HUMIRA® subcutaneous injection
Special use result survey
All case survey concerning gastro-intestinal Behcet disease

Statistical analysis plan (the 6th safety periodic report/reassessment/final report)
Version 1.2

Prepared on November 1, 2017

1. Approval

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Date of approval	DD/MM/YYYY	

Contents

1. History of preparation and revision

Version number	Date of preparation/revision	Prepared/Revised by	Reasons
1.0	2/8/2017	[redacted]	The first version
1.1	4/6/2017	[redacted]	■ 2.Definition of terms and abbreviation ● Patients who were followed up for 52 weeks (patients collected for the first volume), Patients who were followed up for 104 weeks (patients collected for the first/second volume), patients who were followed up for 156 weeks (patients collected for the first/second/third volume) ■ 8.Definition of population used for analysis ● Definition of registered patients to delete the definition of registered eligible patients and registered not eligible patients ● Definition of patients for whom data of the survey sheet was not fixed was changed ■ 10.1 Overall ● Added a description," The test is deemed to have been performed if a box is not checked but laboratory test results are described" to a definition of implementation of "Test for tuberculin reaction or IGRA" ● Added definitions of "Patients excluded from separate volume", "Chest X-ray or CT scanning", "Test for tuberculosis", "Test for Hepatitis B", and "Responding patients" ■ 12.2 Time of evaluation of occurrence

Version number	Date of preparation/revision	Prepared/Revised by	Reasons
			status of adverse reaction ●Deleted evaluation time 2 and 3 to change items for time of evaluation ■ 13.1 Overall ● Changed purpose of analysis and analysis items of 1.1.1,1.6,1.7.1, and 1.12.1 ● Added a description of 1.4.3 Deleted 1.5 and1.6.1 ● Changed items subject to analysis for 1.13 ■ 13.2 Safety ● Changed analysis items of 2.4.1, 2.4.2, 2.4.3, and 2.9 ● Added descriptions of 2.7, 2.19.1, and 2.19.2 ● Deleted 2.7(1), 2.7(2), 2.7(3), 2.8(1), 2.8(2), 2.8(3), and 2.19 ● Added a description of 2.9.xx ■ 13.3 Efficacy ● Changed analysis item of 3.4 ● Changed a method of description to that by which the contents of 3.5 are divided into 3.5.1 and 3.5.2.
1.2	11/1/2017	[redacted]	■ 10.1 Overall Changed the method of description so that condition drawing for “presence or absence of previously used drug (aminosalicylic acid preparation)”, “presence or absence of previously used drug (steroid)”, “presence or absence of previously used drug (immunomodulative drug)”, “presence or absence of previously used drug (antibiotics)”, and “presence or absence of previously used drug (others)” can include information in the check box in survey sheet.

2. ■ 2.Definition of terms and abbreviations

Terms and abbreviations used in this analysis plan are defined as follows:

Terms and abbreviations	Definition
Patients who were followed up for 52 weeks (patients collected for the first volume)	Patients who started to receive this drug between August 16, 2014 and August 15, 2015.
Patients included at the 104th week of follow-up (patients collected for the first and second volume)	Patients who started to receive this drug between August 16, 2013 and August 15, 2014.
Patients included at the 156th week of follow-up (patients collected for the first, second, and third volume)	Patients who started to receive this drug by August 15, 2013.
Adverse events	Any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease, regardless of whether they are related to this drug or not
Adverse events that occurred during the period subject to safety analysis	Adverse events that occurred from the start date of administration until the time as follows should be included. • Patients included at the 52th week of follow-up: The start date of administration of this drug + 392 days (56 weeks) • Patients included at the 104th week of follow-up: The start date of administration of this drug + 756 days (108 weeks) • Patients included at the 156th week of follow-up: The start date of administration of this drug + 1120 days (160 weeks) • Patients who discontinued to receive this drug: The last date of administration of this drug + 28 days
Adverse events that occurred in a period except for the period subject to safety analysis	Adverse events that occurred before the start date of administration or after the following timing should be included • Patients included at the 52th week of follow-up: The start date of administration of this drug + 392 days (56 weeks) • Patients included at the 104th week of follow-up: The start date of administration of this drug + 756 days (108 weeks) • Patients included at the 156th week of follow-up: The start date of administration of this drug + 1120 days (160 weeks) • Patients who discontinued to receive this drug: The last date of administration of this drug + 28 days
Adverse reaction	Among adverse events,those for which causal relationship with this drug cannot be ruled out should be included
Adverse reactions that occurred during the period subject to safety analysis	Among adverse events that occurred during the period subject to safety analysis, those for which causal relationship with this drug cannot be ruled out should be included
Adverse reactions that occurred outside the	Among adverse events that occurred outside the specified safety analysis period, those for which causal relationship with this drug

Terms and abbreviations	Definition
specified safety analysis period	cannot be ruled out should be included
Summary statistics	The number of patients, mean value, standard deviation, the minimum value, the first quartile point, median value, the third quartile point, and the maximum value should be applicable
MedDRA/J	Medical Dictionary for Regulatory Activities / Japanese edition(ICH MedDRA/J)
SOC	System Organ class in MedDRA/J
PT	Preferred Term in MedDRA/J
LLT	lower Level Term in MedDRA/J
IGRA test	Interferon γ free release test
GB	Green Book Guidance for application for reassessment

3. Purpose of this statistical plan

3.1. Purpose of preparation of this statistical plan

Main purpose of this statistics plan is to define items used for operations of statistical analysis conducted according to implementation plan of "Special use result survey of HUMIRA® subcutaneous injection (all case survey concerning gastro-intestinal Behcet disease)" (hereinafter referred to as "this survey"). This survey is one of surveillance conducted according to GPSP ordinance, and a part or all of the analysis results serves as material for reporting of special use result survey of this drug to regulatory authority and for preparation of application for reassessment.

4. Outline of survey

4.1. Objective of survey

Objective of this survey is to understand following matters when HUMIRA® subcutaneous injection (hereinafter referred to as "this drug") is used in patients with gastro-intestinal Behcet disease.

1) Unknown adverse reactions (especially important adverse reactions)
2) Occurrence status of adverse reactions under actual use conditions
3) Factors that may contribute to safety and efficacy

<<Primary survey items>>

Infection, tuberculosis, interstitial pneumonia, malignant tumour, cardiac failure congestive, pancytopenia, autoimmune disease, demyelinating disorder, and administration site reaction

4.2. Planning of survey

Any patients with gastro-intestinal Behcet disease (only those who did not respond to existing treatment) who receive this drug for defined indication for use and dosage and administration are included.

4.3. Scheduled number of patients included in this survey

Not decided

All patients with gastro-intestinal Behcet disease are registered after the approval of this drug for use in patients with gastro-intestinal Behcet disease.

All case survey is decided to be conducted because approval of this drug for treatment of gastro-intestinal Behcet disease in Japan is the first in the world and the clinical trial was open-label trial including only 20 patients. In order to make reporting after reaseessment period, follow-up period requires at least 52 weeks per patient, and therefore, we set the registration period as 2 years and 6 months after the date of approval for additional indication for use. Registration after 2 years and 6 months had passed should be continued for only patients who use this drug.

5. Items subject to analysis and the method

5.1. Analysis items

1) Items related to patient distribution
   - [1] The number of registered patients
   - [2] The number of patients for whom a survey sheet data was fixed
   - [3] The number of patients included in safety evaluation
   - [4] The number of patients included in efficacy evaluation
2) Items related to safety
   - [1] List of occurrence status of adverse reactions and infections
   - [2] Factors that may contribute to safety
     - Incidence of adverse reactions by patient characteristics (sex, disease duration, smoking habit, presence or absence of complications, presence or absence of medical history, presence or absence of allergy, presence or absence of previous treatment, and presence or absence of concomitant drugs)
     - According to symptoms of Behcet disease other than gastrointestinal tract symptoms
     - According to changes in steroid dose in patients who receive steroid
   - [3] Adverse events that occurred during or after administration of this drug

- List of occurrence status of serious adverse events

[4] Occurrence status of Self-administration error

[5] Contribution to safety when anti-adalimumab antibody is detected

3) Items related to efficacy

[1] Comprehensive evaluation of gastrointestinal symptoms, evaluation of gastrointestinal symptoms Behcet disease, evaluation of main symptoms of Behcet disease, evaluation of accessory symptoms, level of improvement in endoscopy findings, and CRP

[2] Factors considered to contribute to efficacy

- Efficacy by patient characteristics (sex, disease duration, smoking habit, presence or absence of complications, presence or absence of medical history, presence or absence of allergy, presence or absence of previous treatment, and presence or absence of concomitant drugs)
- According to symptoms of gastro-intestinal Behcet disease
- According to changes in steroid dose in patients who receive steroid
- Contribution to efficacy when anti-adalimumab antibody is detected

4) Items concerning patients with specific characteristics

List of occurrence status of adverse reactions/infections in patients with specific characteristics including children, the elderly, expectant and nursing mothers, patients with renal impairment, or patients with hepatic function disorder

5.2. Method of analysis

Appropriate method including chi-square test should be used according to scale and property of analysis

6. Implementation status of analysis and the schedule

Objective of analysis	Survey period and deadline for reassessment
The 6th safety periodic report	Between January 1, 2016 and December 31, 2016
Reassessment	Between May 16, 2013 and May 15, 2017

7. Software and dictionary used for analysis

7.1. Software for statistical tabulation and analysis

Information about software and its version used for analysis is described as

follows:

	Software and its version
OS	Microsoft Windows 7 or newer version should be used
Software for statistical analysis	SAS Ver. 9.2 or newer version should be used
Software for statistical tabulation	Microsoft Excel 2010 or newer version should be used

7.2. Dictionary used for analysis

Dictionary used to express term of adverse events, complications, and name of drugs is described as follows:

Items	Name of dictionary and its version	Remarks
Types of adverse events and adverse reactions/infections	ICH Medical Dictionary for Regulatory Activities (MedDRA/J version 19.1)	• After the events are classified into system organ class (SOC), appropriate terms should be chosen and written among preferred term (PT). • When term of the events are displayed as SOC, order according to international consensus should be followed. • Version of MedDRA/J used should be described in the blank space
Name of drug (concomitant drug)	Pharmaceutical product name data file *Appropriate version should be used for data aggregation according to the timing of analysis	• Seven digit cord should be used for aggregation of concomitant drugs by drug in principle • The lowest level cord should be used as priority for a list of concomitant drugs

8. Definition of population used for analysis

Name of population	Definition
Patients who were transferred to another institutions	Patients registered at different institutions in duplicate are applicable.
Registered patients	Patients who are eligible for registration based on registration assessment are applicable.
Not registered patients	Patients not registered for whom survey sheet data was collected are applicable.
Patients for whom a survey sheet data was fixed	Patients for whom a survey sheet data was fixed are applicable.
Patients for whom a survey sheet data was not fixed	Patients for whom a survey sheet data was not fixed are applicable. As a reason for unfixed survey sheet, “patients for which survey sheet cannot be collected” should be chosen for applicable patients extracted from “ [HUMIRA BD] Patients whose survey

Name of population	Definition
	sheet cannot be collected.xls”
Patients excluded from safety analysis	Patients corresponding to exclusion conditions for safety analysis are applicable. For exclusion conditions for safety analysis, standard data “Adoption or not adoption of patients” should be referred to. Items of exclusion are as follows: • Violation of contract: Institutions/departments with which contract is not concluded • Physicians outside the contract • Period excluded from survey period • Patients who have not received this drug • Patients without physician’s evaluation • Duplicated patients • Patients who were transferred to another institutions • Patients in whom safety cannot be assessed • Patients who received this drug before the contract
Patients included in safety analysis	Patients included in those for whom survey sheet was fixed after excluding those excluded from safety analysis
Patients excluded from efficacy analysis	Patients corresponding to exclusion conditions for efficacy analysis are applicable. For exclusion conditions for efficacy analysis, standard data “Adoption or not adoption of patients” should be referred to. Items of exclusion are as follows: • Patients with diseases which is not subject to the survey • Patients in whom efficacy cannot be assessed
Patients included in efficacy analysis	Patients included in those for whom survey sheet was fixed after excluding those excluded from efficacy analysis

9. General arrangements for analysis

9.1. Handling of missing data

When analysis is conducted, missing data at that time is not complemented. However, entry data compliment may be conducted in some items, and therefore, data complement method is defined in items in Chapter 10 or later chapters if any entry data complement is needed.

9.2. Descriptive statistics

Following values should be calculated for categorical data and quantitative data

Types of data	Data required to be calculated
Categorical data	The number or rate of patients When rate of patients is calculated, patients with “unknown” and “not described” data should be included in denominator. In addition, breakdown of patients is displayed as rate, the number of

Types of data	Data required to be calculated
	patients including those with “unknown” and “not described” data from high-order items should be used as denominator. When test is performed, patients with “unknown”or “not described” data should be excluded.
Quantitative data	The number of patients, mean value, standard deviation, median value, the minimum value, and the maximum value should be applicable

9.3. Digits of the values displayed

Digits of the values displayed are as follows:

Types of values	Digits of values displayed
Mean value, standard deviation, and median value	Two digits subsequent to the valid digits for data are rounded off to display the value with valid digits plus 1 digits
The minimum value and maximum value	The number of digits of the value should be the same as that of valid digits of data.
The number of patients	The number should be displayed as integral number
Rate, 95% confidence interval	The second digit after the decimal point should be rounded off to display the value with 1 digit after the decimal point. However, when the value is displayed with 2 digits after the decimal point with the third digit after the decimal point being rounded off, such as the values in Appendix 2 or incidence of adverse events, rules of display should be based on layout of the tables and figures.
p value	The fifth digit after the decimal point should be rounded off to display the value with 4 digit after the decimal point. However, when the value is less than 0.0001, the value should be displayed as <0.0001
Valid number of digit	Disease duration should be displayed as the value with 1 digit after the decimal point. Valid number of digits for other data should be the displayed number of digits of the data

9.4. Rules of display of the value

Case	Rules of display
When the value cannot be calculated	Hyphen, ”-”

9.5. Test method

Unknown or not described classification should not be included in test. In addition, test of data by classification is performed, the first hierarchy should be tested in principle. Multiplicity should not be considered.

9.6. Level of significance

In principle, level of significance should be 5% on both sides. $p<0.05$ (less than 5%) should be considered significant.

