Cover page for Protocol

Sponsor name	Ferring Pharmaceuticals A/S
NCT Number	NCT04852120
Sponsor trial ID:	000373
Official title of study	A post-marketing drug intensive monitoring study of Compound Sodium Picosulfate Granules for bowel preparation in Chinese population
Document Date	25 November 2021

NON-INTERVENTIONAL STUDY (NIS) PROTOCOL

A post-marketing drug intensive monitoring study of
Compound Sodium Picosulfate Granules for bowel preparation in Chinese population

Trial Code: 000373

Medicinal Product:	Compound Sodium Picosulfate Granules
Indication:	- To clean the bowel prior to X-ray examination or endoscopy - To clean the bowel prior to surgery when judged clinically necessary
Phase:	Post-marketing drug intensive monitoring
Name and Address of Sponsor:	Ferring Pharmaceuticals (China) Co., Ltd. No.6, Hui Ling Lu (Ferring Road), National Health Technology Park 528437 Zhongshan City, Guangdong Province, People's Republic of China

Version History

Version 2.0, 25Nov2021		
Chapter	**Change Summary**	**Change Reason**
2	Deleted secondary objective and exploratory objective.	The study is to monitor and assess the safety profile of Compound Sodium Picosulfate Granules in the real-world clinical practice. Secondary objective and explanatory objective are un-mandatory objective.
3	ePRO is replaced by contacting the subject remotely by pharmacist or hospital staff. Deleted DeltaMed relevant description.	ePRO is too complicate for data entry by subjects, the protocol amendment is to simplify data collection method. The DIM trial will be managed by Ferring.
4	Added hospitals as study sites. Deleted planned 3000 subjects	Due to insufficient recruitment from pharmacies, to add hospitals for more subject recruitment. Sponsor will collect as many subjects' safety data as possible.
5	Deleted variables "Patterns and compliance of drug use and liquid intake", "Date and time of X-ray examination, endoscopy or bowel surgery procedure" "Patient self-evaluation", etc. Clarified the necessary study procedures.	Consistent with the updated trial objective.
6	Deleted "definition of Adverse Events of Special Interest".	The study will collect all Adverse Events reported from signing the ICF to about 37(+2) hours after the first medication.
7	Analysis Population "Registry population" and "Complete population" are replaced by "Safety population". Deleted "Compliance of Drug Administration and Liquid Intake" and "Patient Self-evaluation"	Consistent with the updated trial objective
11	Deleted "The results will be submitted for publication in a peer-reviewed journal."	The study will not be used for publication
12	Added "Subject number will consist of study site code "CHN##" and study subjects code "####" (E.g. Subject number: CHN01-0001)"	Clarify subject number rule

Others	Deleted ePRO relevant description. Deleted DeltaMed relevant description. Added hospitals as study sites.	Consistent with the updated protocol.
Version 1.0, 19Nov2020		

SYNOPSIS

TITLE OF STUDY

A post-marketing drug intensive monitoring study of Compound Sodium Picosulfate Granules for bowel preparation in Chinese population

SIGNATORY INVESTIGATOR(S)

Not applicable

STUDY SITE(S)

The study is planned to be carried out in 20 pharmacies and hospitals in Chinese mainland.

PLANNED STUDY PERIOD

Apr 2021- Dec2022

OBJECTIVES

To monitor and assess the safety profile of Compound Sodium Picosulfate Granules in the real-world clinical practice in Chinese population.

METHODOLOGY

This is a post-marketing multi-site, prospective, non-interventional study. Compound Sodium Picosulfate granules or other similar drugs will be prescribed to the subject based on physicians' clinical judgement.

The study will collect all stipulated events reported from signing the informed consent form (ICF) to about 37(+2) hours after first medication. Contacting the subject remotely by pharmacist or hospital staff will be used to collect adverse events/reactions and other relevant information. No additional tests or examinations will be performed on subjects, no drugs will be provided to the subjects.

- The study staff will register the eligible subjects. The subjects will sign the informed consent, provide contact information. Demographic characteristics (gender, age, nation, height, weight) of subjects will be collected.
- Contact the subjects remotely 37(+2) hours after first medication to collect any adverse events and information on the Compound Sodium Picosulfate granules administration.

All adverse events collected will be sent to the sponsor for case processing.

NUMBER OF SUBJECTS

Sponsor will collect as many subjects' safety data as possible.

CRITERIA FOR INCLUSION / EXCLUSION

Inclusion criteria:

- Agree to participate in this study and sign the ICF by subject or the legal representative.
- Subjects taking the Compound Sodium Picosulfate Granules drug in real clinical practice.

Exclusion criteria:

- Subjects who are enrolled in other on-going studies, which prohibit any participation in this non-interventional study.

MONITORING PRODUCT

Compound Sodium Picosulfate Granules

DURATION OF PARTICIPATION

The duration of participation for each subject will be from signing the ICF to about 37(+2) hours after first medication. The sponsor will decide on the requirement for any follow-up of AEs persisting.

STATISTICAL METHODS

As this is a descriptive study, no formal statistical testing will be carried out.

Descriptive statistics on continuous data will include the counts, number of missing data, means, standard deviations, medians, minimum and maximum values, while categorical data will be summarized using frequency counts and percentages.

Adverse events (AE) will be coded according to the latest version of the MedDRA dictionary and presented in "preferred term (PT) and system organ class (SOC)". The incidence of each AE will be calculated.

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LIST OF ABBREVIATIONS

ADR	Adverse drug reaction
AE	Adverse event
AESI	Adverse event of special interest
BHPM	Bis-(p-hydroxyphenyl)-pyridyl-2-methane
BMI	Body Mass Index
CRO	Contract research organization
EC	Ethics committee
ECG	Electrocardiogram
ePRO	Electronic patient reported outcomes
FDA	U.S. Food and drug administration
GPP	Good pharmacoepidemiology practice
ICF	Informed consent form
ICSR	Individual case safety report
INR	International standardized ratio
NMPA	National medical products administration
PEG	Polyethylene glycol
PSUR	Periodic safety update report
PT	Preferred terms
RA	Regulatory authority
RMP	Risk management plan
SAE	Serious adverse event
SADR	Serious adverse drug reaction
SMP	Safety management plan
SOC	System organ classification
SOP	Standard operating procedure

1 INTRODUCTION

1.1 Background

High-quality bowel preparation plays an important role in ensuring a safe and successful X-ray examination, endoscopy or some kinds of bowel surgeries. Inadequate bowel preparation may lead to incomplete examination of the colonic mucosa, may require increased operation time and difficulty, and incur the costs for rescheduling or performing other examinations. Early attention to the influencing factors of bowel cleansing effect and taking positive measures can effectively improve the success rate and diagnosis rate of endoscopic and radiological examinations, and reduce the possibility of postoperative complications and local infections[1–4]. In 2019, China released the latest "Guidelines for Bowel Preparation Related to Digestive Endoscopy", emphasizing the importance of dietary restrictions and patient notification and education. The “Guideline” also recommends that sodium picosulfate, magnesium oxide, and anhydrous citric acid can be used for bowel preparation before endoscopy and is well tolerated (recommended strength: weak; evidence quality: moderate) [5]. The other used colonic cleansing agents also include polyethylene glycol (PEG) electrolyte powder, magnesium salt, sodium phosphate, mannitol and Chinese herbal medicine. Each carries its own properties, indications and safety profiles.

