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

Protocol Number：CSPC-GSS-axSpA-001

Product Name：Acemetacin sustained-release capsules

Funding organization：Shijiazhuang Pharmaceutical Group Ouyi Pharmaceutical Co., Ltd

Version/Date：V2.0/March 5, 2026

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# Revision history of the experimental plan

| Version number | Version date | Main revisions and reasons for revision |
|---|---|---|
| 2.0 | March 5th, 2026 | 1. Revision: Change the inclusion and exclusion criterion 2 from "Subjects aged 18-65 years" to "Subjects aged 18-65 years (inclusive)"<br>Revision reason: Modify the age restriction condition to include a threshold value<br>2. Revised content: The dosage of the test drug has been changed from 90mg per administration, twice a day, to 90mg per administration, once a day<br>Revision reason: Adjustment of the dosage of the test drug |
| 1.0 | January 13, 2026 | Initial version |

# Catalogue

# Glossary

| Abbreviation | English full name |
|---|---|
| ADR | Adverse Drug Reaction |
| AE | Adverse Event |
| ANCOVA | Analysis of Covariance |
| ASAS | Assessment of Spondyloarthritis International Society |
| ASAS HI | ASAS Health Index |
| ASDAS | Ankylosing Spondylitis Disease Activity Score |
| axSpA | Axial Spondyloarthritis |
| BASDAI | Bath Ankylosing Spondylitis Disease Activity Index |
| BASFI | Bath Ankylosing Spondylitis Functional Index |
| BASMI | Bath Ankylosing Spondylitis Metrology Index |
| BMI | Body Mass Index |
| CRF | Case Report Form |
| CRP | C-Reactive Protein |
| csDMARDs | Conventional Synthetic Disease-Modifying Antirheumatic Drugs |
| CTCAE | Common Terminology Criteria for Adverse Events |
| DMP | Data Management Plan |
| eCRF | Electronic Case Report Form |
| ESR | Erythrocyte Sedimentation Rate |
| FAS | Full Analysis Set |

| Abbreviation | English full name |
|---|---|
| GCP | Good Clinical Practice |
| HLA | Human Leukocyte Antigen |
| ICF | Informed Consent Form |
| IEC | Independent Ethics Committee |
| IRB | Institutional Review Board |
| JAK | Janus Kinase |
| NCI-CTCAE | National Cancer Institute Common Terminology Criteria for Adverse Events |
| NMPA | National Medical Products Administration |
| NSAID | Non-Steroidal Anti-Inflammatory Drug |
| PPS | Per Protocol Set |
| SAE | Serious Adverse Event |
| SAS | Statistical Analysis System |
| SPARTAN | Spondyloarthritis Research and Treatment Network |
| SS | Safety Set |
| SUSAR | Suspected Unexpected Serious Adverse Reaction |
| TEAE | Treatment-Emergent Adverse Event |
| VAS | Visual Analog Scale |

# 1. Project Summary

## 1.1 Project Summary

| | |
|---|---|
| Research Topic | A multicenter, prospective, observational real-world study evaluating the efficacy and safety of acemetacin sustained-release capsules in the treatment of active axial spondyloarthritis (axSpA) |
| Product Name | Acemetacin sustained-release capsules |
| Funding organization | Shijiazhuang Pharmaceutical Group Ouyi Pharmaceutical Co., Ltd |
| Research objective | Evaluate the efficacy and safety of acemetacin sustained-release capsules in the treatment of active axial spondyloarthritis |
| Experimental Design | Multi-center, prospective, observational clinical study |
| Study population | Subjects with active axial spondyloarthritis |
| Sample size | 150 cases |
| Selection criteria | 1. Understand the purpose and procedure of the trial and voluntarily sign the informed consent form;<br>2. The subjects should be aged between 18 and 65 (inclusive), with no gender restrictions;<br>3. Meet the revised classification criteria for axial spondyloarthritis in ASAS-SPARTAN in 2025;<br>4. ASDAS score > 2.1. |
| Exclusion criteria | Subjects who meet any of the following conditions will not be eligible to participate in the study:<br>1. Hypersensitivity to acemetacin and other NSAIDs;<br>2. Those with a history of digestive tract ulcer or bleeding;<br>3. Individuals with severe cardiac or renal insufficiency, or abnormal liver function;<br>4. Those with ulcerative colitis or Crohn's disease;<br>5. Having used systemic glucocorticoids or intra-articular injections of glucocorticoids within 3 months prior to the commencement of the study;<br>6. Have used targeted therapy within 3 months before the start of the study;<br>7. The researcher believes that there are any other situations that make the participant unsuitable for participating in this study. |
| Treatment plan | Take acemetacin sustained-release capsules, strictly following the clinical actual prescription. The recommended dosage is 90mg per dose, once daily, for a treatment period of 4 weeks. |
| Study endpoint | Primary endpoint:<br>1. After 4 weeks of acemetacin treatment, the average change in the patient's overall pain score relative to the baseline, as well as the differences in changes among different subgroups.<br>Secondary endpoints:<br>1. The clinical remission rate (clinical remission, i.e., ASDAS $\leqslant$ 1.3) and the proportion of patients achieving low disease activity (i.e., 1.3 < ASDAS $\leqslant$ 2.1) after 4 weeks of acemetacin treatment, as well as the differences among different subgroups. |

| | |
|---|---|
| | 2. The changes in patients' pain, BASDAI, BASFI, ASAS HI, and BASMI after 4 weeks of acemetacin treatment compared to baseline, as well as the differences in these changes across different subgroups compared to baseline.<br>3. The changes in CRP and ESR levels after 4 weeks of acemetacin treatment compared to baseline, as well as the differences in these changes across different subgroups. |
| Pain assessment | The Visual Analogue Scale (VAS) is used to assess the level of pain experienced by patients after medication. The scale primarily consists of a 10cm straight line, with one end indicating "completely pain-free" and the other end indicating "the most severe pain imaginable" or "pain at its peak", etc. Participants are instructed to mark a corresponding point on the line (using a dot or a "×", etc.) to represent the intensity of pain they experienced at that moment after taking the medication. There are three points in total: before taking the oral acemetacin sustained-release capsules, after taking them at W2, and after taking them at W4, to assess the average change in VAS scores relative to the baseline. |
| Evaluation of major adverse events | From the beginning to the end of treatment, clinical manifestations, severity, occurrence time, duration, treatment measures, and outcomes were recorded, and the correlation with the study drug was analyzed. |

