Janssen Research & Development

Statistical Analysis Plan

A Prospective, Multicenter, Open-Label, Single-Arm, Phase 2 Study to Investigate the Safety, Tolerability and Pharmacokinetics of Selexipag in Children with Pulmonary Arterial Hypertension (PAH)Protocol: AC-065A203

Protocol AC-065A203; Amendment 7; Phase 2

ACT-293987/JNJ-67896049 (selexipag)

Status:	Approved
Date:	2 May 2022
Prepared by:	Janssen Research & Development, a division of Janssen Pharmaceutical NV
Document No.:	EDMS-597620, 1.0

Compliance: The study described in this report was performed according to the principles of Good Clinical Practice (GCP).

TABLE OF CONTENTS

LIST OF IN-TEXT TABLES AND FIGURES

VERSION HISTORY

Table 1: SAP Version History Summary

SAP Version	Approval Date	Change	Rationale
Original SAP	10 June 2020	Not Applicable	Initial release
Amendment 1	11 August 2020	See rationale	1) Add outputs for COVID-19 related AEs. 2) Add more analysis for concomitant PAH-specific medications 3) Update AESI definitions and provide more details on AESI definitions as an appendix of SAP to align with selexipag program level AESI definitions: ie. Remove thrombocytopenia from anaemia AESI definition, add PVOD AESI and medication error and pregnancy. 4) Add definitions for persistent and recurrent AESIs and average annualized event rates
Amendment 2	02 May 2022	See rationale	1) Update the SAP based on Protocol Version 8, Amendment 7 to add optional PK Interim Analysis 3. 2) Add Week 16 CSR deliverable, including all participants having Week 16 assessment. 3) Remove the persistent TEAE definition as the team agree that no separate output is need for it

1. INTRODUCTION

The purpose of this study is to confirm the selexipag doses in children from ≥2 to <18 years of age with PAH that led to an exposure similar to that in adult participants. The selection of the selexipag starting dose was based on a PK extrapolation from adults to pediatric participants. In addition, the safety and tolerability of selexipag in children from ≥2 to <18 years of age are assessed.

This statistical analysis plan (SAP) contains definitions of analysis sets, derived variables, and statistical methods for the analysis of safety and exploratory efficacy and other endpoints.

The analyses of pharmacokinetic (PK) data, as well as PK and PK/PD modeling are not included in this document but described in separate analysis plans.

1.1. Study Objectives

Primary:

- The primary objective of the study is to confirm the selexipag starting dose(s), selected based on pharmacokinetic (PK) extrapolation from adults, which leads to similar exposures as adult doses in children from ≥2 to <18 years of age with pulmonary arterial hypertension (PAH) by investigating the PK of selexipag and its active metabolite ACT-333679 in this population.

Secondary:

- To evaluate the safety and tolerability of selexipag in children from ≥2 to <18 years of age with PAH.

Exploratory:

- To explore the relationship between drug exposure at the individual maximum tolerated dose (iMTD) and 6-minute walk distance (6MWD) at each time point of assessment.
- To explore the relationship between drug exposure and N-terminal pro b-type natriuretic peptide (NT pro-BNP) at each time point of assessment.
- To explore the relationship between drug exposure and Echocardiography (Echo) variables at each time point of assessment.
- To explore the time to disease progression/clinical worsening from first study drug dose up to EOT + 7 days.

Other:

- To assess palatability of selexipag formulation at each time point of assessment using a 5-point facial hedonic scale.
- To assess acceptability of selexipag formulation at each time point of assessment using a 3-point categorical scale.

1.2. Study Design

This is a prospective, multi-center, open-label, single-arm, Phase 2 study. Approximately 60 participants will be enrolled in 3 different age cohorts (based on age at baseline/enrollment/Visit 2) to obtain at least 45 participants with evaluable PK profiles:

- Cohort 1: ≥12 to <18 years of age (approximately 20 enrolled participants to obtain at least 15 participants with evaluable PK profiles)

- Cohort 2: ≥6 to <12 years of age (approximately 20 enrolled participants to obtain at least 15 participants with evaluable PK profiles)
- Cohort 3: ≥2 to <6 years of age (approximately 20 enrolled participants to obtain at least 15 participants with evaluable PK profiles).

The starting dose is based on the body weight category of the participants, using the data from the population PK model in the GRIPHON/AC-065A302 study targeting the exposure observed in adult PAH participants at a starting dose of 200 µg, taken orally, twice a day. The continuous relationship between dose and body weight is used to define body weight categories and starting dose for each body weight category such that – on average – the exposure ($AUC_{\tau,ss,combined}$) will be comparable to that of a 70 kg adult but not exceeding the exposure of a 50 kg adult.

