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# Phototherapy achieves significant cost savings by the delay of drug-based treatment in psoriasis

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## Abstract

**Background:** Although used for decades in psoriasis, access to phototherapy is becoming increasingly restricted. Besides patient inconvenience, this is in large part to do with a perception of “high cost.” We previously reported a comprehensive analysis of direct and indirect phototherapy treatment cost. However, no robust data exist on the actual savings associated with providing phototherapy in the treatment pathway. **Objectives:** To quantify the cost savings achieved by phototherapy by delaying alternative treatments.

**Methods:** Costs accruing through the UK-wide established treatment pathway with and without phototherapy were analysed. Direct and indirectly incurred drug treatment costs were calculated using drug tariff, laboratory cost, estate rates and clinic review costs. To enhance reliability, ranges of cost scenarios were calculated by varying parameters such as drug dosing.

**Results:** Medium annual cost savings per patient were £2200 [range: £1800-£2900] for NB-UVB, and £3700 [range: £2500-£5300] if both NB-UVB and PUVA courses were administered, respectively. As the provider treated  $656 \pm 76$  patients per year during the 6-year observational window, this amounted to savings of £Mio 2.4 [range: £Mio 1.6-£Mio 3.4], even excluding additional non-modelled drug-associated costs (eg diagnostics, adverse event management). Since we only consider cost savings by delay of drug treatment for the duration of phototherapy, drug price reductions through biosimilar introduction only have a small effect. We provide spreadsheets allowing adaptation cost savings projections by varying input variables.

**Conclusions:** Healthcare providers may achieve significant cost savings by implementing and/or widening access to phototherapy.

## KEYWORDS

health economics, NB-UVB, psoriasis, treatment pathways

## 1 | INTRODUCTION

Narrowband UVB (NB-UVB) treatment is effective in psoriasis as shown in numerous clinical trials,<sup>1-5</sup> as well as in a recent detailed real-world study which also showed that NB-UVB achieved

significant reduction in the use of steroid creams.<sup>6</sup> Although widely used, the treatment is not uniformly available and, indeed, access appears to be decreasing in the United States.<sup>7</sup> The main limitations of the treatment include inconvenience for patients, as the treatment requires three times weekly attendance, a perception of

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inferior efficacy (compared to biologics treatment), as well as expense. The latter is reflected in treatment guidelines, such as the most recently published British Association of Dermatology (BAD) guidelines which fail to even include NB-UVB in the biologic drug treatment pathway (recommendation R4<sup>8</sup>).

Since high-quality randomized trials are almost always funded by commercial sponsors, there is a relative dearth on both efficacy as well as economics data for phototherapy. In turn, this leads to underrepresentation or even exclusion from comparative treatment analyses aiming a synthesizing clinical trial data (eg Ref.<sup>9,10</sup>). To address this knowledge gap, we recently undertook detailed efficacy analysis under real-world conditions using methodology to minimize reporting and selection bias.<sup>12</sup> Using long-term comprehensive data from a healthcare provider in Scotland (NHS Tayside), we subsequently presented detailed cost figures, showing that this provider had incurred an average cost of £257 ± 64 per completed course over the course of 6 years.<sup>13</sup> This figure included both direct costs (job plan allocations, support staff), as well as an exhaustive list of indirect cost (pension contributions, administration, estate, depreciation, etc),<sup>13</sup> and data were obtained from four independently operated sites, thereby minimizing random effects attributable to site-specific cost efficiency.

In the present study, we extend this analysis towards modelling the savings generated for the healthcare provider through phototherapy by the concomitant delay and/or avoidance of alternative treatments. While large majority of health economics analysis focussing on high-cost treatments focusses on quality-of-life aspects in order to delineate relative cost-effectiveness, no data exist to assess the cost implications of inclusion or exclusion of phototherapy in the psoriasis treatment pathway. The present study addresses this question. By limiting modelling to the provider NHS Tayside as case study, we are able to reduce uncertainty associated with assumptions since we draw on detailed knowledge of direct cost incurred by phototherapy,<sup>13</sup> local treatment pathways, as well as known costs for drug-based treatments. Therefore, various parameters determining costing scenarios can be provided with a high degree of confidence. Despite using a single provider for modelling, the model as such is directly transferable to any other health economic context by adjusting the input variables to reflect local practice, respectively.