## 1.2 Experimental flowchart

| | **Screening** | **Baseline（V1）** | **Week 2（V2）** | **Week 4（V3）** | **Early terminate[20]** |
|---|---|---|---|---|---|
| **visit window** | D-7~D-1 | **First administration D1** | **Telephone follow-up D14±3 天** | **D28±3 天** | **Last dose ±3 天** |
| Informed Consent Form | × | | | | |
| Inclusion/exclusion criteria | × | | | | |
| Demography [1] | × | | | | |
| Smoking history | × | | | | |
| Drinking history | × | | | | |
| Past medical history/present medical history [2] | × | | | | |
| previous axSpA treatment [3] | × | | | | |
| family history [4] | × | | | | |
| height and weight [5] | × | | | | |
| Radiology (Sacroiliac Joint)[6] | × | | | | |
| vital signs [7] | × | × | | × | × |
| physical examination [8] | × | × | | × | × |
| hematology [9] | × | × | | × | × |
| Liver and kidney function [10] | × | × | | × | × |
| urinalysis [11] | × | × | | × | × |
| C-reactive protein | × | × | | × | × |
| Erythrocyte Sedimentation Rate | × | × | | × | × |
| Drug treatment regimen | | × | × | × | × |
| VAS score[12] | | × | × | × | × |
| ASDAS score [13] | × | × | | × | × |
| BASDAI score [14] | | × | × | × | × |
| BASFI score [15] | | × | × | × | × |
| ASAS HI score [16] | | × | × | × | × |
| BASMI score [17] | | × | | × | × |

| | | |
|---|---|---|
| adverse event [18] | | × |
| Combined medication/treatment [19] | × | |

Note：

1. Demographic information: including date of birth, gender, height, weight, BMI, education level, etc.
2. Past medical history/current medical condition: Past medical history includes cardiovascular and cerebrovascular diseases, hypertension, diabetes, hyperlipidemia, respiratory diseases, arthritis, osteoporosis, psoriasis, tumor history, etc.; current medical condition includes axSpA diagnosis time, disease duration, clinical symptoms, and HLA-B27.
3. Previous treatment for axSpA: including treatment regimen, medication dosage, medication duration, and reasons for medication change;
4. Family history: Record the family history of axSpA.
5. Height and weight: Height is only measured during the screening period, while weight can be collected at each visit point according to actual clinical needs.
6. Radiology (Sacroiliac Joint): Radiological examination is essential for diagnosis and classification. Before the first administration of medication, MRI, CT, and X-ray examinations must be completed.
7. Vital signs: including body temperature, breathing, heart rate, and blood pressure. These are checked during the screening period and before each follow-up visit.
8. Physical examination: The screening period includes examinations of general conditions, mucous membranes, lymph nodes, head and neck, chest, abdomen, spine and limbs, nervous system, etc. For disease-related positive signs (such as chest expansion, occipitofrontal distance, fingertip-to-ground distance, etc.), detailed descriptions and changes should be recorded. The examination should be conducted during the screening period and before each follow-up visit. For V1, the screening results within 7 days before the first dose are acceptable.
9. Blood routine examination: including white blood cell count, neutrophil count, red blood cell count, hemoglobin, platelet count, and lymphocyte count. It should be conducted during the screening period and before each follow-up visit. For V1, screening results within 7 days before the first dose are acceptable.
10. Liver and kidney function: Liver function includes alanine aminotransferase, aspartate aminotransferase, and total bilirubin; kidney function includes serum creatinine. These tests should be conducted during the screening period and before each follow-up visit. For V1, screening test results within 7 days before the first dose are acceptable.
11. Urine routine test: including urine protein, urine glucose, urine occult blood, urine red blood cells, and white blood cells. It should be conducted during the screening period and before each follow-up visit. For V1, results from the screening period within 7 days before the first dose are acceptable.
12. VAS score: See Appendix 1 for overall pain scores. VAS scores were taken before medication and during follow-up.
13. ASDAS score: ASD disease activity score, which is assessed during the screening period, V1, V3, and early withdrawal visits. For V1, the screening period score within 7 days before the first dose is acceptable.
14. BASDAI score: See Appendix 2, Bath Ankylosing Spondylitis Disease Activity Index, with scores recorded at V1, V2, V3, and early withdrawal visits.
15. BASFI score: See Appendix 3, Bath Ankylosing Spondylitis Functional Index, scores at V1, V2, V3, and early withdrawal visits.
16. ASAS HI score: See Appendix 4, ASAS Health Index, scores at V1, V2, V3, and early withdrawal visits.
17. BASMI score: refer to Appendix 5, Bath Ankylosing Spondylitis Measurement Index, which is scored at V1, V3, and at early withdrawal from the visit.
18. Adverse events: From the beginning to the end of treatment, record the clinical manifestations, severity, occurrence time, duration, treatment measures, and outcomes, and analyze the correlation with the study drug.
19. Concurrent medication/treatment: It is necessary to record the medication use within 30 days prior to signing the informed consent form, including the type of concurrent medication, the dosage of the therapeutic drug used, the time of medication administration, and the reason for medication use.

20. Early withdrawal: If a subject discontinues treatment for various reasons, an early withdrawal visit is required. The early withdrawal visit should be completed within ±3 days after the subject's last dose, except for subjects who are lost to follow-up, deceased, or have withdrawn their informed consent.

# 2. Research Background

## 2.1 Theoretical basis of the study

Axial spondyloarthritis (axSpA) is a chronic inflammatory disease primarily affecting the axial skeleton, characterized by inflammatory low back pain, morning stiffness, enthesitis, and arthritis [1,2]. It may also be accompanied by extra-articular manifestations such as uveitis and psoriasis [3,4]. This disease is more common in young adult males, with symptoms typically appearing between the ages of 20 and 30. It poses a serious threat to patients' quality of life, functional status, and social productivity [5,6]. If not promptly diagnosed and adequately treated, patients may face persistent pain, morning stiffness, fatigue, and loss of spinal mobility and function [7].

Globally, the estimated prevalence of axSpA ranges from 0.3% to 1.4%. According to Chinese research data, its prevalence among the mainland population is approximately 0.3% [8], indicating that over 4 million individuals, particularly young and middle-aged males, are deeply affected by it, posing a significant economic burden on both individuals and the national healthcare system [9-11].

In terms of treatment, non-steroidal anti-inflammatory drugs (NSAIDs), such as diclofenac, celecoxib, and acemetacin, are recommended as first-line drugs for the treatment of axSpA by clinical practice guidelines both domestically and internationally [12-14]. Acemetacin is a non-selective NSAID that is itself a prodrug, metabolizing to indomethacin in the body to exert its anti-inflammatory effect. This unique metabolic pathway may alleviate the direct irritation of the original drug, indomethacin, on the gastrointestinal tract to some extent, offering potential gastrointestinal safety advantages [15].

Currently, there is a lack of systematic prospective research data on the evidence-based medical efficacy of acemetacin in the treatment of axSpA, especially in real-world clinical practice, regarding the treatment outcomes for patients with different disease phenotypes - radiographically positive axSpA (r-axSpA) and radiographically negative axSpA (nr-axSpA) -

as well as those with varying disease durations. Therefore, this study aims to provide evidence for the application of acemetacin in the individualized treatment of active axSpA through a prospective, observational real-world study.

### 2.2 Background

#### 2.2.1 Investigational drugs

Common name: Acemetacin Sustained-release Capsules

#### 2.2.2 Assessment of potential risks and benefits

Acemetacin sustained-release capsules have been launched in China. Clinical studies both domestically and internationally have confirmed their good safety profile. Preliminary data have demonstrated that the investigational drug is similar to the originator drug in terms of pharmacy, pharmacokinetics, and pharmacodynamics, with no significant differences in safety data. Therefore, it is expected that the efficacy and safety of the investigational drug will be similar to those of the originator drug. This study will conduct regular follow-ups on subjects, promptly handle and observe any adverse reactions that occur, until they return to normal or achieve clinical stability.