Dosing scheme (by body weight) is defined as follows:

- 100 µg starting dose for participants with a body weight from ≥9 to <25 kg
- 150 µg starting dose for participants with a body weight from ≥25 to <50 kg
- 200 µg starting dose for participants with a body weight ≥50 kg

Selexipag is to be dosed twice daily (bid) and during the up-titration period of 12 weeks, it is recommended that the doses are increased weekly in increments equal to the starting dose until the participants reach their individual maximum tolerated dose (iMTD), or until the maximum dose corresponding to 8-fold that of the starting dose (based on their baseline weight category) is achieved.

The starting dose selection will be confirmed or adjusted after completion of each age cohort by updating the population PK model (interim and final PK analysis).

Enrollment started with both Cohort 1 and Cohort 2 (participants ≥12 to <18 years, and ≥6 to <12 years of age, respectively). After completion of PK assessments in at least 15 participants in Cohort 1 at Week 12, the dose-exposure relationship was established using a population PK model (interim analysis 1). Enrollment of Cohort 3 (children ≥2 to <6 years of age) was started once the appropriate doses were confirmed by modelling and simulation in a second interim analysis of PK data from the children older than 6 years (i.e., Cohorts 1 and 2) and the confirmation that there was no safety concern based on IDMC reviews.

The PK data pooled from all 3 age cohorts will be modelled to allow dosing recommendations for all children ≥2 years of age. A final PK analysis will be prepared based on the overall PK and safety data up to Week 16 evaluation. The selection of the dosing regimen for the Phase 3 study will be based on the safety, tolerability, and PK results evaluated in the interim or final PK analysis (as applicable).

Participants who discontinue the treatment any time before the profile PK sampling day will be replaced within the age cohort.

Study Periods

The study consists of the following consecutive periods:

Screening period: Lasts up to 42 days; starts with the signature of the informed consent and ends with the administration of the first study treatment dose.

Treatment period: Starts from the first dose of study treatment at Baseline/enrollment visit and ends on the day of the last dose of selexipag (End of Treatment [EOT]). This includes:

- **Up-titration period:**
  From the first dose of study treatment until the participant reaches individual maximum tolerated dose (iMTD). This period is estimated to last up to 12 weeks.
- **Maintenance period:**
  After Week 12: the participants will continue study treatment at the same dose up to Week 16.
  After Week 16: study treatment will continue as long as it remains beneficial for the participant up to maximum of 5 years after last (Cohort 3) participant first visit.

EOT visit: this visit should be conducted within 1 week of the last dose of study treatment.

Safety Follow-up period: Starts on the day after the last dose of study treatment and ends about 30 days thereafter with a phone call that indicates the End of Study (EOS).

2. ANALYSIS DETAILS

2.1. Analysis Sets

- **Screened Analysis Set:** Screened analysis set includes all participants who are screened and have a participant identification number.
- **Full Analysis Set:** Full analysis set includes all enrolled participants who were eligible to receive the study drug.
- **Safety Analysis Set:** Safety analysis set includes all participants included in Full Analysis Set who receive at least one dose of the study drug. Since all enrolled participants received at least one dose of study drug, the Full Analysis Set and Safety Analysis Set are the same in this study. For simplicity, the Safety Analysis Set will be used for all safety and efficacy analyses.
- **Pharmacokinetic Analysis Set (PKS):** PK analysis set comprises all participants included in the Safety Analysis Set who complied with the protocol sufficiently and did not deviate from the protocol in a way that might affect the PK outcome of the study. Criteria for sufficient compliance include exposure to treatment, availability of PK measurements, and absence of major protocol deviations that have an impact on the PK. Further details are provided in the PK and modeling analysis plan.

For all analyses, except the time to disease progression event, only the scheduled visits data will be used in summary outputs; both the scheduled and unscheduled visits data will be included in the listings.

