



## Translating Patient Value to Commercial Value in the Development of Digitally Measured Nocturnal Scratch

### Objective

Atopic dermatitis has a substantial impact on patients' day-to-day wellbeing. When considering therapies to treat atopic dermatitis, payers and health care providers want assurances that therapies yield patient-relevant improvements in conditions. However, existing measures in atopic dermatitis trials do not capture a crucial dimension of the patient experience: scratch. Patients report that the discomfort caused by scratching is an important and burdensome symptom of atopic dermatitis (Blome et al., 2016), but measures of scratch are rarely incorporated into atopic dermatitis trials. Accordingly, drug developers are working to use digital technologies to measure “nocturnal scratch,” scratching that occurs while patients are asleep, with the ultimate goal of deploying digitally measured nocturnal scratch as an endpoint in clinical trials.

While digitally measured nocturnal scratch has the potential to offer a more complete assessment of the lived experience for patients with atopic dermatitis, developing and deploying a new endpoint is time-consuming and costly. This document provides recommendations specifically targeted toward increasing the commercial value of digitally measured nocturnal scratch by increasing **payer acceptance** of the measure. DiMe and our partners are also currently [engaged in complimentary work](#) targeted toward increasing regulatory acceptance of digitally measured nocturnal scratch and other digital endpoints.

### Key Insights

- Drug developers should engage with patients to collect evidence that nocturnal scratch is relevant to their experience with atopic dermatitis. This engagement means drug developers should demonstrate that nocturnal scratch offers unique information about disease burden in atopic dermatitis beyond existing visual assessments and patient-reported outcomes.
- Payers will be more willing to accept digital nocturnal scratch if drug developers can show that nocturnal scratch is correlated with existing

endpoints and payer-relevant outcomes, including health care utilization and patient quality of life.

- Whether digitally measured nocturnal scratch is developed for use in clinical practice will affect its value as an endpoint. Payers are more likely to value digitally measured nocturnal scratch if they can track it in their patient populations in real time, but payers may also tie utilization management to digital nocturnal scratch thresholds and limit patient access to treatments.

## Background

### Digitally Measured Nocturnal Scratch as an Endpoint in Atopic Dermatitis Trials

Atopic dermatitis (AD), also known as atopic eczema, is a chronic inflammatory skin disease affecting both adults and children. In the United States, atopic dermatitis affects 7% to 10% of adults (Silverberg et al., 2013; Chiesa Fuxench et al., 2019) and 13% to 15% of children (Silverberg et al., 2021; Fu et al., 2014). The estimated prevalence is similar in other developed countries (Cork et al., 2020; Theodosiou et al., 2020). The features of AD include acute, subacute, or chronic eczematous skin lesions represented by skin redness, thickness, and lichenification. Patients frequently report that scratching brought on by AD is painful and disrupts sleep, while changes in appearance caused by AD can cause embarrassment and depression (Blome et al., 2016). Atopic dermatitis is associated with higher comorbidity burdens (Shrestha et al., 2017), development of anxiety and depression (Schonmann et al., 2020), increased work absenteeism among adults (Silverberg et al., 2015), increased school absenteeism among children (Cheng et al., 2021), and greater health care use and spending (Shrestha et al., 2017; Smith Begolka et al., 2021).

Digitally measured nocturnal scratch uses digital technologies to assess whether patients scratch themselves during sleep. Digitally measured nocturnal scratch is intended to measure symptoms of atopic dermatitis that have a large impact on patient wellbeing: scratching and sleep disruptions. Multiple modalities of digitally measured nocturnal scratch are being developed, including wearable accelerometers and wireless monitors. DiMe is currently working with multiple stakeholder groups in a pre-competitive space to create a standardized ontology that defines key terminology (e.g., when does sleep start and end) and units of measurement such that drug developers can consistently deploy a uniform digital measure of nocturnal scratch as an outcome in clinical trials.