Therefore, the risks of this study are controllable, and the expected benefits to the subjects outweigh the risks.

## 3. Research objective

Evaluate the efficacy and safety of acemetacin sustained-release capsules in the treatment of axial spondyloarthritis.

### 3.1 Primary research endpoint

After 4 weeks of acemetacin treatment, the average change in the patient's overall pain score relative to baseline, as well as the differences in changes among different subgroups.

### 3.2 Secondary research endpoints

1. The clinical remission rate (clinical remission, i.e., ASDAS $\leqslant$ 1.3) and the proportion of patients achieving low disease activity (i.e., 1.3 < ASDAS $\leqslant$ 2.1) after 4 weeks of acemetacin treatment, as well as the differences among different subgroups.

2. The changes in patient pain, BASDAI, BASFI, ASAS HI, and BASMI after 4 weeks of acemetacin treatment compared to baseline, as well as the differences in these changes between different subgroups compared to baseline.

3. The changes in CRP and ESR levels after 4 weeks of acemetacin treatment compared to baseline, as well as the differences in these changes across different subgroups.

# 4. Research Plan

## 4.1 Experimental Design

### 4.1.1 Overall Design

This study is a multicenter, prospective, observational clinical study. The study process includes a screening period and a treatment period.

**Screening：**

After the subjects sign the Informed Consent Form (ICF), they enter the study screening period and will be visited according to the trial flowchart. It is planned to complete the screening period evaluation, which will last up to 7 days. Subjects who meet all the inclusion criteria of the study and do not meet the exclusion criteria will enter the study treatment period. The study plans to include 150 subjects with axial spondyloarthritis, who will all be treated with acemetacin sustained-release capsules.

**Treatment period：**

All subjects received treatment with acemetacin sustained-release capsules for a period of 4 weeks.

**Early terminate visit：**

If the subject needs to terminate the study drug treatment in advance due to treatment failure, intolerable drug side effects, or any other reason, an early withdrawal visit is required. This visit should be completed within ±3 days after the last study medication.

**Efficacy evaluation：**

The pain assessment during the screening period and throughout the entire study will be conducted using the Visual Analogue Scale (VAS). The overall pain score for patients is based on a 10cm VAS pain scale, where 0 indicates no pain and 10 indicates the most severe pain.

**Safety assessment：**

The safety of the subjects must be assessed during each visit. Safety indicators encompass adverse events, serious adverse events, laboratory tests, vital signs, physical examinations, concomitant medications, etc. Adverse events and serious adverse events are graded according to CTCAE5.0. Special attention is paid to gastrointestinal adverse events

(such as nausea, abdominal pain, indigestion, gastrointestinal bleeding) and cardiovascular events.

#### 4.1.2 Study on dose design

Acemetacin sustained-release capsules: 1 capsule per dose, once daily, for 4 weeks.

### 4.2 Sample size

Based on previous research, the standard deviation of overall pain score changes after 4 weeks of NSAID treatment is 2. Assuming a significance level $\alpha$ =0.5 (two-tailed) and a test power of 80%, the minimum sample size required to detect clinically meaningful changes in pain scores is calculated to be 136 cases. This study is a real-world study. Considering the dropout rate of follow-up samples, it is planned to include 150 patients with active axSpA to ensure that the final effective sample size meets statistical requirements.

### 4.3 Research period

#### 4.3.1 Safety monitoring period

After signing the informed consent form, safety monitoring commences and continues until the end of treatment. During this period, clinical manifestations, severity, occurrence time, duration, treatment measures, and outcomes are recorded, and their correlation with the study drug is analyzed.

#### 4.3.2 Treatment cycle

Patients will be treated for a maximum of 4 weeks, except in the following circumstances: if patients experience intolerable drug side effects, do not agree to continue participating in the clinical study, or achieve complete clinical remission, treatment can be terminated. See Section 5.3.1 "Termination Criteria" for details.

## 5. Study population

### 5.1 Inclusion criteria

1. Understand the purpose and procedure of the trial and voluntarily sign the informed consent form;

2. The subjects should be aged between 18 and 65 (inclusive), with no gender restrictions;

3. Meet the revised classification criteria for axial spondyloarthritis in ASAS-SPARTAN 2025;

4. ASDAS score > 2.1.

**5.2 Exclusion criteria**

1. Hypersensitivity to acemetacin and other NSAIDs and their excipients;

2. Those with a history of digestive tract ulcer or bleeding;

3. Individuals with severe cardiac or renal insufficiency or abnormal liver function;

4. Those with ulcerative colitis or Crohn's disease;

5. Have used systemic glucocorticoids or intra-articular injections of glucocorticoids within 3 months prior to the start of the study;

6. Have used targeted therapy within 3 months before the start of the study;

7. The researcher believes that there are any other situations that make the participant unsuitable for participating in this study.

**5.3 Termination criteria and exclusion criteria**

**5.3.1 Termination criteria**

1. The subject withdraws the informed consent;

2. Subjects who experience intolerable drug side effects that remain unrelieved despite symptomatic treatment;

3. The drug was delayed for more than 4 weeks and was deemed unsuitable for continued administration by the investigator;

4. The subject becomes pregnant;

5. Subjects were lost to follow-up;

6. The researcher determines that the study should be terminated in the best interest of the subjects;

7. The subject fails to comply with the relevant research regulations, and the researcher deems it necessary to terminate the study;

8. The regulatory authority or sponsor notifies the termination of the clinical study.

If the termination of patient treatment research is due to any of the above reasons, the researcher must fill out the case summary page in the case report form, as well as specify the date and reason for the termination of treatment.

If the termination of a treatment study is due to an adverse event, follow-up should be conducted on the adverse event until it is properly resolved and the condition stabilizes.

**5.3.2 Steps to terminate study treatment**

It is imperative to diligently complete the effectiveness and safety checks stipulated in the protocol at the end of the study treatment, and thoroughly document adverse events (AEs) and outcomes. Researchers may suggest or provide new or alternative treatment methods to the subjects based on their actual conditions.

If the subject refuses to visit the research center for further follow-up, relevant research information should still be continuously collected and tracked, unless the subject withdraws from disclosing further information or withdraws consent to be contacted further. In this case, no further research evaluation should be conducted, and no further data should be collected.

#### 5.3.3 Exclusion criteria

1) Those who have not taken any medication since enrollment;
2) During the trial, simultaneous receipt of any other investigational treatment or any other treatment for axial spondyloarthritis;
3) Subjects with a significant lack of research data, or whose effectiveness cannot be determined due to the use of prohibited drugs;
4) Seriously violating the protocol and requiring exclusion as determined by the investigator.

# 6. Research treatment

## 6.1 Investigational drugs

### 6.1.1 Investifational drugs

Common name: Acemetacin Sustained-release Capsules

Trade name: Gaoshun Song®

Storage: Keep in a dark and dry place. Keep out of reach of children.

### 6.1.2 Packaging of test drugs

The label attached to each drug package includes dosage form, specification, quantity, usage, storage conditions, expiration date, and the drug supply unit, with the indication of "exclusively for clinical research use".

### 6.1.3 Drug inventory

According to the requirements of each center, the investigator or the central pharmacy is responsible for ensuring the counting and organization of all study drugs received by the research center throughout the study period. The study drugs allocated to the subjects need to be recorded on the medication administration record sheet.

