bumps and/or cysts of rosacea that is of mild-to-moderate severity. Finacea decreases skin protein buildup and also stops bacteria from growing. It is not known exactly how it works in rosacea. Finacea is to be applied to the skin only. It is available as a 15% topical gel, and the Health Canada-approved dose is 0.5 grams applied twice daily.

Summary of CEDAC Considerations:
To make their decision, the Committee considered the following information prepared by the Common Drug Review (CDR): a review of the medical studies of Finacea and a review of the economic information prepared by the manufacturer of Finacea. Also, CEDAC considered information that patient groups submitted about outcomes and issues important to patients who have the condition for which the drug is indicated or who might use the drug.

Clinical Trials

CEDAC reviewed four studies conducted in a total of 1,075 adult patients with mild-to-moderate rosacea. Two studies, A03125 with 329 patients and A03126 with 335 patients, compared Finacea with the vehicle gel (i.e., the gel without the drug). Study A08681 with 251 patients and the Wolf study with 160 patients compared Finacea with another medication as described below.

Studies A03125 and A03126 compared Finacea with vehicle gel, both applied twice daily for 12 weeks. The proportion of patients who stopped taking part in the studies was 14% and 12% for A03125 and A03126 respectively.

Study A08681 compared Finacea with MetroGel 0.75% (metronidazole 0.75% gel), both applied twice daily for 15 weeks; 10% of patients stopped taking part in the study (11% for Finacea and 8% for MetroGel). The Wolf study compared Finacea applied twice daily with MetroGel 1% (metronidazole 1% gel) applied once daily for 15 weeks, and overall 15% of patients stopped taking part in the study (the percentage of patients who stopped using Finacea versus MetroGel was not reported).

The three studies that were funded by the manufacturer of Finacea (A03125, A03126, and A08681) were designed to see if Finacea was better than the comparators (vehicle gel or MetroGel 0.75%). The Wolf study was funded by a manufacturer of metronidazole gel, and was designed to see if MetroGel 1% was not worse than Finacea.

Outcomes

The main purpose of the studies comparing Finacea with vehicle gel was to measure the change in the number of inflammatory lesions (red swollen bumps) during the duration of the study and to determine the investigator global assessment of severity (IGAS) score at end of treatment. The main purpose of study A08681 was to measure the change in the number of inflammatory lesions during the duration of the study. The main purpose of the Wolf study was to measure the per cent change in inflammatory lesion count during the duration of the study; it would be concluded that MetroGel was not worse than Finacea if the per cent decrease in lesion count with Finacea was not more than 15% greater than with MetroGel.

Other results were defined in advance by the CDR protocol. Of these, the Committee discussed the following: quality of life, investigator global assessment of improvement (IGAI), patient global assessment of improvement (PGAI), investigator assessment of improvement in erythema (redness) and telangiectasia (visible blood vessels), patient assessment of cosmetic acceptability (e.g., the look and feel of the gels), and side effects.

Results

Efficacy or Effectiveness

- Quality of life was not evaluated in any of the four studies.
- In study A08681, Finacea was better than MetroGel 0.75%, with an average of 2.9 less inflammatory lesions per patient by the end of the treatment. In the Wolf study, MetroGel 1% once daily was not considered to be worse than Finacea twice daily, as the average percentage decrease in lesion count with MetroGel was only 5% less than that with Finacea.

- Compared with vehicle gel, patients taking Finacea had a greater reduction in the number of inflammatory lesions at end of treatment in studies A03125 and A03126; an average of 3.6 and 2.7 less lesions per patient respectively.
- The proportion of patients who improved with treatment (defined as an IGAS score of clear or minimal) at study end was greater for Finacea compared with vehicle gel in A03125, but not in A03126. In study A08681 and the Wolf study, the proportion of patients achieving an IGAS score of clear or minimal at study end was about the same for Finacea and MetroGel.
- In A08681, patients in the Finacea group showed more overall improvement compared with MetroGel 0.75%, as measured by the IGAI. In studies A03125 and A03126, patients in the Finacea group showed more overall improvement compared with vehicle gel, as measured by the IGAI and the PGAI. The Wolf study did not include the measures of IGAI or PGAI.
- Investigator assessed improvement in erythema (redness) was greater for Finacea compared with vehicle gel (in studies A03125 and A03126) and compared with MetroGel 0.75% (in study A08681).
- Telangiectasia (visible blood vessels) assessed by the investigator were about the same with Finacea and MetroGel 0.75% (in study A08681) and also with Finacea and vehicle gel (in studies A03125 and A03126).