## 2 | METHODS

### 2.1 | Ethics statement

All data generated in this study were obtained in accordance with the Declaration of Helsinki and in compliance with local governance approval regulations (Caldicot number CSAppJF2101; the use of local Tayside phototherapy data was approved by the National Managed Clinical Network for Phototherapy, Photonet).

### 2.2 | NB-UVB treatment data

Numbers of treated patients were ascertained from the PhotoSys database, as previously described.<sup>6</sup> The cost of NB-UVB phototherapy

has been detailed recently.<sup>13</sup> The cost of one course of PUVA incurred by NHS Tayside has been calculated as follows: The number of staff hours, estate cost, technician, supervision, admin etc detailed in Reference<sup>13</sup> (Tables S2-S6 therein) is identical between NB-UVB and PUVA, respectively. PUVA incurs extra cost owing to the need for medication (8-methoxypsoralen tablets, 5-methoxypsoralen tablets, 8-MOP bath additive and 8-MOP gel, respectively), as well as different acquisition cost for UVA cabinets instead of UVB cabinets. The difference of these factors has previously been calculated to amount to an aggregate 3.3-fold higher cost of a PUVA treatment session compared to a NB-UVB session<sup>14</sup> (pp 85-89 therein). The overall cost of an entire course is furthermore directly proportional to the number of treatment sessions which average  $21.8 \pm 12.1$  for PUVA and  $27.2 \pm 13.7$  for NB-UVB across all NHS Tayside sites, respectively. Therefore, the cost of PUVA = [cost-NB-UVB] × 3.3 × [sessions-PUVA/sessionsNB-UVB] = £257 × 3.3 × 0.8 = £678.

### 2.3 | Cost factors in third-line treatment

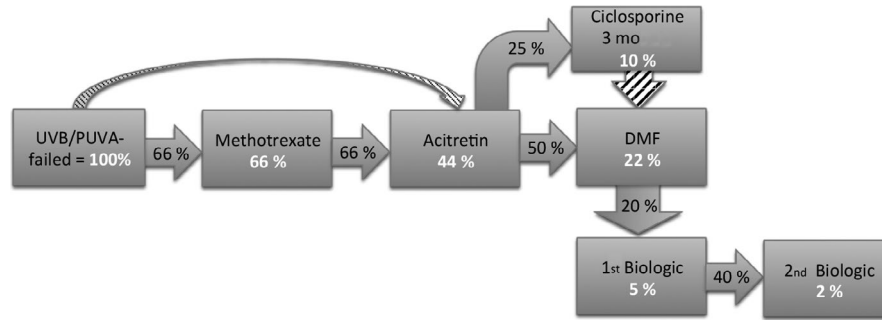
Laboratory monitoring cost incurred by the provider was supplied by NHS Tayside Blood Sciences and is detailed in their application to various drugs in Figure S1. The frequency of laboratory review was set at four times annually (low and medium) or six times annually (high). Cost for clinic review (Tayside Dermatology outpatient appointment) was supplied by NHS Tayside Directorate of Finance/Operational Unit as £167 (2018/19 rate), which is also in line with the Scottish average of £160. The figure represents full economic costing, including direct, indirect and overhead costs, respectively. The frequency of clinic review was set at 4 × per year, assuming (conservatively) steady state rather than the review frequency encountered during initial treatment induction.

### 2.4 | Non-modelled cost elements

A number of cost emerging with drug treatment were not modelled due to difficulty in establishing precise actual frequencies of episodes. These include (a) treatment failures occurring at less than months after drug initiation, thereby incurring added compound expenditures for more than one drug, (b) various/ additional monitoring required in a subset of patients only (eg tests in concurrent diabetes/ thyroid disease/ haemochromatosis), (c) unscheduled review and additional medication in response to adverse effects (eg significant nausea), (d) additional safety measures (vaccinations, chest x-ray according to local SOP). In addition, not modelled were (e) savings achieved through phototherapy replacing non-psoriasis conditions (eg urticaria, atopic dermatitis, prurigo, pruritus in the elderly).

