Non-Interventional Study Protocol
B3391001

AMEPAROMO Capsules 250 mg
Drug Use Investigation

Statistical Analysis Plan

Version: 3.0

Author: PPD (Clinical Statistics Department)

Date: 10-SEP-2018

[redacted]

TABLE OF CONTENTS

1. AMENDMENTS FROM THE PREVIOUS VERSION

Version	Date	Author(s)	Summary of Changes/Comments
1.0	22-OCT-2014	PPD	Initial version
2.0	04-OCT-2017	PPD	Study status: Ongoing 5.1 Safety Analysis Set - Changes were made to coordinate with the revision of the "Guidance for Criteria for Inclusion in Analysis Sets and Handling of Data in Drug Use Investigations". 5.2.1. Cyst Analysis Set - Non-target disease of the study was added to the criteria for patients to be excluded. 5.2.2. Clinical Response Analysis Set - Non-target disease of the study was added to the criteria for patients to be excluded. 5.3. Subgroups - Categories that serve as a reference in comparisons between subgroups were underlined. - Items of subgroups were added. - A description on patients who may meet contraindications in the package insert of this drug was added. - The SMQs of the definitions of hepatic dysfunction and renal dysfunction were changed to the narrow scope only. 6.1. Safety Endpoints - Based on the results of internal review, adverse drug reactions were changed to adverse events determined to be related to AMEPAROMO by the investigator. 8.1.3. Analysis of Binary Data - Calculation of risk difference and 95% confidence interval were added to analyses between subgroups, and graphical presentation of risk ratio was deleted. 8.2.2. Patient Background and Treatment History of AMEPAROMO - Other diagnostic names and the description of prior medications other than those for intestinal amebiasis were added to patient background. - The presence or absence of overdose and the definition of overdose were added to the status of treatment of AMEPAROMO. 8.2.3. Safety Analysis - The definition of main analysis period for safety analysis was added.

Version	Date	Author(s)	Summary of Changes/Comments
			8.2.3.1. Adverse Drug Reactions - A statement was added to note that the listing of contraindicated patients will be prepared and adverse drug reactions will be tabulated by SOC and PT by patients who do or do not meet contraindications, as necessary. - The status of development of adverse drug reactions by whether they developed within or outside of the observation period was added. 8.2.3.4. Subgroup Analysis - Risk difference was added to analyses between subgroups. - The analysis of serious adverse drug reactions and the analysis of risk ratio and risk difference of serious adverse drug reactions were deleted. 8.2.4.3. Subgroup Analysis - The description of subgroup analysis was clarified. 9. LISTINGS - The listing of contraindicated patients was added. 10. APPENDIX - Appendix 1 was deleted. Other description adjustments were made.
3.0	10-SEP-2018	PPD	Study status: Ongoing 2.1. Study Design - A description on design and registration system was modified in association with a protocol amendment. 5.3. Subgroups - Clinical response evaluation to be performed when prior treatment for intestinal amebiasis is present was deleted from factors for subgroup analysis. - To examine the relationship between adverse drug reactions and concomitant medications, concomitant medications were added to subgroup analysis of safety as a factor. Concomitant medications here refer to drugs concomitantly used by the onset of the last adverse drug reaction observed during the observation period plus 28 days. 6.1. Safety Endpoints - The definition of serious adverse events or adverse drug reactions was added as an endpoint. 7. HANDLING OF MISSING DATA - A description on handling in the case the causal relationship of adverse events is missing was added. 8.1.3. Analysis of Binary Data - A statement was added to note that risk ratio and risk

Version	Date	Author(s)	Summary of Changes/Comments
			difference will not be calculated if the number of patients in subgroups compared is less than 10. 8.2.2. Patient Background and Treatment History of AMEPAROMO - The presence or absence of concomitant medication and prior treatment for intestinal amebiasis were added. - The definition of overdose was modified, and the definition was shown in a footnote. 8.2.3. Safety Analysis - The tabulation and analysis period was changed from the observation period to the observation period plus follow-up period (28 days) as a result of review, and a description adjustment was made. - The status of development of adverse drug reactions by whether they developed within or outside the observation period was deleted because of the above change. 8.2.3.4. Subgroup Analysis - A statement was added to note that the number and proportion of patients with adverse drug reactions will be tabulated by SOC and PT if the risk ratio is ≥2 or ≤0.5. - A statement was added to note that the number and proportion of patients with adverse events by age (elderly, non-elderly), presence or absence of hepatic dysfunction, presence or absence of renal dysfunction, and presence or absence of HIV infection will be tabulated by SOC and PT. 8.2.3.5. Exploratory Analysis - An analysis was added to examine the relationship of concomitant medications with the development of adverse drug reactions. 9. LISTINGS - The listing of concomitant medications by patient was added. - The listing of patients with overdose was added. - In accordance with PSEHB/PED Notification No. 1128-2 and PSEHB/PSD Notification No. 1128-4 “Partial Revision on Appendix Forms of Periodic Safety Update Reports and Their Entry Methods,” Appendix Form 2 to be prepared in periodic safety update reports was added, Appendix Form 2 was changed to Appendix Form 15, and Appendix Form 3 was changed to Appendix Form 16. Other description adjustments were made.