Compound Sodium Picosulfate Granules is a compounded preparation consisting of sodium picosulfate and magnesium citrate. Each sachet contains 10 mg of sodium picosulfate, 3.5 g of magnesium oxide and 12.0 g of citric acid. It is white to slightly yellow crystalline powder, with a slight orange flavour. Sodium picosulfate is transformed by colonic bacteria to form an active metabolite: bis-(p-hydroxyphenyl)-pyridyl-2-methane, BHPM, which acts directly on the colonic mucosa to stimulate colonic peristalsis. Magnesium oxide and citric acid react to create magnesium citrate (when dispersed in a solution), which is an osmotic agent that causes water to be retained within the gastrointestinal tract. The stimulant laxative activity of sodium picosulfate together with the osmotic laxative activity of magnesium citrate produces a purgative effect, which can be used to clean the bowel prior to X-ray examination, endoscopy or bowel surgery.

Since its first marketing in the UK in December 1980, Compound Sodium Picosulfate Granules has been approved in more than 80 countries and regions, including Germany (2010), France (2010), Spain (2011), Italy (2011) and the United States (2012), Japan (2016), under the tradename PICOLAX, PICOPREP or PREPOPIK. In 2018, Compound Sodium Picosulfate Granules was officially approved in China with the indication: for preparation of bowel cleansing prior to X-ray examination, endoscopy or surgery when judged clinically necessary.

1.2 Preliminary Safety Evaluation

1.2.1 *Preclinical Safety Data*

The preclinical safety data related to Compound Sodium Picosulfate Granules are summarized as follows:

General Safety Pharmacology

Anesthetized rats were injected with sodium picosulfate intravenously and tested their cardiac function parameters. Under the maximum dose of 160 mg/kg, no abnormal changes in blood pressure and electrocardiogram were observed [6].

Irwin screen test was used to evaluate the effect of one-time oral gavage of sodium picosulfate on the central nervous system of mice. Single oral administration of sodium picosulfate 40mg/kg and 80mg/kg in mice has no effect on the central nervous system [6].

In a 4-week repeated oral dose toxicity study of Compound Sodium Picosulfate Granules in dogs (n = 6), no abnormal ECG changes were observed under the maximum dose of 1000 mg/kg (twice a day, every 8 hours apart).

Repeat-Dose Toxicity

Repeated dose toxicity studies with sodium picosulfate (2 weeks) and Compound Sodium Picosulfate Granules (4 weeks) in both the rat and the dog showed expected treatment and dose related pharmacology with soft stools and diarrhoea and with no observed adverse effects.

Carcinogenicity

No published studies of carcinogenic potential of sodium picosulfate have been identified.

Genotoxicity

Sodium picosulfate was not mutagenic in the Ames test, the mouse lymphoma assay and the mouse bone marrow micronucleus test.

Reproductive toxicity

Male and female rat fertility was not affected by oral doses of sodium picosulfate up to 100 mg/kg.

Prenatal developmental studies in rats and rabbits did not reveal any teratogenic potential after oral dosing of sodium picosulfate, but embryotoxicity has been observed in rats at 1000 and 10000 mg/kg/day and in rabbits at 1000 mg/kg/day. The corresponding safety margins were 3000 to 30000 times the anticipated human dose. In rats, daily doses of 10 mg/kg during late gestation (fetal development) and lactation reduced body weights and survival of the offspring.

In an oral fertility study in rats, Compound Sodium Picosulfate Granules did not cause any significant adverse effect on male or female fertility parameters up to a maximum dose of 2000 mg/kg twice daily (about 1.2 times the recommended human dose based on the body surface area). During the perinatal period, rats were given Compound Sodium Picosulfate Granules 2000 mg/kg twice daily, and no significant effect on pup growth and development was observed.

Drug interactions

Sodium picosulfate and its active metabolite are not absorbed to any significant degree and there is no evidence of direct, time dependent or metabolism dependent inhibition on the major drug metabolizing cytochrome P450 enzymes in human liver microsomes and hepatocytes.

Some medicines (e.g. tetracycline and fluoroquinolone antibiotics, iron, digoxin, chlorpromazine and penicillamine) have the potential to chelate with magnesium.

1.2.2 *Clinical Safety Data*

Up to May 2019, the cumulative number of subjects from completed clinical trials, for Compound Sodium Picosulfate Granules, is estimated to 1,974 subjects.

The key efficacy, safety results and exposures to investigational drug from the completed Ferring sponsored Phase 3-4 clinical trials are presented in the table below.

Trial Code/Phase	Trial Design	Country	Compound Sodium Picosulfate Granules Dose/Schedule	No. of Subjects	Results
2009-01 (Phase 3)	Multicentre, randomized, assessor-blinded, active control, parallel-group	US	Split-day[a]	Compound Sodium Picosulfate Granules: 305; HalfLytely: 298; Total: 603	Compound Sodium Picosulfate Granules superior to HalfLytely in overall colon cleansing (Aronchick Scale). No drug-related safety concerns or novel adverse events were observed. No clinically meaningful changes in laboratory tests, ECGs, or physical examinations, including multiple orthostatic pulse and blood pressure measurements were observed. The safety profile supported a positive benefit/risk ratio.
2009-02 (Phase 3)	Multicentre, randomized, assessor-blinded, active	US	Day-before[b]	Compound Sodium Picosulfate Granules: 296;	Compound Sodium Picosulfate Granules non-inferior to HalfLytely in overall colon cleansing (Aronchick Scale). No drug-related safety concerns or novel adverse