### 2.5 | Drug costs

Costs for methotrexate, acitretin, ciclosporine were accessed through NHS drug tariff (<http://www.drugtariff.nhsbsa.nhs.uk>), respectively. Cost for dimethyl fumarate was accessed at <https://>



**FIGURE 1** Model used to calculate cost of treatment for psoriasis incurred by NHS Tayside in the absence of phototherapy. Numbers printed in white denote percentages of original “UVB/PUVA failed” patient pool. Numbers in black print denote fraction of the population-pool progressing from one to the next step in the treatment pathway, respectively. Dashed arrows denote alternate treatment pathways not included in the overall cost scenario. “DMF”—Dimethyl fumarate (brand name currently marketed in the UK “Skilarence”)

www.sps.nhs.uk/medicines/dimethyl-fumarate/. Cost for 1st and 2nd line Biologics is confidentially negotiated between NHS Tayside (and many other healthcare providers) and manufacturers, respectively. In order to achieve more realistic modelling, therefore, annual cost of £9000 and £11 000, respectively, was set for the medium cost scenario (see Results) but can be altered to reflect local cost figures.

### 3 | RESULTS

#### 3.1 | The post-phototherapy psoriasis treatment pathway

In order to delineate the cost for treatment of psoriasis that the provider would have incurred in the absence of phototherapy, we used the treatment pathway currently operative in NHS Tayside (Figure 1, see below for the details) which is similar to that applied across the UK and indeed worldwide.<sup>15</sup> NHS Tayside local practice includes consideration of PUVA in patients ahead of third-line systemic treatment. For that reason, we performed two analyses, one for NB-UVB only and another for a combination of NB-UVB/PUVA into a single phototherapy treatment (and cost) block into the model, respectively (Figure 1). In terms of specific drugs, their relative prevalence will vary regionally, as well as by older drugs being superseded by new drugs. For example, in the present case study, use of apremilast, licensed in 2015, is low and has further decreased in NHS Tayside (Financial year 2016/17:66 prescriptions/10,000 population; financial year 2017/18:54; data from HMUD available at ISD Scotland). In view of negligible cost implications of apremilast, apremilast has therefore been omitted from the NHS Tayside case study.

#### 3.2 | Basic modelling parameters

The basic assumption is simply that completion of a course of NB-UVB and PUVA, respectively, will delay the use of alternative treatment by 12 months. This is an extremely conservative assumption since many patients, who do well with phototherapy,

will in fact undergo repeat treatment for years before moving on to drug treatment. In addition, we have previously shown that NB-UVB produces good clinical outcomes and sustained decrease in corticosteroid treatment for at least 12 months after treatment in the majority of patients.<sup>12</sup> Therefore, the cost difference for one course of NB-UVB will be the delay of subsequent treatments by 1 year.

#### 3.3 | Modelling phototherapy-based delay of drug treatment

For any given financial year, therefore, the difference in cost between the current practice and the alternative scenario is (Equation 1):

$$\text{Cost difference} = [\text{Cost (NB - UVB)} + \text{Cost (PUVA)} + \text{Review}] \times 1.2 - 2 \times \sum (P_{\text{Drug}} \times \text{cost}_{\text{Drug}}) \quad (1)$$

“Review” refers to a clinician review appointment which is scheduled between NB-UVB and PUVA courses, respectively.  $P$  = probability (termed “likelihood” in Table 1) of drug usage given as % (representing the relative discount for each drug in the treatment pathway) in Figure 1 (see Table 1) for the successive pathway elements methotrexate, ciclosporine, dimethyl fumarate, 1st line biologic, 2nd line biologic, respectively.  $P$  incorporates the 3% discount rate commonly applied in cost-effectiveness modelling,<sup>16</sup> reflected in successively lower values along the treatment pathway. Importantly, even for the treatment directly replacing phototherapy,  $P$  was set to a conservative value of 66% to account for the fact that, in practice, a number of patients do not opt for any alternative/additional treatments for a variety of reasons.