10. Data derivation and calculation method

10.1. Overall

Name of data	Derivation and calculation method
The number of institutions	When a institution have an identical DCF institution cord in “List of [HUMIRA BD] DCF cords_Company A” and “List of [HUMIRA BD] DCF cords_Company E” , such institution is counted as one institution.
The number of patients per institution	The number of patients should be calculated by institution with the identical DCF institution cord.
The number of patients who continue to participate in clinical study	Patients with box being checked in “Patients who participate in clinical trial of this drug” in a section of administration status in registration sheet are applicable.
Patients in whom adverse events occurred outside the specified safety analysis period	Patients who experienced at least one adverse event that occurred outside the specified safety analysis period.
Patients who are excluded from separate volume	Patient number and volume number that are excluded from analysis should be specified from “[HUMIRA BD] patients included in separate volume.xlsx” to exclude applicable data at the analysis.
Patients in whom infection occurred	When patients have at least one event corresponding to conditions of infection in “20161110_MedDRA18.1 and 19.1 List of primary survey item_PV”, such patients should be applicable.
Patients in whom tuberculosis occurred	When patients have at least one event corresponding to conditions of tuberculosis in “20161110_MedDRA18.1 and 19.1 List of primary survey item_PV”, such patients should be applicable.
Patients in whom malignant tumour occurred	When patients have at least one event corresponding to conditions of malignant tumour in “20161110_MedDRA18.1 and 19.1 List of primary survey item_PV”, such patients should be applicable.
Patients in whom administration site reaction occurred	When patients have at least one event corresponding to conditions of administration site reaction in “20161110_MedDRA18.1 and 19.1 List of primary survey item_PV”, such patients should be applicable.
Patients in whom autoimmune disease occurred	When patients have at least one event corresponding to conditions of autoimmune disease in “20161110_MedDRA18.1 and 19.1 List of primary survey item_PV”, such patients should be applicable.

Name of data	Derivation and calculation method
Patients in whom pancytopenia occurred	When patients have at least one event corresponding to conditions of pancytopenia in "20161110_MedDRA18.1 and 19.1 List of primary survey item_PV", such patients should be applicable.
Patients in whom demyelinating disorder occurred	When patients have at least one event corresponding to conditions of demyelinating disorder in "20161110_MedDRA18.1 and 19.1 List of primary survey item_PV", such patients should be applicable.
Patient in whom cardiac failure congestive occurred	When patients have at least one event corresponding to conditions of cardiac failure congestive in "20161110_MedDRA18.1 and 19.1 List of primary survey item_PV", such patients should be applicable.
Patients in whom interstitial pneumonia occurred	When patients have at least one event corresponding to conditions of interstitial pneumonia in "20161110_MedDRA18.1 and 19.1 List of primary survey item_PV", such patients should be applicable.
Patients in whim AAA was measured	Patients included in "BD survey AAA measurement (Safety periodic report)" should be applicable.
Patients who have contraindicated drugs	Patients whose registration sheet includes a check mark in box for any of contraindicated drugs should be applicable.
Start date of the initial treatment with this drug	Of dates described in "Administration status of this drug", the oldest date should be the start date of the initial treatment with this drug.
The last date of the final treatment with this drug	Of dates described in "Administration status of this drug" in survey sheet, records corresponding to following conditions should not be used for analysis. Records of patients who started to receive this drug by August 15, 2013: The start date of the initial treatment with this drug + 1092 days < the start date Records of patients who started to receive this drug between August 16, 2013 and August 15, 2014: The start date of the initial treatment with this drug + 728 days < the start date Records of patients who started to receive this drug between August 16, 2014 and August 15, 2015: The start date of the initial treatment with this drug + 364 days < the start date Of the last date of the treatment complemented by following [1] to [4], the latest date should be the last date of the final treatment with this drug. [1] Data should be sorted by the start date of the treatment, separate volume, and the number of the cycle of treatment described in "Administration status of this drug" in that order. [2] The start date of each data should be complemented at the last date of the initial and second treatment with this drug. When a date is described in the section for the last date of the third or subsequent treatment, and there is no check mark in "Ongoing" box so that last date of the treatment can be

Name of data	Derivation and calculation method
	identified, the date described as the last date of the treatment should be employed. [3] When there is no description in the section for the last date of the third or subsequent treatment or there is a check mark in "Ongoing" box so that the last date of the treatment cannot be identified, following rules are applied. ● When the patients are included in the last period in the volume: The date should be complemented by the last follow-up date for relevant volume or a date obtained by subtracting 1 day from start date of the subsequent treatment, which is earlier. ● When the patients are included in not last period in the volume: The date should be complemented by a date obtained by subtracting 1 day from the start date of the subsequent treatment with this drug. The last follow-up date should be defined as follows: • The initial volume: Start date of the treatment with this drug + 364 days • The second volume: Start date of the treatment with this drug + 728 days • The second volume: Start date of the treatment with this drug + 1092 days [4] When there is description in the section for the last date of the third or subsequent treatment but the date is incomplete so that the last date of the treatment cannot be identified, following rules are applied. ● When the date include year and month, but date is unknown: The date should be complemented by the last date of relevant month. ● When the date include year, but month and date is unknown: The date should be complemented by the last date in the last month of relevant year. In addition, when records in the subsequent treatment are created and the start date of the subsequent treatment is earlier than the complemented last date in the last month of the relevant year, the last date of the treatment should be complemented by the date obtained by subtracting 1 day from the start date of the subsequent treatment. However, if description in the last date of the treatment in the records for which last date of the treatment was complemented according to above rules and there is a check mark in "Ongoing" box, following rules are applied: ● When the described last date of the treatment is later than the last date complemented according to above rules, the date complemented should be employed as the last date of the final treatment of this drug. ● When the described last date of the treatment is earlier than the last date complemented according to above rules, the date described should be employed as the last

Name of data	Derivation and calculation method
	date of the final treatment of this drug. In addition, the last date identified according to above rule is later than the last follow-up date, the last follow-up date should be employed as the last date of the final treatment with this drug.
Days to the last date of the final treatment with this drug	The last date of the final treatment with this drug - the start date of the initial treatment with this drug + 1
Administration status (dosage and administration)	Data should be sorted by the start date of the treatment described in "Administration status of this drug" in survey sheet [1] The initial administration: Patients who receive this drug at the dose of 160 mg [2] The second administration: Patients who receive this drug at the dose of 80 mg [3] The third administration: Patients who receive this drug at the dose of 40 mg [4] The fourth or subsequent administration: Patients whose survey sheet includes a check mark in "once per 2 weeks" box and a description of 40 mg as the dose *If a description of fourth or subsequent administration is found, any administration status in the fourth and subsequent administration should be described as specified in [4]. • If patients receive this drug four times or more, conditions [1] to [4] described above are satisfied. If patients receive this drug 3 times but does not receive fourth administration, conditions [1] to [3] described above are satisfied. If patients correspond to either of these 2 patterns, the dosage should be aggregated as "160mg→80mg→40mg/2 weeks, no change was made thereafter". • If conditions [1], [2], and [3] described above are satisfied and the dose in the fourth and subsequent administration is 160 mg or 80 mg, the dosage should be aggregated as "160mg→80mg→40mg/2 weeks, and 160 mg or 80 mg in the subsequent administration". • If [1] described above is satisfied and the second and subsequent administrations are not given, the dosage should be aggregated as "160 mg, and no administration was given for the second and subsequent administration". • If [1][2] described above is satisfied and the second and subsequent administrations are not given, the dosage should be aggregated as "160 mg, and no administration was given for the second and subsequent administration". • If the initial dose is 80 mg: the dosage is aggregated as "80 mg". • If the initial dose is 40 mg: the dosage is aggregated as "40 mg".

Name of data	Derivation and calculation method
	• The dose is other than above, the dosage is aggregated as "Other".
Patients in whom dose increase was made	Patients in whom 160 mg/2 weeks was administered as the initial dose, 80 mg/2 weeks as the second dose, 40 mg/2 weeks as the third and subsequent dose, and 160 mg or 80 mg was administered at least once thereafter are applicable.
Administration status (total number of administrations, total dose)	• The number of administrations [1] Data should be sorted by the start date of the treatment, separate volume, and the number of the cycle of treatment described in "Administration status of this drug" in that order. [2] Administration intervals should be calculated by administration status. The administration interval should be 14 days for the initial and second administration. The third and subsequent administration should be given according to following rules. If there is a check mark in "once/2 weeks" box, the administration intervals should be 14 days, and in any other situations, a data should be obtained from "[HUMIRA BD] converted data to be provided for analysis". [3] The number of administrations by administration status should be calculated. The number of administrations = (The last date of the administration (after complement) - the start date of the administration (after complement))/the administration intervals (days) [4] Result obtained according to [3] is larger than 0 and smaller than 1, the number of administrations should be 1. In addition, that number is 1 or larger, the number of administrations should be obtained by rounding off the decimal point. [5] The number of administrations should be sum total of [4] by patients • Dose [1] If the dose of this drug is classified as other, the data should be obtained from "[HUMIRA BD] converted data to be provided for analysis". [2] The dose by administration status should be calculated. The dose = The number of administrations × the dose [3] Total dose should be sum total of [2] by patients • Mean daily dose Mean dose = Total dose/Total number of administrations
Patients who discontinued the administration	If the last date of the final administration of this drug corresponds to following conditions, the patients are deemed to be those who discontinued the administration.

Name of data	Derivation and calculation method
	Patients who started to receive this drug by August 15, 2013: The start date of the initial administration + less than 1064 days Patients who started to receive this drug between August 16, 2013 and August 15, 2014: The start date of the initial administration + less than 700 days Patients who started to receive this drug between August 16, 2014 and August 15, 2015:The start date of the initial administration + less than 350 days
Presence or absence of reasons for discontinuation	If patients correspond to those who discontinued the administration and there is at least one check mark in any "Reasons for discontinuation" boxes in "Discontinuation of the survey" section in the survey sheet, the patients are deemed as having reasons for discontinuation and if no description is found in the "Reasons for discontinuation" box in the survey sheet of patients defined as those who discontinued the administration, such patients are defined as patients whose reason for discontinuation is "unknown or not described reason".
Patients who continue to participate in the survey	Patients who do not correspond to those who discontinued administration are deemed as patients who continue to participate in the survey.
Presence or absence of complications	If there is a check mark in a box for complication in "patient information" in survey sheet, such patients are deemed to have complication, and if a column for "presence or absence of complications" is not completed and cannot be assessed, whether patients have complication or not is deemed as unknown or not described, and in any other situations, patients are deemed to have no complication.
Presence or absence of medical history	If there is a check mark in a box for medical history in "patient information" in the survey sheet, patients deemed to have medical history, and a column for "presence or absence of medical history" is not completed and cannot be assessed, whether patients have medical history or not is deemed as unknown or not described, and in any other situations, patients are deemed to have no medical history.
Medical history Presence or absence of tuberculosis	Patients who had data indicating presence or absence of medical history of tuberculosis in "161207 medical history (FIX) CRO" are deemed to have tuberculosis, and patients without such data are deemed to not have tuberculosis.
Medical history Presence or absence of nontuberculous mycobacterial infection	Patients who had data indicating presence or absence of medical history of nontuberculous mycobacterial infection in "161207 medical history (FIX) CRO" are deemed to have nontuberculous mycobacterial infection, and patients without such data are deemed to not have nontuberculous mycobacterial infection.
Medical history Presence or absence of interstitial pneumonia	Patients who had data indicating presence or absence of medical history of interstitial pneumonia in "161207 medical history (FIX) CRO" are deemed to have interstitial pneumonia, and patients without such data are deemed to not have interstitial pneumonia.
Medical history Presence	Patients who had data indicating presence or absence of medical

Name of data	Derivation and calculation method
or absence of bacterial bronchitis	history of bronchitis bacterial in “161207 medical history (FIX) CRO” are deemed to have bacterial bronchitis, and patients without such data are deemed to not have bacterial bronchitis.
Medical history Presence or absence of aplastic anaemia	Patients who had data indicating presence or absence of medical history of aplastic anaemia in “161207 medical history (FIX) CRO” are deemed to have aplastic anaemia, and patients without such data are deemed to not have aplastic anaemia.
Medical history Presence or absence of pancytopenia	Patients who had data indicating presence or absence of medical history of pancytopenia in “161207 medical history (FIX) CRO” are deemed to have pancytopenia, and patients without such data are deemed to not have pancytopenia.
Medical history Presence or absence of malignant tumour	Patients who had data indicating presence or absence of medical history of malignant tumour in “161207 medical history (FIX) CRO” are deemed to have malignant tumour, and patients without such data are deemed to not have malignant tumour.
Medical history Presence or absence of other conditions	Patients who had data indicating presence or absence of medical history of other conditions in “161207 medical history (FIX) CRO” are deemed to have other conditions, and patients without such data are deemed to not have other conditions.
Complications Presence or absence of hepatic function disorder	Patients who had data indicating presence or absence of liver disorder in “161207 complication (FIX) CRO” are deemed to have hepatic function disorder, and patients without such data are deemed to not have hepatic function disorder.
Complications Presence or absence of renal impairment	Patients who had data indicating presence or absence of renal disorder in “161207 complication (FIX) CRO” are deemed to have renal impairment, and patients without such data are deemed to not have renal impairment.
Complications Presence or absence of circulatory disturbance	Patients who had data indicating presence or absence of renal disorder in “161207 complication (FIX) CRO” are deemed to have circulatory disturbance, and patients without such data are deemed to not have circulatory disturbance.
Complications Presence or absence of hematologic disorder	Patients who had data indicating presence or absence of hematologic disorder in “161207 complication (FIX) CRO” are deemed to have blood disorder, and patients without such data are deemed to not have hematologic disorder.
Complications Presence or absence of respiratory disorder	Patients who had data indicating presence or absence of respiratory disorder in “161207 complication (FIX) CRO” are deemed to have respiratory disorder, and patients without such data are deemed to not have respiratory disorder.