Trial Code/Phase	Trial Design	Country	Compound Sodium Picosulfate Granules Dose/Schedule	No. of Subjects	Results
	control, parallel-group			HalfLytely: 302; Total: 598	events were observed. No clinically meaningful changes in laboratory tests, ECGs, or physical examinations, including multiple orthostatic pulse and blood pressure measurements were observed. The safety profile supported a positive benefit/risk ratio.
999169 CS2 (Phase 3)	Multicentre, randomized, assessor-blinded, active control, parallel-group	China	Split-day[c]	Compound Sodium Picosulfate Granules:150; PEG-ELS:150; Total: 300	Compound Sodium Picosulfate Granules non-inferior to PEG-ELS (polyethylene glycol 4000-electrolyte powder for oral solution) in overall bowel cleansing (Ottawa Scale), cleansing of each colon section, and overall fluid retention. There were no clinically significant differences in changes from baseline to post-treatment in clinical safety laboratory values, vital signs, ECG parameters, or physical examination findings. Compound Sodium Picosulfate Granules was superior to PEG-ELS in subject-rated outcomes.
000121 (Phase 3)	Multicentre, randomized, assessor-blinded, parallel-group	EU	Split-dose[d] vs. Day-before[e]	Split-dose: 73; Day-before: 131; Total:204	Subjects receiving the tailored schedule had 7-9 times greater odds of being a responder (Ottawa Scale) with regard to colon cleansing status when compared with day-before schedule. Subject convenience and satisfaction (ease of consuming, overall experience, taste, willingness and acceptance to use for future colonoscopy) were high for each schedule. No new safety signals were seen with either schedule.
000176 (Phase 3)	Multicentre, randomized, assessor-blinded, active control, parallel-group	Japan	Split-day[f] vs. Day-before[b]	Compound Sodium Picosulfate Granules Split-day: 214; Compound Sodium Picosulfate Granules Day-before: 212;	Results showed that both Compound Sodium Picosulfate Granules dosing schedules were non-inferior to Niflec, as judged by an Independent Central Judging Committee (Japanese Colon Cleansing Scale). Subjects considered Compound Sodium Picosulfate Granules more acceptable than Niflec, according to a questionnaire administered on the day of colonoscopy. No new safety

Trial Code/Phase	Trial Design	Country	Compound Sodium Picosulfate Granules Dose/Schedule	No. of Subjects	Results
				PEG-ELS: 211; Total: 637	signals were seen with either schedule.
000253 (Phase 3)	Multicentre, randomized, assessor-blinded, active control, parallel-group	US	Split-day[a]	Compound Sodium Picosulfate Granules: 453; Sodium picosulfate, magnesium oxide, and anhydrous citric acid pre-mixed oral solution: 448; Total: 901	The Sodium picosulfate, magnesium oxide, and anhydrous citric acid pre-mixed oral solution treatment demonstrated statistically significant superiority over Compound Sodium Picosulfate Granules for the primary endpoint and the key secondary endpoint. Overall, the safety results did not indicate any safety concerns or signals for either bowel preparation.
000180 (Phase 4)	Multicentre, randomized, assessor-blinded, active control, parallel-group	Brazil	Split-day[a]	Compound Sodium Picosulfate Granules: 90; Mannitol/ Bisacodyl: 89; Total: 179	Results showed that Compound Sodium Picosulfate Granules is a tolerable and safe preparation for colon cleansing in preparation for a colonoscopy in adult subjects, but the objective of demonstrating superior efficacy over the active control was not achieved.

a：Split-day schedule: On the day before colonoscopy, first dose between 5:00 pm and 9:00 pm; on the day of colonoscopy, second dose approximately 5 hr before but no more than 9 hr prior to the procedure.

b：Day-before schedule: On the day before colonoscopy, one dose between 4:00 pm and 6:00 pm and another dose 6 to 8 hr later between 10:00 pm and 12:00 am.

c：Split-day schedule: On the day before colonoscopy, first dose between 8:00 pm and 9:00 pm; on the day of colonoscopy, second dose 4 to 6 hr before colonoscopy.

d：Split-dose schedule: First dose 10 to 18 hr before colonoscopy and second dose 4 to 6 hr before colonoscopy.

e：Day-before schedule: On the day before colonoscopy, one dose prior to 8:00 am and another dose 6 to 8 hr later.

f：Split-day schedule: On the day before colonoscopy, first dose between 5:00 pm and 9:00 pm; on the day of colonoscopy, second dose at least 4 and up to 9 hr prior to colonoscopy.

* HalfLytely: (Powder: PEG-El (polyethylene glycol electrolyte solution) 3350/Sodium Chloride/Sodium Bicarbonate/KCL) and Bisacodyl Tablets Bowel Prep Kit.

In randomized, multicentre, controlled clinical trials, nausea, headache, and vomiting were the most common adverse reactions (>1%) following Compound Sodium Picosulfate Granules administration. Since abdominal bloating, distension, pain/cramping, and watery diarrhoea are known

to occur in response to bowel cleansing preparations, these effects were documented as adverse events in the clinical trials only if they required medical intervention (such as a change in study drug or led to study discontinuation, therapeutic or diagnostic procedures, met the criteria for a serious adverse event), or showed clinically significant worsening during the study that was not in the frame of the usual clinical course, as determined by the investigator.

Limitations in respect to populations typically under-represented in clinical trial development programmes are presented as follows:

Paediatric population	In completed Ferring sponsored clinical trial for the paediatric population (000103), a total of 78 paediatric subjects were included (48 paediatric subjects were randomised to Compound Sodium Picosulfate Granules and 30 to PEG). The subjects were randomised to one of the treatment arms by age groups from 9-12 years and 13-16 years. The Compound Sodium Picosulfate Granules age group 9-12 years received either 1/2 sachet x 2 or 1 sachet x 2, whilst the Compound Sodium Picosulfate Granules age group 13-16 years received 1 sachet x 2. The results of the trial demonstrated that the '1 sachet x 2 dose' of Compound Sodium Picosulfate Granules is a safe and efficacious preparation for colonoscopy in children aged 9-16 years.
Elderly	In the completed Ferring sponsored clinical trials 20% of patients were of ≥ 65 years of age. The overall incidence of treatment emergent adverse events was similar among patients of ≥ 65 and < 65 years of age, 73% and 71% respectively.
Pregnant/breastfeeding women	**Pregnancy** Compound Sodium Picosulfate Granules should not be used during pregnancy unless the clinical condition of the woman requires treatment. There are no adequate and well-controlled studies with Compound Sodium Picosulfate Granules in pregnant women. **Breastfeeding women** Several drugs are excreted in human milk and caution should be exercised when Compound Sodium Picosulfate Granules is administered to a lactating woman. No formal studies have evaluated the transfer of Compound Sodium Picosulfate Granules products into human milk, or its effect on lactation or on breastfed infants. The active metabolite of sodium picosulfate, BHPM is absorbed from the gastrointestinal tract. BHPM, however, remained below the limit of detection (1 ng/mL) in breast milk after both single and multiple doses of 10 mg/day [7]. Although it is known that magnesium contained in Compound Sodium Picosulfate Granules is systemically absorbed in healthy volunteers, no information is available on the clinical use of magnesium citrate during lactation.
Patients with hepatic impairment	Not included in the clinical development program. A dosage adjustment in patients with hepatic impairment is not considered needed as sodium picosulfate is converted to its active metabolite BHPM by colonic bacteria. Sodium picosulfate and its metabolite BHPM are mainly excreted in urine.
Patients with renal impairment	Severely reduced renal function (creatinine clearance less than 30 mL/minute) is a contraindication. In patients with severely reduced renal function accumulation of magnesium in plasma may occur. Another preparation should be used in such cases.