The study drugs must be handled strictly in accordance with the study protocol and instructions on the packaging labels. The study drugs should be stored in a secure area or a locked cabinet under appropriate environmental conditions. Unused study drugs and unused portions of drugs must be retained for verification during monitoring visits. When the research center is an authorized destruction center and the study drugs are destroyed on-site, all details must be recorded on the drug recovery form.

### 6.2 Treatment plan

Subjects with axial spondyloarthritis who meet the inclusion criteria and do not meet any of the exclusion criteria will be treated with the following regimen: administration of acemetacin sustained-release capsules, fully adhering to the actual clinical prescription. The commonly recommended dosage is 90mg per dose, once daily, for a treatment duration of 4 weeks. During the study, detailed records of each patient's actual medication dosage, frequency, and treatment duration must be maintained.

### 6.3 Concurrent medication/treatment

#### 6.3.1 Prohibited drugs and treatments

The use of other non-steroidal anti-inflammatory drugs (NSAIDs) and glucocorticoids is prohibited during the study period.

#### 6.3.2 Permissible drugs and treatments

During the study treatment period, in consideration of the subjects' interests, the researchers will provide necessary treatment according to clinical diagnosis and treatment routines. The following drugs/treatments are allowed to be used as appropriate:

（1） Patients who have been stably using traditional synthetic disease-modifying antirheumatic drugs (csDMARDs) such as sulfasalazine for more than 3 months before enrollment are allowed, but specific medication use needs to be recorded.

（2） Medications for other concomitant diseases: such as medications for hypertension, diabetes, etc.

（3） If an adverse event occurs to a subject during the study treatment period, the investigator should provide appropriate treatment according to clinical diagnosis and treatment routines.

## 7. Test procedure

Overall requirements and regulations for experimental evaluation and procedures

### 7.1 Screening

The preparation phase of clinical research includes the preparation, distribution, and confirmation of research documents, as well as personnel training; signing of informed consent forms, and screening of subjects.

Initiate the clinical research phase, and patients who meet the inclusion criteria and do not meet the exclusion criteria will be enrolled in this study after screening. During the screening period, the following assessment steps should be completed and recorded:

① Days -7 to -1 before enrollment

1) Informed consent;
2) Inclusion/exclusion criteria;
3) Demographic information: date of birth, gender, ethnicity, height, weight, BMI, and education level;
4) Smoking history;
5) Alcohol consumption history
6) Past medical history/current medical condition: Past medical history includes cardiovascular and cerebrovascular diseases, hypertension, diabetes, hyperlipidemia, respiratory diseases, arthritis, osteoporosis, psoriasis, tumor history, etc.; current medical condition includes axSpA diagnosis time, disease duration, clinical symptoms, and HLA-B27.
7) Previous axSpA treatment: including treatment regimen, medication dosage, medication duration, and reasons for medication change;
8) Family history: Record the family history of axSpA;
9) Height and weight: Height and weight (measured in kilograms), with weight data collected at each visit point as clinically necessary;
10) Radiology (Sacroiliac Joint): Radiological examination is necessary for diagnosis and classification. Before the first administration, MRI, CT, and X-ray examinations must be completed.
11) Vital signs: including body temperature, breathing, heart rate, and blood pressure;
12) Physical examination: including general condition, skin and mucous membranes, lymph nodes, head and neck, chest, abdomen, spine and limbs, nervous system, etc. For disease-related positive signs (such as chest expansion, occipitofrontal distance,

fingertip-to-ground distance, etc.), detailed description and recording of changes are required;

13) Blood routine test: including white blood cell count, red blood cell count, neutrophil count, hemoglobin, platelet count, and lymphocyte count;
14) Liver and kidney function: Liver function includes alanine aminotransferase, aspartate aminotransferase, and total bilirubin; kidney function includes serum creatinine.
15) Urine routine test: including urine protein, urine glucose, and urine occult blood (urine red blood cells, white blood cells);
16) C-reactive protein;
17) Erythrocyte sedimentation rate;
18) ASDAS score;
19) Concurrent medication/treatment;

**7.2 Baseline（V1）**

Collect, record, and report patient information and data in a timely manner, ensuring that the data and information are timely, consistent, complete, reliable, and accurate. Adverse events, especially serious adverse events, should be handled promptly and appropriately, with timely tracking, follow-up, recording, and reporting, and original records should be preserved.

The plan is to administer the medication for 4 weeks.

1) Body weight (collected as needed);
2) Vital signs;
3) Physical examination: For V1, the screening period test results within 7 days before the first dose are acceptable;
4) Laboratory tests: including blood routine, liver and kidney function, urine routine, C-reactive protein, and erythrocyte sedimentation rate. For V1, results from the screening period within 7 days before the first dose are acceptable;
5) The research center administers the medication;
6) Efficacy evaluation: VAS score, ASDAS score (V1 can accept the screening period test results within 7 days before the first dose), BASDAI score, BASFI score, ASAS HI score, BASMI score;
7) Concurrent medication/treatment;
8) Adverse events.

**7.3 Week 2（V2）**

1) The research center administers the medication;
2) Efficacy evaluation: VAS score, BASDAI score, BASFI score, ASAS HI score;
3) Concurrent medication/treatment;
4) Adverse events.

**7.4 Week 4（V3）**

1) Body weight (collected as needed);
2) Vital signs;
3) Physical examination;
4) Laboratory tests: including blood routine, liver and kidney function, urine routine, C-reactive protein, and erythrocyte sedimentation rate;
5) The research center administers the medication;
6) Efficacy evaluation: VAS score, ASDAS score, BASDAI score, BASFI score, ASAS HI score, BASMI score;
7) Concurrent medication/treatment;
8) Adverse events.

**7.5 Early withdrawal visit**

The early withdrawal visit needs to be completed within ±3 days after the last administration.

The tasks that need to be completed before early withdrawal from the visit are as follows:

1) Weight (collected as needed);
2) Vital signs;
3) Physical examination;
4) Laboratory tests: including blood routine, liver and kidney function, urine routine, C-reactive protein, and erythrocyte sedimentation rate;
5) Efficacy evaluation; VAS score, ASDAS score, BASDAI score, BASFI score, ASAS HI score, BASMI score;
6) Concurrent medication/treatment;
7) Adverse events;

**7.6 Selection and confirmation of primary measurement indicators or outcome indicators**

**7.6.1 Primary outcome measure: Mean change in VAS score relative to baseline.**

Utilize the VAS scoring scale to quantify patients' subjective pain sensation, employing a visual analog scale

A straight line without any divisions, and only marking pain at both ends of the line. One end of the horizontal line is marked as 0,

One end represents no pain; the other end represents severe pain, and the middle part represents varying degrees of pain, for recording purposes

The change in VAS score from baseline after 4 weeks of medication.

VAS pain score: 0 indicates no pain; less than 3cm is defined as mild pain, tolerable; 4cm-6cm indicates moderate pain affecting sleep, still tolerable; 7cm-10cm indicates severe pain, unbearable, affecting appetite and sleep.

# 8. Research evaluation

## 8.1 Study endpoint

（1）Primary study endpoint

After 4 weeks of acemetacin treatment, the average change in the patient's overall pain score relative to baseline, as well as the differences in changes among different subgroups.