The analysis set usage is summarized as following:

Table 2: Study Analysis Set Usage

	Screened Analysis Set	Full Analysis Set	Safety Analysis Set	PK Analysis Set	PK
Participant disposition	x	x	x		
Participant information (medical history, concomitant medication, contraceptives)			x		
Participant information (demographics, baseline characteristics, baseline disease characteristics)			x		
Treatment exposure, treatment discontinuation, drug accountability and compliance, protocol deviation			x		
Safety analyses			x		
Other endpoints analyses			x		
PK analyses				x	x
Efficacy exploratory analyses			x		
Sensitivity Analysis, for Efficacy exploratory analyses			x		
All listings for disposition/Recruitment	x	x	x		
All listings for Participant information	x	x	x		
All other Listings			x		

2.2. Study Analysis Periods

For each dosed participant, the screening, treatment and follow-up phases of the study will be structured as following:

Table 3: Study periods definition

Period	Period Start	Period End
Screening	Starts with the signature of the informed consent form (ICF), may be as early as Day -42	Prior to the administration of the first study treatment dose
Treatment		
Up-Titration	the first dose of study treatment	the participant reaches their iMTD (iMTD for each participant is determined at Week 12, or EOT + 3 days in case of premature treatment discontinuation before Week 12)
Maintenance after Week 12 to 16 (continue treatment at same dose)	Day of Up-Titration end plus 1.	Up to Week 16 or EOT + 3 days in case of premature treatment discontinuation before Week 16

Period	Period Start	Period End
Maintenance after Week 16	Day of Week 16 visit plus 1	EOT (up to 5 years after last participant, first visit)
EOT visit	This visit should be conducted within 1 week of the last dose of study treatment. The participant will then enter the Safety follow-up period.	
Safety follow-up	Day after EOT	EOS - Day of Safety follow-up Phone call (about 30 days after last dose)

In case a participant drops out during a treatment period, the participant will have a Follow-Up period after the last applicable treatment period only if a Follow-Up visit was performed.

Each of these analysis periods is associated with a treatment. Treatments for the Screening and Follow-Up periods are defined as 'None (screening/follow-up)', respectively.

2.3. Study Output Deliverable

This SAP will be used for Final Analysis CSR, Canada Health Authority Submission and Week 16 CSR. The data used by these deliverables are described as follows:

The Data Presentation Plan (DPS) will describe the details regarding which analyses and outputs are created for which purpose.

Outputs Deliverables	Analysis Coverage/Data to include/Cut point
Analysis for Canada Health Authority Submission	Data cut-off: 04MAY2020 Data extract: 05MAY2020 Outputs for efficacy and safety
Week 16 CSR	All available participants' data in all age cohorts when all enrolled participants have finished all required Week 16 assessments or discontinued earlier from study permanently. Outputs for efficacy and safety
Final Analysis CSR	All datasets Outputs for efficacy and safety

2.4. Baseline Definition

Baseline: Baseline will be defined as the last non-missing assessment available prior to the first dose administration. Any unscheduled measurement performed before administration of study drug should also be used for determination of baseline across all the domains, as some tests may be repeated for confirmation.

3. PARTICIPANT AND TREATMENT INFORMATION

3.1. Demographics and Baseline Disease Characteristics

For all Safety Analysis Set participants, descriptive summary statistics will be provided for the following by age cohort, body weight and in the overall population, and listings by age cohort, country, site.

- Demographic and baseline characteristics: Age (year with decimal for month) at enrollment, Sex, Childbearing Potential for female participants, Race, Ethnicity, Weight (kg), Height (cm), and BMI (kg/m^2).
    - Childbearing Potential and sexual activity for female participants at Screening (or eventually at re-screening) will be summarized together with the above demographics.

- Baseline disease characteristics:
  From the 'PAH Etiology' eCRF module:
    - Etiology of PAH, association of PAH with congenital heart disease (CHD),
    - Date of first observed/assumed PAH symptoms (only for listing),
    - Time from first observed/assumed symptoms (days) (date of first observed/assumed PAH symptoms – date of screening + 1),
    - Date of PAH diagnosis (only for listing),
    - Time from PAH diagnosis (days) (date of PAH diagnosis – date of screening + 1).

  From the 'WHO Functional Class' eCRF module:
    - Baseline WHO Functional Class.

  From the 'Panama Functional Class for Pediatrics' eCRF module:
    - Baseline Panama FC.

  From the 'Right Heart Catheterization' eCRF module:
    - Date of Diagnosis of right heart catheterization (RHC),
    - Mean pulmonary arterial pressure (mPAP[mmHg]),
    - Pulmonary arterial wedge pressure (PAWP[mmHg]) (or LAP or LVEDP),
    - Pulmonary vascular resistance index (PVRi[Wood units x m^2]).
- Medical history (previous and ongoing clinically significant diseases) investigator original terms and preferred terms coded using the latest implemented MedDRA version dictionary will be listed.