	An analysis was performed as a post-approval commitment to the FDA. The objective was to retrospectively identify risk factors associated with the development of persistent or potential late decrease in renal function in subjects who had undergone colon cleansing with Compound Sodium Picosulfate Granules or HalfLytely in preparation for colonoscopy in Ferring Trials FE2009-01 and FE2009-02[8,9]. This retrospective analysis of renal function in subjects supports the current labelling when the product is used per label instructions as well as confirming the validity of the current renal prescribing information to physicians and subjects.
Population with relevant different ethnic origin	Phase 3 trials have been conducted in different regions involving patients of different racial and ethnic origin. Although no formal analysis has been carried out, the safety and efficacy profile of Compound Sodium Picosulfate Granules is well established in these various populations.
Patients with low body weight (BMI)	Limited data is available for treatment of patients with low body weight (BMI less than 18).

1.2.3 *Post-authorisation Experience*

The cumulative exposure to Compound Sodium Picosulfate Granules from marketing experience calculated from 01 January 1999 up to and including 31 May 2019 is estimated to 53,654,394 patients. The calculation of exposure is based upon an assumption that the number of treatments is equivalent with number of patients exposed to Compound Sodium Picosulfate Granules. One treatment consists of 2 sachets, which corresponds to an adult dose.

The frequencies of the side effects are based on post-marketing experience and as outlined in the Compound Sodium Picosulfate Granules label.

System Organ Class	Common (≥1/100, ＜1/10)	Uncommon (≥1/1000,＜ 1/100)	Not known (cannot be estimated from the available data)
Immune system disorder		Anaphylactic reaction, hypersensitivity	
Metabolism and nutrition disorders		Hyponatraemia hypokalaemia	
Nervous system disorders	Headache	Epilepsy, grand mal convulsion, convulsions, confusional state	
Gastrointestinal disorders	Nausea and proctalgia	Vomiting, abdominal pain, aphthoid ileal ulcers	Diarrhoea, faecal incontinence
Skin and subcutaneous tissue disorders		Rash (including erythematous and maculopapular rash, urticaria, purpura)	

1.3 Study Rationale

Based on nearly 40 years' clinical experience, Compound Sodium Picosulfate Granules has a well-

established safety profile and treatment regimen that support a positive benefit/risk ratio.

According to the review of non-clinical, clinical and post-marketing data, the known adverse effects of Compound Sodium Picosulfate Granules include anaphylactic reaction, hypersensitivity, hyponatraemia, hypokalaemia, confusional state including disorientation, headache, epilepsy, generalised tonic-clonic seizure, seizure, loss of consciousness or depressed level of consciousness, syncope, presyncope, dizziness, vomiting, nausea, abdominal pain, diarrhoea, ileal ulcers, anal incontinence, proctalgia, rash (including erythematous rash, maculo-papular rash, urticaria, purpura).

According to the latest Compound Sodium Picosulfate Granules Risk Management Plan (RMP) (Ver. 2.0, 11 OCT 2019), Compound Sodium Picosulfate Granules has no important identified risks, no important potential risks, and no important missing information. Compound Sodium Picosulfate Granules's label and its package leaflet give essential information to healthcare professionals and patients on how the Compound Sodium Picosulfate Granules product should be used. Measures to minimise the risks identified for medicinal products include:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and label addressed to patients and healthcare professionals;
- Important advice on the medicine’s packaging;
- The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine’s legal status — the way a medicine is supplied to the patient (e.g. with prescription) can help to minimise its risks.

Together, these measures constitute routine risk minimisation measures. In addition, information about adverse reactions is collected continuously and regularly analysed, including individual case assessment and Periodic safety update report (PSUR) assessment so that immediate action can be taken as necessary. These measures constitute routine pharmacovigilance activities. According to NMPA Regulation Order No. 81 of Ministry of Health, the safety profile of a newly approved medicine needs to be intensively monitored in a real-world setting. This study will further assess Compound Sodium Picosulfate Granules utilisation and safety profile in bowel preparation prior to X-ray examination, endoscopy or surgery when judged clinically necessary in real-world clinical practice in Chinese population.

2 STUDY OBJECTIVES

The objectives of this drug intensive monitoring study are to monitor and assess the safety profile of Compound Sodium Picosulfate Granules in the real world clinical practice in Chinese population, including：

- Incidence of known ADRs
- Observe occurrence of unexpected AEs/ADRs
- Incidence and risk factors of SAEs/SADRs

3 METHODS

3.1 Study Design

This is a multi-site, prospective, non-interventional study. The subject's recruitment should not be influenced by the study protocol and should fall within the current practice.

Subjects who meet the requirements will be followed from signing the informed consent form (ICF) to about 37(+2) hours after first medication to collect AEs, medications and other relevant information with remotely contacted by pharmacist and/or hospital staff. No additional assessments or tests considered as interventional will be required. Any adverse events collected during the subject's interview will be sent to the sponsor for case processing.

3.2 Medicinal Product

This study does not provide treatment, the subjects must already have been prescribed Ferring Compound Sodium Picosulfate Granules. All directions for drug usage are solely at the discretion of the subject's primary physician in accordance with his/her usual practice and should be consistent with the local prescribing information.

3.3 Bias and Limitations

3.3.1 *Method to Minimize Bias*

In order to limit this potential selection bias in the recruitment of subjects, the recruiter will be required to include all subjects who have been prescribed Ferring Compound Sodium Picosulfate Granules in a naturalistic fashion.

Since the AE information is collected through the report of subjects, while the missing information of AEs due to subjects failing to declare may be immeasurable.