（2）Secondary research endpoints

1) The clinical remission rate (clinical remission, i.e., ASDAS ≤ 1.3) and the proportion of patients achieving low disease activity (i.e., 1.3 < ASDAS ≤ 2.1) after 4 weeks of acemetacin treatment, as well as the differences between different subgroups.

2) The changes in patient pain, BASDAI, BASFI, ASAS HI, and BASMI after 4 weeks of acemetacin treatment compared to baseline, as well as the differences in these changes between different subgroups compared to baseline.

3) The changes in CRP and ESR levels after 4 weeks of acemetacin treatment compared to baseline, as well as the differences in these changes among different subgroups.

# 9. Adverse event

## 9.1 Definition of adverse event

Adverse Event (AE): Refers to all adverse medical events that occur in subjects after receiving the trial medication, which may manifest as symptoms, signs, diseases, or abnormalities in laboratory tests, but not necessarily have a causal relationship with the trial medication.

Treatment Emergent Adverse Event (TEAE): Any event that occurs newly or worsens relative to before treatment, from the first administration of acemetacin sustained-release capsules to the completion of the last administration.

Adverse Drug Reaction (ADR) refers to any harmful or unexpected reaction to the test drug that may occur during clinical trials. There is at least a reasonable possibility of a causal relationship between the test drug and the adverse event, meaning that the correlation cannot be ruled out.

Serious Adverse Event (SAE): Refers to adverse medical events that occur after a subject receives the trial medication, such as death, life-threatening conditions, permanent or severe disability or loss of function, hospitalization or prolonged hospitalization of the subject, as well as congenital abnormalities or birth defects.

Adverse events that lead to hospitalization or prolongation of hospitalization duration in clinical studies should be considered as serious adverse events. Any initial hospitalization (even if it is shorter than 24 hours) by a medical institution meets this criterion.

Hospitalization does not include the following situations:

① Rehabilitation institutions;

② Sanatorium;

③ Admitted for observation in the emergency department or other departments of the hospital, and it will not result in hospitalization (unless it is considered a significant medical event or life-threatening);

④ Hospitalization or prolonged hospitalization unrelated to the deterioration of adverse events is not a serious adverse event in itself, for example:

- Admitted to the hospital due to pre-existing conditions, with no new adverse events occurring and no exacerbation of the pre-existing conditions (e.g., to investigate persistent laboratory abnormalities that have existed since before the study);
- Hospitalization due to management reasons (such as annual routine physical examination);
- Hospitalization as stipulated in the research protocol during the clinical study period (i.e., following the requirements outlined in the research protocol);

- Elective hospitalization unrelated to the exacerbation of adverse events (such as elective cosmetic surgery);
- The scheduled treatment or surgery should be recorded in the entire research protocol and/or the baseline information of individual subjects;
- Admission is unrelated to health status and does not require medical or surgical intervention (such as lack of housing, financial difficulties, need to care for a patient, family reasons, or medical insurance reasons);

Diagnostic or therapeutic invasive procedures (such as surgery) and non-invasive procedures should not be reported as adverse events. However, when the disease condition leading to such procedures meets the definition of an adverse event, it should be reported. For example, acute appendicitis that occurs during the reporting period of an adverse event should be reported as an adverse event, and the appendectomy performed as a result should be recorded as the treatment method for that adverse event.

Based on appropriate medical judgment, significant medical events that do not result in death, life-threatening situations, or hospitalization can be considered as serious adverse drug events. These events may pose harm to the subjects and may require medical or surgical intervention to prevent the aforementioned outcomes.

Suspected Unexpected Serious Adverse Reaction (SUSAR): This refers to a suspected and unexpected serious adverse reaction whose nature and severity exceed the information provided in existing materials such as the investigator's brochure for trial drugs, the instructions for marketed drugs, or the summary of product characteristics. It is required to be reported promptly as a case report in accordance with the standards and procedures mandated by regulatory authorities.

For example: (1) Acute renal failure is listed as an adverse reaction in the investigator's brochure, but if interstitial nephritis occurs during the trial, it should be judged as an unexpected serious adverse reaction; (2) Hepatitis is listed as an adverse reaction in the investigator's brochure, but if acute severe hepatitis occurs during the trial, it should be judged as an unexpected serious adverse reaction.

### 9.2 Evaluation and classification of adverse events

Researchers evaluated and recorded all adverse events according to the following criteria.

Severity: For each adverse event, the severity must be determined according to the definition of SAE.

Severity: The severity of adverse events is recorded using the National Cancer Institute's Common Terminology Criteria for Adverse Events (NCI-CTCAE, version 5.0).

The NCI-CTCAE (5.0) grading is as follows:

Grade 1: Mild: Asymptomatic or with minor symptoms; only clinically or diagnostically observed; no intervention treatment required.

Level 2: Moderate: Slight, localized, or non-invasive intervention; age-related limitations in instrumental activities of daily living (instrumental activities of daily living refer to tasks such as cooking, shopping for groceries or clothing, making phone calls, managing finances, etc.).

Grade 3: Severe or medically significant, but not immediately life-threatening; resulting in hospitalization or prolonged hospitalization; disability; limited ability to perform self-care activities of daily living (self-care activities of daily living refer to bathing, dressing, eating, grooming, taking medication, and not requiring bed rest).

Level 4: Life-threatening; requires emergency intervention.

Grade 5: Death related to AE.

### 9.3 Assessment of the correlation between adverse events and study drugs

The causality between adverse events and the study drug should be assessed by the investigator based on all available information at the time of completing the Clinical Record Form (CRF). For all adverse events (AEs), the investigator should individually evaluate the causality between each event and each study drug. If the investigator believes that the event cannot be definitively attributed to a specific study drug (e.g., due to suspected potential interactions), the same assessment should be recorded under each study treatment. Important factors to consider when evaluating the causality between adverse events and the study drug include:

a. The event related to the timing of drug administration should occur after administration. The duration from drug exposure to the occurrence of the event should be evaluated in the clinical context of that event.

b. The reactions after drug withdrawal (dechallenge) and after re-administration (rechallenge) should be assessed in conjunction with the common clinical course of related events to evaluate the patient's response after dechallenge or rechallenge.

c. For underlying diseases, comorbidities, and concurrent diseases, each case should be evaluated in conjunction with the current treatment of the disease and the natural history and course of other diseases that the patient may have.

d. For concomitant medication or treatment, it is necessary to examine other medications or treatments that the patient is currently receiving at the time of the adverse event, in order to determine whether they may have contributed to the event.

e. Known types of reactions (clinical/preclinical) for such drugs.

f. Exposure to physiological/psychological stress may induce adverse changes in patients and provide a more reasonable explanation for the event.

g. The pharmacology and pharmacokinetics of the investigational treatment should be studied comprehensively, taking into account the pharmacokinetic characteristics of the investigational treatment (absorption, distribution, metabolism, and excretion).

The relationship between the study drug and AE is classified as: unrelated, possibly unrelated, possibly related, likely related, and definitely related.