Digitally measured nocturnal scratch has several potential advantages relative to existing outcomes. Unlike existing primary outcomes, digitally measured nocturnal scratch directly captures scratch. This information is collected continuously, rather than in discrete snapshots, allowing for more comprehensive assessment of outcomes in a disease characterized by flares and relapses. And in contrast to existing secondary outcomes reliant on patient recall, the measure is objective and not subject to potential environmental confounders. However, work is still needed to

standardize digitally measured nocturnal scratch and communicate the value of the measure to payers.

### 3Ps for Digital Endpoint Value

DiMe and partners have developed the [3Ps of Digital Endpoint Value toolkit](#), a set of resources for developing and deploying digital endpoints as value evidence in reimbursement decisions. The toolkit helps drug developers create integrated evidence plans that meet the requirements of various stakeholders needed to secure regulatory approval and payer coverage of new therapies.



The 3Ps framework identifies three stakeholder groups critical to acceptance of new endpoints. First, **pharmaceutical companies** must develop evidence that demonstrates the value of a new endpoint across the total lifecycle of a product, from clinical trials to patient adoption. Second, **payers** must weigh relative clinical benefits against financial burdens placed on their enrollees as new therapies are covered. Third and finally, **patients** must be at the center of any evidence development process; developing evidence to please regulators and payers does little good if patients are not convinced that a product is worthwhile.

Drug developers can use the 3Ps framework to guide evidence development in order to satisfy the diverse stakeholders that will ultimately determine the success of digitally measured nocturnal scratch.

## 3P Considerations for Digitally Measured Nocturnal Scratch

### For Patients

#### *Relevance of Measure*

Patient relevance is crucial when developing any new measure. Endpoints must capture an important aspect of a patient's disease, and drug developers must perform the necessary methodological work to establish minimal clinically important differences in endpoints.

In the context of nocturnal scratch, drug developers will need to demonstrate that scratch is a patient-relevant feature of AD, independent from burden of itch and skin appearance. If drug developers do not meaningfully engage patients to collect evidence on the unique burden that scratching places on patients, payers may believe that digitally measured nocturnal scratch does not offer meaningful additional information beyond what is already captured in existing endpoints. If drug developers can demonstrate that scratch is conceptually distinct from itch (preferably through qualitative research published in peer-reviewed journals), payers will be more likely to consider digitally measured nocturnal scratch in coverage decisions. In other workstreams, DiMe has conducted qualitative interviews providing preliminary evidence documenting the conceptual importance of scratch and its connection to meaningful aspects of patients' lives.

*“When looking at new endpoints within trials, we’re asking: is this clinically significant for patients? Because sometimes we see evidence included in the medication approvals that may not translate into clinical significance for the patients in terms of daily living or experience.”*

*- US Integrated Delivery Network Expert*

### **Trial Representativeness of Population**

Digital endpoints may raise issues of patient representation in clinical trials. If the digital tools used to measure nocturnal scratch are dependent on access to specific technologies or reliable internet service, patient enrollment in trials with digitally measured nocturnal scratch may not be reflective of target populations for new therapies. This concern may be especially relevant to the US population of patients with atopic dermatitis, given that approximately 20% of office visits for atopic dermatitis are covered by Medicaid or other state-based programs<sup>1</sup>, while nearly 25% of Medicaid enrollees in the US have limited computer or internet access (Corallo, 2021).

At the same time, digitally measured nocturnal scratch also has the potential to improve representation in clinical trials. Typical visual assessments used in clinical trials require patients to visit a clinician once a week or once every other week, while patient-reported outcomes require patients to regularly document their disease progression; both may represent a barrier to patient participation in trials. In contrast, digitally measured nocturnal scratch is by definition a passively collected measure. Patients may be more willing to enroll in trials or less likely to drop out of trials with nocturnal scratch as an endpoint.

Ultimately, trials employing digitally measured nocturnal scratch should be no less representative of patient populations than existing trials. Drug developers might consider offering Wi-Fi hotspot devices or pre-paid data plans for cellular networks in addition to scratch sensors if study participation is dependent on reliable internet access.