Harms (Safety and Tolerability)

- Serious side effects were uncommon in all of the four studies.
- The proportion of patients who had skin-related side effects was higher among those treated with Finacea compared with vehicle gel (in studies A03125 and A03126) and also compared with MetroGel 0.75% (in study A08681). Skin-related side effects that were more common with Finacea than with comparators included, burning sensation or pain, paresthesia (numbness and tingling), and pruritus (itching). Most of the skin-related side effects seen with Finacea were mild or moderate in studies A03125, A03126, and A08681.
- In the Wolf study the percentage of patients with moderate or severe stinging or burning was 5% greater for Finacea compared with MetroGel 1%.

Cost and Cost-Effectiveness

The manufacturer submitted economic information to compare the cost of Finacea with that of MetroGel 0.75%. Both medications have similar efficacy (as shown in study A08681) and are applied twice daily, and the manufacturer assumed patients would use 1 g daily of either gel. When looking at the cost per gram, Finacea ($0.60) is similar in cost to MetroGel 0.75% ($0.66).

Finacea at 0.5 grams twice daily ($0.60) is more costly than MetroGel 1% gel at 0.5 grams daily (dosed as per product monograph) ($0.30).

Patient Input Information

- Patient input was received from one patient group.
- Patients mentioned that keeping the symptoms under control is very important in order to improve the quality of life. The type and frequency of side effects of the treatment should also be acceptable to patients.
- Patients pointed out that there are few approved treatments for rosacea.

Other Discussion Points:

- The Committee felt that the main result of the studies (lesion count) was an appropriate measure of the effectiveness of the treatments because it is fairly easy to measure, and because the number of lesions present is linked closely with the disease severity as measured by the patients.
- The Committee noted that there were not any good quality data available comparing Finacea with other non-metronidazole products used for rosacea, such as benzoyl peroxide.
- Although there were more skin-related side effects with Finacea compared with MetroGel, this was not felt to be much of a problem because patients easily notice such side effects and can switch to a different treatment.
- The reviewed studies do not provide information on whether patients who do not improve on MetroGel will improve with Finacea.
- As rosacea tends to go through cycles of improvement and worsening, it can be difficult to assess whether or not the patient is not improving with the medication.
- How often the different products would be applied in real life was not clear. The Committee was concerned that Finacea, used at the recommended frequency of twice daily, may be more costly compared with MetroGel 1% used once daily. However, it was noted that patients are the ones who decide how often and for how long to use these products as their condition worsens and improves over time.

CEDAC Members Participating:

Dr. Robert Peterson (Chair), Dr. Anne Holbrook (Vice-Chair), Dr. Michael Allan, Dr. Ken Bassett, Dr. Bruce Carleton, Dr. Doug Coyle, Mr. John Deven, Dr. Alan Forster, Dr. Laurie Mallery, Mr. Brad Neubauer, Dr. Lindsay Nicolle, and Dr. Yvonne Shevchuk.

Regrets:

None

Conflicts of Interest:

None

About this document

The information contained within this plain language version of the Canadian Expert Drug Advisory Committee (CEDAC) Recommendation about this drug is based on the information found within the corresponding technical version of the CEDAC Recommendation.

In making its recommendation, CEDAC considered the best clinical and pharmacoeconomic evidence available, up to that time. Health care professionals and those requiring more detailed information are advised to refer to the technical version available in the CDR Drug Database on the CADTH website (www.cadth.ca).

Background on CEDAC
CEDAC is a committee of the Canadian Agency for Drugs and Technologies in Health (CADTH). The Committee is made up of drug evaluation experts and public members. CEDAC provides recommendations about whether or not drugs should be listed for coverage through the participating publicly funded drug plans; however, the individual drug plans make their own decision about whether or not to cover a drug.

In making its recommendations, CEDAC decides if the drug under review ought to be covered by the participating public drug plans based on an evidence-informed review of the medication's effectiveness and safety, and based on an assessment of its cost-effectiveness in comparison with other available treatments. Patient information submitted by Canadian patient groups is included in the CDR reviews and used in the CEDAC deliberations.

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The manufacturer has reviewed this document and has not requested the deletion of any confidential information.