- Irrelevant: There is evidence indicating that the cause of the adverse event is not the test drug (such as previous conditions, underlying diseases, concurrent diseases, or concomitant medications).
- Potentially unrelated: The event is not reasonably temporally associated with the use of the study drug and may be caused by many other factors, such as clinical conditions, other treatments, or concomitant medications.
- Possibly related: There was a transient relationship between the onset of the event and the administration of the test drug, but the subject's clinical condition or concurrent treatment is difficult to interpret. At the same time, based on the known therapeutic and pharmacological effects of the drug, there seems to be a certain degree of correlation. If the drug is discontinued or the dosage is reduced, the event may alleviate or disappear. However, it recurs when re-exposed to the stimulus. It

must be emphasized that ineffective treatment should not be considered as a causative factor for adverse events (AEs) when reporting them.

- Likely related: The event has a reasonable temporal association with the use of the study drug, and it is known or suspected that the study drug can cause the event. After experimentally discontinuing the study drug, the event lessened or disappeared. Upon reintroduction of the study drug, the adverse event reappeared.
- Definitely related: The temporal sequence since the medication was administered is reasonable; the reaction is consistent with known drug adverse drug reactions (ADR) (as reported in similar literature); the reaction ceased after drug discontinuation; upon re-administration, the event recurred.

| | definitely related | Most likely related | possibly related | possibly irrelevant | irrelevant |
|---|---|---|---|---|---|
| a. Does the event have a reasonable temporal relationship with the study drug? | + | + | + | + | — |
| b. Does the event conform to the known types of adverse reactions associated with the drug? | + | + | ± | — | — |
| c. After drug withdrawal or dosage reduction, did the event alleviate or disappear? | + | + | ±? | ±? | — |
| d. After re-administration of the medication, did the event recur? | + | ? | ? | ? | — |
| e. Can the event be explained by the effects of concomitant medications, the progression of the patient's condition, or the impact of other treatments? | — | — | ± | ± | + |

Note: + indicates affirmation, - indicates negation, ± indicates uncertainty, and ? indicates unclear.

Causal relationship between adverse events and protocol procedures and clinical operations:

Based on the question of whether the adverse event has a "reasonable causal relationship" with the protocol procedures and clinical operations, the assessment result

should be recorded as "related (yes)" or "unrelated (no)" in the Clinical Record Form (CRF). Generally, it refers to one of the following situations: adverse events caused by injury/damage resulting from any clinical operation (such as tissue biopsy); adverse events caused by drug withdrawal (such as elution), reduction, or adjustment of treatment regimen required by the protocol procedures; adverse events caused by other preventive medications before the administration of the trial drug, etc.

**9.4 Measures taken for research treatment**

Record all measures taken for the study drug to address adverse events (AEs) according to the following categories. Specific measures should be detailed in the Clinical Record Form (CRF).

- Discontinue medication
- Suspend drug administration
- Reduce the dosage
- Increase the dosage
- Dose remains unchanged
- Not applicable
- Unknown

**9.5 Other specific treatments for adverse events (Yes/No?)**

- None
- Pharmacotherapy
- Others

**9.6 Outcome**

The AE (Adverse Event) outcome record is as follows:

- Recovery/healing
- Recovery/healing with sequelae
- Improvement
- No improvement/No relief/Persistent
- Aggravate
- Death
- Unknown

**9.7 Adverse event assessment and recording**

The researcher must ensure that all adverse medical events occurring from the signing of the informed consent form to the end of follow-up are recorded on the CRF.

For AEs (regardless of causality) that have not fully recovered by the end of follow-up, follow-up must be continued until recovery (to baseline level or full recovery) or clinical stability is achieved, or a reasonable explanation is provided. If the subject dies, the cause or symptom leading to death should be reported as the name of the AE, and "death" should be considered as the outcome of the AE. If the cause of death is unknown, "death of unknown cause" should be reported as the name of the AE.

The investigator shall be responsible for grading the severity of recorded AEs and determining the causal relationship between the AEs and the study drug, protocol procedures, and clinical operations. For details, see 9.2 and 9.3.

For SAEs, the sponsor must conduct a separate assessment of their predictability, severity, and causality with the study drug. The reference documents for the predictability assessment include the latest version of the drug's package insert and other relevant documents.

### 9.8 Report of adverse events

#### 9.8.1 The responsibilities of researchers

During the clinical research process, regardless of whether the adverse event is related to the trial medication, the investigator should truthfully and thoroughly fill out the adverse event record form, documenting the clinical manifestation, occurrence time, severity, duration, measures taken, and outcome of the adverse event. Additionally, the investigator should record in detail the concomitant medication used, to facilitate analysis of the correlation between the adverse event and the study drug.

For all Serious Adverse Events (SAEs) that occur during the observation period described in Section 9.1, regardless of whether they are related to the trial drug, the investigator should provide timely emergency treatment and report to the ethics committee of the clinical trial responsible unit and the sponsor via telephone/fax within 24 hours of being informed. At the same time, the investigator should report to the hospital's adverse reaction monitoring center and prepare a written report within 72 hours. The sponsor should promptly investigate the serious adverse events that have occurred with the investigator and take necessary measures to ensure the safety and rights of the subjects.

Researchers must fill out the "Serious Adverse Event Report Form" and record in the original data when, how, and to whom the serious adverse event was reported. The sponsor guarantees compliance with all legal and regulatory reporting procedures.

### 9.8.2 Responsibilities of the sponsor

（1）Report to regulatory agencies

The sponsor shall handle relevant events (such as SAE) in accordance with all applicable regulations and report relevant events (such as SUSAR) to regulatory agencies as required.

SUSAR's reporting deadline:

- For fatal or life-threatening SUSARs, report within 7 days after first learning of it (Day 0 is the day the applicant first learns of it), and report and complete follow-up information within the subsequent 8 days.
- For non-fatal or non-life-threatening SUSARs, report within 15 days.
- For follow-up reports, report within 15 days of obtaining new information.

（2）Notify the Research Center

The sponsor will notify all research centers of relevant events (e.g., SUSAR) in accordance with all applicable regulations.

（3）Other

For serious adverse events that occur after the observation period specified in the plan, the sponsor will handle them in accordance with all relevant regulations.

**Contact information for reporting serious adverse events:**

| Unit | Contact | Tel. | Fax | Mailbox |
|---|---|---|---|---|
| Shijiazhuang Pharmaceutical Group Ouyi Pharmaceutical Co., Ltd | | | —— | 202512090003@cspc.cn |

### 9.9 Pregnancy

Researchers must report all pregnancy events that occurred during the participation of female participants in this study. Pregnancy outcomes should be carefully followed up and any abnormal outcomes of the mother or infant should be reported. Report to the hospital ethics committee (if applicable).

If the partner of a male subject becomes pregnant, information about the pregnancy process and outcome should be obtained as much as possible with their consent.

Once a female subject experiences a pregnancy event during the trial period, the researcher should immediately terminate the clinical trial and discontinue the study drug. Researchers should communicate scientifically and rigorously with subjects based on medication information, informing them of the possible effects and risks of the research drug on pregnant women and fetuses.

Within 24 hours of confirming the occurrence of a pregnancy event in the subject (or subject partner), the researcher shall complete a pregnancy report form and report it to the sponsor.

After learning about the pregnancy outcome, the researchers completed a pregnancy report form tracking report within 24 hours of learning and reported it to the sponsor.