Name of data	Derivation and calculation method
Complications Presence or absence of other conditions	Patients who had data indicating presence or absence of complication classified into other detailed classification (diabetes mellitus, gastrointestinal disorder, osteoporosis, malignant tumour, and collagen disorder, and others) in "161207 complication (FIX) CRO" are deemed to have other conditions, and patients without such data are deemed to not have other conditions. In addition, if there is applicable data for Presence or absence of any conditions by "complications including other detailed classification", patients are deemed as having such conditions and those without such data, they are deemed to not have such conditions.
Presence or absence of history of allergy	If there is a check mark in a box for history of allergy in "patient information" in survey sheet, such patients are deemed to have allergy, and if there is a check mark in a box for "unknown about allergy", whether patients have allergy is deemed as unknown, and if a column for "presence or absence of allergy" is not completed and in any other situations, patients are deemed to have no history of allergy.
Patients with hepatitis B viral infection	Patients with description as "hepatitis→ viral" in "complication" and "Type B" in "hepatitis virus carrier" in "patient information", are deemed to be patients with hepatitis B infection. In addition, patients have events corresponding to MedDRA PT code described in "161207 Hepatitis B (FIX) CRO" are deemed to have hepatitis B infection.
Presence or absence of smoking habit	If there is a check mark in a box for presence or absence of smoking habit in the survey sheet, patients are deemed to have smoking habit. If there is a check mark in a box for absence of smoking habit in the survey sheet, patients are deemed to have no smoking habit. If there is a check mark in a box for unknown about smoking habit in the survey sheet, whether patients have smoking habit or not is deemed as unknown. If a column for "smoking habit" is not completed, whether patients have smoking habit or not is deemed as not described.
Patients in whom deviation from rules for administration of this drug is noted	Patients who receive this drug at the dose other than "160 mg→80 mg→40 mg/2 weeks", "only 160 mg", or "160 mg→80 mg/2 weeks", deviation is deemed to have occurred.
Presence or absence of self-administration	If there is at least one check mark in a column for "Self-administration" in "Administration status" in the survey sheet, the patients are deemed to do self-administration. In any other situations, patients are deemed not to do self-administration.
Presence or absence of self-administration error	If there is a check mark in a box for "self-administration error was present" in the survey sheet, self-administration error is deemed to be present, and if there is a check mark in a box for "self-administration error was absent", self-administration is deemed to be absent. In addition, regardless of presence or absence of check mark in

Name of data	Derivation and calculation method
	"self-administration error was present" or "self-administration error was absent", if details are described about onset date of self-administration error, self-administration error is deemed to be present. If there is no description about onset date of self-administration error, whether there is self-administration error or not is deemed as "Unknown/not described".
Sex	Data should be extracted from an item, sex, in patient information in the survey sheet. If there are multiple check marks or data without description, sex is deemed to be "unknown/not described".
Pregnancy/lactation	Data should be extracted from pregnancy/lactation in patient information in the survey sheet. If there are multiple check marks or data about pregnancy/lactation is not completed although "female" is chosen as sex, whether the patients correspond to pregnancy/lactation is deemed to be "unknown/not described". If any description about this item are found, data should not be aggregated as "female" if "female" is not chosen.
Race	Data is extracted from an item, race, in the survey sheet. If there are multiple check marks or data without description, sex is deemed to be "unknown/not described".
Age	Data should be extracted from an item, "Year and month of birth", and the start date of initial administration in the survey sheet. Date of birth should be complemented by the first day of the month and derived by following SAS codes. floor((intck('month', birth data, start date of the initial administration) - (day(start date of the initial administration) < day(birth date)))/12) However, if derivation could not be executed because birth date or start date of the initial administration is incomplete or unknown, age described in the survey sheet should be employed. If derivation could not be executed by birth date and age is not described, age should be defined as "unknown/not described".
Child	Patients aged younger than 15 should be applicable.
The elderly	Patients aged 65 or older should be applicable.
body weight	Data should be derived from an item, body weight, in patient information in the survey sheet. If there is a check mark in a box for unknown, or data about bod weight is not completed, body weight is deemed to be "unknown/not described".
Body height	Data should be derived from an item, body height, in patient information in the survey sheet. If there is a check mark in a box for unknown, or data about body height is not completed, body height is deemed to be "unknown/not described".
BMI	Body weight (kg) / (body height(cm)/100)^2
Disease duration (Year)	"YY/MM" in "disease duration" in "patient information" should be converted to description on an annual basis.

Name of data	Derivation and calculation method
	In a case where there are both values for year and month: Year + month/12 In a case where there is only value for year: Year In a case where there is only value for month: Month/12 In any other situations, disease duration should be defined to be "unknown/not described" as derivation cannot be executed.
Reasons for use	If there are duplicated check marks in gastro-intestinal Behcet disease and other conditions for reasons for use, data should be aggregated as "gastro-intestinal Behcet disease".
• Diagnostic classifications of gastro-intestinal Behcet disease	Diagnostic classification should be determined based on check marks in boxes for main symptoms and accessary symptoms in the survey sheet. • Complete type: 4 items of main symptoms • Incomplete type: Any of following conditions are met [1] Any 3 items of main symptoms [2] Any 2 items of main symptoms and 2 items of accessary items [3] Either item of eye symptoms of main symptoms or any main symptoms other than eye symptoms [4] Either item of eye symptoms of main symptoms or any 2 accessary symptoms • Suspected: In a case where at least 1 main symptom is met although conditions for incomplete type are not met • Other: There is no main symptom • Unknown/not described: Other than above situations
Tuberculin test or IGRA test	Tests were implemented: Either of "Tuberculin test" or "Interferon γ free release test" is implemented (if there is no check mark in box for implementation although test results are described, tests are deemed to have been implemented". Test were not implemented: Both "Tuberculin test" and "Interferon γ free release test" were not implemented. Unknown/not described: Other than above situations
HBs antigen test	Test was implemented: In a case where "Hbs antigen test" in the survey sheet was implemented Test was not implemented: In a case where "Hbs antigen test" in the survey sheet was not implemented Unknown/not described: Other than above situations
HBs antibody test	Test was implemented: In a case where "Hbs antibody test" in the survey sheet was implemented Test was not implemented: In a case where "Hbs antibody test" in the survey sheet was not implemented Unknown/not described: Other than above situations
HBc antibody test	Test was implemented: In a case where "Hbc antibody test" in the survey sheet was implemented Test was not implemented: In a case where "Hbc antibody test" in the survey sheet was not implemented

Name of data	Derivation and calculation method
	Unknown/not described: Other than above situations
HBV-DNA quantitative test	Test was implemented: In a case where “HBV-DNA quantitative test” in the survey sheet was implemented Test was not implemented: In a case where “HBV-DNA quantitative test” in the survey sheet was not implemented Unknown/not described: Other than above situations
Chest X-ray test	When the start date of the initial administration of this drug is defined as 1 and previous day of the start date of the initial administration is defined as -1, patients in which date of chest X-ray is included between -90 and -1, are deemed to undergo chest X-ray. In addition, data included in the survey sheet should be used.
CT scanning	When the start date of the initial administration of this drug is defined as 1 and previous day of the start date of the initial administration is defined as -1, patients in which date of CT scanning is included between -90 and -1, are deemed to undergo CT scanning. In addition, data included in the survey sheet should be used.
Other image tests	When the start date of the initial administration of this drug is defined as 1 and previous day of the start date of the initial administration is defined as -1, patients in which date of other image tests is included between -90 and -1, are deemed to undergo other image tests. In addition, data included in the survey sheet should be used.
Chest X-ray and CT scanning	Either of “Chest X-ray” or “CT scanning” is implemented (if there is no check mark in box for implementation although test results are described, tests are deemed to have been implemented”. Tests were not implemented: Other than above situations
Drug previously used	Of data in which there are any descriptions about “previously used drug/previous treatment for gastro-intestinal Behcet disease”, data excluding that about previous treatment method is deemed to be previously used drug. Patients with description about previously used drug is deemed to have drug previously used. If there is no description in “previously used drug/previous treatment method for gastro-intestinal Behcet disease” and whether patients have drug previously used cannot be assessed, where there is drug previously used is deemed to be unknown/not described, and in any other situations, patients are deemed to have no drug previously used.
Presence or absence of use of previously used drug (aminosalicylic acid preparation)”	Based on “161206 drug list_addtion (Fix)CRO”, if there is a data on previously used drug corresponding to relevant drug code or there is a check mark in a box for aminosalicylic acid preparation in the survey sheet, patients are deemed to have previously received aminosalicylic acid preparation and in any other situations, patients are deemed not to have received aminosalicylic acid preparation.

Name of data	Derivation and calculation method
Presence or absence of previously used drug (steroid)	Based on "161206 drug list_addtion (Fix)CRO", if there is a data on previously used drug corresponding to relevant drug code or there is a check mark in a box for steroid in the survey sheet, patients are deemed to have previously received steroid and in any other situations, patients are deemed not to have received steroid.
Presence or absence of previously used drug (immunomodulative drug)	Based on "161206 drug list_addtion (Fix)CRO", if there is a data on previously used drug corresponding to relevant drug code or there is a check mark in a box for immunomodulative drug in the survey sheet, patients are deemed to have previously received immunomodulative drug and in any other situations, patients are deemed not to have received immunomodulative drug.
Presence or absence of drug used for previously used drug (antibiotic)	Based on "161206 drug list_addtion (Fix)CRO", if there is a data on previously used drug corresponding to relevant drug code or there is a check mark in a box for antibiotic in the survey sheet, patients are deemed to have previously received antibiotic and in any other situations, patients are deemed not to receive antibiotic.
Presence or absence of previously used drug (other drug)	Based on "161206 drug list_addtion (Fix)CRO", if there is a data on "Other drugs than biological preparations" in the survey sheet and any data on previously used drug except for aminosalicylic acid preparation, steroid, immunomodulative drug, or antibiotic, patients are deemed to have previously received other drugs and in any other situations, patients are deemed not to have received other drugs.
Presence or absence of drug used for previously used drug (adalimumab)	Based on "161206 drug list_addtion (Fix)CRO", if there is a data on previously used drug corresponding to relevant drug code, patients are deemed to have previously received adalimumab and in any other situations, patients are deemed not to have received adalimumab.
Presence or absence of previously used drug (infliximab)	Based on "161206 drug list_addtion (Fix)CRO", if there is a data on previously used drug corresponding to relevant drug code, patients are deemed to receive infliximab and in any other situations, patients are deemed not to have previously received infliximab.
Presence or absence of previously used drug (other biological preparations)	Based on "161206 drug list_addtion (Fix)CRO", if there is a data on "Biological preparations" in the survey sheet and any data on previously used drug except for adalimumab or infliximab, patients are deemed to have previously received other biological preparations and in any other situations, patients are deemed not to have previously received other biological preparations.
Presence or absence of previous treatment	Of data in which there are any descriptions about "previously used drug/previous treatment for gastro-intestinal Behcet disease", data excluding that about previously used drug is deemed to be previous treatment. Patients with description about previous treatment is deemed as patients who received previous treatment. If there is no description in "previously used drug/previous treatment for gastro-intestinal Behcet disease" and whether previous treatment is present or not cannot be assessed, previous treatment is deemed to be unknown/not described, and

Name of data	Derivation and calculation method
	in any other situations, patients are deemed to have received no previous treatment.
Presence or absence of previous treatment (operation/others)	If there is a check mark in a box for operation in “previously used drug/previous treatment for gastro-intestinal Behcet disease” and description corresponding to operation in “[HUMIRA BD] converted data for provision for analysis”, previous treatment is deemed to be operation, and in any other situations, it is deemed to be others. If there is a data corresponding to operation, patients are deemed to have undergone operation, and in any other situations, patients are deemed to have not undergone operation. If there is a data corresponding to others, patients are deemed to have received other previous treatment, and in any other situations, patients are deemed to have not received previous treatment.
Presence or absence of previously used drug/previous treatment	If data corresponds to presence or absence of previously used drug and previous treatment, patients are deemed to have previously used drug or have received previous treatment. Whether previously used drug or previous treatment is present or not is “unknown/not described”, “unknown/not described” should be described for presence or absence of previously used drug/previous treatment, and in any other situations, “none” should be described.
Presence or absence of concomitant drugs	If there is data corresponds to following condition, patients are deemed to have concomitant drugs. Patients with description about concomitant drug are deemed to have concomitant drug. If there is no description in “concomitant drug” and whether patients have concomitant drug cannot be assessed, “unknown/not described” should be described for presence or absence of concomitant drug, and in any other situations, “none” should be described. □ Data with description about “Administration status of concomitant drugs” • If there is clear description in start date of administration of concomitant drug with year and month, “date” is complemented by “1”. • If there is clear description in start date of administration of concomitant drug with yea, “month” and “date” each is complemented by “1”. • If there is clear description in last date of administration of concomitant drug with year and month, “date” is complemented by the end day of the month. • If there is clear description in last date of administration of concomitant drug with year, “month” and “date” are complemented by “12” and “1”, respectively. • If last date of administration of concomitant drug is earlier than start date of the initial administration of this drug and last date of the final administration of this drug is earlier

Name of data	Derivation and calculation method
	than start date of administration of concomitant drug, the data should be excluded from aggregation of concomitant drugs. If date cannot be complemented by above rules or the order of start date and last date of administration of concomitant drug is reversed, the data should be included in aggregation of concomitant drugs. □ Data with description about "Previously used drug" • If there is clear description in start date of administration of previously used drug with year and month, "date" is complemented by "1". • If there is clear description in start date of administration of previously used drug with year, "month" and "date" each is complemented by "1". • If last date of administration of previously used drug is earlier than start date of the initial administration of this drug, the data should be included in aggregation of concomitant drugs. If date cannot be complemented by above rules, last date of administration of previously used drug is deemed as unknown and it is not handled as concomitant drug. □ Data with description about "Administration status of antituberculosis drug" • If there is clear description in start date of administration of antituberculosis drug with year and month, "date" is complemented by "1". • If there is clear description in start date of administration of antituberculosis drug with year, "month" and "date" each is complemented by "1". • If there is clear description in last date of administration of antituberculosis drug with year and month, "date" is complemented by the end day of the month. • If there is clear description in last date of administration of antituberculosis drug with year, "month" and "date" are complemented by [12] and [31], respectively. • If last date of administration of antituberculosis drug is earlier than start date of the initial administration of this drug and last date of the final administration of this drug is earlier than start date of administration of antituberculosis drug, the data should be excluded from aggregation of concomitant drugs. If date cannot be complemented by above rules or the order of start date and last date of administration of antituberculosis drug is reversed, the data should be included in aggregation of concomitant drugs. (A term, "clear" means a situation where there is no ambiguous description such as "around" or "middle of month" and only numerical value is described)
Presence or absence of	Based on "161206 drug list_addtion (Fix)CRO", if there is a data