3.3.2 *Study Limitations*

This is a single arm observational study provides no comparative data. Therefore, whether the incidence of AEs in the Compound Sodium Picosulfate Granules group is higher or lower than the incidence in a non-exposed group can't be determined.

In addition, observational data may miss some relevant information or loss follow-up, the quality of data is not compatible to interventional study. The participants are voluntarily enrolled which may

have certain bias would not truly represent real world population or data.

4 SELECTION OF STUDY POPULATION

4.1 Study Population

4.1.1 *Inclusion Criteria*

1) Agree to participate in this study and sign the ICF by subject or the legal representative.
2) Subjects taking the compound sodium picosulfate granules drug in real clinical practice.

4.1.2 *Exclusion Criteria*

1) Subjects who are enrolled in other on-going studies, which prohibit any participation in this non-interventional study.

4.2 Withdrawal Criteria

As this is a non-interventional study, no specific withdrawal criteria are specified. Subjects are free to withdraw consent at any time. Data will be collected up to the time of withdrawal of consent, and no additional information will be collected after this time.

4.3 Site Selection

This study is planned to be conducted in 20 pharmacies and hospitals in China mainland.

4.4 Duration of Study

The overall duration of the study for each subject will be from signing the ICF to about 37 (+2) hours after the first medication. The sponsor will decide on the requirement for any follow-up of AEs persisting (see section 6.6).

The study will be considered as started when the first subject signs the ICF and will be considered as finished when the last subject's data are fully collected. The overall study duration will be approximately 2 years.

The sponsor has the right to terminate this study/close the study sites in advance after consulting the relevant regulatory agency.

5 STUDY PROCEDURES

The study procedure includes following steps:

1. Provide signed and dated written informed consent form prior to any procedure related to the study.
2. Evaluate subjects agreed to participate in study to make sure they meet inclusion and exclusion criteria.
3. Register eligible subjects and collect subject demographics and characteristics (gender, age, nation, height and body weight).
4. Follow up the eligible subjects 37 (+2) hours after the first medication.

For the subject who experienced AE, the following information will be collected to evaluate the safety profile of Compound Sodium Picosulfate Granules in real-world clinical practice.

- Medicinal information (administration time and dosage) and indication
- Concomitant medications
- Medical history
- Relevant lab test and its result: for the subject who experienced AE, collect relevant lab tests and its results subjects may receive as much as possible
- Safety evaluation

All stipulated events reported from signing the ICF to about 37(+2) hours after the first medication. AE information include the nature, the start date and end date, the relationship to the medicinal product, the seriousness, the outcome, and the use of corrective treatment, etc.

6 SAFETY REPORTING

6.1 Definition of Adverse Events

Adverse event (AE) is any untoward medical condition or the deterioration of a pre-existing medical condition in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with the treatment. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product, whether or not related to the medicinal product. An AE may be caused by the use of any medication (e.g. non-indications, combined use), any route of administration, prescription, dose (including overdose) and accidental injuries.

6.2 Definition of Adverse Drug Reactions

An adverse drug reaction (ADR), contrary to an AE, is characterized by the suspicion of a causal relationship between the medicine and the occurrence, i.e. judged as being at least possibly related to treatment by the reporter or a reviewing health professional.

An ADR is a response to a medicinal product which is noxious and unintended. This includes adverse reactions which arise from:

- The use of a medical product within the terms of the marketing authorization;
- The use outside the terms of the marketing authorization, including overdose, off-label use, misuse, abuse and medication errors;
- Occupational exposure.

6.3 Definition of Unexpected Adverse Drug Reactions

Unexpected adverse reaction refers to a drug reaction whose nature, severity, specificity, or outcome is not consistent with the term or description listed in the current local/regional label. This includes events that may be symptomatically and pathophysiological related to an event listed in the labelling but differ from the event because of greater severity or specificity. For example, under this definition, hepatic necrosis would be unexpected (by virtue of greater severity) if the labelling only referred to elevated hepatic enzymes or hepatitis. Similarly, cerebral thromboembolism and cerebral vasculitis would be unexpected (by virtue of greater specificity) if the labelling only listed cerebral vascular accidents.

"Unexpected," as used in this definition, refers to an adverse drug experience that has not been previously observed (i.e. not included in the label) rather than from the perspective of such experience not being anticipated from the pharmacological properties of the pharmaceutical product.

6.4 Definition of Serious Adverse Events

A serious adverse event (SAE) is defined as any untoward medical occurrence that at any dose that:

- Results in death [a]
- Is life-threatening [b]
- Is a congenital anomaly/birth defect [c]
- Results in persistent or significant disability/incapacity [d]
- Results in unplanned inpatient hospitalisation or prolongation of existing hospitalisation [e]
- Is an important medical event that may jeopardise the subject or may require intervention to prevent one of the outcomes listed above [f]

Further explanations for SAEs are as follows:

a. Any deaths caused by AEs during the study period, including those that are completely unrelated to the medicinal product. Note: AE terms should be described as the lead cause of death (e.g. multiple organ dysfunction syndrome, pneumonia, myocardial infarction, etc. and with a fatal outcome but not death as an event), with the only exception being unknown causes of death (i.e. sudden or unexplained death), in which case the event term may be "death" or "sudden death".

b. Life-threatening is an event that places the patient at immediate risk of death from the reaction as it occurred. It does not include a reaction that, had it occurred in a more severe form, might have caused death, e.g. drug-induced liver injury without hepatic failure.

c. The term refers to any congenital anomaly/birth defect in the offspring of either patient who exposed to the medicinal product.

d. The term refers to any condition that impairs physical/psychological well-being to the extent that the subject is unable to function normally. Physical disability may include, but is not limited to, permanent disability of locomotion or motility, but also systemic permanent dysfunction as development of heart failure, liver insufficiency or pulmonary fibrosis.

e. Hospitalisation is defined as at least one overnight formal admission into hospital, usually to perform additional tests, provide treatment that it is not possible to provide at home and/or to allow specific monitoring of the subject due to their unstable medical condition. Hospitalisation for a pre-planned or elective treatment/surgical procedure should not be reported as an SAE unless there are complications or sequelae which meet the criteria for seriousness described above. Hospitalization or prolongation of existing hospitalisation due to non-medical reasons / convenience or purely for the purpose of study does not meet the criteria for medical events and cannot be considered an SAE.

f. Important medical events that may not result in death, be life-threatening, or require hospitalisation may be considered a significant adverse drug experience when, based upon appropriate medical judgment, they may jeopardize the patient and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalisation, or the development of drug dependency or drug abuse.