### 9.10 Other security assessments

Other safety assessments such as vital signs, physical examinations, laboratory tests, etc.

## 10.Statistical analysis

### 10.1 Statistical analysis of population

Full Analysis Set (FAS): Includes all enrolled subjects. And those who have used the medication at least once and have at least one follow-up record.

Per Protocol Set (PPS): Conduct statistical analysis on the efficacy of all cases that comply with the trial protocol, complete the visit plan, have good compliance, did not use prohibited drugs during the trial, completed the CRF requirements, and meet the visit window requirements.

Safety Analysis Set (SS): All cases that have used the investigational drug at least once and have safety evaluation data after medication constitute the safety dataset of this study. This dataset is used to evaluate the safety of this study.

### 10.2 Statistical Analysis Methods

#### 10.2.1 Sample size calculation

According to previous studies, the standard deviation of overall pain score changes after 4 weeks of NSAID treatment was 2, with a significance level of $\alpha$ =0.05 (bilateral) and a test efficacy of 80%. To detect clinically significant changes in pain scores, the minimum sample size was calculated to be 136 cases. This study is a real-world research. Considering the

dropout of follow-up samples, we plan to include 150 active axSpA patients to ensure that the final effective sample size meets statistical requirements.

#### 10.2.2 Statistical Analysis Plan

Measurement data is described using mean ± standard deviation or median (interquartile range) for statistical analysis; Count data is described using frequency (percentage) for statistical analysis. The primary and secondary endpoints were compared before and after treatment using paired t-test or Wilcoxon signed rank sum test. Categorical variables such as ASDAS response rate are tested using chi square test or exact probability method. Covariance analysis (ANCOVA) or non parametric tests will be used for subgroup analysis to compare the differences in primary and secondary efficacy indicators between r-axSpA vs. nr-axSpA and short course vs. long course, respectively. Conduct descriptive analysis on the incidence and types of adverse events. All statistical analyses were conducted using a two-sided test, and $P<0.05$ was considered statistically significant. Use SAS software (version 9.4 or above) for analysis.

## 11.Data management

### 11.1 Responsibilities for data collection and management

Before conducting clinical trial data management, the data management department shall develop a Data Management Plan (DMP) based on the actual situation of the project. The data management plan is a dynamic document written by data management personnel based on the clinical trial protocol, which specifies and records in detail the data management tasks of a specific clinical trial, including personnel roles, job responsibilities, operational standards, etc.

### 11.2 Data Collection and Methods

The data recorded in the Case Report Form (CRF) should come from the source file and be consistent with the source data. All source files should be kept clear and tidy to ensure accurate data identification. The permanent copy of the research visit record will be considered as the source file for recording the data of the selected subjects. The data entry personnel should promptly and accurately enter the data from research medical records and other source files into the CRF.

### 11.3 Data Cleaning and Doubt Resolution

The data cleaning work includes data verification, raising questions, researchers/research assistants answering questions, data updates, and the process until the questions are resolved.

The data management related work that was not specified in detail in the plan shall be executed in accordance with the data management plan of this experiment.

# 12.Quality Control and Quality Assurance

## 12.1 Quality Control

1. Quality control measures in the laboratory

Establish unified experimental testing indicators, standard operating procedures, and quality control procedures in each participating clinical trial hospital laboratory.

2. Requirements for participants

Corresponding professional expertise, qualifications, and research abilities. After qualification review, it was determined that the personnel are relatively fixed.

3. Training for participants

Through pre clinical trial training, participants will have a full understanding and recognition of the clinical trial protocol and its specific indicators (such as research objectives, inclusion and exclusion criteria, prohibited drugs, etc.).

The objective indicators specified should be checked according to the time, place, and method specified in the plan.

Pay attention to observing adverse events or unexpected side effects, and track and observe them. The description of subjective symptoms should be objective and should not induce or prompt.

CRF filling should be timely, truthful, and accurate, ensuring that all conclusions in clinical trials are derived from raw data.

Blood sample storage and transportation follow standard operating procedures.

1. Measures to ensure subject compliance

The participating doctors should patiently explain to the subjects, so that they fully understand and cooperate with the experiment.

2. Other

Inform the subjects of possible adverse events of the investigational drug, and immediately notify the doctor or hospital by phone if any adverse events occur.

## 12.2 Quality Assurance

To ensure the quality of the trial, the sponsor and researchers jointly discuss and develop a clinical research plan before the formal trial begins. Each research center must manage research drugs in accordance with standard operating procedures, including acceptance, storage, distribution, and retrieval. It is not allowed to use research drugs with non participants of this clinical trial, and it is necessary to ensure that the drugs used are only for the subjects of this clinical trial.

The coordination committee is composed of the main researchers, heads of each participating unit, and funding parties, responsible for the implementation of the entire experiment and researching solutions to issues related to the experiment. The sponsor is responsible for maintaining contact with the National Medical Products Administration.

The sponsor shall appoint a monitor for this trial to ensure the rights and interests of the subjects in the clinical trial are protected. Verify the accuracy, authenticity, completeness, and accuracy of the data in the trial records and reports by the inspector, ensuring that the trial follows the approved protocol, the Good Clinical Practice for Drugs, and relevant regulations.

# 13.Responsibilities of Researchers

## 13.1 Responsibilities of Researchers

Researchers have the responsibility to ensure that clinical studies are conducted in accordance with the trial protocol, current GCP, and relevant regulations of the National Medical Products Administration (NMPA) of China.

## 13.2 Independent Ethics Committee (IEC)/Institutional Review Board (IRB)

Before initiating the study, researchers must provide the following documents to IEC:

1. Final draft of the experimental plan (and supplements);

2. The informed consent form provided by the sponsor and other written materials provided to the subjects;

3. Drug user manual;

4. Materials to assist in the selection of subjects;

5. Other documents required by IEC.

The trial can only begin after IEC fully agrees with the research protocol, informed consent form, materials used to assist in subject selection, and the sponsor receives a copy of the IEC approval document. The approval letter document must indicate the approved research topic (number), research document name (including version number), and approval date.

During the trial period, researchers may submit the following documents for IEC approval at an appropriate time for some reason:

1. Supplement to the experimental plan;

2. Modifications to the informed consent form and any other written information provided to the subjects;

3. Revised information regarding compensation for experimental injuries or compensation for participant participation in the trial;

4. Supplementary or updated versions of drug instructions for use;

5. New information regarding potential negative impacts on the safety of participants and the conduct of the study;

6. Deviation and modification of the research protocol to avoid immediate harm to the subjects;

7. Report of deceased subjects;

8. Notice of change of main researchers in the research unit;

9. Other requirements of IEC.

When the supplementary plan increases the risk for the subjects, the supplementary plan and its corresponding modified informed consent form must be promptly submitted to IEC for review and approved before implementation.

**13.3 Informed Consent**

Each participant (or their legal representative) must provide written consent after fully understanding the purpose and content of the study, and this written consent must be signed (signed and dated) before any experimental procedures are carried out. The informed consent form should comply with the Helsinki Declaration, current GCP guidelines, and relevant regulations.