2. INTRODUCTION

This statistical analysis plan describes the statistical analysis plan for the drug use investigation of AMEPAROMO Capsules 250 mg (hereinafter referred to as AMEPAROMO). In this plan, sentences cited from the Protocol are shown in *Italics*.

2.1. Study Design

This investigation is a multicenter open study in patients who received AMEPAROMO for treatment of intestinal amebiasis. Patients who have never been treated with AMEPAROMO will be enrolled using a central registration system. The observation period shall start on the day the treatment with AMEPAROMO begins (Day 1) and end on Day 10. The main effectiveness analysis item will be the proportion of cyst negative based on the results of examination of cysts up to 3 months after the completion of observation period (or discontinuation of treatment), and clinical response assessed by the investigator will also be evaluated. A target sample size of 100 patients was selected. The rationale for the target sample size is shown below.

- *Rationale*

The number of patients who will receive AMEPAROMO may be extremely small, but 100 patients were chosen as a sample size that can be collected during a certain period of time from the viewpoint of the feasibility of the study.

2.2. Study Objectives

This study will be conducted to investigate the safety and effectiveness of AMEPAROMO in daily medical practice in terms of: 1) Adverse drug reactions unexpected from precautions (unknown adverse drug reactions); 2) Occurrence of adverse drug reactions under daily medical practice; and 3) Factors that may affect safety, effectiveness and other relevant matters.

3. INTERIM AND FINAL ANALYSIS

In this study, interim analyses for periodic safety update report will be performed periodically. At the time of interim analyses, only the analyses of items necessary for periodic safety update report among the statistical analyses specified in this plan will be performed. In addition, the final analysis for the application for reexamination will be performed. At the time of the final analysis, all analyses specified in this plan will be performed.

4. HYPOTHESES AND DECISION RULES

4.1. Statistical Hypotheses

Because this study is not a confirmatory investigation, the tests are considered as exploratory tests.

4.2. Statistical Decision Rules

Not applicable.

5. ANALYSIS SETS

5.1. Safety Analysis Set

The safety analysis set is the full analysis set that is as close as possible to all AMEPAROMO-treated patients. Specifically, the safety analysis set includes all registered or reported patients excluding any patients who meet any of the following criteria:

a. The case report form (CRF) could not be collected at all (description in the report, "case report form not collected")

b. There was a violation or deficiency in the contract (description in the report, "contract violation/deficiency")

c. There was a violation of registration (description in the report, "registration violation")

d. Administration of the drug under investigation is not reported at all (description in the report, "no administration information")

e. Information on adverse events is not reported at all - no visits after the first prescription day (description in the report, "no adverse event information - no visits")

f. Information on adverse events is not reported at all - there is a visit after the first prescription day but no description of safety information (description in the report, "no adverse event information - no description")

Details for each criterion should follow the "Guidance for Criteria for Inclusion in Analysis Sets and Handling of Data in Drug Use Investigations".

5.2. Effectiveness Analysis Sets

There are two effectiveness analysis sets: the cyst analysis set, in which effectiveness will be determined based on the results of examination of cysts; and the clinical response analysis set.

5.2.1. Cyst Analysis Set

The cyst analysis set consists of the patients in the safety analysis set who have undergone the examination of cysts after AMEPAROMO treatment. Patients who meet any of the following criteria will be excluded:

g. Examination of cysts has not been performed (description in the report, "no information on examination of cysts")

h. Non-target disease of the study (description in the report, "Non-target disease of the study") [That is, "others" is checked with no other information in the CRF item that asks the disease (diagnosis) that required the use of AMEPAROMO.]