3.2. Participant Recruitment, Disposition and Study Completion/Withdrawal Information

To describe participant disposition, the number of participants screened will be presented, and in addition, the following will be tabulated:

- Number (and % based on the Screened Analysis Set) of screening failures (all screened participants who were not enrolled)
    - Reasons for failure (from the “Enrollment” eCRF module)

- Number (and % based on the Screened Analysis Set) of enrolled participants (from the "Enrollment" eCRF module)

- Number (and % based on the Full Analysis Set) of dosed participants (with at least one record in the "Study Treatment Log" eCRF module)

- Number (and % based on the Safety Analysis Set) of participants who prematurely discontinued the study drug (from the "Premature Discontinuation of Study Treatment" and "Study Treatment Log eCRF modules)
    - Reasons for treatment discontinuation

- Number (and % based on the Safety Analysis Set) of participants who completed the study as per protocol (with completed EOS follow-up telephone call)

- Date and time of informed consent with the protocol version will be listed together with enrollment data (including reasons for not enrolling the participants) for all participants in the Screened Analysis Set.

- Unmet inclusion criteria and met exclusion criteria will be also listed for participants in the Screened Analysis Set.

- A participant listing of recruitment by country and center will be provided based on the Screened Analysis Set. In addition, for the same analysis set the number of participants recruited in each country and center (within country) will be tabulated.

- Study completion/Study premature discontinuations along with relevant reasons will also be listed for all Safety Analysis Set participants ("Study Discontinuation" eCRF modules).

For an individual participant, per protocol study completion is reached when the EOS follow-up telephone call is completed.

Participants who prematurely discontinued study treatment for any reason before completion of the last study visit phase will not be considered to have completed the study.

Check the details for prematurely discontinuation of study treatment in Protocol 5.1.9.

3.3. Previous and Concomitant Therapies and PAH-Specific Medications

All medications recorded in the 'Previous/Concomitant Medication' eCRF pages will be coded to preferred term using the latest version of the WHO Drug code and Anatomic Therapeutic Chemical class code dictionaries.

Previous medications are any medication/therapy with end date prior to the study drug start date.

Concomitant medications are defined as any medication/therapy with start date missing, or start date prior to, or on, or after the first study drug dose date but before last study drug dose, and with end date after the first study drug dose date, or end date missing.

In general, **concomitant medications** during study treatment include all medications taken whilst the participant is on study treatment, regardless of whether the start of intake is before the start of study drug. Concomitant medications include therefore concomitant medications at baseline and concomitant new medications.

Previous and concomitant medications (regardless of being PAH-specific or not) will be summarized by previous/concomitant medications class and preferred term and will be ordered according to decreasing frequency overall.

In addition, concomitant PAH-specific medications at baseline (i.e., used on the same day as the first dose of study drug but excluding the cases in which the medication ended on the day of first study drug dose), will be summarized. In this summary, PAH-specific medications will be presented by preferred term and PAH-specific medication subgroup name (as defined below). Also, the proportions of participants who received none, 1, 2, and 3 or more PAH-specific concomitant medications at baseline will be included.

The following preferred terms will define PAH-specific medications (except study treatment): "Ambrisentan", "Bosentan" (including "Bosentan Monohydrate"), "Sitaxentan", "Macitentan", "Sildenafil" (including "Sildenafil Citrate"), "Tadalafil", "Vardenafil", "Udenafil", "Riociguat", "Iloprost", "Epoprostenol", "Treprostinil", "Beraprost".

All other medications will be classified as non-PAH-specific medication.

PAH-specific medications at baseline summary will be provided by preferred term with the following subgroup treatment categories:

- Treatment with Endothelin Receptor Agonist (ERA) monotherapy – identified by the following preferred terms ("Ambrisentan" OR "Bosentan" OR "Sitaxentan" OR "Macitentan") AND NOT ("Sildenafil" OR "Tadalafil" OR "Vardenafil" OR "Udenafil") AND NOT "Riociguat".

- Treatment with phosphodiesterase type 5 (PDE-5) inhibitor monotherapy – identified by the following preferred terms ("Sildenafil" OR "Tadalafil" OR "Vardenafil" OR "Udenafil") AND NOT ("Ambrisentan" OR "Bosentan" OR "Sitaxentan" OR "Macitentan") AND NOT "Riociguat".

- Treatment with combination of both ERAs and PDE-5 inhibitors – identified by the following preferred terms ("Ambrisentan" OR "Bosentan" OR "Sitaxentan" OR "Macitentan") AND ("Sildenafil" OR "Tadalafil" OR "Vardenafil" OR "Udenafil") AND NOT "Riociguat".

- Treatment with prostacyclin/analogs (irrespective of treatment with ERAs or PDE-5 inhibitors or "Riociguat") – identified by the following preferred terms "Iloprost" OR "Epoprostenol" OR "Treprostinil" OR "Beraprost" (it is expected to be rare as prostacyclin/analogs are not allowed to be co-administered according to the study protocol).

