Clinical Outcome Assessments (COA) Qualification Program
DDT COA #000101: Patient-Reported Symptoms and Impacts of Alopecia Areata
Letter of Intent

Administrative Structure:

Description of the submitter including, but not limited to, principal investigator(s), working group member(s), institutions, and contact information not contained within the cover letter.

The National Alopecia Areata Foundation (NAAF) is collaborating with a number of pharmaceutical companies to form a Consortium with the intent of developing a patient-centered and patient-reported outcome (PRO) measure for alopecia areata (AA) for qualification as a Drug Development Tool (DDT). NAAF, in collaboration with Evidera, a leading Health Economics Outcomes Research organization, and other key opinion leaders in PRO measurement, AA research and treatment, and engagement of patients in patient-focused drug development, will work with industry partners, patients and other stakeholders to develop the instrument. The purpose of this consortium is to develop a single, evidence-based PRO instrument that will support the evaluation of treatment benefit in terms of health-related quality of life (HRQol) in medical product clinical trials for patients with AA, with the intention to support product approval and labeling, health technology assessment (HTA), reimbursement, and patient care.

NAAF's role is to serve as a recognized and respected neutral third party that provides overall administrative support and oversight for the management of the Consortium to establish a PRO instrument to benefit all stakeholders and the public health. The Working Group Members named in this proposal are experts in the fields of: PRO measurement; validation studies; questionnaire development; AA research and treatment; trial management and implementation; and engagement of patients in patient-focused drug development.

The administrative structure for the NAAF PRO Consortium is as follows:

Working Group Members

Gale Harding, Evidera	Co-Principle Investigator; PRO Methodologist
Natasha Mesinkovska, UC Irvine	Co-Principle Investigator; Alopecia Areata KOL
Abby Ellison, National Alopecia Areata Foundation	Patient Advocate
Stephen Chavez, Health Advocacy Partners	Patient Engagement/PFDD KOL
Nancy Kline Leidy, Evidera	Peer Reviewer
To Be Assigned	FDA COA Staff Representative
To Be Assigned	Industry Partner Representative(s)
To Be Assigned	Patient Representative

External Advisors

Laurie Burke, LORA Group, LLC
Eleanor Perfetto, National Health Council

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Concept(s) of Interest (COI) for Meaningful Treatment Benefit:

A description of the meaningful aspect of patient experience that will represent the intended benefit of treatment (e.g., presence/severity of symptoms, limitations in performance of daily activities)

This DDT described in this LOI will be used to measure underlying concepts related to hair loss and regrowth deemed important by patients with AA.

Based on a review of the literature and initial qualitative interviews with AA patients, important concepts are anticipated to include, but not necessarily limited to, amount and area/location of hair coverage, type and quality of hair regrowth, and impact on daily activities, well-being; and psychological and social functioning.

Provide a conceptual framework for the COA(s)

The conceptual framework will be developed based on the findings from concept elicitation interviews and item generation. The draft conceptual framework for the PRO will be presented in diagram format (as recommended by the FDA [2009]), and will link the individual items with hypothesized PRO domains and overall summary scores (if applicable) (FDA 2009). This conceptual framework will be considered a draft, based on the initial item pool, and will be refined and finalized as the PRO is modified and finalized after the next phase of work (cognitive interviews) to confirm the content of the PRO.

COU for COA Qualification:

Targeted study population including a definition of the disease and selection criteria for clinical trials (e.g., baseline symptom severity, patient demographics, comorbidities, language/culture groups)

The AA PRO instrument will be used in clinical trials evaluating treatment efficacy in adult patients, 18 years of age and older, diagnosed with alopecia areata with at least ≥ 25% hair loss on scalp and current episode of hair loss lasting at least six months.

It should be noted that during the qualitative phase of instrument development, information from adolescents (ages 12–17 years) will be elicited during concept elicitation interviews. Findings will be used to explore if the important underlying concepts are the same (or different) between the two age groups and whether a single "core" instrument would be appropriate for both adolescents and adults.

Targeted study design and statistical analysis plan (includes the role of the planned COA in future drug development clinical trials, including the planned set of primary and secondary endpoints with hierarchy, if appropriate)

The PRO scale scores will be used as key secondary or secondary endpoints, with results used to support any or all of the following target claims. The selection, positioning, and precise wording will be refined by the sponsors in keeping with their proposed target product profiles and in consultation with FDA, as appropriate. The name of the instrument may be included in the claim, at the discretion of the FDA.

1) Patients treated with TXa compared to placebo reported improvements in the severity of alopecia areata at (time point).
2) Patients treated with TXa compared to placebo reported improvements in the amount of hair coverage on their scalp at (time point).

3) Patients treated with TXa compared to placebo reported improvements in the amount of hair regrowth on their scalp at (time point).
4) Patients treated with TXa compared to placebo reported improvements in the quality of hair regrowth on their scalp at (time point).
5) Patients treated with TXa compared to placebo reported improvement in (daily impact of alopecia areata) at (time point).

Under the proposed framework, the Severity of Alopecia Tool (SALT or SALT II) will continue to serve as the primary clinician-reported endpoint in clinical trials. PRO measure scores will serve as key secondary, or secondary endpoints for proposed United States Prescribing Information (USPI). Sample endpoint models are provided in Tables 1 and 2.

Table 1. Sample Endpoint Model A

Concept	Measure	Endpoint Type
Change from baseline of Severity of Alopecia Tool (SALT) [percent] scalp hair loss and [percent] regrowth score	SALT or SALT II	Primary
Change from baseline in patients' perceptions of symptom severity and interference of AA in daily functioning	PRO measure	Key Secondary

Table 2. Sample Endpoint Model B

Concept	Measure	Endpoint Type
Change from baseline of Severity of Alopecia Tool (SALT) [percent] scalp hair loss and [percent] regrowth score	SALT or SALT II	Primary
Change from baseline in patients' perceptions of symptom severity and interference of AA in daily functioning	PRO measure	Secondary

Applicable study settings for future clinical trials

- ***Geographic location with language/culture groups***
- ***Other study setting specifics (e.g., inpatient versus outpatient)***

The AA PRO instrument will be developed in English and intended for use in clinical trials evaluating treatment efficacy in outpatients with AA who adequately represent the targeted study population as described in Section 3A. Efforts will be made to recruit an even distribution of males to females within the target age ranges (adolescents and adults) as well as soft targets with regards to obtaining a range in terms of race and ethnicity, AA severity (i.e., amount of hair loss) and time since diagnosis. Under the NAAF PRO Consortium initiative—a multi-sponsor project involving multi-disciplinary experts— efforts will be made to ensure the instrument is developed appropriately for use in multinational clinical trials and words and phrases in US English can be translated for use in multiple language and culture groups.

COA Type: Patient Reported Outcome (PRO)