5.2.2. Clinical Response Analysis Set

The clinical response analysis set consists of the patients in the safety analysis set in whom clinical response (assessed by the investigator) has been evaluated. Patients who meet any of the following criteria will be excluded:

i. Information on clinical response assessment is not reported at all (description in the report, "no clinical response information")

j. Non-target disease of the study (description in the report, "Non-target disease of the study") [That is, "others" is checked with no other information in the CRF item that asks the disease (diagnosis) that required the use of AMEPAROMO.]

5.3. Subgroups

Subgroup analyses of safety will be performed for the following patient background factors. Underlined categories will be used as a reference in comparisons between subgroups.

- Sex [male, female]
- Children (<15 years), adults (≥15 to <65 years), elderly (≥65 years)
- Inpatient/outpatient status at the first prescription [inpatient, outpatient]
- Diagnostic name [intestinal amebiasis, others]
- Severity [mild, moderate, severe, unknown]
- Initial onset/recurrence [initial onset, recurrence]
- HIV infection [absent, present]
- Past medical history other than HIV infection [absent, present]
- Concurrent illness other than HIV infection [absent, present]
- Presence or absence of prior treatment for intestinal amebiasis [absent, present]
- Presence or absence of hepatic dysfunction [absent, present]
- Presence or absence of renal dysfunction [absent, present]
- Presence or absence of concomitant medication up to the development of adverse drug reactions[a] [absent, present]

Subgroup analyses of safety will be performed for the other factors shown below.

- Pregnant and parturient women (pregnancy present)

[a]: The presence or absence of concomitant medications will be determined by excluding concomitant medications started to be used after the day of onset of the last adverse drug reaction observed during the observation period plus 28 days.

- Overdose[b] (overdose present)

Patients in whom AMEPAROMO might have been contraindicated per the package insert (hereinafter referred to as contraindicated patients) will be sampled from the registry according to separately-specified criteria and be analyzed for the safety of AMEPAROMO as a subgroup analysis.

Subgroup analyses of effectiveness will be performed for the following patient background factors. Underlined categories will be used as a reference in comparisons between subgroups.

- Sex [male, female]
- Presence or absence of hepatic dysfunction [absent, present]
- Presence or absence of renal dysfunction [absent, present]
- Children (<15 years), adults (≥15 to <65 years), elderly (≥65 years)
- Severity [mild, moderate, severe, unknown]
- Initial onset/recurrence [initial onset, recurrence]
- HIV infection [absent, present]
- Past medical history other than HIV infection [absent, present]
- Concurrent illness other than HIV infection [absent, present]
- Presence or absence of prior treatment for intestinal amebiasis [absent, present]

Hepatic and renal dysfunction will be considered "present" if there is at least one complication falling under the following MedDRA SMQs and HLGTs. The judgment will be made using the MedDRA version at the data cutoff for periodic safety update report or the final database release because SMQs, HLGTs, etc. may be changed due to version updates.

- Hepatic dysfunction: SMQ (narrow) "hepatic disorders" and HLGT "hepatic and hepatobiliary disorders" + "hepatobiliary neoplasms"
- Renal dysfunction: SMQ (narrow) "acute renal failure" + "renal vessel disorders" + "chronic kidney diseases" and HLGT "nephropathies" + "renal disorders"

[b]: Because the dosage and administration of AMEPAROMO is "the usual dosage for adults is 1500 mg (potency) of paromomycin sulfate administered orally after meals, divided into 3 doses per day for 10 days", overdose present was defined as "daily total dose exceeded 1500 mg on at least 1 day, or the duration of treatment is 12 days or more". Only dose per single dose, number of doses, start day, and end day are collected as records on treatment with AMEPAROMO in the CRF. If AMEPAROMO is taken a total of 30 times in 10 days and the initial dose on the start day (Day 1) is given after lunch or supper, the last dose on the last day (Day 11) will be after breakfast or lunch. Because the duration of treatment from the start day to the end day is calculated to be 11 days in tabulation, the duration of treatment of 12 days or more was selected.

6. ENDPOINTS AND COVARIATES

6.1. Safety Endpoints

- Adverse drug reactions: Adverse events determined to be related to AMEPAROMO by the investigator
- Adverse events: All-causality adverse events
- Serious adverse events or reactions: Adverse events or adverse drug reactions in which the seriousness was determined to be serious by the investigator

6.2. Effectiveness Endpoints

- Proportion of cyst negative:

Results in patients who underwent the examination of cysts after AMEPAROMO treatment

  - Cyst negative
  - Cyst positive
  - Indeterminate

- Clinical Response (assessed by the investigator)

On the day of completion of the observation period (or the day of completion of the study), the clinical response of AMEPAROMO should be comprehensively assessed based on the course of the general condition, laboratory findings and other relevant data after the start of AMEPAROMO treatment.