- Treatment with soluble guanylate cyclase stimulator (irrespective of ERAs or PDE-5 inhibitors or prostacyclin/analogs) – identified by the preferred term "Riociguat".

All medications/therapies will be listed together. A different flag will indicate if the medication is previous or concomitant respectively. Additionally, forbidden and PAH-specific medications will be flagged.

All summaries will be provided by age cohort and body weight group.

All PAH-related non-pharmacological interventions recorded on the dedicated eCRF form will be listed.

If missing end date or the medications ended on or after first dose date of the study drug, the medication will be classified as concomitant medication. If both start date and end date are missing, then this medication will be considered as both previous and concomitant medications.

3.4. Protocol Deviations

Major protocol deviations and COVID-19 related deviations will be reported in the database.

A listing of participants with major protocol deviations will be provided as well as a listing with any COVID-19 related deviations, including all available details about these deviations.

Between visits, compliance is expected to be between 80% and 120%. Compliance values outside of this range will be considered as protocol deviations (see details in Protocol 5.1.7.2.).

3.5. Extent of Exposure and Compliance

Exposure data are taken from the "Study Treatment Log" eCRF module.

All data recorded will be listed, together with treatment exposure duration (weeks) derived as defined below. The listing will also display the body weight at baseline, as this parameter triggers the starting dose.

Treatment duration (days) is defined as date of last intake of study drug minus date of first intake of study drug plus 1. It includes therefore any possible treatment interruption.

The treatment exposure duration (days) takes account of periods of drug interruption. To calculate the treatment exposure duration per participant, the number of days the participant took no study treatment is subtracted from the treatment duration defined above.

The treatment exposure duration (weeks) will be then calculated by dividing the treatment exposure duration (days) by 7.

Treatment duration or treatment exposure duration (weeks) will be summarized as categorical data. The duration categories will be cumulative for <=4 weeks, <=8 weeks, <=12 weeks, <=16 weeks, <=52 weeks.

Study treatment compliance is based on study treatment accountability. Study treatment compliance will be calculated by site personnel at visits as indicated in the assessment schedule using the below formula and entered in the eCRF:

> Compliance = 100 x (number of tablets dispensed − number of tablets returned) / Total number of tablets that should have been taken during the period*
>
> *The period is defined as the number of days of treatment from the date of dispensation / start of study treatment until the next accountability visit. The number of tablets that should have been taken should be calculated on a participant basis, based on the investigator's prescription.

Study treatment compliance, reason of non-compliance will be summarized at each timepoint. Details of study treatment dispensing and accountability will be listed for each participant.

3.6. Individual maximum tolerated dose(iMTD)

The iMTD is defined as the last dose received before the Week 12 visit (for participants who prematurely discontinued study drug) or the dose received on the day of the Week 12 visit (for participants who completed the 12-week up-titration period).

For each iMTD, the number and percentage of participants who reached this dose will be summarized by age cohort and body weight group categories (≥9 to <25 kg, ≥25 to <50 kg, ≥50 kg) at baseline.

The iMTD reached for each participant will be indicated in the study drug administration listing.

3.7. Other Participant Information

Contraceptive methods used by female participants who are of childbearing potential and heterosexually active (or who become heterosexually active at any time after enrollment), collected on a dedicated eCRF module, will be listed.

4. SAFETY ANALYSIS

Safety and tolerability will be assessed throughout the study, from signing of the Informed Consent Form (ICF) until the participant's last study-related activity. The study will include the following evaluations of safety and tolerability: adverse events, clinical laboratory tests (including TSH, thyroid antibodies, T3, T4, pregnancy tests, Plasma NT pro-BNP), ECG, vital signs, growth (weight, height and BMI), sexual maturation (Tanner Stage), childbearing potential and physical examinations.

Unless otherwise specified, all safety analyses will be carried out descriptively (using the Safety Analysis Set) in the overall population, by age cohort and body weight group.

4.1. Adverse Events

Adverse Events and Treatment-Emergent Adverse Events

- Summaries of below adverse event categories will be summarized according to the study periods *Up-Titration*, *Maintenance after Week 12*, *Maintenance after Week 16* as defined in Table 2.
- All reported adverse events with onset following the start of study treatment, or pre-existing conditions that have worsened since baseline, will be defined as treatment-emergent (TEAE) and will be included in the analysis. TEAEs will be recorded up to EOT + 3 days.
- AEs will be analyzed by period, and the start or worsened date-time of the AEs will be used to determine the period the AE falls in.
- For each TEAE, the percentage of participants who have experienced at least 1 occurrence of the given event will be summarized by system organ class, preferred term, and age cohort.
- TEAEs will be tabulated by severity and relationship and will be summarized by system organ class, preferred term, and age cohort.
- Serious AEs and AEs occurring up to EOT + 3 days that lead to death, hospitalization, treatment discontinuation, dose reduction/interruption will be tabulated and listed.
- AEs that occur during screening and that start prior to first dosing will be included in data listings only.
- All reported adverse event terms will be coded with the latest available MedDRA dictionary version.
- COVID-19 related AEs will be listed.