Name of data	Derivation and calculation method
use of concomitant drug (aminosalicylic acid preparation)	on concomitant drug corresponding to relevant drug code, patients are deemed to concomitantly received aminosalicylic acid preparation and in any other situations, patients are deemed not to concomitantly receive aminosalicylic acid preparation.
Presence or absence of use of concomitant drug (steroid)	Based on "161206 drug list_addtion (Fix)CRO", if there is a data on concomitant drug corresponding to relevant drug code, patients are deemed to concomitantly receive steroid and in any other situations, patients are deemed not to concomitantly receive steroid.
Presence or absence of concomitant drug (immunosuppressive drug)	Based on "161206 drug list_addtion (Fix)CRO", if there is a data on concomitant drug corresponding to relevant drug code, patients are deemed to concomitantly received immunosuppressive drug and in any other situations, patients are deemed not to concomitantly receive immunosuppressive drug.
Presence or absence of concomitant drug (immunomodulative drug)	Based on "161206 drug list_addtion (Fix)CRO", if there is a data on concomitant drug corresponding to relevant drug code, patients are deemed to concomitantly receive immunomodulative drug and in any other situations, patients are deemed not to concomitantly receive immunomodulative drug.
Presence or absence of concomitant drug (enteral nutrient)	Based on "161206 drug list_addtion (Fix)CRO", if there is a data on concomitant drug corresponding to relevant drug code, patients are deemed to concomitantly received enteral nutrient and in any other situations, patients are deemed not to concomitantly receive enteral nutrient.
Presence or absence of concomitant drug (colchicine)	Based on "161206 drug list_addtion (Fix)CRO", if there is a data on concomitant drug corresponding to relevant drug code, patients are deemed to concomitantly received colchicine and in any other situations, patients are deemed not to concomitantly receivecolchicine.
Presence or absence of concomitant drug (Others)	If there is data with descriptions about concomitant drug other than immunosuppressive drug, immunomodulative drug, enteral nutrient, and colchicine, patients are deemed to have use of other concomitant drug, and in any other situations, patients are deemed to have no concomitant drug.
Presence or absence of combination therapy	Data including descriptions in "combination therapy" in the survey sheet obtained between the start date of the initial administration and the last date of the final administration of this drug should be applicable. Even if the start date or last date of combination therapy is not identified, the data should be applicable. (the data should be excluded only if the administration period is not obviously overlapped with that of this drug) Patients with description about combination therapy are deemed to receive combination therapy. If there is no description in "treatment except for drug treatment/presence or absence of combination therapy" and whether patients receive combination therapy or not cannot be assessed, whether patients receive combination therapy is deemed to be unknown/not described, and in any other situations, patients are deemed to receive no

Name of data	Derivation and calculation method
	combination therapy.
Presence or absence of combination therapy (operation/others)	If there is a check mark in a box for operation in name of treatment except for drug treatment/therapy in "treatment except for drug treatment/combination therapy for gastro-intestinal Behcet disease (including operation)" and there is description corresponding to operation as combination therapy in "[HUMIRA BD] converted data for provision for analysis", combination therapy provided in the patients is deemed to be operation, and there is data about other therapy than operation, the patients are deemed to receive other combination therapy. If there is data corresponding to operation, patients are deemed to have received operation, and in any other situations, patients are deemed to have not undergone operation. If there is data corresponding to others, patients are deemed to receive other combination therapy, and in any other situations, patients are deemed not to receive combination therapy.
Presence or absence of implementation of endoscopy	If at least one description of date between the start date of the initial administration of this drug and the last date of the final administration of this drug in implementation date of endoscopy in "level of improvement in endoscopy findings" in the survey sheet, endoscopy is deemed to have been implemented. If there is a check mark in a box for not implemented, endoscopy is deemed to have not been implemented. In any other situations, whether endoscopy has been implemented or not is deemed to be unknown/not described. The site of endoscopy should be derived from data with check mark in "site of ulcer with the maximum diameter" in the survey sheet.
Presence or absence of drug used after discontinuation of administration of this drug	If there is data with description in "drugs used after discontinuation of administration of this drug", patients are deemed to have drugs after discontinuation of administration of this drug. If there is data about drugs used after discontinuation, patients are deemed to have drugs used after discontinuation of administration of this drug. If whether patients have drugs used after the discontinuation of administration of this drug or not is not described or cannot be assessed, presence or absence of drug used after the discontinuation of this drug is deemed to be unknown/not described, and in any other situations, patients are deemed to have no drug used after the discontinuation of administration of this drug.
Presence or absence of use of drug used after the discontinuation of administration of this drug (aminosalicylic acid preparation)	If there is data about aminosalicylic acid preparation in "drugs used after the discontinuation of this drug" in the survey sheet, patients are deemed to have received aminosalicylic acid preparation, and in any other situations, patients are deemed to have not received aminosalicylic acid preparation.
Presence or absence of use of concomitant drug (steroid)	If there is data with description in steroid in "drugs used after the discontinuation of this drug" in the survey sheet, patients are deemed to have received steroid, and in any other situations,

Name of data	Derivation and calculation method
	patients are deemed to have not received steroid.
Presence or absence of drugs used after the discontinuation of this drug (immunomodulative drug)	If there is data with description in immunomodulative drug in “drugs used after the discontinuation of this drug” in the survey sheet, patients are deemed to have received immunomodulative drug, and in any other situations, patients are deemed to have not received immunomodulative drug.
Presence or absence of drugs used after the discontinuation of this drug (antibiotic)	If there is data about antibiotic in “drugs used after the discontinuation of this drug” in the survey sheet, patients are deemed to have received antibiotic, and in any other situations, patients are deemed to have not received antibiotic.
Presence or absence of drugs used after the discontinuation of this drug (biological preparation)	If there is data with description in biological preparation in “drugs used after the discontinuation of this drug” in the survey sheet, patients are deemed to have received biological preparation, and in any other situations, patients are deemed to have not received biological preparation.
Presence or absence of drugs used after the discontinuation of this drug (other drug)	If there is data about other drugs in “drugs used after the discontinuation of this drug” in the survey sheet, patients are deemed to have received other drug, and in any other situations, patients are deemed to have not received other drug after the discontinuation of administration of this drug.
Main symptoms of Behcet's disease: presence or absence of recurrent oral mucosa aphthous ulcer	If there is a check mark in “1,2,3” in “recurrent oral mucosa aphthous ulcer” at the start of administration of this drug in survey sheet with the date before the start date of the initial administration of this drug, mucosal aphthous ulcer is deemed to be present, and in any other situations, it is deemed to be absent.
Main symptoms of Behcet's disease: presence or absence of cutaneous symptoms	If there is a check mark in “1,2,3” in “cutaneous symptoms” at the start of administration of this drug in survey sheet with the date before the start date of the initial administration of this drug, cutaneous symptoms is deemed to be present, and in any other situations, cutaneous symptom is deemed to be absent.
Main symptoms of Behcet's disease: presence or absence of eye symptoms	If there is a check mark in “1,2,3” in “eye symptoms” at the start of administration of this drug in survey sheet with the date before the start date of the initial administration of this drug, eye symptoms is deemed to be present, and in any other situations, it is deemed to be absent.
Main symptoms of Behcet's disease: presence or absence of ulcer of vulva	If there is a check mark in “1,2,3” in “ulcer of vulva” at the start of administration of this drug in survey sheet with the date before the start date of the initial administration of this drug, ulcer of vulva is deemed to be present, and in any other situations, it is deemed to be absent.
Main symptoms of Behcet's disease: presence or absence of arthritis without deformity or rigidity	If there is a check mark in “1,2,3” in “arthritis without deformity” at the start of administration of this drug in survey sheet with the date before the start date of the initial administration of this drug, arthritis without deformity is deemed to be present, and in any other situations, it is deemed to be absent.
Accessary symptoms of Behcet's disease: presence or absence of	If there is a check mark in “epididymitis” at the start of administration of this drug in survey sheet with the date before the start date of the initial administration of this drug,

Name of data	Derivation and calculation method
epididymitis	epididymitis is deemed to be present, and in any other situations, it is deemed to be absent.
Accessary symptoms of Behcet's disease: presence or absence of vascular lesion	If there is a check mark in “vascular lesion” at the start of administration of this drug in survey sheet with the date before the start date of the initial administration of this drug, vascular lesion is deemed to be present, and in any other situations, it is deemed to be absent.
Accessary symptoms of Behcet's disease: presence or absence of moderate or higher degree central nervous lesion	If there is a check mark in “moderate or higher degree central nervous lesion” at the start of administration of this drug in survey sheet with the date before the start date of the initial administration of this drug, moderate or higher degree central nervous lesion is deemed to be present, and in any other situations, it is deemed to be absent.
Test for tuberculosis	Test was implemented: If “test for tuberculosis or IGRA test” were implemented and “chest X-ray or CT scanning” was implemented. Tests were not implemented: Other than above situations
Test of hepatitis B	Test was implemented: If “HBV-DNA quantitative test” was implemented or patients are negative for “Hbs antigen test”, “Hbs antibody test”, and “Hbc antibody test”. Tests were not implemented: Other than above situations
Responding patients	Patients who were assessed to have obtained “improvement” and “significant improvement” as level of overall improvement are defined as responding patients.

10.2. Safety analysis

Name of data	Derivation and calculation method
Adverse events	Of events described in “Humira BD_AE matching list (for application for reassessment)(after linking)_20170110”, events derived from survey sheet or events listed in detailed survey report described by physician of contracted departments and institutions although they are not derived from survey sheet are deemed to be adverse events included in analysis. Adverse events occurred: At least one record of adverse event is found. No adverse event: Other than above When the number of adverse events is counted, in a case where the events are aggregated by SOC, the events expressed in same SOC in the same patient is deemed as 1 event, and in a case where they are aggregated by PT, the events expressed in same PT in the same patient is deemed as 1 event. If there is no applicable patient, “0” for the number of patients and “0.00” for rate of patients should be displayed.

Name of data	Derivation and calculation method
Serious adverse events	Of adverse events, those assessed as serious using seriousness criteria for company's seriousness assessment described in "Humira BD_AE matching list (reassessment) (after linking)_20170110" are deemed as serious adverse events. Serious adverse events occurred: At least one record of serious adverse event is found. No adverse event: Other than above The same counting method as that for adverse events shall be used for the number of serious adverse events.
Adverse reaction	Of adverse events, adverse events except for those assessed as "Not related" based on criteria for company's causality assessment described in "Humira BD_AE matching list (reassessment) (after linking)_20170110" are deemed to be adverse reaction. Adverse reactions occurred: At least one record of adverse reaction is found. Adverse reactions did not occur: Other than above The same counting method as that for adverse events shall be used for the number of adverse reactions.
Serious adverse reactions	Of adverse events, those assessed as serious using seriousness criteria for company's seriousness assessment described in "Humira BD_AE matching list (reassessment) (after linking)_20170110" are deemed as serious adverse reactions. Serious adverse reactions occurred: At least one record of serious adverse reaction is found. Serious adverse reactions did not occur: Other than above The same counting method as that for adverse events shall be used for the number of serious adverse reaction.
Outcome	When adverse event, adverse reaction, serious adverse event, and serious adverse reaction are aggregated by outcome, if multiple events with same SOC or those with same PT were present in 1 patient, such events should be identified using outcome in company's outcome assessment described in "Humira BD_AE matching list (reassessment) (after linking)_20170110" according to the priority as follows: [1] Death [2] Sequela [3] Not resolved [4] Unknown [5] Not described [6] Resolving [7] Resolved
Days from the start date of the initial administration of this drug until the onset date of adverse event	Onset date described in company's assessment in "HumiraBD_AE matching list (for reassessment) (after linking)_20170110" should be used. Derivation can be executed if the start date of the initial administration of this drug and onset date of adverse event is identified with complete date. If the start date of the initial administration of this drug is the same as or earlier than the onset date of the adverse events: The onset date of adverse event - the start date of the initial administration of this drug + 1

Name of data	Derivation and calculation method
	The start date of the initial administration of this drug is later than the onset date of adverse event: The onset date of adverse event - the start date of the initial administration of this drug If there are multiple events with same PT in 1 patient, the onset date of the event that occurred first should be used to identify the events to be aggregated.
Days from the onset date until the outcome (resolved or resolving) date of the adverse event	Outcome (resolved or resolving) date described in "HumiraBD_AE matching list (for reassessment) (after linking)_20170110" should be used. Derivation can be executed if the onset date and outcome date of adverse event are identified with complete date. Outcome date - onset date of the adverse event + 1 If there are multiple events with same PT in 1 patient, the value of the event with the longest duration until the outcome of resolved or resolving should be used.
Incidence of adverse reactions, serious adverse reactions, adverse events, and serious adverse events	Incidence of adverse reactions, serious adverse reactions, adverse events, and serious adverse events should be calculated by using the number of patients in whom at least one of these events occurred as a numerator and the number of patients included in safety analysis as denominator. If different calculation method from above method is used, it should be described in each table in the Chapter 13 and subsequent chapter.

10.3. Efficacy analysis

Name of data	Derivation and calculation method
Level of overall improvement	Description of level of overall improvement in the survey sheet (assessment provided by attending physician) should be employed.
Clinical improvement	Patients with the level of improvement in endoscopy findings in the survey sheet of "2. shrinkage" or lower and comprehensive evaluation of gastrointestinal symptoms in the survey sheet of "1" or lower (0, 1) are assessed as patients with clinical improvement.
Complete remission	Patients with the level of improvement in endoscopy findings in the survey sheet of "1. remission or scar" and comprehensive evaluation of gastrointestinal symptoms in the survey sheet of "0" are assessed as patients with complete remission.
Improvement in gastrointestinal symptoms (abdominal pain, diarrhoea, other gastrointestinal symptoms)	If comprehensive evaluation of gastrointestinal symptoms or evaluation of each gastrointestinal symptom differs by 1 point or higher compared to those at the start of the administration of this drug (points of evaluation at the start of administration - those at each evaluation≥1), patients are assessed as those who obtained improvement.

Name of data	Derivation and calculation method
Level of improvement in endoscopy findings	Description in “level of improvement in ulcer with the maximum diameter” in the level of endoscopy findings in the survey sheet should be emplpyed.
Main symptoms and accessary symptoms of Behcet disease	Description in evaluations for each main and accessary symptom in efficacy evaluation in the survey sheet should be employed. “0” should be defined as “no symptom”, “1,2,3” should be defined as “there are any symptoms”, unknown or not described data should be defined as “unknown/not described”
CRP	Measurement in the survey sheet should be employed. If measurement is undetectable, the measurement should be deemed as undetectable limit.