### **Key Action Items on Patient Relevance & Representation**

- Conduct qualitative surveys with patients to demonstrate that scratch is a uniquely burdensome symptom of atopic dermatitis, distinct from itch and skin appearance
- Establish a minimal clinically important difference for digitally measured nocturnal scratch.



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<sup>1</sup> Derived from analysis of 2018 National Ambulatory Medical Care Survey (NAMCS)

- Provide technological resources (e.g., pre-paid data plans) to reduce patient barriers to participating in trials with digitally measured nocturnal scratch as an outcome.

## **For Pharma**

### **Comparing Nocturnal Scratch to Existing Measures**

Drug developers will need to demonstrate how digitally measured nocturnal scratch relates to current measures of efficacy. Payers will be skeptical of digitally measured nocturnal scratch if the measure is not significantly correlated with existing measures such as the Eczema Area and Severity Index or the Pruritus Numerical Rating Scale. At the same time, the goal of developing digital nocturnal scratch is to offer novel information about disease severity beyond what existing measures already capture. As such, drug developers should also consider demonstrating how the measure relates to more general measures used outside the atopic dermatitis space. Payers may be more likely to accept digitally measured nocturnal scratch if reductions in nocturnal scratching lead to improvements in existing quality of life measures that payers may be familiar with, such as the EuroQol-5D or the Dermatology Life Quality Index. Dimension reduction statistical analysis techniques may help clarify how digitally measured nocturnal scratch relates to existing atopic dermatitis-specific measures versus general quality of life measures.

### **Comparing Nocturnal Scratch Performance Across Therapies**

Payers are generally more likely to consider new endpoints if evidence is presented in a comparative framework, showing that one drug is superior to another when using a new endpoint. There may be a “first mover” disadvantage to new endpoint development, where a certain number of drug developers need to deploy an endpoint before that endpoint is meaningfully considered when payers make coverage decisions.

*“If only one company would come up with a new measure that shows the drug is great - and there was no other general validation or external adoption of this measure - it would not be meaningful. If there's literature and a lot of advocacy around the measure, discussion in specialty circles, and validation in other sources - we'd support using this endpoint. It would help P&T committees understand the impact on the patients.”*

*- US Integrated Delivery Network Expert*

Fortunately, any first mover disadvantage is less applicable to digitally measured nocturnal scratch specifically, largely due to ongoing work by DiMe and our partners. In other workstreams, DiMe is working with drug developers and regulatory experts to create a standardized ontology that defines key terminology and units of measurement such that drug developers can consistently deploy a uniform digital measure of nocturnal scratch as an outcome in clinical trials. Payer experts have

commended DiMe and our partners for this work and stated that payers would be more likely to consider early evidence derived from digitally measured nocturnal scratch, given that diverse stakeholders were involved in developing and validating the measure in a pre-competitive environment.

## Key Action Items on Pharma Evidence Development & Communication



- Develop evidence showing that digitally measuring nocturnal scratch is correlated with existing measures used in atopic dermatitis trials.
- Demonstrate that improvements in digitally measured nocturnal scratch lead to improvements in both general and dermatology-specific quality of life measures.
- Ground discussion with payers about evidence derived from digitally measured nocturnal scratch in the pre-competitive measure development work by DiMe and partners.

## For Payers

### Value of Objective Evidence

One potential advantage of digitally measured nocturnal scratch relative to other measures of efficacy is that digital nocturnal scratch is objective. European payers may be especially receptive to the objective nature of digitally measured nocturnal scratch, given the use of cost-effectiveness analysis and other decision analysis techniques employed by health technology assessment bodies. Even if digitally measured nocturnal scratch did not offer any meaningfully different information relative to other measures, simply using an additional modality to measure disease severity would boost payers' confidence that products worked as intended. Health technology assessment bodies may reward this increased certainty in treatment effectiveness with higher prices in European markets. However, it should be cautioned that Europe is not homogenous in how it approaches drug coverage, and the relationship between certainty in treatment effectiveness and prices is likely not universally true across Europe.