Adverse Events of Special Interest(AESI):

Adverse events of special interest (AESI) for this study have been defined in Appendix 2.

For each AESI category, the percentage of participants who have experienced at least 1 occurrence of the given event will be summarized by system organ class, dictionary derived preferred term, and age cohort.

AESIs will be also tabulated by severity and will be presented by treatment periods, age cohort, body weight and overall. AESIs will also be summarized by relationship to the study drug.

Number of recurrent AESIs will be counted as the total number of occurrences of any TEAEs, i.e., multiple occurrences for the same preferred term for the same participant will be counted multiple times. Average annualized event rate will be calculated as follows:

1) Calculate total number of recurrent TEAEs.
2) Calculate participant-years of treatment duration (sum of individual participant time-years in a treatment group)
3) Average annualized event rate = (total number of recurrent TEAE) / (subject-years of treatment duration)

The prostacyclin-associated Treatment-Emergent Adverse Events will be summarized by age cohort and body weight group during study period separately.

Deaths

All AEs leading to death occurring up to 3 days after end of treatment, will be listed.

Hospitalization

All hospitalization data from Hospitalization and Adverse Event CRF page will be listed.

4.2. Clinical Laboratory Tests

The following laboratory parameters are evaluated:

- Hematology:
  - Hemoglobin (g/L)
  - Hematocrit (L/L)
  - Erythrocyte count (10^9/L)
  - Leukocyte count with differential counts (10^9/L)
  - Platelet count (10^9/L)
- Clinical chemistry:
  - Alanine aminotransferase (U/L)
  - Aspartate aminotransferase (U/L)
  - Alkaline phosphatase (U/L)
  - Total and direct bilirubin (µmol/L)
  - Creatinine (µmol/L)
  - Creatinine clearance (mL/min)
  - Serum urea nitrogen (mmol/L)
  - Uric acid (µmol/L)
  - Glucose (mmol/L)
  - Cholesterol, triglycerides (mmol/L)
  - Sodium, potassium, chloride, calcium (mmol/L)
  - Albumin (g/L)
  - NT-pro BNP (pmol/L)
  - TSH (mU/L)
  - Free T3 and free T4 (pmol/L)
  - Thyroid antibodies (U/mL)

In addition, local laboratory parameters might be available under certain circumstances and recorded in the CRF.

All recorded assessments, whether from central or local laboratory (including unscheduled) will be assigned to the most appropriate visit time points according to the best fitting time-window for that assessment

If data from a local laboratory and from the central laboratory are available for the same date, the central laboratory value will be used; if more than one valid assessment are available on the same timepoint window in the same lab, the mean value will be considered.

A laboratory test abnormality is defined as any value outside the normal range as provided by the laboratory. The direction of the abnormality (below or above the normal range) is indicated using 'H' and 'L', if applicable.

A marked (alert) laboratory test abnormality is defined as any value that fulfills the applicable condition listed in the table below for LL / HH (or LLL / HHH, respectively):

Safety parameter	Marked Abnormally Low Values		Marked Abnormally High Values	
	LL	LLL	HH	HHH
Hematology				
Hemoglobin (g/L)	< 100	< 80	Increase (> 20 g/L) above ULN or above baseline if baseline is above ULN	Increase (> 40 g/L) above ULN or above baseline if baseline is above ULN
Hematocrit (L/L)	< 0.28 F < 0.32 M	< 0.20	> 0.55 F > 0.60 M	> 0.65
Erythrocyte count (10^9/L)	NA	NA	NA	NA
Leukocyte count with differential counts (10^9/L)	< 3.0	< 2.0	> 20.0	> 100.0
Platelet count (10^9/L)	< 75	< 50	> 600	> 999
Clinical chemistry				
AST (U/L)	NA	NA	> 3 ′ ULN	> 5 ′ ULN
ALT (U/L)	NA	NA	> 3 ′ ULN	> 5 ′ ULN
Alkaline phosphatase (U/L)	NA	NA	> 2.5 ′ ULN	> 5 ′ ULN
Total bilirubin (µmol/L)	NA	NA	> 2 ′ ULN	> 5 ′ ULN
Direct bilirubin (µmol/L)	NA	NA	> 2 ′ ULN	> 5 ′ ULN
Creatinine (µmol/L)	NA	NA	> 1.5 ′ULN or > 1.5 ′ baseline if baseline is above ULN	> 3 ′ ULN or > 3 ′ baseline if baseline is above ULN
Serum urea nitrogen	NA	NA	> 2.5 x ULN	> 5 x ULN
Glucose (mmol/L)	< 3.0	< 2.2	> 8.9	> 13.9
Sodium (mmol/L)	NA	< 130	> 150	> 155
Potassium (mmol/L)	< 3.2	< 3.0	NA	> 6.0
Calcium (mmol/L)	< 2.0	< 1.75	> 2.9	> 3.1