11. Method of dividing hierarchy of data

data	Method of dividing hierarchy
Dosage and administration	160mg→80mg→40mg/2 weeks, no changes thereafter 160mg→80mg→40mg/2 weeks, and160mg or 80mg is administered at least once thereafter 160mg, and not administered thereafter 160mg→80mg, and not administered thereafter 80mg, and not administered thereafter 40mg, and not administered thereafter others
the number of administrations	at least once and less than 4 times at least 4 times and less than 12 times at least 12 times and less than 26 times at least 26 times and less than 39 times at least 39 times and less than 52 times at least 52 times and less than 65 times at least 65 times and less than 78 times at least 78 times
Total dose	lower than 500mg at least 500mg and lower than1000mg at least 1000mg and lower than 2000mg, at least 2000mg and lower than 3000mg at least 3000mg unknown
Mean daily dose	lower than 40 mg at least 40 mg and lower than 60 mg at least 60 mg and lower than 80 mg at least 80 mg and lower than 100 mg at least 100 mg unknown

data	Method of dividing hierarchy
Administration duration	at least 0 week and shorter than 4 weeks (1-28 days) at least 4 week and shorter than 12 weeks (29-84 days) at least 12 weeks and shorter than 24 weeks (85-168 days) at least 24 weeks and shorter than 52 weeks (169-364 days) at least 52 weeks and shorter than 104 weeks (365-728 days) at least 104 week and shorter than 156 weeks (729-1093 days) unknown * When the start date of the administration is defined as 1
Reasons for discontinuation	Occurrence of adverse events, insufficient effect, patient's request, not visiting, others, multiple reasons, unknown, and not described
Sex	male, female, unknown, not described
Pregnancy/lactation	Without pregnancy/lactation, during pregnancy, during lactation, unknown, not described
Race	Japanese, other Asians, others, unknown, not described
Age (years)	Younger than 15 years, 15 years or older and younger than 65 years, 65 years or older, unknown/not described
Body weight (kg)	Lower than 30, 30 or higher and lower than 40, 40 or higher and lower than 50m, 50 or higher and lower than 60, 60 or higher, unknown/not described
Body height (cm)	Lower than 140, 140 or higher and lower than 150, 150 or higher and lower than 160, 160 or higher and lower than 170, 170 or higher and lower than 180, 180 or higher and lower than 190, 190 or higher, unknown/not described
BMI	Younger than 18.5 years, 18.5 years or older and younger than 25 years, 25 years or older and younger than 30 years, 30 years or older, unknown
Smoking habit	Absent, present, unknown, not described
Disease duration (years)	Shorter than 2, 2 or longer and shorter than 5, 5 or longer and shorter than 10, 10 or longer, unknown/not described
Reasons for use	Gastro-intestinal Behcet disease, other conditions, unknown, not described
Diagnostic classifications of Behcet disease	Complete type, incomplete type, suspected, others, unknown/not described
Main symptoms of Behcet disease	Recurrent oral mucosa aphthous ulcer, cutaneous symptoms, eye symptoms, ulcer of vulva
Evaluation of main symptoms of Bechet disease	0,1,2,3 Recurrent oral mucosa aphthous ulcer Cutaneous symptoms (erythema nodosum, subcutaneous phlebitis, folliculitis-like skin eruption, acne-like skin eruption) Ulcer of vulva Eye symptoms
Presence or absence of eye symptoms of	There is no symptom: Point for evaluation of main symptoms of Bechet disease is 0

data	Method of dividing hierarchy
Bechet disease	There are any symptoms: Points for evaluation of main symptoms of Bechet disease are 1,2,3 Unknown/not described: Other than above situations
Accessary symptoms of Bechet disease	Arthritis without deformity or rigidity, epididymitis, gastrointestinal lesions characterized by ulcer of ileocecum, vascular lesion, moderate or higher degree central nervous lesion
Presence or absence of accessary symptoms of Bechet disease	There are any symptoms: there are check marks in boxes for each accessary symptom There is no symptom: Other than above
History of allergy	Absent, present, unknown, not described
Tuberculin test or IGRA test	Not implemented, implemented, unknown, not described
HBs antigen	Not implemented, implemented, unknown, not described
HBs antibody	Not implemented, implemented, unknown, not described
HBc antibody	Not implemented, implemented, unknown, not described
HBV-DNA quantitative	Not implemented, implemented, unknown, not described
Complications	Absent, present, unknown, not described
Detailed classification of complications	Liver disorder, renal disorder, circulatory disorder, blood disorder, respiratory disorder, others
Other classifications of complications	Diabetes mellitus, gastrointestinal disorder, osteoporosis, malignant tumour, collagen disorder, others
Medical history	Absent, present, unknown, not described
Detailed classifications of medical history	tuberculosis, bacterial bronchitis, nontuberculous mycobacterial infection, aplastic anaemia, pancytopenia, malignant tumour, others
Previously used drug/previous treatment	Absent, present, unknown, not described
Classification of biological preparation as previously used drug/previous treatment	Adalimumab, infliximab, others
Classification of drugs other than biological preparation as previously used drug/previous treatment	Biological preparation, aminosalicylic acid preparation, steroid, immunomodulative drug, antibiotic, other previously used drug, operation, other previous treatment
Concomitant drug	Absent, present, unknown, not described
Detailed classification of concomitant drugs	Aminosalicylic acid preparation, oral adrenocortical steroid, immunomodulative drug, immunosuppressive drug, enteral nutrient, colchicine, others
Combination therapy	Absent, present, unknown, not described
Detailed classification of combination therapy	Operation, others
Endoscopy	Absent, present, unknown, not described

data	Method of dividing hierarchy
Detailed classifications of endoscopy	Ileocecum, colon, esophagus, others
Level of improvement in endoscopy findings	Remission or scar, shrinkage, no change, aggravation, not assessed
Evaluation of gastrointestinal symptoms	0,1,2,3,4 0: No symptom 1: There was symptom in last 2 weeks but daily living activities were rarely disturbed. 2: There was symptom in last 2 weeks and daily living activities were slightly disturbed. 3: There was symptom in last 2 weeks and daily living activities were disturbed. 4: There was symptom in last 2 weeks and daily living activities were severely disturbed.
Detailed classifications of gastrointestinal symptoms	Abdominal pain, diarrhoea, others (including bloating, abcominal tenderness, haemorrhage)
Self-administration	Absent, present
Self-administration error	Absent, present, unknown, not described
Drug used after the discontinuation of this drug	Absent, present, unknown, not described
Detailed classifications of drug used after the discontinuation of this drug	Aminosalicylic acid preparation, steroid, immunomodulative drug, biological preparation, other drug
Level of overall improvement	Significant improvement, improvement, ineffective
Detailed classifications of level of overall improvement for patients with improvement or higher level of improvement	Significant improvement, improvement

12. Handling of data at test and evaluation

12.1. Time of evaluation of administration status of this drug

Time Allowance at evaluation when the start date of the initial administration of this drug is defined as 1 is as follows:

Time of evaluation	Time Allowance(Day)
At least 0 week and shorter than 4 weeks	1-28
At least 4 week and shorter than 12 weeks	29-84
At least 12 week and shorter than 24 weeks	85-168
At least 24 week and shorter than 52 weeks	169-364
At least 52 weeks and shorter than 104 weeks	365-728
At least 104 weeks and shorter than 156 weeks	729-1093

12.2. Time of evaluation of occurrence status of adverse reactions

Time Allowance at evaluation when the start date of the initial administration of this drug is defined as 1 is as follows:

Time of evaluation	Time Allowance(Day)
Within 4 weeks after the administration start	1-28
From 4 weeks within 12 weeks after the administration start	29-84
From 12 weeks within 24 weeks after the administration start	85-168
From 24 weeks within 52 weeks after the administration start	169-364
From 52 weeks within 104 weeks after the administration start	365-728
From 104 weeks within 156 weeks after the administration start	729-1092
Patients who received this drug for over156 weeks	1093-

12.3. Time of evaluation of level of overall improvement

At the final follow-up: The evaluation at the last follow-up in which level of improvement for each patient was assessed as “1. significant improvement”, “2. improvement”, or “3. ineffective” is employed.

Patients who discontinued the administration of this drug should be followed-up until 14 days after the last date of the final administration of this drug, and within this period, the evaluation at the last follow-up in which level of improvement was assessed as “1.significant improvement”, “2. improvement”, or “3. ineffective” is employed.

In patients in whom follow-up was continued, the evaluation for following period should be included in analysis: Time Allowance at evaluation when the start date of the initial administration of this drug is defined as 1 is as follows:

Time of evaluation	Time Allowance(Day)
The last follow-up (patients who were continuously followed up)	• Patients who were followed up for 52 weeks: the start date of the initial administration of this drug + 37 (52 weeks + 14 days)

Time of evaluation	Time Allowance(Day)
	• Patients who were followed up for 104 weeks: the start date of the initial administration of this drug + 756 (104 weeks + 28 days) • Patients who were followed up for 156 weeks: the start date of the initial administration of this drug + 1120 (156 weeks + 28 days)

12.4. Time of evaluation of rate of clinical improvement, rate of complete remission, and level of improvement in endoscopy findings

Time Allowance at evaluation when the start date of the initial administration of this drug is defined as 1 is as follows:

Time of evaluation	Time Allowance(Day)
Within 24 weeks after the administration start	1-168
At least 24 weeks and within 52 weeks after the administration start	169-364
At least 52 weeks and within 76 weeks after the administration start	365-532
At least 76 weeks and within 104 weeks after the administration start	533-728
At least 104 weeks and within 128 weeks after the administration start	729-896
At least 128 weeks and within 160 weeks after the administration start	897-1121

Data of rate of clinical improvement and complete remission with evaluation of endoscopy findings obtained within Time allowance and evaluation of gastrointestinal symptoms within 4 weeks before and after the date of endoscopy implementation should be employed.

If there are multiple measurements during the same period, the measurement obtained on the latest date should be employed.

12.5. Time of evaluation of gastrointestinal symptoms

Time Allowance at evaluation when the start date of the initial administration of this drug is defined as 1 is as follows:

Time of evaluation	Time Allowance(Day)
Administration start	until 1 (record date is day 1)
4 weeks after the administration start	15-42 (record date is day 29)
8 weeks after the administration start	43-70 (record date is day 57)
12 weeks after the administration start	71-98 (record date if day 85)
24 weeks after the administration start	155-183 (record date if day 169)

Time of evaluation	Time Allowance(Day)
52 weeks after the administration start	351-379 (record date is day 365)
76 weeks after the administration start	505-561 (record date is day 533)
104 weeks after the administration start	701-757 (record date is day 729)
128 weeks after the administration start	869-925 (record date is day 897)
156 weeks after the administration start	1065-1121 (record date is day 1093)

The latest data of that obtained within Time allowance should be included in analysis and if there is multiple data for the same day, data with the worse value (in the order of 4,3,2,1,0) should be included in analysis.

12.6. Time of evaluation of main and accessary symptoms of Bechet disease

Time Allowance at evaluation when the start date of the initial administration of this drug is defined as 1 is as follows:

Time of evaluation	Time Allowance(Day)
Administration start	until 1 (record date is day 1)
52 weeks after the administration start	351-379 (record date is day 365)
104 weeks after the administration start	701-757 (record date is day 729)
156 weeks after the administration start	1065-1121 (record date is day 1093)

The data on the closest day to the record date should be included in analysis and if there is multiple data for the same day, data with the worse value should be included in analysis.

12.7. Changes in CRP levels

Time Allowance at evaluation when the start date of the initial administration of this drug is defined as 1 is as follows:

Time of evaluation	Time Allowance(Day)
Administration start	-14-1(record date is day 1)
24 weeks after the administration start	155-183 (record date is day 169)
52 weeks after the administration start	351-379 (record date is day 365)
76 weeks after the administration start	505-561 (record date is day 533)
104 weeks after the administration start	701-757 (record date is day 729)
128 weeks after the administration start	869-925 (record date is day 897)
156 weeks after the administration start	1065-1121 (record date is day 1093)

The data on the closest day to the record date should be included in analysis and if there is multiple data for the same day, data with the worse value should be included in analysis.

13. Tables and figures prepared (Table and figure number and name)

13.1. Overall

"1.1 figure for distribution of patients"

Data included in analysis: Registered patients

Objective of analysis: Changes in the number of patients are shown as follows:

Analysis items: The number of registered institutions, the number of registered patients, the number of institutions in which survey sheets of unregistered patients were collected, the number of unregistered patients whose survey sheets were collected, the number of institutions in which survey sheet data was fixed, the number of patients whose survey sheet data was fixed, the number of patients whose survey sheet data was not fixed, the breakdown of reasons for not fixed survey sheet data, the number of patients included in safety analysis, the number of patients excluded from safety analysis, the breakdown of reasons for exclusion from safety analysis, the number of patients included in efficacy analysis, the number of patients excluded from efficacy analysis, the breakdown of reasons for exclusion from efficacy analysis

Notes: If there is no unregistered patients, the number of institutions in which survey sheets of unregistered patients were collected and the number of unregistered patients whose survey sheets were collected should be excluded from analysis.

In addition, items with no data of ineligible patients, patients whose survey sheet data was not fixed, or patients who have no reasons for exclusion, data by item should not be output.

"1.1.1 Progress of survey sheet"

[1] Patients with fixed data by separate volumes

Data included in analysis: Patients for whom a survey sheet data was fixed

Objective of analysis: The number of patients with fixed data by separate volumes is shown.

Analysis items: The number of patients with fixed data for the initial, second, and third volume should be calculated by patients whose survey sheet data was fixed, patients included in safety analysis, and patients included in efficacy analysis.

[2] Patients included in analysis by follow-up period

Patients included in analysis: Patients for whom a survey sheet data was fixed

Objective of analysis: The number of patients included in analysis by follow-up period is shown

Analysis items: The number of patients included in analysis for each follow-up period should be calculated by patients included in safety analysis and patients included in efficacy analysis.

"1.2 the number of institutions and patients included in the survey"
Patients included in analysis: Patients for whom a survey sheet data was fixed
Objective of analysis: The number of patients per institution is shown
Analysis items: The number of patients whose survey sheet data was fixed, mean, maximum, and minimum number of patients per institution is shown.

"1.3 List of patients excluded from safety analysis and efficacy analysis for use result survey, etc. (including reasons for exclusion)"
Patients included in analysis: Patients for whom a survey sheet data was fixed
Objective of analysis: List of patients excluded from each analysis population and reasons for exclusion are shown.
Analysis items: Reasons for exclusion in patients excluded from safety and efficacy analysis should be output.
If there are multiple reasons for exclusion in one patient, these reasons should be displayed by separating by comma.

"1.3.1 patients excluded (aggregated by reasons for exclusion)"
Patients included in analysis: Registered patients
Objective of analysis: For all patients included in analysis, reasons for exclusion in patients excluded from each analysis population are shown.
Analysis items: Patients whose survey sheet data was not fixed, patients excluded from safety analysis, breakdown of reasons for exclusion from safety analysis, patients excluded from efficacy analysis, and breakdown of reasons for exclusion from efficacy analysis

Notes: Data of all patients is output and [1] should be displayed for relevant items and brank space should be left for item which is not applicable.