*“Digital measurement can be more granular and demonstrate long-term reductions in scratch. The HTAs would be more likely to accept more robust documentation for a drug with digital evidence, reducing the degree of uncertainty in decision making. In the EU, different countries have different frameworks for decision making, but usually it's a good thing to reduce the uncertainty of the decision.”*

*- European Payer*

### ***Tying New Outcomes to Cost Considerations***

One of the largest factors in determining US payers' acceptance of a new endpoint is cost. While US payers might appreciate the clinical significance of new endpoints, they are far more likely to consider an endpoint if drug developers show that changes in an endpoint lead to changes in utilization and spending. Ideally, drug manufacturers could demonstrate that reductions in nocturnal scratch cause reductions in overall health care spending or utilization. Developers might also consider linking nocturnal scratch to work absenteeism; while large national insurers may not consider missed days of work when making coverage decisions, this measure could be relevant to large self-insured employers. Prior studies have found that unmanaged atopic dermatitis is associated with more health care utilization, work absenteeism, and health care spending (Shrestha et al., 2017; Silverberg et al., 2015; Smith Begolka et al., 2021), suggesting that linking digital nocturnal scratch to health care costs may be feasible. Drug developers might specifically explore the relationship between the measure and spending on topical therapies to treat skin lesions or psychiatric costs related to sleep and mental health concerns.

*"The payers want the patients to do well, but show the payers that this disease costs more than they think. Prove that, and you'll have a winner on your hands."*

*- US National Payer*

### ***Considerations for Bringing Digital Nocturnal Scratch into Clinical Care***

Payers' acceptance of digital endpoints may be partially tied to their potential applications in clinical practice. Integrated delivery networks in particular value the ability to directly track the outcomes of patients initiating new therapies. As such, if a manufacturer were able to demonstrate that a drug was effective according to digitally measured nocturnal scratch, and payers were able to monitor patients' outcomes with digitally measured nocturnal scratch, then the measure would be more meaningful and useful from a payer perspective.

At the same time, moving digital endpoints into clinic use may not be entirely beneficial for drug manufacturers. Payers could hypothetically "weaponize" digital measures and use them to justify overly restrictive utilization management practices, where patients would not have access to certain therapies unless their digitally measured scratch exceeded some threshold.

The evidence needed to demonstrate that digitally measured nocturnal scratch is appropriate for clinical use will differ from the evidence needed to establish digital nocturnal scratch as an endpoint in clinical trials. Manufacturers will need to weigh the cost of developing this additional evidence against potential increases in coverage facilitated by greater acceptance of digitally measured nocturnal scratch, along with potential reductions in utilization due to new utilization management practices.

## Key Action Items on Payer Considerations

- Demonstrate that improvements in digitally measured nocturnal scratch lead to reductions in health care utilization and spending.
- Weigh whether the benefits of introducing digitally measured nocturnal scratch into clinical practice are outweighed by the potential development of new utilization management tied to the measure.



## Conclusion

In order for payers to accept digital nocturnal scratch, drug developers must demonstrate that digitally measured nocturnal scratch is relevant to patients and related to payer-relevant outcomes. Key action items include:

- Conducting qualitative studies to demonstrate that the concept of scratch is relevant to patients and distinct from skin appearance and itch (*note: DiMe and the project partners are running such a study as part of the [Nocturnal Scratch Project](#)*)
- Validating digitally measured nocturnal scratch by comparing it to existing measures used in atopic dermatitis trials
- Tying digitally measured nocturnal scratch to payer-relevant outcomes including health care utilization and patient quality of life

The [3Ps toolkit](#) has resources for drug developers to develop this evidence, such that digitally measured nocturnal scratch can satisfy the demands of regulators, payers, and patients alike. Doing so can empower drug developers to bring commercially successful products to market that improve the day-to-day experience of patients with atopic dermatitis.



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