ALT = alanine aminotransferase; AST = aspartate aminotransferase; F = female; M = male; ULN = upper limit of normal range.

Treatment-emergent marked laboratory abnormalities are defined as all marked laboratory abnormalities with onset after the study treatment start and up to EOT+3 days, that were not present at baseline or worsened during the course of the study. They will be analyzed on the Safety Analysis Set overall, by age cohort and body weight group.

For each category (i.e., LL, LLL, HH, HHH), treatment-emergent marked laboratory abnormalities are summarized for each laboratory variable overall, by age cohort and body weight group, displaying counts and percentages of participants with at least one marked treatment-emergent abnormality. Percentages are calculated by dividing the number of participants with at least one marked abnormality for the parameter under consideration by the number of participants with any post-baseline measurement.

The number of participants with laboratory abnormalities/marked abnormalities (any value outside the normal ranges for the laboratory) will be also tabulated as shift tables against baseline.

Absolute values and changes from baseline will be determined for each parameter and participant at the different timepoints of assessment and summarized overall, by age cohort and body weight group for the Safety Analysis Set. For graphs or tables with mean values, to account for changing reference ranges across age and gender, certain central and local laboratory values (Y_{ori}) and their reference ranges (LLN_{ori}, ULN_{ori}) will be normalized as Y_{norm} using a standard range (LLN, ULN) as follows:

$$Y_{norm} = LLN + \frac{(Y_{ori} - LLN_{ori})}{(ULN_{ori} - LLN_{ori})} \times (ULN - LLN)$$

If the value is negative after normalization, zero will be assigned.

The laboratory tests that require normalization and their standard ranges to be used are:

- TSH: 0.34 - 5.60 (mIU/L)
- Free T3: 4.5 - 7.8 (pmol/L)
- Free T4: 10 - 24 (pmol/L)
- Hemoglobin: 116 - 164 (g/L)
- Hematocrit: 0.34 - 0.48 (L/L)
- Erythrocyte count: 4.1 - 5.6 (10^{12}/L)
- Leukocyte count: 3.80 - 10.70 (10^9/L)
- Neutrophil count: 1.65 - 8.15 (10^9/L)
- Lymphocyte count: 0.95 - 5.25 (10^9/L)
- Monocyte count: 0.40 - 0.90 (10^9/L)
- Monocyte/leukocyte: 4.0 - 7.0 (%)
- Eosinophil count: 0.00 - 0.20 (10^9/L)
- Eosinophil/leukocyte: 0.0 - 4.1 (%)
- Platelet count: 140 - 400 (10^9/L)
- Creatinine: 40 - 83 (µmol/L)
- Alkaline phosphatase: 31-110 (U/L)

- Alanine aminotransferase: 6-34 (U/L)
- Aspartate aminotransferase: 10-40 (U/L)
- Uric Acid: 137-404 (µmol/L)
- Albumin: 33 - 47 (g/L)
- Triglyceride: 0.44 - 1.40 (mmol/L)
- Cholesterol: 3.23 - 5.48 (mmol/L)

All individual laboratory data will be listed and a separate listing for participants with laboratory abnormalities will also be provided, as well as a separate listing of participants with treatment-emergent marked laboratory abnormalities.

4.3. TSH, Thyroid antibodies and T3 and T4

In addition, TSH (mU/L), thyroid antibodies (U/mL), free T3 (pmol/L) and free T4 values (pmol/L) will be presented separately.

4.4. Pregnancy Test

Serum pregnancy test will only be performed at screening. Afterwards urine pregnancy test will be performed. All results, as recorded in the eCRF, will be listed.

4.5. Electrocardiograms

ECG will be evaluated by a central ECG service. All ECG data from scheduled and unscheduled visits will be listed.