"1.4 List of patients"
Patients included in analysis: Patients for whom a survey sheet data was fixed
Objective of analysis: List of patient characteristics, adverse events, administration status by patients prepared using data for analysis is shown.
Analysis items: Patient number, sex, age, body weight, disease duration, adverse event (presence or absence of adverse events, adverse event that occurred outside the period subject to analysis, SOC code, system organ class, PT code, disease name [PT of MedDRA], adverse event terms described by physician, onset date, days from start of administration of this drug to onset, seriousness, causal relationship, outcome, outcome

date, days to outcome date), level of overall improvement, administration status of this drug (start date of administration, last date of administration, days of administration, initial dose, maximum dose), presence or absence of complications, presence or absence of medical history, hepatitis B viral test (HBs antigen, HBs antibody, HBc antibody, HBV-DNA quantitative), tests for tuberculosis (tuberculin test, QuantiFERON test, T-spot test, chest X-ray, CT scanning, other image tests), retrieving flag (patients included in safety analysis, patients included in efficacy analysis, patients who continue to participate in clinical study, patients in whom adverse events occurred outside the period subject to safety analysis, patients who died, children, the elderly, pregnant women, patients who are lactating, patients with liver disorder, patients with renal impairment, patients with hepatitis B viral infection, patients in whom infection occurred, patients in whom malignant tumour occurred, patients in whom administration site reaction occurred, patients in whom autoimmune disease occurred, patients in whom pancytopenia occurred, patients in whom demyelinating disorder occurred, patients in whom cardiac failure congestive occurred, patients in whom interstitial pneumonia occurred, patients in whom deviation from administration rule of this drug occurred, patients in whom dose increase was made, patients with complete type Behcet disease, patients with incomplete type Behcet disease , patients with suspected Behcet disease, patients with recurrent aphthous ulcer, patients with cutaneous symptoms, patients with eye symptoms, patients with ulcer of vulva, patients with arthritis without deformity or rigidity, patients with epididymitis, patients with vascular disease, patients with moderate or higher degree central nervous lesion, patients with self-administration error, patients with detected AAA, patients who have contraindicated drug)

Notes: Level of overall improvement to be output should be according to “12.3 Time of evaluation of overall improvement”.
In addition, level was defined as “Significant improvement”, “improvement,” “ineffective”, or “efficacy could not be assessed”.
For adverse events that occurred outside the period subject to safety analysis, retrieving flag should be displayed as 1 (applicable) or 2 (not applicable).
Retrieving flag for complete type Behcet disease, incomplete type Behcet disease, and suspected Behcet disease, 10.1 diagnostic classifications of Behcet disease should be referred to.

“14.1.1 List of adverse events”
Patients included in analysis: Patients for whom a survey sheet data was fixed
Objective of analysis: List of adverse events by patients prepared using data for analysis

is shown.
Analysis items: Patient number, sex, age, SOC code, system organ class, PT code, disease name (PT of MedDRA), adverse event term described by physician, onset date, days from administration start, seriousness, causal relationship, outcome, outcome date, days to outcome, presence or absence of complications, presence or absence of medical history

Notes: Same definition should be used for analysis items

"1.4 List of patients who died"
Patients included in analysis: Patients for whom a survey sheet data was fixed
Objective of analysis:List of adverse events that occurred in patients who died prepared using data for analysis is shown.
Analysis items: Patient number, sex, age, SOC code, system organ class, PT code, disease name (PT of MedDRA), adverse event term described by physician, onset date, days from administration start, seriousness, causal relationship, outcome, outcome date, days to outcome, complications, start date of administration, last date of administration, days of administration

"14.3 List of patients aged 18 or younger"
Patients included in analysis: Patients for whom a survey sheet data was fixed
Objective of analysis:List of adverse patients aged 18 or younger prepared using data for analysis is shown.
Analysis items: Patient number, sex, age, body height, body weight, BMI, disease duration, presence or absence of discontinuation, reasons for discontinuation, adverse events (SOC code, system organ class, PT code, disease name [PT of MedDRA], onset date, seriousness, causal relationship, outcome, outcome date), level of overall improvement, administration status of this drug (start date of the initial administration of this drug, last day of the final administration of this drug), complications (PT code, disease name [PT of MedDRA], medical history (PT code, disease name [PT of MedDRA], comprehensive evaluation of gastrointestinal symptoms (time of administration start, the 52th week of administration, the 104th week of administration, the 156th week of administration), adalimumab as previously used drug, infliximab as previously used drug, aminosalicylic acid preparation as previously used drug, steroid as previously used drug, immunomodulating drug as previously used drug, antibiotic as previously used drug

"1.6 Administration status (total number of administrations, total dose)"
Patients included in analysis: Patients included in safety analysis, patients included in

efficacy analysis
Objective of analysis: Distribution of the number of administration, total dose, mean daily dose, days to last date of administration are shown
Analysis items: For the number of administration, total dose, and mean daily dose, the number of patients according to the classifications defined in “11 method of dividing hierarchy of data” and rate of the patients to those included in analysis should be calculated. In addition, summary statistics should be calculated for each measurement. Day to the last date of administration should be calculated according to “days to last date of the final administration of this drug” in “10.1 Overall”, and the number of patients by Time Allowance containing corresponding to days of administration in each patient defined in “12.1 time of evaluation of administration status of this drug” and rate of the patients to those included in analysis should be calculated. Summary of statistics of days of administration should be calculated.

“1.7 Reasons for discontinuation of survey”
Patients included in analysis: Patients included in safety analysis
Objective of analysis: Breakdown of patients who discontinued the survey and the reasons should be shown.
Analysis items: The number of patients included in analysis, the number of patients who discontinued survey and rate of these patients to those included in analysis, the number of patients with reasons for discontinuation and patients for which reasons for discontinuation is unknown or not described, and rate of these patients to those discontinued the survey, the number of patients by “Reasons for discontinuation” defined in “11. method of dividing hierarchy of data” and rate of these patients to those included in patients with reasons for discontinuation should be calculated.
Notes:Reasons for discontinuation may be overlapped at time of aggregation.
In addition, there is no patient corresponding to “patients in whom multiple reasons were chosen”, output by items should not be conducted.

“17.1 Reasons for discontinuation of survey (list of other reasons)”
Patients included in analysis: Patients included in safety analysis
Objective of analysis: Breakdown of other reasons for discontinuation is shown.
Analysis items: In patients who discontinued the survey for “Other reasons” defined in “11 Method of dividing hierarchy of data”, the number of patients by contents of other reasons for discontinuation should be calculated.

“1.12.1 Distribution of patient characteristics”
Patients included in analysis: Patients included in safety analysis, patients included in efficacy analysis, patients whose survey sheet data was fixed

Objective of analysis: Distribution of patient characteristics is shown
Analysis items: The number of patients included in analysis should be calculated.
The number of patients according to following classifications defined in “11 method of dividing hierarchy of data” and rate of these patients to those included in analysis should be calculated.
Sex, pregnancy/lactation, race, age (years), body weight (kg), body height (cm), BMI (kg/m2), smoking habit, disease duration (years), reasons for use, diagnostic classifications of Behcet disease, main symptoms of Behcet disease, accessary symptoms of Behcet disease, allergy history, tests for tuberculosis, test for hepatitis B, complications, detailed classifications of complications (liver disorder, renal disorder), medical history, previously used drug/previous treatment, classifications of biological preparations as previously used drug/previous treatment, classifications of drugs other than biological preparations as previously used drug/previous treatment, concomitant drugs, detailed classifications of concomitant drugs, combination therapy, detailed classifications of combination therapy, endoscopy, detailed classifications of endoscopy
In addition, summary statistics should be calculated for following items.
Age (years), body weight (kg), body height (cm), BMI (kg/m2), disease duration (years)

Notes:Rate of pregnancy/lactation should be calculated as that to female patients.
In addition, breakdown of each item should be represent the rate of patients to the aggregated number of patients corresponding to the item at one-step higher hierarchical level.
(Example: Rate of patients according to detailed classifications of complication to all patients who have complications should be calculated)
Main symptoms of Behcet disease, accessary symptoms of Behcet disease, detailed classifications of complications, other classifications of complications, detailed classifications of medical history, classifications of biological preparations as previously used drug/previous treatment, classifications of drugs other than biological preparations as previously used drug/previous treatment, detailed classifications of concomitant drugs, detailed classifications of combination therapy, and detailed classifications of endoscopy may be overlapped.

“1.13 Distribution of self-administration”
Patients included in analysis: Patients included in safety analysis
Objective of analysis:Distribution of presence or absence of self-administration and self-administration error is shown.
Analysis items: The number of patients included in analysis should be calculated.
The number of patients by “self-administration“ defined in “11 method of dividing hierarchy of data” and rate of these patients to those included in analysis should be

calculated. In addition, the number of patients with “self-administration error” and rate of these patients to patients in whom self-administration is present should be calculated.

“1.16 List of patients in whom AAA was detected”

Patients included in analysis: Patients included in safety analysis

Objective of analysis:List of patients in whom AAA was detected is shown.

Analysis items: Following items should be output for “patients in whom AAA was detected” defined in “10.1 Overall”.

Patient number, administration status (start date of the administration, last date of the administration), concomitant drugs, serum anti-adalimumab antibody (Date of blood test, positive/negative), adverse event term described by physician, disease name (PT of MedDRA), system organ class, onset date, seriousness, causal relationship, outcome date, outcome, and level of overall improvement

Notes: “Ongoing” should be displayed if patients continue to participate in the survey.

Information about serum anti-adalimumab antibody should be obtained from “AAA measurement (safety periodic report) in BD survey”.

Level of overall improvement should be evaluated using data at the last follow-up defined in “12.3 Time of evaluation of level of overall improvement”.

13.2. Safety

“2.1 List of occurrence status of adverse reactions and infections (Appendix 2)”

Patients included in analysis: Patients included in safety analysis

Objective of analysis: Occurrence status of adverse reactions is shown.

Analysis items: The number of patients should be calculated by the period for following items in patients in whom adverse reaction occurred in the period subject to safety analysis.

The number of institutions, the number of patients included in survey, the number of patients in whom adverse reaction occurred, the number of adverse reactions, rate of patients in whom adverse reactions occurred, the number of patients in whom adverse reactions occured by types of adverse reactions (SOC, PT) and the rate of these patients to all patients included in the survey should be calculated.

Notes: Classifications of period is as follows:

The 6th safety periodic report: between May 16, 2013 and December 31, 2015; between January 1, 2016 and December 31, 2016: Accumulation and total

Reassessment: At approval: between May 16, 2013 and December 31, 2015; between January 1, 2016 and December 31, 2016; between January 1 and May 15, 2017: Accumulation and total

“*” should be put before PT for events that cannot be expected based on “Precaution”.

“2.1.1 List of occurrence status of adverse reactions and infections (patients excluded from safety analysis)”

Patients included in analysis: Patients excluded from safety analysis

Objective of analysis: Occurrence status of adverse reactions in patients excluded from safety analysis is shown.

Analysis items: The number of adverse reactions should be calculated by following items in adverse reactions that occurred in the period subject to safety analysis.

The number of institutions, the number of patients included in survey, the number of patients in whom adverse reaction occurred, the number of adverse reactions, rate of patients in whom adverse reactions occurred, the number of patients in whom adverse reactions occured by types of adverse reactions (SOC, PT) and the rate of these patients to all patients included in the survey should be calculated.

“2.1.2 List of occurrence status of adverse reactions and infections that occurred outside the follow-up period”

Patients included in analysis: Patients for whom a survey sheet data was fixed

Objective of analysis: Occurrence status of adverse reactions that occurred outside the follow-up period is shown.

Analysis items: The number of adverse reactions should be calculated by following items in adverse reactions that occurred outside the period subject to safety analysis.

The number of institutions, the number of patients included in survey, the number of patients in whom adverse reaction occurred, the number of adverse reactions, rate of patients in whom adverse reactions occurred, the number of patients in whom adverse reactions occured by types of adverse reactions (SOC, PT) and the rate of these patients to all patients included in the survey should be calculated.

“2.2 List of occurrence status of serious adverse events (Appendix 10)”

Patients included in analysis: Patients included in safety analysis

Objective of analysis:Occurrence status of serious adverse events is shown.

Analysis items: The number of patients should be calculated by the period for following items in patients in whom adverse event occurred in the period subject to safety analysis.

The number of patients in whom serious adverse events occurred according to the number of institutions, the number of patients in whom serious adverse events occurred, the number of serious adverse events, rate of the number of patients in whom serious adverse events occurred, types of adverse events (SOC, PT) and rate of these patients to patients included in the survey should be calculated.

Notes:“2.1 List of occurrence status of adverse reactions and infections (Appendix 2)” should be referred to for classifications of the period.
“*” should be put before PT for events that cannot be expected based on “Precaution”.

“2.3 List of summary of patients included in analysis (Appendix 3)”
Patients included in analysis: Patients for whom a survey sheet data was fixed
Objective of analysis:List of patients is shown.
Analysis items: Analysis items and definitions are shown as follows.

(1) Patient number
Consecutive number starting from 1 should be provided by patients.

(2) Name of institutions (Company code)
The name should be displayed as Japanese official name. Name of institutions should be obtained from “[HUMIRA BD] list of DCF cords_Company A” and “[HUMIRA BD] list of DCF cords_Company E”.

(3) Main body of establishment/code
Code should be obtained from “Nippon Ultmarc Inc. classification of reassessment”

(4) Name of prefecture where the company is located
Company should be displayed as name Name of prefecture should be obtained from “Nippon Ultmarc Inc. classification of reassessment”

(5) Abbreviated name of patients
According to GB, “Not applicable” should be used

(6) Sex
According to GB, description should be as male, female, unknown, or not described

(7) Birth date (or age)
Description should be unified to age. According to GB, description should be as ”A + age + "0000"”

(8) Distinction between inpatient and outpatient
According to GB, description should be as inpatient, outpatient, unknown, or not described.

(9) Reasons for use
Code, disease name: LLT code and name displayed as LLT of MedDRA should be obtained based on reason for use of this drug described in the survey sheet

(10) Severity before administration
“items not collected” should be applied.

(11) Complications
Presence or absence: “presence or absence of complications” defined in “10.1

Overall".

The number of complications described: The number of PT codes applied to the complications based on MedDRA should be employed. Complication with the same PT code in one patient should be counted as 1. If there is no complication, "0" should be applied.