6.5 Collection of Adverse Events

The study will collect all stipulated events reported from signing the ICF to about 37(+2) hours after the first medication. Sponsor will capture any adverse events collected during the subject's remotely contact by pharmacist or hospital staff.

Pharmacist or hospital staff will report any adverse events collected during the subject's remotely contact to Ferring (E-mail: PPD) within the following timelines:

1) Fatal events, whether they are related/unrelated, must inform the sponsor immediately (within 24 hours of the knowledge of the event).

2) All other AE reports must be sent to the sponsor within 3 calendar days of knowledge of the event or receipt of significant follow-up information.

6.6 Follow-up of Adverse Events

The sponsor will decide on the requirement for any follow-up of AEs persisting after 37(+2) hours after the first medication. Generally, for all ADRs, pharmacist or hospital staff needs to follow up until:

1) Sufficient information has been obtained from the reporter;

2) The reporter clearly stated that there was no further information or refused to follow up;

3) There is no new information after two follow-ups, and further follow-up cannot obtain more information;

4) The reporter cannot be contacted more than 3 times on different days. Follow-up records should be kept properly;

5）Mails and letters are returned and there are no other contact methods available.

For Fatal SADR, the following information should be collected promptly, includes: verifying, supplementing and improving information on death cases, drug use, occurrence, diagnosis and treatment of adverse reactions; information about drug storage, use, and occurrence of similar adverse reactions from medical institutions; if the subject is transferred for treatment, investigation should be carried out on the transfer treatment. In addition, the subject's medical records, autopsy reports and other information should be collected according to the actual situation. During the investigation process, the quality of the product should also be reviewed, and quality inspection should be carried out if necessary.

6.7 Adverse Events Recording during Case Processing

The sponsor is responsible for case processing. During case processing, AE recording must be based on subject's reliable reporting. For each AE the following variables will be recorded:

- Verbatim;
- Date/time of AE start and stop;
- Relationship to the medicinal product;
- Action taken with regard to the medicinal product;
- Outcome;
- Seriousness;
- Criteria for seriousness (if applicable);
- Date AE met criteria for seriousness (if applicable);
- Date of hospitalisation and discharge (if applicable);
- Date of death and reason (if applicable);
- Autopsy report (if applicable).

6.7.1 *Verbatim/Description of AE*

The recording of AEs should use diagnostic terms whenever possible. If the diagnosis cannot be confirmed, AE can be recorded for the symptoms, signs and abnormal examinations. The record should be updated and reported as follow-up information if later diagnosis is confirmed. It should be ensured that each AE verbatim term consists of a single event, and one diagnosis, sign or symptom is an AE.

6.7.2 *Time Recording of AE*

The start date of the AE should be the date when the symptoms appear. If the AE is the deterioration of a pre-existing medical condition at the baseline, the start date is the date of the deterioration of the condition in the study. If the AE is new event in the study and upgraded to SAE, the SAE start date is still the original AE start date.

6.7.3 *Outcome of AE*

The outcome of the event will be described in terms of:

- **Recovered**: Subject returned to the baseline state.
- **Recovering**: Event has not been fully resolved, but the subject is already in the recovery phase.
- **Not recovered**: Event is ongoing. e.g. irreversible congenital malformation.
- **Recovered with sequelae**: Used only with persistent incapacity/life-long sequelae, e.g. blindness after diabetes mellitus, hemiparesis after stroke.
- **Fatal**: (S)AE stop date is the date of death.
- **Unknown**: Unknown to investigational personnel, e.g. patient lost to follow-up.

If the outcome is “recovered” or “recovered with sequelae” or “fatal” the AE stop date must be entered.

6.7.4 *Assessment of AE*

Causality Classification

Subject will assess causal relationship between the medicinal product and each AE, and answer “yes” or “no” to the question “Do you consider that there is a reasonable possibility that the event may have been caused by Compound Sodium Picosulfate Granules?”

During case processing, the sponsor will also assess the causality. The relationship of an AE with the medicinal product will be classified according to the following:

– **Related**: The AE follows a reasonable temporal sequence from the medicinal administration and cannot be reasonably explained by the subject's clinical state or other factors (e.g. disease under study, concurrent diseases, and concomitant medications). It may be a known reaction to the drug under study or its chemical group or is predicted by known pharmacology and could not be ruled out with certainty.

– **Not related**: The AE does not follow a reasonable sequence from the medicinal product administration or can be reasonably explained by the subject's clinical state or other factors (e.g. disease under study, concurrent diseases, and concomitant medications).

Assessment of Expectedness

The sponsor is responsible for assessment of expectedness.

6.7.5 *Special Situations of AE Recoding*

Persistent or Recurrent AEs

Persistent AEs are events that persist between assessment time points and no remission. During case processing, such events should be recorded only once. The initial date of the event should be recorded. If the event progresses into an SAE, a corresponding update should be made to reflect the situation.

Recurrent AEs are events that have been resolved between assessment time points but then recurred. Each recurrence of an AE should be recorded separately.

AEs Secondary to other Events

During case processing, in general, AEs secondary to other events (e.g. cascade events or clinical sequelae) should be recorded based on their main etiology, except for severe or serious secondary AEs. For a medically significant AE secondary to an initial event with a time interval, the AE should be recorded as an independent event.

Abnormal Medical Exam

Clinically significant medical exam abnormalities (such as vital signs, physical examination, blood routine, urine routine, blood biochemistry, ECG, etc.) found before the first medication can be recorded as a medical history/concomitant disease. The results of various medical exam after medication will be compared with the data from baseline and judged whether they are of clinical significance.

During case processing, medical exam abnormalities should be recorded as an AE if any one of

the following criteria is met:

- The abnormality is associated with symptoms/signs.
- The abnormality requires required medical intervention (such as a change in medicinal product or led to study discontinuation, therapeutic or diagnostic procedures).

If the abnormality is a manifestation of a disease (e.g. increased alkaline phosphatase and total bilirubin levels accompanied by cholecystitis), only the diagnosis (i.e. cholecystitis) should be recorded as an AE. If the abnormality does not belong to any disease, the abnormality itself should be recorded as an AE, using relevant descriptors to indicate that the test result is higher or lower than the normal range (e.g. "blood sodium decreased" instead of "blood sodium abnormal"). If the diagnostic criteria are met, the clinical diagnosis should be used to record the AE. For example, a serum sodium level < 135 mmol/L can be recorded as "hyponatremia".