  - Effective
  - Not effective
  - Indeterminate

6.3. Other Endpoints

Not applicable.

6.4. Covariates

As for the safety and effectiveness of AMEPAROMO, there are no covariates identified from clinical study data thus far obtained or potential covariates.

7. HANDLING OF MISSING DATA

When the causal relationship of adverse events is missing, the data will be handled as “related” for counting. When the seriousness/outcome of adverse events and action taken with

AMEPAROMO for the adverse events are missing, the data will be handled as "unknown" for counting.

For effectiveness endpoints, missing data will not be imputed.

8. STATISTICAL METHODS AND STATISTICAL ANALYSIS

8.1. Statistical Methods

8.1.1. Analysis of Continuous Data

Summary statistics (number of patients, mean, standard deviation, median, maximum, and minimum) will be calculated.

8.1.2. Analysis of Categorical Data

The number of patients and proportion of each category will be calculated.

8.1.3. Analysis of Binary Data

The number of patients and proportion will be calculated. If the confidence interval of proportion is calculated, two-sided 95% confidence interval (exact method) will be calculated.

If the proportion is compared between subgroups, risk ratio and its 95% confidence interval, and risk difference and its 95% confidence interval will be calculated. If the number of patients in subgroups compared is less than 10, the number and proportion of patients will be calculated but risk ratio and its 95% confidence interval, and risk difference and its 95% confidence interval will not be calculated.

8.2. Statistical Analysis

8.2.1. Overview of Patients

- **Number of sites by establisher and number of patients**

In CRF-collected patients, the number and proportion of sites by establisher shown below and the number and proportion of patients will be calculated.

- University hospitals
- National hospitals established by the Ministry of Health, Labour and Welfare
- Prefectural and municipal hospitals
- Public organizations
- Hospitals other than the above four established by corporations and individuals
- General practitioners/clinics

In addition, the mean, minimum, and maximum will be calculated for the number of patients per site.

- **Dispositions of patients**

In patients who registered to the study, the number of registered patients, the number of completed patients, the number of patients included in the analysis of safety, and the number of patients included in the analysis of effectiveness will be tabulated. In addition, the number of patients excluded from the analysis of safety and effectiveness and the number of patients by reason for exclusion will be tabulated.

- **Listing of discontinuations and dropouts**

In the safety and effectiveness analysis sets, the number and proportion of discontinued patients will be tabulated. In addition, the number and proportion of patients by reason for discontinuation will be tabulated.

- **Listing of excluded patients**

The listing of reasons for exclusion in patients excluded from the analysis of safety and effectiveness will be prepared.

8.2.2. Patient Background and Treatment History of AMEPAROMO

- **Patient background**

In the safety and effectiveness analysis sets, the following patient background factors will be tabulated in accordance with Section 8.1.

- Sex [male, female]
- Age (continuous)
- Age group [<15 years, ≥15 to <65 years, ≥65 years]
- Inpatient/outpatient status at the first prescription [inpatient, outpatient]
- Body weight (continuous)
- Body Mass Index (continuous)
- Diagnostic name [intestinal amebiasis, others]
- Diagnostic name [details of others]
- Severity [mild, moderate, severe, unknown]
- Initial onset/recurrence [initial onset, recurrence]
- Hepatic dysfunction [absent, present]
- Renal dysfunction [absent, present]
- HIV infection [absent, present]
- Past medical history [absent, present]
- Concurrent illness [absent, present]
- Presence or absence of prior treatment for intestinal amebiasis [absent, present]
- Clinical response of prior treatment [effective, not effective, indeterminate]

In the safety analysis set, the number and proportion of the following patients will be tabulated by SOC and PT of MedDRA.

- Past medical history
- Concurrent illness

In the safety and effectiveness analysis sets, the number and proportion of the following patients will be tabulated.