Any cost savings for each treatment step will not be realized instantaneously, but at various subsequent time points, wherefore Equation 1 represents cumulative savings (effects of inflation and varying interest rates are ignored). The cost for each treatment step was set for a 12-month treatment window, which is also conservative, since most treatments are dispensed for longer (eg we have previously reported median treatment duration of methotrexate as significantly longer than that<sup>17</sup>). This setting allows calculation of

	Likelihood of use (%) <sup>b</sup>			Cost displaced per patient by UVB (£) <sup>c</sup>		
	Low	Medium	High <sup>d</sup>	Low	Medium	High
Methotrexate	50	66	70	349	461	492
Acitretin	30	40	44	221	303	337
Ciclosporine	5	10	15	38	77	141
Fumarate	18	22	25	831	916	1,138
1st biologic	3	5	7	292	487	682
2nd biologic	1	2	4	117	234	469

**TABLE 1** Drug-associated costs displaced by phototherapy<sup>a</sup>

<sup>a</sup>The table details costs (given in £) arising as a result of the drug tariff-based or listed drug prices (see Figure S1) for each drug at the assumed annual dose requirement detailed in Figures S1, F2.

<sup>b</sup>The costs shown in the table only detail costs accruing during the year of treatment displaced by phototherapy. Therefore, the theoretical treatment cost, for example for a first biologic, only occurs with a 3%-7% likelihood, respectively. This likelihood ("discount") has been applied to the annual treatment cost to yield the net cost displaced by phototherapy treatment.

<sup>c</sup>The cost accruing for each drug includes clinic review (4 per year for "low/medium," 6 per year for "high") as well as laboratory cost specific for each drug (see Figure S1).

<sup>d</sup>The likelihood of use and selection of drugs (eg a medium scenario of two-thirds of patients not offered phototherapy, to be offered methotrexate) is based on known figures in NHS Tayside but can be adapted to any other economical context.

cost savings incurred by delay of the subsequent treatment step by one financial year.

### 3.4 | Actual versus theoretical phototherapy treatment cost

In clinical practice, a subset of patients may in fact undergo subsequent courses of either UVB or PUVA in less than 12 months, thereby increasing the cost incurred. For NHS Tayside, this factor can be readily quantified. Thus, across the previous six financial years an average of  $656 \pm 76$  patients underwent  $788 \pm 98$  courses of phototherapy (either UVB or PUVA). Therefore, the actual cost incurred for the provider NHS Tayside has in fact been  $788/656 = 1.20$  times the cost of one treatment course, which has accordingly incorporated as correction factor into Equation 1.

### 3.5 | Actual- versus Qaly-based costs

For high-cost drug treatment, most healthcare providers require objective outcome measures, most commonly the so-called PASI or IGA indices. A drop below PASI50 (that is: 50% worsening from baseline) is then used to trigger moving to the next treatment in the pathway. These scores are not commonly recorded for traditional treatments including phototherapy, and we therefore have refrained from incorporating assumptions. However, it is worth noting that we have previously shown that the degree of disease control by NB-UVB is comparable to that achieved by methotrexate under real-world conditions,<sup>6,17,18</sup> and that response rates are similar to clinical study results reported for apremilast, DMF and etanercept.<sup>19-21</sup> Although the subjectively experienced degree of disease control, that is the "health benefit," is likely higher using a biologic drug, it is therefore

reasonable to assume that any given patient will not continue phototherapy in the absence of a subjective benefit justifying treatment attendance.

### 3.6 | Modelling of NB-UVB-only cost differences

Since many providers may only offer NB-UVB treatment, it is instructive to calculate hypothetical cost differences associated only with NB-UVB. In this alternative scenario, the delay in the use of third-line treatment is shortened from 24 to 12 months and no CR review is required prior to PUVA, yielding Equation 2:

$$\text{Cost difference} = [\text{Cost (NB - UVB)}] \times 1.2 - \sum (P_{\text{Drug}} \times \text{cost}_{\text{Drug}}) \quad (2)$$

### 3.7 | Modelling the likelihood of alternative treatments

For the calculation of cost savings by NHS Tayside, the most frequently used dose ranges are summarized in Table 2. The likelihood for alternative treatments (Table 1) was set based on the economical impact at the time of initiation of NB-UVB. Thus, biologics treatments, for example, although expensive, do not account for a large proportion of cost savings in this particular scenario, since their position in the treatment pathway is further removed in time. However, all parameters, including drugs, assumed treatment duration, dosing, numbers of patients treated can be adapted and altered to reflect practice operative in other healthcare providers (Figure S1).