6.7.6 *Special Situations with No Need to Record as AEs*

During case processing, the following situations collected will not be recorded as AEs:

- The clinical adverse events that occurred before the medication will be recorded as pre-treatment events rather than AEs.
- Since abdominal bloating, distension and watery diarrhoea are known to occur in response to bowel preparations, these effects should be documented as AEs only if they require medical intervention (such as a change in study drug or led to study discontinuation, therapeutic or diagnostic procedures), or show clinically significant worsening during the study that is not in the frame of the usual clinical course.
- X-ray examination, endoscopy or bowel surgery findings such as polyps and/or colorectal cancer do not need to be recorded as an AE as their diagnosis is the goal of the endoscopic examination. However, injuries / damages caused by inspections or surgical operations must be recorded as AEs.

6.8 Reporting of Adverse Drug Reactions to Regulatory Authorities

The sponsor will submit the ADR to the Regulatory Authorities according to current legislation, and all have to comply with local legislation for safety reporting.

6.9 Post-study Safety Collection

If pharmacist or hospital staff becomes aware of an ADR reported by subjects spontaneously after the end of the study, the case will have to be sent to the sponsor, regardless how long after the end of the study.

6.10 Special Situations

The following information must be collected and recorded during case processing regardless of the occurrence of AE.

- Medication error (including potential medication error and intercepted medication error)
- Off-label use
- Lack of efficacy
  - The drug was ineffective, did not work, or similar wording, or that the expected effect was not obtained (e.g. subject did not reach the clear yellow liquid poop stage) under the usage and dosage according to the locally approved label.
- Accidental/Occupational exposure
- Misuse/Abuse
- Overdose/Underdose
- Counterfeit/falsified products
- Suspected transmission of an infectious agent *via* a medicinal product
- Drug exposure to foetus *via* mother or father
  - The pregnancy must be reported immediately and within 24 hours from the date of the awareness to the sponsor by completing and sending the “Pregnancy form”. Pregnancy itself is not regarded as an AE, however, any congenital anomaly/birth defect, spontaneous miscarriage, elective termination for medical reasons should be reported and handled as SAE. Pharmacist or hospital staff will continue to provide and record further information about the course and outcome of the pregnancy (spontaneous miscarriage, elective termination, ectopic pregnancy, normal birth, or congenital abnormality) by telephone follow-up.
- AEs in infants following drug exposure from breastfeeding

- Treatment non-compliance
  - In this study, non-compliance of drug administration and liquid intake (see Section 7.3.4) will be recorded as treatment non-compliance.
- Unexpected benefit
- Cases where the reported term does not reflect a specific reaction, for example “Adverse reaction or Adverse event”
- Product use issues
- Product quality issues (only when reported alongside other safety information e.g. an ICSR or other surveillance event (e.g. medication error)).

Details will be described in safety management plan (SMP).

7 STATISTICAL METHODS

7.1 Sample Size

Since the drug regulatory authority did not require specific population surveillance in this project, general population surveillance will be adopted. This study will not impose rigid rules on the sample size of specific populations. Sponsor will collect safety data as much as possible.

7.2 Analysis Population Definitions

- **Safety population**: Subjects who has signed an ICF and has at least partially taken the drug. It is the primary population for safety evaluation in post-marketing intensive monitoring.

7.3 Statistical Analysis

Analyses will be performed by sponsor or its representatives. Statistical methods will be primarily descriptive in nature. No formal statistical tests will be performed.

All statistical analyses will be presented overall.

7.3.1 *Demographics and other Baseline Characteristics*

Demographic and baseline clinical characteristics analysis will be performed on the safety population. Descriptive summary statistics (number of available data, number of missing data, mean, standard deviation, median, minimum and maximum for continuous data, and frequency count and percentage for categorical data) will be calculated for demographic and baseline clinical characteristics (e.g. gender, age, weight, etc.).

Missing data will not be replaced but they will be displayed in all relevant tables.

7.3.2 *Subject Disposition*

The following will be summarized:

- Subject signed ICF;
- Subject has at least partially taken the drug;
- Subject allocation by site.

7.3.3 *Safety Evaluation*

AEs will be coded using the latest version of MedDRA and presented as “Preferred Terms (PT)

and System Organ Classification (SOC)".

Descriptive summary statistics of SAEs, AESIs and other nonserious AEs, related or unrelated to Compound Sodium Picosulfate Granules, will be presented. The main contents include the incidence, seriousness. of known ADRs/AEs and unexpected ADRs/AEs, as well as the occurrence of ADRs/AEs in specific populations. The covariates like age, gender and relevant risk factors (e.g. decreased renal function, non-compliance of drug administration or liquid intake, etc.) for the AE will be examined. Analyses and summary tables will be based upon the registry population.

Statistical analyses will present the overall results as well as separately for the specific populations.

7.4 Interim Analyses

No interim analyses are planned for this study.

8 DATA HANDLING

This study collect AEs, medications and other relevant information with remotely contacted by pharmacist and hospital staff. The subjects' data will be input into the database by the delegated staff. The subjects will be identified only by Study ID and subject number in the export database for analysis.

If the written informed consent of a subject is known not to be available in spite of it being required, data for this subject is not entered into or is deleted from the export database.

The safety data (AEs report) filed in AE form will be input into Ferring global safety database. The sponsor is responsible for processing AE/ADR in the safety database.

The coding of AE, medical history, concomitant medication, concomitant non-drug therapies and concomitant surgery terms will be performed. Concomitant medications will be coded using the World Health Organisation Drug Dictionary (WHODRUG) and AEs/medical and surgical history and nondrug therapy terms will be coded using the latest version of MedDRA.

On request, Pharmacist or hospital staff will provide the sponsor with additional data relating to the study, duly anonymised and protected in accordance with applicable requirements.

9 QUALITY CONTROL

9.1 Monitoring

Before the first subject is recruited into the study, sponsor will work with the investigational personnel to review and discuss the study protocol and related documents, as well as their responsibilities with regards to protocol compliance. Training will be conducted in accordance with the prescribed study procedures, and records of all participants will be kept.

Sponsor reserves the rights of monitoring the data to verify that they are accurate and complete and that the study is conducted in compliance with the protocol, GPP and regulatory requirements. Assigned monitors will conduct a combination of remote data reviews (with email and telephone contacts) and periodic local visits to address specific requirements and data quality. The monitor can access all original data, documents and records of the study and perform source data verification including verification of informed consent of participating subjects.

All the monitoring activities will be performed in accordance with sponsor SOP.

9.2 Audit/Inspection

Similarly, audits/inspections may be conducted during the study and/or at the end of the study by representatives of the sponsor or external competent authorities. In this later case, the sponsor will be informed immediately. The auditor can review all medical records, study-related documents, and the ICF. The purpose of an audit is to ensure that ethical, regulatory and quality requirements are fulfilled in all studies performed by the sponsor.