Name of complication: It should represent a name of PT based on MedDRA Description should include detailed classification of complications, disease name as complication, and consecutive number of complications in that order. This item should be left as blank space if the number of complication described is "0".

(12) Administration route

"SC" should be employed.

(13) The maximum dose (daily dose/one time dose)

The one time maximum dose should be employed. According to "Administration status (dosage and administration)" defined in "10.1 Overall", the maximum value by patients should be employed.

(14) Mean dose (daily dose/one time dose)

Mean one time dose should be employed.

According to "Administration status (total number of administration, total dose)" defined in "10.1 Overall", "total number of administration/total dose" should be employed.

(15) unit

"MG" should be employed.

(16) The number of administrations per day (the maximum)

"1" should be applied.

(17) Duration of use

According to "Administration status (total number of administration, total dose)" defined in "10.1 Overall", value for "total number of administration" should be employed.

(18) Concomitant drug

Pharmaceutical product code, name of main drug: Drugs should be displayed placing priority on those used for Behcet disease, with consecutive number, and the drug at the top of list should be employed. If there is no concomitant drug, a column for pharmaceutical product code should be left as blank and name of main drug should be "none".

The number of concomitant drugs described: The number of pharmaceutical codes put in order defined as above should be counted. The number of codes when there are multiple same codes in one patient should be 1. If there is no concomitant drug, "0" should be described.

(19) Extent of effect

The extent of improvement according to "12.3 Time of evaluation of level of overall improvement" should be output. However, if there is no level of overall improvement calculated according to 12.3, but description of level of overall improvement is found in the survey sheet, "unknown" or "not described" when no description was found should be output. If improvement could not be assessed, "unknown" should be applied.

(20) Adverse reaction

The number of records of adverse reactions that occurred in the period subject to safety analysis with the same PT code in one patient should be counted as 1.

Cord for organ name: SOC code should be applied. This item should be left as blank if "absent" is chosen as description for presence or absence.

Code for adverse reactions: PC code should be applied. This item should be left as blank if "absent" is chosen as description for presence or absence.

Name of adverse reaction: Name of PT should be applied This item should be left as blank if "absent" is chosen as description for presence or absence.

Presence or absence: Adverse reactions that occurred in the period subject to safety analysis with data indicating presence or absence of adverse event and causal relationship with this drug should be "present". If whether there is adverse events or not is unknown, "unknown" should be applied. If there is no description about presence or absence of adverse event, "not described" should be applied. In any other situations, "absent" should be applied. If a reason for exclusion from safety analysis is incapability of evaluating safety, "unknown" should be applied.

The number of adverse events: The number of PT codes should be counted. The number of records of PT codes in one patient should be 1.

This item should be left as blank if "absent" is chosen as description for presence or absence.

(21) Outcome

Outcome with the first priority among "Outcome" according to definition of "10.2 safety analysis" for PT code output as adverse reaction should be applied. This item should be left as blank if "absent" is chosen as description for presence or absence.

(22) Survey sheet number

Patient number described in this survey sheet should be applied.

(23) Withdrawn

Patients who were excluded from safety analysis and those excluded from efficacy analysis are defined as "patients withdrawn from both analysis".

Patients excluded from safety analysis except for patients defined as above are defined as "patients withdrawn from safety analysis".

Patients excluded from efficacy analysis except for patients defined as above

are defined as “patients withdrawn from efficacy analysis”.

Notes: For items subject to aggregation, if the number of relevant data is 0, “0” should be output without leaving it as blank.

“2.4.1 List of occurrence status of events defined as primary survey item”

Patients included in analysis: Patients included in safety analysis

Objective of analysis: In adverse events that occurred in the period subject to safety analysis, summary statistics of days to onset of the events, the number of patients by the outcome, and days to outcome (Resolved or resolving) is shown.

Analysis items: The number of patients in whom the events occurred and rate of these patients to those included in analysis and the number of patients with serious adverse events and rate of these patients included in analysis by types of adverse events (primary survey item and PT) that occurred in the period subject to safety analysis should be calculated. In addition, summary of statistics (the number of patients, the mean, median, maximum values) of days to onset of adverse events by PT and primary survey items (the number of PT code), the number of patients by outcome, summary of statistics of days from onset to outcome (Resolved or resolving) (the number of patients, the mean, median, minimum, and maximum values) should be calculated.

Notes: If there are events with the same PT in one patient, days to onset, outcome, and days to outcome (Resolved or resolving) should be aggregated as 1 event (1 patient) according to following rules.

- Priority for seriousness: Serious > non-serious
- Days to onset: It is identified based on the description in 10.2 days from start date of the initial administration of this drug to onset of adverse event.
- Outcome: It is identified based on the description as outcome in 10.2.
- Days to outcome (Resolved or resolving): It is identified based on the description in 10.2 days from onset of adverse event to outcome (Resolved or resolving).

“2.4.2 List of occurrence status of events defined as primary survey item (adverse reaction)”

Patients included in analysis: Patients included in safety analysis

Objective of analysis: In adverse reactions that occurred in the period subject to safety analysis, summary statistics of days to onset of the reactions, the number of patients by the outcome, and days to outcome (Resolved or resolving) is shown.

Analysis items: The number of patients in whom adverse reactions occurred and rate of these patients to those included in safety analysis, the number of patients in whom serious adverse reactions occurred and rate of these patients to those included in

analysis by types of the adverse reactions in the period subject to safety analysis should be calculated. In addition, summary of statistics (the number of patients, the mean, median, maximum values) of days to onset of adverse events by PT and primary survey items (the number of PT code), the number of patients by outcome, summary of statistics of days from onset to outcome (Resolved or resolving) (the number of patients, the mean, median, minimum, and maximum values) should be calculated.

Notes: If there are events with same PT in one patient, “2.4.1 List of occurrence status of primary items” should be referred to.

“2.4.3 List of occurrence status of adverse reactions (Important identified risk)”

Patients included in analysis: Patients included in safety analysis

Objective of analysis: In adverse reactions that occurred in the period subject to safety analysis, summary statistics of days to onset of important identified risks, the number of patients by the outcome, and days to outcome (Resolved or resolving) is shown.

Analysis items: The number of patients in whom adverse reactions occurred and rate of these patients to those included in analysis, the number of patients in whom serious adverse reactions occurred and rate of these patients to those included in analysis by types of important identified risks (important identified risk, PT) in the period subject to safety analysis should be calculated. In addition, summary of statistics of days to onset of adverse reactions (the number of patients, the mean, median, maximum values), the number of patients by outcome, summary of statistics of days from onset to outcome (Resolved or resolving) (the number of patients, the mean, median, minimum, and maximum values) by PT and important identified risks (total number of PT code) should be calculated.

Notes: If there are events with same PT in one patient, “2.4.1 List of occurrence status of primary items” should be referred to.

“2.5 List of occurrence status of adverse reactions by presence or absence of self-administration”

Patients included in analysis: Patients included in safety analysis

Objective of analysis: Occurrence status of adverse reactions by presence or absence of self-administration is shown.

Analysis items: Following items should be aggregated by presence or absence of self-administration in adverse reactions that occurred in the period included in safety analysis.

The number of patients included in the survey, the number of patients in whom adverse reaction occurred, the number of adverse reactions, the number of patients in whom

adverse reactions occurred and rate of these patients to those included in analysis by types of adverse reactions (SOC, PT) should be calculated.

"2.7 List of occurrence status of adverse reactions"

Patients included in analysis: Patients included in safety analysis

Objective of analysis: Occurrence status of adverse reactions by the time of onset is shown.

Analysis items: The number of patients should be calculated by the period for following items in patients in whom adverse reaction occurred in the period subject to safety analysis.

The number of patients included in survey, the number of patients in whom adverse reaction occurred, the number of adverse reactions (95% confidence interval), the number of patients in whom adverse reactions occurred and rate of these patients to those included in analysis by types of adverse reactions (SOC, PT) should be calculated.

Notes: The event that occurred first of all events with same PT in one patient should be included in analysis. Aggregation of data including the time of onset for the first-onset adverse reaction in Time Allowance defined in "12.2 Time of evaluation of adverse reactions". When the number of patients for events included in analysis is counted, data should be made invalid according to patient number and time of onset, and when the number of SOC is counted, data should be made invalid according to patient number, time of onset, and SOC for aggregation.

The number of patients included should be counted according to following definitions except for patients who discontinued the survey (patients who used this drug within the follow-up period) so that patients included in evaluation corresponding to Time Allowance defined in "12.2 Time of evaluation of occurrence status of adverse reactions" can be included. For patients who discontinued the survey, the patients included in the period until the time when 28 days has passed from the last date of the final administration of this drug should be counted.

- Patients who were followed up for 52 weeks:
  Patients who received this drug "for 52 weeks or longer and shorter than 104 weeks after the administration start" should be included.
- The number of patients who were followed up for 104 weeks:
  Patients who received this drug "for 104 weeks or longer and shorter than 156 weeks after the administration start" should be included.
- The number of patients who were followed up for 156 weeks:
  Patients who received this drug for longer than 156 weeks after the administration start should be included.

The number of patients in whom adverse reactions occurred should be counted by the period during which at least one adverse reaction is noted.
Incidence should be calculated by the time of evaluation to calculate Clopper-Pearson confidence interval.

"2.9 Incidence of adverse reactions (serious adverse reaction and adverse reaction) by patient characteristics"

Patients included in analysis: Patients included in safety analysis
Objective of analysis: Incidence of adverse reactions should be shown by patient characteristics and factor analysis should be conducted.
Analysis items: In patients in whom adverse reactions occurred in the period subject to safety analysis, the number of all the patients, the number of patients with serious adverse reactions, and rate of these patients to those included in analysis, the number of the patients with adverse reactions and rate of these patients to those included in analysis, and test provided for the adverse reactions (Fisher's exact test for nominal scale factors, and Mann-Whiteny u test for ordinal scale factors) should be calculated by following patient characteristics:
Notes:Patient characteristics are as follows: Age (years), sex, disease duration (years), complication, hepatic function disorder as complication, renal impairment as complication, medical history, allergy history, smoking habit, self-administration as administration status of this drug, previously used drug/previous treatment, biological preparation adalimumab as previously used drug, biological preparation infliximab as previously used drug, steroid as previously used drug, immunomodulative drug as previously used drug, immunosuppressive drug as previously used drug, oral adrenocortical steroid as concomitant drug, oral mucosa recurrent aphthous ulcer as main symptoms of Behcet disease other than gastrointestinal symptoms, cutaneous symptoms as main symptoms of Behcet disease other than gastrointestinal symptoms, eye symptoms as main symptoms of Behcet disease other than gastrointestinal symptoms, ulcer of vulva as main symptoms of Behcet disease other than gastrointestinal symptoms, arthritis without deformity or rigidity as accessary symptoms of Behcet disease other than gastrointestinal symptoms, epididymitis as accessary symptoms of Behcet disease other than gastrointestinal symptoms, vascular lesion as accessary symptoms of Behcet disease other than gastrointestinal symptoms, moderate or higher degree central nervous lesion as accessary symptoms of Behcet disease other than gastrointestinal symptoms, diagnostic classification of Behcet disease, days until the last date of the administration, and mean daily dose.

"2.9 incidence of adverse reactions by seriousness by patient characteristics"

Patients included in analysis: Patients included in safety analysis

Objective of analysis: Based on test result described in 2.9, occurrence status of adverse reactions by patient characteristics with significant differences is shown by dividing them into serious and non-serious adverse reactions.
Analysis items: In adverse reactions that occurred in the period included in safety analysis, following items should be aggregated by patient characteristics and seriousness.
The number of patients, the number of patients in whom adverse reactions occurred, rate of patients in whom adverse reactions occurred, the number of adverse reactions, the number of patients in whom adverse reactions occurred and rate of these patients to those included in analysis by types of the reactions (SOC, PT) should be calculated.

"2.13.1 Incidence of adverse reactions by presence or absence of hepatic function disorder"

Patients included in analysis: Patients included in safety analysis
Objective of analysis: Occurrence status of adverse reactions by presence or absence of hepatic function disorder should be shown by dividing them into serious and non-serious ones.
Analysis items: Following items should be aggregated by presence or absence of hepatic function disorder in adverse reactions that occurred in the period included in safety analysis.
The number of patients, the number of patients in whom adverse reactions occurred, rate of patients in whom adverse reactions occurred, the number of adverse reactions, the number of patients in whom adverse reactions occurred and rate of these patients to those included in analysis by types of the reactions (SOC, PT) should be calculated.

Notes: The event with the highest seriousness of all the events with same PT in one patient should be included in analysis. When the number of patients for events included in analysis is counted, data should be made invalid according to patient number and seriousness, and when the number of SOC is calculated, data should be made invalid according to patient number, seriousness, and SOC for aggregation.

"2.13.5 Incidence of adverse reactions by presence or absence of moderate or higher degree central nervous lesion"

Patients included in analysis: Patients included in safety analysis
Objective of analysis: Occurrence status of adverse reactions by presence or absence of moderate or higher degree central nervous lesion should be shown by dividing them into serious and non-serious ones.
Analysis items: Following items should be aggregated by presence or absence of moderate or higher degree central nervous lesion in adverse reactions that occurred in

the period included in safety analysis.
The number of patients, the number of patients in whom adverse reactions occurred, rate of patients in whom adverse reactions occurred, the number of adverse reactions, the number of patients in whom adverse reactions occurred and rate of these patients to those included in analysis by types of the reactions (SOC, PT) should be calculated.

Notes: Notes for "2.13.1 Incidence of adverse reactions by presence or absence of hepatic function disorder by seriousness" should be referred to.

"2.14.1 Incidence of adverse reactions by presence or absence of renal impairment by seriousness"

Patients included in analysis: Patients included in safety analysis
Objective of analysis: Occurrence status of adverse reactions by presence or absence of renal impairment should be shown by dividing them into serious and non-serious ones.
Analysis items: Following items should be aggregated by presence or absence of renal impairment in adverse reactions that occurred in the period included in safety analysis.
The number of patients, the number of patients in whom adverse reactions occurred, rate of patients in whom adverse reactions occurred, the number of adverse reactions, the number of patients in whom adverse reactions occurred and rate of these patients to those included in analysis by types of the reactions (SOC, PT) should be calculated.

Notes: Notes for "2.13.1 Incidence of adverse reactions by presence or absence of hepatic function disorder by seriousness" should be referred to.