### 3.8 | Phototherapy-associated cost savings

The results pertinent for NHS Tayside are summarized in Table 3 with exact data sources provided in Figures S1 and S2. The data indicate

that the provider would have incurred significant additional cost in the absence of either combined phototherapy (NB-UVB + PUVA) or NB-UVB only. The numbers in the “medium” scenario reflect actual savings most closely based on local treatment patterns (including both retention time and dosing ranges) and costings, including staff-related factors. Even when assuming a 50% discounted cost for clinic review appointments (ie allowing that the actual cost incurred is only half to that stated by the provider), savings remain significant (Table 3, bottom two lines). Furthermore, the data shown represent

a conservative estimate as follows: First, a number of yet additional cost factors associated with drug treatment were not added in order to minimize assumption based uncertainty (see Methods, section “non-modelled cost elements”). Second, a significant fraction of patients on NB-UVB achieves retention times for several years before (if ever) requiring third-line drug treatment, adding further savings. Importantly, due to the discounting incorporated, any change in pricing in biologics (eg biosimilar replacement) would only have a minor impact on the savings.

**TABLE 2** Drug doses and fixed drug prices used to calculate cost savings associated with displacement of drug treatment by phototherapy (UVB/PUVA)<sup>a</sup>

Treatment scenario <sup>b,g</sup>	Low <sup>b,c</sup>	Medium	High
Methotrexate	12.5 mg	15 mg	20 mg
Acitretin	10 mg	25 mg	30 mg
Ciclosporine	200 mg <sup>f</sup>	200 mg	300 mg
Dimethyl fumarate	4 tabs <sup>d</sup>	4.5 tabs	5 tabs
1st line biologic	£7000 <sup>e</sup>	£9000	£9000
2nd line biologic	£9000 <sup>e</sup>	£11 000	£11 000

<sup>a</sup>For details see text; the “medium savings” scenario is represented in Figure 1. Treatment likelihoods and dosing are modelled according to NHS Tayside local practice.

<sup>b</sup>Scenarios calculated using Equation 1 and 2, respectively, see Figure S1.

<sup>c</sup>Dose is daily except for methotrexate (weekly) and biologics (annual flat cost rate). In accordance with common usage, ciclosporine dosage is assumed 6 mo for medium/high scenarios and 3 mo for low scenario, respectively.

<sup>d</sup>Long-term average daily steady-state dosing; initial dose induction is not modelled.

<sup>e</sup>For most providers, including NHS Tayside, confidential flat annual rates are negotiated with suppliers. Cost figures shown represent annual cost likely incurred per patient.

<sup>f</sup>Low scenario ignores initial high-frequency laboratory for up-dosing.

<sup>g</sup>Low and medium scenarios assume steady-state review; high scenario incorporates higher frequency due to adverse effects and/or need to change treatment.

## 4 | DISCUSSION

### 4.1 | Modelling cost savings in pathway-organized medical care

When assessing cost-effectiveness, models are commonly applied to account for variable health benefits afforded by alternative or sequential health interventions. For the chronic condition psoriasis, for example, Health Technology Appraisals by the UK economics watch dog NICE commonly assume greater health benefit for biologic drugs, impacting on a “value for money” type of approach for these high-cost drugs. By contrast, we here exploit detailed knowledge of the response of psoriasis to phototherapy as well as comparator treatments<sup>6,17-21</sup> in order to simplify modelling by aligning it with clinical practice: regardless of a specific PASI improvement, a given patient is likely to progress along the treatment pathway if a subjectively “insufficient” experienced level of disease control is encountered, as shown previously in detail for methotrexate.<sup>17</sup> We therefore also disregard potential savings by reduced requirement for steroid cream treatment, which we have previously shown for NB-UVB,<sup>6</sup> as this specific is likely be comparable for any effective intervention. Because of conservative discounting, the overall contribution of both 1st and 2nd line biologic combined only amounts to 30% of the overall savings (Supporting Excel files 1, 2) obviating any further need to adjust for greater health benefit. Importantly, discounting means that even changing

**TABLE 3** Cost savings associated with delay/avoidance of third-line treatment by NHS Tayside.<sup>a</sup>

		Medium	Range	
		Cost (£)	Low	High
Per Patient	NB-UVB + PUVA	3727	2469	5284
For all patients <sup>b</sup>		Mio 2.44	Mio 1.62	Mio 3.47
Per Patient	NB-UVB only <sup>c</sup>	2169	1849	2948
For all patients		Mio 1.42	Mio 1.21	Mio 1.93
Per Patient	NB-UVB discounted <sup>d</sup>	1685	1479	2397
For all patients		Mio 1.11	0.97	1.57

<sup>a</sup>Data shown represent net savings hypothetically achieved by NHS Tayside, using input variables detailed in Table 2 and Equation 1 (for details see Supporting Excel file 1).