- Presence or absence of concomitant medication [absent, present]
- Concomitant medication
- Concomitant non-drug therapy
- Prior medication for intestinal amebiasis
- Prior medication other than those for intestinal amebiasis

- **Status of treatment of AMEPAROMO**

In the safety analysis set, the following status of treatment of AMEPAROMO will be tabulated:

- Duration of treatment (continuous)
- Dose per single dose (continuous)
- Number of doses (continuous)
- Daily dose (continuous)
- Presence or absence of overdose[c] [absent, present]

The duration of treatment is from the day of initial dose in the study to the last confirmed day of dosing including the treatment suspension period.

8.2.3. Safety Analysis

Safety will be analyzed using data collected during the observation period (from the start day of AMEPAROMO treatment to the end day of AMEPAROMO treatment) plus 28 days[d]. All adverse events reported in the study will be included in listings.

[c]: Because the dosage and administration of AMEPAROMO is "the usual dosage for adults is 1500 mg (potency) of paromomycin sulfate administered orally after meals, divided into 3 doses per day for 10 days", overdose present was defined as "daily total dose exceeded 1500 mg on at least 1 day, or the duration of treatment is 12 days or more". Only dose per single dose, number of doses, start day, and end day are collected as records on treatment with AMEPAROMO in the CRF. If AMEPAROMO is taken a total of 30 times in 10 days and the initial dose on the start day (Day 1) is given after lunch or supper, the last dose on the last day (Day 11) will be after breakfast or lunch. Because the duration of treatment from the start day to the end day is calculated to be 11 days in tabulation, the duration of treatment of 12 days or more was selected.

8.2.3.1. Adverse Drug Reactions

- **All adverse drug reactions**

The number and proportion of patients with adverse drug reactions will be tabulated by SOC and PT.

- **Serious adverse drug reactions**

The number and proportion of patients with serious adverse drug reactions will be tabulated by SOC and PT.

- **Details of adverse drug reactions**

The number and proportion of patients with adverse drug reactions will be tabulated by SOC and PT for each of the following items.

- Seriousness [serious, non-serious]
- Expected/unexpected [expected, unexpected]
- Intervention [discontinuation, temporarily discontinued or dose reduced]
- Outcome [not recovered, recovered with sequela, recovering, resolved/recovered, unknown]

In addition, the number and proportion of patients with adverse drug reaction that meets all of the following items will be tabulated by SOC and PT:

- The seriousness was considered “non-serious”;
- The intervention was “discontinuation”, “temporary discontinued”, or “dose reduced”
- The outcome was “not recovered” or “recovered with sequela”.

If the same adverse drug reaction (the same PT) occurs more than once in the same patient, it will be handled as follows in the tabulation of the number of patients with events:

- Seriousness: If both serious and non-serious events are reported, “serious” will be adopted.
- Expected/unexpected: If both expected and unexpected events are reported, “unexpected” will be adopted.
- Number of days to onset: The number of days to the first event will be adopted.
- Intervention: If multiple types of action are reported, one of discontinuation, temporarily discontinued or dose reduced, or other (none, dose increased), in descending order of precedence, will be adopted.

[d]: The collection period was specified as the observation period plus 28 days because the period of reporting of safety information collected using the NIS AE Report Form of the study is up to 28 days after the end day of treatment.

- Outcome: The outcome of the last occurring event will be used.

- **Time to adverse drug reaction**

The number of patients who experienced an adverse drug reaction will be tabulated by time to first development (<3 days, ≥3 to <7 days, ≥7 to <10 days, ≥10 days), by SOC and PT.

- **Details of serious adverse drug reactions**

The number and proportion of patients with serious adverse drug reactions will be tabulated by expected/unexpected status by SOC and PT.

- **Adverse drug reactions by patients of included/excluded in the safety analysis set**

In CRF-collected patients, the listing of adverse drug reactions in patients excluded from the safety analysis set will be prepared. In addition, the number of patients with events will be tabulated by SOC and PT.

- **Status of development of adverse drug reactions in contraindicated patients**

The listing of contraindicated patients including the status of development of adverse drug reactions will be prepared. The number and proportion of patients with adverse drug reactions will be tabulated by patients who do or do not meet contraindications by SOC and PT as necessary.

8.2.3.2. Adverse Events

- **All adverse events**

The number and proportion of patients with adverse events will be tabulated by SOC and PT.

- **Adverse events by serious/non-serious**

The number and proportion of patients with serious adverse events will be tabulated by SOC and PT. The same tabulation will be performed for non-serious adverse events.

8.2.3.3. Other Endpoints

Not applicable.