"2.16.1 Incidence of adverse reactions in elderly patients and that in non-elderly patients by seriousness"

Patients included in analysis: Patients included in safety analysis
Objective of analysis: Occurrence status of adverse reactions in elderly patients and that in non-elderly patients should be shown by dividing them into serious and non-serious ones.
Analysis items: In adverse reactions that occurred in the period included in safety analysis, following items should be aggregated according to whether the patients were elderly or not and by seriousness.
The number of patients, the number of patients in whom adverse reactions occurred, rate of patients in whom adverse reactions occurred, the number of adverse reactions, the number of patients in whom adverse reactions occurred and rate of these patients to those included in analysis by types of the reactions (SOC, PT) should be calculated.

Notes: Notes for "2.13.1 Incidence of adverse reactions by presence or absence of

hepatic function disorder by seriousness" should be referred to.

"2.17 List of occurrence status of adverse reactions and infections in this survey"
Patients included in analysis: Patients included in safety analysis
Objective of analysis: Occurrence status of adverse reactions and serious adverse reactions is shown.
Analysis items: In adverse reactions that occurred in the period included in safety analysis, adverse reactions and serious adverse reactions should be aggregated for following items.
The number of patients included in the survey, the number of patients in whom adverse reactions occurred, the number of adverse reactions, rate of patients in whom adverse reactions occurred, the number of patients in whom adverse reactions occurred and rate of these patients in those included in the survey by types of the reactions (SOC, PT) should be calculated.

Notes: If there are events with same PT in one patient, these events should be counted as 1 event (1 patient) according to following rules for seriousness.
Priority for seriousness: Serious > non-serious

"2.18 List of occurrence status of adverse events in this survey"
Patients included in analysis: Patients included in safety analysis
Objective of analysis: Occurrence status of adverse events, serious adverse events, and non-serious adverse events is shown.
Analysis items: Adverse events, serious adverse events, and non-serious adverse events should be aggregated for following items in adverse events that occurred in the period subject to safety analysis.
The number of patients, the number of patients in whom adverse events occurred, the number of adverse events, rate of patients in whom adverse events occurred, the number of patients in whom adverse events occurred and rate of these patients to those included in analysis by types of the events (SOC, PT) should be calculated.

Notes: If there are events with same PT in one patient, these events should be counted as 1 event (1 patient) according to following rules for seriousness.
Priority for seriousness: Serious > non-serious

"2.19.1 Treatment for patients who showed insufficient response to treatment"
Patients included in analysis: In patients included in safety analysis, patients who discontinued the survey because of "insufficient effect" or patients in whom dose or the number of administration was adjusted because of "insufficient effect" should be

included.
Objective of analysis: Presence or absence of drugs used after discontinuation of this drug and distribution of the drugs used after discontinuation of this drug are shown.
Analysis items: The number of patients included in analysis should be calculated.
The number of patients and rate of these patients by “drugs used after discontinuation of this drug“ and ”detailed classifications of drug used after the discontinuation of this drug“ defined in “11 method of dividing hierarchy for data” should be calculated.
Date of patients in whom dose or the number of administration was adjusted because of “insufficient effect” should be obtained from “[HUMIRA BD] converted data for provision for analysis”.

Notes: Detailed classifications of drug used after the discontinuation of this drug may be overlapped.

“2.19.2 Dosage and administration for patients who showed insufficient response to treatment”

Patients included in analysis: In patients included in safety analysis, patients who discontinued the survey because of “insufficient effect” or patients in whom dose or the number of administration was adjusted because of “insufficient effect” should be included.
Objective of analysis: Distribution of dosage and administration for patients who showed insufficient response to treatment is shown.
Analysis items: The number of patients included in analysis should be calculated.
The number of patients and rate of these patients to those included in analysis should be calculated by presence or absence of discontinuation and classification of dosage and administration (patients discontinued by the initial or second administration, patients who received this drug 3 times or more, the maximum dose for the third or subsequent administration is 40 mg/2 weeks, 40 mg/1 week, 80 mg/2 weeks, 80 mg/1 week, 160 mg/2 weeks, 160 mg/1 week, and others). Items with the number of 0, output by items should not be made.
Date of patients in whom dose or the number of administration was adjusted because of “insufficient effect” should be obtained from “[HUMIRA BD] converted data for provision for analysis”.

13.3. Efficacy

“3.1 Level of overall improvement”

Patients included in analysis: Patients included in efficacy analysis
Objective of analysis: Level of overall improvement at the last follow-up is shown.
Analysis items: The number of patients included in analysis should be calculated.

The patients who achieved overall improvement and rate of these patients to those included in analysis based on the level of overall improvement calculated at last follow-up according to “12.3 Time of evaluation of level of overall improvement should be calculated by “The level of overall improvement” and “detailed classification of overall improvement at the level of improved or higher” defined in “11 method of dividing hierarchy of data”.

> “3.1.1 Level of clinical improvement (level of improvement in endoscopy findings is “2. shrinkage” or lower and comprehensive evaluation of gastrointestinal symptoms is “1” or lower”

Patients included in analysis: Patients included in efficacy analysis
Objective of analysis: Level of clinical improvement is shown by time of evaluation.
Analysis items: The number of patients included in analysis, the number of patients who achieved clinical improvement and rate of these patients to those included in analysis should be calculated by the time of evaluation.

Notes: The number of patients should be that of patients with data of evaluation of endoscopy findings within relevant period subject to analysis and evaluation of gastrointestinal symptoms in 4 weeks before and after the date of implementation of endoscopy. Time Allowance for the time of evaluation should be according to “12.4. Rate of patients who achieved clinical improvement, rate of patients who achieved complete remission, and time of evaluation of level of improvement in endoscopy findings”.

> “3.1.2 Rate of patients who achieved complete remission (level of improvement in endoscopy findings is “1. remission or scar” and comprehensive evaluation of gastrointestinal symptoms is “0” or lower”.

Patients included in analysis: Patients included in efficacy analysis
Objective of analysis: Level of complete remission is shown by time of evaluation.
Analysis items: The number of patients included in analysis, the number of patients who achieved complete remission and rate of these patients to those included in analysis should be calculated by the time of evaluation.

Notes: The number of patients should be that of patients with data of evaluation of endoscopy findings within relevant period subject to analysis and evaluation of gastrointestinal symptoms in 4 weeks before and after the date of implementation of endoscopy. Time Allowance for the time of evaluation should be according to “12.4. Rate of patients who achieved clinical improvement, rate of patients who achieved complete remission, and time of evaluation of level of improvement in endoscopy

findings".

"3.2.1 Comprehensive evaluation of gastrointestinal symptoms at each time of evaluation"

Patients included in analysis: Patients included in efficacy analysis

Objective of analysis: Comprehensive evaluation of gastrointestinal symptoms is shown by time of evaluation.

Analysis items: The number of patients included in analysis, the number of patients have comprehensive evaluation of gastrointestinal symptoms (0,1,2,3,4) and rate of these patients to those included in analysis, the number of patients who achieved improvement in gastrointestinal symptoms and rate of these patients to those included in analysis should be calculated by time of evaluation.

Notes: Time Allowance at time of evaluation should be according to "12.5 Time of evaluation of gastrointestinal symptoms". Only patients who have evaluation corresponding to administration start and Time Allowance of each time of evaluation should be included in analysis.

"3.2.2 Evaluation of gastrointestinal symptoms at each time of evaluation"

Patients included in analysis: Patients included in efficacy analysis

Objective of analysis: Evaluation of gastrointestinal symptoms is shown by time of evaluation.

Analysis items: The number of patients included in analysis, the number of patients who have evaluation of gastrointestinal symptoms (0,1,2,3,4) and rate of these patients to those included in analysis, the number of patients who achieved improvement in detailed classifications of gastrointestinal symptoms and rate of these patients to those included in analysis should be calculated by time of evaluation.

Notes: Time Allowance at time of evaluation should be according to "12.5 Time of evaluation of gastrointestinal symptoms". Only patients who have evaluation corresponding to administration start and Time Allowance of each time of evaluation should be included in analysis.

"3.3.1 Level of improvement in endoscopy findings"

Patients included in analysis: Patients included in efficacy analysis

Objective of analysis: Level of improvement in endoscopy findings is shown by time of evaluation.

Analysis items: The number of patients included in analysis, the number of patients who achieved improvement in endoscopy findings and rate of these patients to those

included in analysis should be calculated by the time of evaluation.

Notes: Time Allowance for the time of evaluation should be according to “12.4. Rate of patients who achieved clinical improvement, rate of patients who achieved complete remission, and time of evaluation of level of improvement in endoscopy findings”. Patients who have evaluation corresponding to Time Allowance of each time of evaluation should be included in analysis.

“3.3.2 Level of improvement in endoscopy findings (ileocecum)”

Patients included in analysis: Patients included in efficacy analysis

Objective of analysis: Level of improvement in endoscopy findings (ileocecum) is shown by time of evaluation.

Analysis items: The number of patients included in analysis, the number of patients who achieved improvement in endoscopy findings and rate of these patients to those included in analysis should be calculated by the time of evaluation.

Notes: Patients with a check mark in a box “1.ileocecum” in a description about endoscopy before administration start in “Level of improvement in endoscopy findings” in the survey sheet should be included in analysis.

Time Allowance for the time of evaluation should be according to “12.4. Rate of patients who achieved clinical improvement, rate of patients who achieved complete remission, and time of evaluation of level of improvement in endoscopy findings”. Patients who have evaluation corresponding to Time Allowance of each time of evaluation should be included in analysis.

“3.3.3 Level of improvement in endoscopy findings (colon)”

Patients included in analysis: Patients included in efficacy analysis

Objective of analysis: Level of improvement in endoscopy findings (colon) is shown by time of evaluation.

Analysis items: The number of patients included in analysis, the number of patients who achieved improvement in endoscopy findings and rate of these patients to those included in analysis should be calculated by the time of evaluation.

Notes: Patients with a check mark in a box “2. colon” in a description about endoscopy before administration start in “Level of improvement in endoscopy findings” in the survey sheet should be included in analysis.

Time Allowance for the time of evaluation should be according to “12.4. Rate of patients who achieved clinical improvement, rate of patients who achieved complete remission, and time of evaluation of level of improvement in endoscopy findings”.

Patients who have evaluation corresponding to Time Allowance of each time of evaluation should be included in analysis.

"3.3.4 Level of improvement in endoscopy findings (esophagus)"
Patients included in analysis: Patients included in efficacy analysis
Objective of analysis: Level of improvement in endoscopy findings (esophagus) is shown by time of evaluation.
Analysis items: The number of patients included in analysis, the number of patients who achieved improvement in endoscopy findings and rate of these patients to those included in analysis should be calculated by the time of evaluation.

Notes: Patients with a check mark in a box "3. esophagus" in a description about endoscopy before administration start in "Level of improvement in endoscopy findings" in the survey sheet should be included in analysis.
Time Allowance for the time of evaluation should be according to "12.4. Rate of patients who achieved clinical improvement, rate of patients who achieved complete remission, and time of evaluation of level of improvement in endoscopy findings". Patients who have evaluation corresponding to Time Allowance of each time of evaluation should be included in analysis.

"3.4 Aggregation of efficacy by patient characteristics"
Patients included in analysis: Patients included in efficacy analysis
Objective of analysis: As primary survey item, efficacy ratio in level of improvement at the last follow-up for factor analysis.
Analysis items: The number of patients included, the number of responding patients regarding level of overall improvement (significant improvement and improvement) and rate of these patients to those included in analysis, the number of patients who showed ineffectiveness in level of overall improvement and rate of these patients to those included in analysis, and test provided for effectiveness (Fisher's exact test for nominal scale factors, and Mann-Whiteny u test for ordinal scale factors) were calculated by following patient characteristics.

Notes: Patient characteristics are as follows:
Age (years), sex, disease duration (years), complication, hepatic function disorder as complication, renal impairment as complication, medical history, allergy history, smoking habit, self-administration as administration status of this drug, previously used drug/previous treatment, biological preparation adalimumab as previously used drug, biological preparation infliximab as previously used drug, steroid as previously used drug, immunomodulative drug as previously used drug, immunosuppressive drug as

previously used drug, oral adrenocortical steroid as concomitant drug, oral mucosa recurrent aphthous ulcer as main symptoms of Behcet disease other than gastrointestinal symptoms, cutaneous symptoms as main symptoms of Behcet disease other than gastrointestinal symptoms, eye symptoms as main symptoms of Behcet disease other than gastrointestinal symptoms, ulcer of vulva as main symptoms of Behcet disease other than gastrointestinal symptoms, arthritis without deformity or rigidity as accessary symptoms of Behcet disease other than gastrointestinal symptoms, epididymitis as accessary symptoms of Behcet disease other than gastrointestinal symptoms, vascular lesion as accessary symptoms of Behcet disease other than gastrointestinal symptoms, moderate or higher degree central nervous lesion as accessary symptoms of Behcet disease other than gastrointestinal symptoms, diagnostic classification of Behcet disease, days until the last date of the administration, and mean daily dose.

"3.5.1 Main symptoms of Behcet disease"
Patients included in analysis: Patients included in efficacy analysis
Objective of analysis: Presence or absence of main symptoms of Behcet disease is shown by time of evaluation.
Analysis items: The number of patients included in analysis, the number of patients with Behcet disease by main symptoms and rate of these patients to those included in analysis should be calculated by time of evaluation.

Notes: Time Allowance at time of evaluation should be according to "12.6 Time of evaluation of main and accessary symptoms of Behcet symptoms". Patients who have evaluation corresponding to Time Allowance of each time of evaluation should be included in analysis.

"3.5.2 Accessary symptoms of Behcet disease"
Patients included in analysis: Patients included in efficacy analysis
Objective of analysis: presence or absence of accessary symptoms of Behcet disease is shown by time of evaluation.
Analysis items: The number of patients included in analysis, the number of patients with Behcet disease by accessary symptoms and rate of these patients to those included in analysis should be calculated by the time of evaluation.

Notes: Time Allowance at time of evaluation should be according to "12.6 Time of evaluation of main and accessary symptoms of Behcet symptoms". Patients who have evaluation corresponding to Time Allowance of each time of evaluation should be included in analysis.

"3.6 Changes in CRP levels"

Patients included in analysis: Patients included in efficacy analysis

Objective of analysis: Measurement of CRP levels is shown by time of evaluation.

Analysis items: Summary statistics of CRP (the number of patients, mean value, standard deviation, the minimum, median, maximum value) should be calculated by time of evaluation.

Notes: Time Allowance at time of evaluation should be according to "12.7 Time of evaluation of changes in CRP levels". Patients who have evaluation corresponding to Time Allowance of each time of evaluation should be included in analysis.