Before potential subjects are enrolled, researchers or their authorized personnel should explain to them the purpose, methods, potential benefits, potential risks, and any discomfort that may arise from the study. Participants should be informed that their participation in the trial is voluntary and they can withdraw at any time. If the subject refuses to participate in the study, they can still choose other treatments, and whether or not they choose to participate in the study will not have any impact on their disease treatment. Finally, participants should be aware that the researcher will keep their identity records for long-term follow-up if necessary, and their records may be viewed by personnel from the drug administration and funding

agencies within the scope permitted by relevant laws and regulations. The privacy rights of the subjects will be protected. By signing the informed consent form, the subject authorizes the aforementioned actions.

The subjects (or their legal representatives) should have sufficient time to read the informed consent form and ask questions. After the researcher explains and before the subject is enrolled, the subject (or their legal representative) should sign their name and date on the informed consent form for record purposes. After signing the informed consent form, the subjects should obtain a copy of the informed consent form.

If the subject (or their legal representative) is unable to read and write, there should be a fair witness involved in the entire process of informed consent (including reading and interpreting all written information), and the subject (or their legal representative) should personally sign their name and date after verbal consent.

Subjects who cannot understand the content of informed consent can only participate in the trial after their legal representative has obtained informed consent.

**13.4 Confidentiality of Personal Information**

This study only collects and processes data from subjects who are essential for studying the effectiveness, safety, quality, and application of drugs.

When collecting and using this data, we will fully ensure its confidentiality and comply with relevant laws and regulations that protect the privacy of the subjects.

The sponsor will ensure that:

The process of collecting data is fair and legal;

The purpose of collecting data is specific, clear, and legal; And will not further process these data in a way that is inconsistent with the purpose and goes against other ways of processing data that violate these purposes;

3. The collected data is sufficient, relevant, and not excessive relative to the research purpose, and data unrelated to the research purpose is not collected;

4. The collected data is accurate and should be updated to the latest when necessary.

Before collecting personal data, researchers will obtain the consent of the subjects and their legal representatives. This agreement should include an emphasis on the transfer of data to other institutional entities and countries.

The subjects and their legal representatives have the right to obtain personal information through the researchers and may request the correction of any errors or incomplete data.

Appropriate responses should be given to such requirements, taking into account their content and purpose, the status of the experiment, and relevant laws. Consider the nature of the requirements, the state of the experiment, and relevant laws and regulations.

Appropriate technical and management measures must be taken to organize steps to protect the personal information of subjects from unauthorized access and disclosure by others, from accidental and illegal destruction, as well as accidental loss and alteration. During the entire research period, the sponsor personnel who have the right to access the personal information of the subjects will keep it confidential.

## 14.Responsibilities assumed by all parties

The sponsor is responsible for initiating, applying for, and inspecting the clinical trial, organizing and monitoring the trial, and providing the investigational drug to the researchers to ensure quality compliance.

After completing the trial summary, each clinical trial unit may publish papers and participate in domestic and international academic conferences with the consent of the sponsor; When publishing a paper, it should be clearly stated in the appropriate section of the paper: the production unit of the experimental drug, the clinical research team leader unit; Clinical research papers that win awards belong to the clinical trial unit. When applying for medical achievement awards for treatment-related papers and treatment techniques, the clinical trial unit should jointly negotiate and apply with the drug production unit and the clinical research team leader unit.

## 15. Expected Progress

From January 2026 to March 2026: Revise and improve the research plan and its accompanying documents, and submit them to the ethics committee for approval.

From March 2026 to September 2026: The first subject enrolled until the last subject completed treatment.

September 2026 December 2026: Data processing and data summary, completion of clinical research summary report, writing of articles and submission.

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# Appendix 1

## Overall situation (VAS score)

Please fill in the numerical values that represent your answer after the following questions. All questions refer to your situation in the past week. The total score is 10 points.


0 points is not at all. 10 points is very serious

1、How did you feel the overall level of back pain throughout the day this week? Rating ()
（ ）

2. How severe do you feel about your back pain at night this week? Rating ( )

3、How do you feel about the overall severity of your illness this week? Rating （ ）

# Appendix 2

## Ankylosing spondylitis disease activity index (BASDAI score)

| |
|---|
| Over the past week, please indicate the following situations and the degree of discomfort you have experienced<br>  <br>0 points no discomfort, 10 points very serious |
| 1、The degree to which you feel weak, fatigued, or powerless. Rating () |
| 2、The degree of pain you feel in your neck, back, and hip area. Rating () |
| 3、he degree to which you feel pain or swelling in other joints besides the neck, back, and hip area. Rating () |
| 4、The degree of pain you feel when other parts are compressed. Rating () |
| 5、The degree of discomfort felt upon waking up in the morning. Rating () |
| 6、Time score for feeling stiff after waking up in the morning ()<br>  <br>0 hours ----------1 hour ----------2 hours or more |

# Appendix 3

## Ankylosing spondylitis functional index (BASFI score)

| |
|---|
| The following is a test of your joint function over the past month. Please score after each item.<br>  <br>0 points is easy, 10 points is difficult |
| 1、Wear socks and shoes (such as using a shoehorn). Rating () |
| 2、Bend down and pick up a pen. Rating () |
| 3、Touch the upper level of the wardrobe. Rating () |
| 4、Stand up from the chair. Rating () |
| 5、Lie down on the floor and get up. Rating () |
| 6、Standing for ten minutes without any discomfort. Rating () |
| 7、Climbing 12 to 15 steps does not require crutches or handrails (usually 1-2 floors). Rating () |
| 8、You don't need to turn your body to see your shoulders. Rating () |
| 9、Can one engage in strong physical exercise and household chores? Rating () |
| 10、Can you stick to a whole day's work? Rating () |

# Appendix 4

## Ankylosing spondylitis health index (ASAS health index)

| | | |
|---|---|---|
| 1 | Sometimes pain can affect my normal life | □ No □Yes |
| 2 | I found myself unable to stand for a long time | □ No □Yes |
| 3 | I have difficulty running | □ No □Yes |
| 4 | I have difficulty using assistive devices when going to the bathroom | □ No □Yes |
| 5 | I often feel exhausted | □ No □Yes |
| 6 | I feel a lack of motivation to participate in physical activities | □ No □Yes |
| 7 | I am not interested in sexual activity | □ No □Yes |
| 8 | I have difficulty stepping on the pedal while driving | □ No □Yes |
| 9 | I find it difficult to communicate with others | □ No □Yes |
| 10 | I cannot take a walk on flat ground | □ No □Yes |
| 11 | I find it difficult to concentrate | □ No □Yes |
| 12 | Due to my limited mobility, I am restricted from traveling outside | □ No □Yes |
| 13 | I often feel frustrated | □ No □Yes |
| 14 | I find it difficult to wash my hair | □ No □Yes |
| 15 | Due to my rheumatism, I am facing financial difficulties | □ No □Yes |
| 16 | I have very poor sleep at night | □ No □Yes |
| 17 | I am unable to overcome the difficulties I have encountered | □ No □Yes |

# Appendix 5

## Ankylosing spondylitis measurement index (BASMI score)

| | |
|---|---|
| 1、Lumbar lateral curvature (bilateral average): cm | 2、Ear wall distance: cm |
| 3、Lumbar spine range of motion (revised Schober): cm | 4、Maximum ankle distance: cm |
| 5、Cervical range of motion (bilateral average): degrees | total score： |