10 CHANGES IN CONDUCT OF THE STUDY

10.1 Protocol Amendments

Any change to this protocol will be documented in a protocol amendment, issued by the sponsor. Amendments will be submitted for consideration to the approving central ethics committee (EC) and/or RA, as applicable. Approval is required for amendments which could affect the safety of the subjects, or which entails a change to the scope/design of the study.

10.2 Premature Termination of Study Sites

The sponsor reserves the rights to terminate the participation of individual study sites. Conditions that may warrant termination include but are not limited to, insufficient adherence to protocol requirements and failure to enter subjects at an acceptable rate.

11 REPORTING AND PUBLICATION

11.1 Non-Interventional Study Report

The data and information collected during this study will be reported in a drug intensive monitoring study report prepared by the sponsor or its designee.

11.2 Confidentiality and Ownership of Study Data

Any information relating to the medicinal product or the study, including any data and results from the study is confidential information and will be the property of the sponsor. The investigational personnel will protect the confidentiality of this proprietary information belonging to the sponsor and not disclose such information unless in accordance with the drug intensive monitoring study agreement agreed between the sponsor and the implementing party.

11.3 Publication and Public Disclosure

11.3.1 *Publication Policy*

The procedures for scientific result publication and authors involved in these publications and communications will be defined by the sponsor which reserves the worldwide copyright of all-important publications, including translations into other languages.

The sponsor reserves the rights to:

- Use the study results for any regulatory procedure, on its own behalf or that of subsidiaries.
- Present the results in its medical information letter on drugs.
- Distribute reprints of the publications.

No one may use these rights without the prior written authorization of the sponsor.

11.3.2 *Public Disclosure Policy*

The sponsor will register non-interventional studies in an appropriate registry, i.e. www.ClinicalTrials.gov, (a website maintained by the National Library of Medicine (NLM) at the U.S. National Institutes of Health (NIH)) and any local registries as required by local/national legislation.

12 ETHICAL AND REGULATORY ASPECTS

12.1 Ethics Committee

A central EC will review the protocol and amendments in accordance with applicable national requirements. The central EC will review the Subject Information and the ICF, their updates (if any), and any written materials given to the subjects.

12.2 Regulatory Authority(ies) Authorisation / Approval / Notification

The permission to perform the study will be obtained in accordance with applicable national regulatory requirements. All ethical and or regulatory approvals in accordance with national legislation must be available before the study is initiated.

12.3 Subject Information and Consent

Prior to any procedure related to the study, informed consent must be obtained from subjects. Informed consent can be expressed verbally or in writing, an official ICF must be dated and signed personally by the subject (or witness/legal representative, if applicable).

The investigational personnel will explain the nature, purpose, possible risk and benefit of the study to each subject (or witness/legal representative, if applicable). The subject must be given ample time to consider participation in the study, before the consent is obtained. Each subject will be informed that he/she is completely free to refuse to enter the study or to withdraw from it at any time, without any consequences for his/her further care and without the need to justify their decision. In case the subject decides to withdraw from the study, the data collected up to this point will be used.

Concerning the study data, the subject will accept by signing the ICF that their medical records may be viewed by the sponsor, RA, a mandated auditor and/or the study monitor in compliance with the statement of confidentiality.

12.4 Confidentiality of Subject Data

The investigational personnel will ensure that the confidentiality of the subjects' data will be preserved. In the database or any other documents submitted for AE reporting or publication, the subjects will not be identified by their names, but by an identification system, which consists of an

assigned number in the study. Subject number will consist of site code "CHN##" and subject code "####" (E.g. Subject number: CHN01-0001). Documents that contain the confidential subject identification, e.g. the signed ICF, will be maintained in strict confidence.

13 ARCHIVING

All relevant materials related to this study must be properly preserved, including original medical records (raw data), statistical data and the resulting documents. No local study document may be destroyed without the sponsor's prior written agreement. The sponsor must be notified if the study documents are transferred to another party or moved to another location.

The intensive monitoring data and study documents should be retained in Ferring in accordance with its procedures and applicable regulatory requirements for at least 10 years after the completion of the study report.

14 MILESTONES

Milestone	**Planned date**
Registration of drug intensive monitoring	Dec 2020
Start of data collection	Apr 2021
End of data collection	Dec 2022
Final report of study results	Feb 2023

15 REFERENCES

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16 APPENDICES

Drug intensive monitoring synopsis (for RA China)

Generic Name: Compound Sodium Picosulfate Granules	Trade Name:
Formulation and Specification: Packaged in two sachets, each sachet contains 16.1 g of white or faintly yellow crystalline granules or powder.	Ingredient/Component: Each sachet contains: 10 mg sodium picosulfate, 3.5 g magnesium oxide, 12.0 g citric acid.
Domestic first approval date: 23 Oct 2018	New drug monitoring period starting and end date: 23 Oct 2018 to 22 Oct 2021
Domestic marketing date:18 Mar 2019	International birth date: 22 Dec 1980
Intensive monitoring reasons: New drug monitoring period first import within 5 years, regulatory authority's requirement	Implementation provinces:
Intensive monitoring (proposed) start date: Apr 2021	Intensive monitoring end date: Dec 2022
Funding support：	Total expenditure：
Relevant information of responsible party: Ferring Pharmaceuticals (China) Co., Ltd. Address: No.6, Hui Ling Lu (Ferring Road), National Health Technology Park 528437 Zhongshan City, Guangdong Province, People's Republic of China Leader Name: PPD E-Mail: PPD	
Materials submission (List in chronological order) ：	

Intensive monitoring objectives：

To monitor and assess the safety profile of Compound Sodium Picosulfate Granules in the real-world clinical practice in Chinese population.

Summary of monitoring methods：

This is a post-marketing multi-centre, prospective, non-interventional study. Subjects who have been prescribed Ferring Compound Sodium Picosulfate Granules at the participating sites will be enrolled. The study will collect all stipulated events reported from signing the ICF to about 37(+2) hours after first medication. Pharmacist or hospital staff will contact subjects remotely to collect adverse events/reactions and other relevant information. No additional tests or examinations will be performed on subjects.

- The investigational personnel (e.g. pharmacy pharmacist or hospital staff) will register the eligible subjects. The subjects will sign the informed consent, record contact information.
- After the procedure (about 37 (+2) hours after first drug administration) will report any adverse events and relevant information.
- Follow up, if necessary, pharmacist or hospital staff will collect AEs and other relevant information.

Summary of monitoring results：

Notes：