8.2.3.4. Subgroup Analysis

To evaluate the relationship between patient background factors and the development of adverse drug reactions, risk ratio and risk difference between subgroups will be calculated for the incidence of adverse drug reactions in accordance with Section 8.1.3. For subgroups with risk ratio ≥2 or ≤0.5, the number and proportion of patients who experienced adverse drug reaction will be summarized for each factor, using SOCs and PTs.

In addition, the number and proportion of patients who experienced adverse drug reaction will be tabulated by SOC and PT for each of the following factors.

- Age [elderly (≥65 years), non-elderly (<65 years)]
- Hepatic dysfunction [absent, present]
- Renal dysfunction [absent, present]
- HIV infection [absent, present]

8.2.3.5. Exploratory Analysis

The following exploratory analysis will be performed for factors affecting safety:

- For adverse drug reactions with high incidence (>10%), factors for development of adverse drug reactions will be examined using methods such as logistic regression analysis.
- To examine the effects of concomitant medications on development of adverse drug reactions, the number and proportion of patients by name of concomitant drug[e] (drug subclassification and nonproprietary name) will be calculated by presence or absence of adverse drug reactions.

Additional exploratory analysis may be performed, as necessary. Among those exploratory analyses, only those that resulted in important interpretations will be reported.

8.2.4. Effectiveness Analysis

8.2.4.1. Proportion of Cyst Negative

In the cyst analysis set, the number and proportion of patients with negative results in the examination of cysts after AMEPAROMO treatment will be calculated. The 95% confidence interval of the proportion of cyst negative will be calculated. The proportion of cyst negative will be calculated using the following equation:

$$\text{Proportion of cyst negative (\%)} = \frac{\text{Number of patients with cyst negative}}{\text{Number of patients with cyst positive + number of patients with cyst negative}} \times 100$$

8.2.4.2. Clinical Response Rate (assessed by the investigator)

In the clinical response analysis set, the number and proportion of patients in whom the clinical response (assessed by the investigator) after AMEPAROMO treatment is effective will be

[e]: The presence or absence of concomitant medications will be determined by excluding concomitant medications started to be used after the day of onset of the last adverse drug reaction observed during the observation period plus 28 days.

calculated as the clinical response rate. The 95% confidence interval of the AMEPAROMO rate will be calculated. The clinical response rate will be calculated using the following equation:

$$\text{Clinical Response rate (\%)} = \frac{\text{Number of patients with “effective”}}{\text{Number of patients in the clinical response analysis set excluding “indeterminate”}} \times 100$$

8.2.4.3. Subgroup Analysis

For each factor specified in Section 5.3, risk ratio and risk difference between subgroups will be calculated for the proportion of cyst negative and clinical response rate in accordance with Section 8.1.3.

8.2.4.4. Exploratory Analysis

The following exploratory analysis will be performed for factors affecting effectiveness:

- Clinical response of prior treatment [effective, not effective, indeterminate]

Additional exploratory analysis may be performed, as necessary. Among those exploratory analyses, only those that resulted in important interpretations will be reported.

9. LISTINGS

The following listings will be prepared. Listings with “Intext” specified following the listing title indicate listings that will be specified in the text of periodic safety update reports and documents for application for reexamination as they are.

- Listing of patients
- Listing of patients with adverse events
- Listing of patients with adverse drug reactions (Intext)
- Listing of patients with adverse drug reactions among patients excluded from the safety analysis set
- Listing of patients with serious adverse drug reactions (Intext)
- Listing of patients with serious adverse events
- Listing of patients with adverse drug reactions among patients with hepatic dysfunction (Intext)
- Listing of patients with adverse drug reactions among patients with renal dysfunction (Intext)
- Listing of elderly patients with adverse drug reactions (Intext)
- Listing of patients with adverse drug reactions among pregnant and parturient women (Intext)
- Listing of effectiveness in pregnant and parturient women (Intext)
- Listing of contraindicated patients

- Listing of concomitant medications by patient
- Listing of patients with overdose
- Patient listing of changes in intestinal bacterial flora (Intext)

Furthermore, the following tables corresponding to appendix forms to periodic safety reports (PSUR) and documents for application for reexamination will be prepared:

- PSUR: Appendix Form 2 (Status of development of adverse drug reactions and infections in post-marketing surveillance, etc.)
- Reexamination: Appendix Form 15 (List of adverse drug reactions and infections)
- Reexamination: Appendix Form 16 (Overview of patients in post-marketing surveillance, etc.)