<sup>b</sup>Data shown for n = 656 ± 76 of psoriasis patient treated on average across NHS Tayside during the previous three financial years.

<sup>c</sup>For NB-UVB only, the cost of PUVA was omitted and the delay in third-line treatment was shortened from 24 to 12 mo. Details are shown in Supporting Excel file 2.

<sup>d</sup>Assuming a fifty per cent discounted cost of Clinician Review from fully economical cost.



the drug cost from £9000 to £3000, as currently the case after biosimilar introduction, only has a minor impact on the overall cost savings. Since the model shown in Figure 1 in fact represents the actual, not hypothetical, post-phototherapy treatment pathway, the cost figures summarized in Table 3 represent a rather realistic model scenario.

## 4.2 | Limitations

Our study has two main limitations. First, we do not consider patient-incurred cost, in particular absence from work place enforced by treatment attendance. In this regard, it should be noted that many providers attempt to minimize such cost by offering out-of-hours access, home treatment, or hospital-based self-treatment NB-UVB units,<sup>22,23</sup> requiring more differentiated modelling of this factor. One intriguing aspect emerging from the current data, however, is that the potential savings for the provider are likely substantial enough to warrant incentivizing patients to utilize phototherapy by integration of fractional savings achieved into health plan contributions. A second major limitation is that quality-of-life cost implications were not modelled due to lack of data.

In terms of the dominant cost factor, staff time, we previously detailed direct and indirect staff hours required to supply NB-UVB, facilitating more predictive model building.<sup>6</sup> The key factor, identified therein, driving cost-effectiveness was low actual hands-on time, requiring only  $0.45 \pm 0.14$  staff hours (including both direct and support staff roles) per completed NB-UVB course. The obvious fundamental difference to drug-based treatment is that costs decrease with increase of patients treated, which is the direct opposite of pharmacotherapy, as recently reported for Spain.<sup>24</sup>

The considerable cost savings potential of phototherapy demonstrated here is of particular relevance given huge financial pressures placed on providers. In that regard, it is notable that NB-UVB is appropriate as long-term intercurrent treatment and can be administered in clinical settings often limiting for drug treatment, such as late pregnancy, anticipated family planning, or hepatic dysfunction. Although we have shown that even for treatment sites with small patient throughput (around 100 courses per year) cumulative cost are similar to larger sites,<sup>6</sup> the cost savings potential is of particular relevance to large providers.

## 4.3 | NB-UVB and phototherapy in psoriasis treatment pathways

The cost savings potential in conjunction with established efficacy begs the question as to why this treatment is not more widely made available. For example, the current British Association of Dermatologist (BAD) guidelines do not even consider NB-UVB on the pathway to Biologics treatment.<sup>8</sup> Similarly, many guidelines consider NB-UVB as a treatment option but not one which should be actively encouraged. The current guidelines of the US American Academy of Dermatology also do not even suggest that NB-UVB ought to be actively considered before moving to systemic treatments. Likewise,

the National Psoriasis Foundation opposes any effort to apply cost-effective treatments ahead of more expensive alternatives (which the NPF terms “step therapy”), lobbying actively for legislation to ban this approach.<sup>25</sup> In some cases, safety concerns are cited even in the absence of data. Specifically, in terms of safety, available studies have not identified any skin cancer risks for NB-UVB.<sup>26-30</sup> In this regard, we are currently analysing data on >50 000 individual patients treated with NB-UVB throughout Scotland since the mid-1980s. Preliminary results do not indicate increased incidence in cancer levels in this cohort (RD, manuscript in preparation). We anticipate that the data presented here will encourage providers to re-evaluate phototherapy, and in particular NB-UVB, within psoriasis treatment pathways.

Finally, phototherapy is also used for many other diseases, with good controlled study evidence supporting efficacy in eczema and chronic urticaria,<sup>31-33</sup> offering further potential economical synergy.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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