A multicenter, prospective, observational real-world study evaluating the efficacy and safety of Aximexine sustained-release capsules in the treatment of active axial spondyloarthritis (axSpA)

Statistical Analysis Plan

Version number: 1.0

Version date: March 5th, 2026

1. Objective

To evaluate the efficacy and safety of acemetacin sustained-release capsules (90 mg once daily for 4 weeks) in patients with active axial spondyloarthritis (axSpA) in a real-world clinical setting.

2. Study Endpoints

2.1 Primary Endpoint

- Mean change in Visual Analog Scale (VAS) pain score (0–10 cm) from baseline to Week 4, and differences in changes among subgroups (r-axSpA vs. nr-axSpA; short disease duration vs. long disease duration).

2.2 Secondary Endpoints

- Clinical remission rate (ASDAS ≤ 1.3) and low disease activity rate (1.3 < ASDAS ≤ 2.1) at Week 4.
- Changes from baseline to Week 4 in:
    - BASDAI
    - BASFI
    - ASAS HI
    - BASMI
    - CRP and ESR levels
- Subgroup differences for all secondary endpoints.

3. Analysis Populations

Population	Definition
Full Analysis Set (FAS)	All enrolled subjects who received at least one dose of study drug and have at least one post-baseline efficacy assessment.
Per Protocol Set (PPS)	Subjects in FAS who completed the 4-week treatment without major protocol deviations (e.g., prohibited medication, poor compliance).
Safety Set (SS)	All subjects who received at least one dose of study drug and have post-baseline safety data.

Primary efficacy analyses will be based on **FAS**, with **PPS** used for sensitivity analysis.

4. Sample Size

- Based on a standard deviation of 2.0 for VAS change, $\alpha = 0.05$ (two-sided), power = 80%, minimum required sample size = 136.
- Accounting for ~10% dropout, **150 subjects** will be enrolled.

5. Statistical Methods

5.1 Descriptive Statistics

- **Continuous variables** (e.g., VAS, BASDAI, CRP): mean, SD, median, IQR, min, max.
- **Categorical variables** (e.g., remission rate, gender): frequency and percentage.

5.2 Primary Endpoint Analysis

- **Within-group change** from baseline to Week 4: paired t-test (if normally distributed) or Wilcoxon signed-rank test (if non-normal).
- **Subgroup comparisons** (r-axSpA vs. nr-axSpA; short vs. long disease duration): ANCOVA or non-parametric tests, adjusted for baseline VAS score.

5.3 Secondary Endpoint Analysis

- **Continuous secondary endpoints** (BASDAI, BASFI, ASAS HI, BASMI, CRP, ESR): same as primary analysis.
- **Categorical secondary endpoints** (remission, low disease activity): Chi-square test or Fisher's exact test.

5.4 Subgroup Analyses

Subgroups will be defined as:

- **r-axSpA** (radiographic) vs. **nr-axSpA** (non-radiographic)
- **Disease duration**: ≤ 2 years vs. > 2 years

For each subgroup, treatment effect (change from baseline) will be estimated with 95% confidence intervals.

5.5 Sensitivity Analysis

- Repeat primary analysis using **PPS**.
- Multiple imputation for missing data if dropout rate > 10%.

5.6 Missing Data Handling

- Missing VAS scores at Week 4 will not be imputed for primary analysis unless dropout

rate > 10%, in which case multiple imputation will be applied.

- Reasons for missing data will be summarized.

6. Safety Analysis (SS population)

- **Incidence of AEs and SAEs**: summarized by system organ class (SOC) and preferred term (PT) using MedDRA.
- **Grading**: NCI-CTCAE v5.0.
- **Causality**: assessed as unrelated, possibly unrelated, possibly related, likely related, definitely related.
- **Laboratory parameters, vital signs, physical exams**: descriptive statistics and shift tables (normal to abnormal).

7. Software

All statistical analyses will be performed using **SAS version 9.4 or higher**.

8. Significance Level

All hypothesis tests will be **two-sided** with a significance level of $\alpha = 0.05$. No adjustment for multiplicity will be applied for secondary endpoints.

9. Reporting

Results will be reported in accordance with **STROBE guidelines** for observational studies. A final clinical study report (CSR) will be prepared.