The quantitative ECG variables up to EOT + 3 days that will be summarized are heart rate (bpm), RR interval (msec), PR interval (msec), QRS interval (msec), QT interval (msec), QTcB (msec) and QTcF (msec), the corrected QT (QTc) using Bazett's and Fridericia's methods, respectively. Values at all scheduled visits and changes from baseline (last value assessed before first study dose intake) over time will be summarized by parameter, time point, age cohort and body weight, and will be presented in figures as well.

In addition, QTcB and QTcF will also be summarized by age cohort and the following categories:

- Value ≤ 450 (normal)
- Value > 450 - ≤ 480
- Value > 480 - ≤ 500
- Value > 500
- Increase from baseline ≤ 30
- Increase from baseline > 30 - ≤ 60
- Increase from baseline > 60
- Value > 480 and increase from baseline > 30 - ≤ 60
- Value > 480 and increase from baseline > 60

For Week 1 and Week 12, where two additional ECG assessments are done at 2H and 4H post-dose, only pre-dose data will be included in the overall analysis. In addition, separate analyses will be done with only Week 1 and Week 12 ECGs data, where values and change from pre-dose to post-dose at each visit will be summarized by parameter, abnormality category for QTcB/F, time

point, and age cohort. Furthermore, summary of QTcF/B abnormalities by category over time and shift tables will be provided for both the overall analysis and Week 1 & 12-focused analysis.

The qualitative ECG abnormal findings at study baseline will be summarized by age cohort and are defined as following:

- Atrioventricular Conduction - 1st Degree Av Block
- Chamber Hypertrophy or Enlargement - Left Atrial Abnormality
- Chamber Hypertrophy or Enlargement - Left Ventricular Hypertrophy
- Chamber Hypertrophy or Enlargement - Right Atrial Abnormality
- Chamber Hypertrophy or Enlargement - Right Ventricular Hypertrophy
- Interpretation - Abnormal
- Interpretation - Not Evaluable
- Intraventricular-Intraatrial Conduction - Incomplete Right Bundle Branch Block
- Intraventricular-Intraatrial Conduction - Intraventricular Conduction Delay, Nonspecific
- Intraventricular-Intraatrial Conduction - Left Posterior Fascicular Block
- Intraventricular-Intraatrial Conduction - Right Bundle Branch Block
- ST Segment. T wave, and U wave - QTc Prolongation
- ST Segment. T wave, and U wave - St Depression
- ST Segment. T wave, and U wave - T Wave Inversion
- Sinus Node Rhythms and Arrhythmias - Sinus Bradycardia
- Sinus Node Rhythms and Arrhythmias - Sinus Tachycardia
- Supraventricular Arrhythmias - Ectopic Atrial Rhythm

Treatment-emergent qualitative ECG abnormalities, defined as any ECG abnormal finding assessed up to EOT + 3 days and reported by the central ECG reader that was not present at study baseline (last assessment before first study drug intake), will also be summarized by age cohort. ECG abnormalities will be also presented in figures.

4.6. Vital Signs

The vital signs parameters up to EOT + 3 days that will be analyzed are heart rate and blood pressure (systolic and diastolic). Position and location will only be listed.

Values and change from baseline over time will be summarized by parameter and time point, age cohort and be presented in figures as well.

All individual vital signs data will be listed.

Body Weight and Height

Height (m) (measured at Screening and Week 16) and weight (kg) data will be used in calculating the BMI.

BMI (kg/m^2) will be calculated at each of these time-points. Before Week 16, BMI is calculated by using height from screening, and at Week 16 will be calculated by using height collected at

Week 16. After Week 16, BMI will be calculated from the height and weight collected at each visit.

Values and changes from baseline over time for weight, height and BMI will be summarized by age cohort and body weight group.

All individual height, weight and BMI data will be listed, and the growth curves will be presented for height, weight, and BMI as well.

4.7. Sexual maturation (Tanner Stage)

Sexual maturation of pediatric participants in long-term studies is assessed by using Tanner Stage.

Tanner stage is assessed in female participants ≥8 years of age and in male participants ≥9 years of age. For participants who enter the study below these ages sexual maturity assessments will start once they reach the ages of 8 or 9 years. Tanner stage assessment is stopped once full sexual maturation is reached.

Tanner stage data will be listed and summarized along with changes from baseline (Screening) over time.

Females of Childbearing Potential Status Change

Childbearing potential status assessed at screening will be listed with participant information, while changes in the status assessed for female participants at later timepoints will also be listed.

4.8. Physical examination

All data will be listed.

5. EXPLORATORY EFFICACY ANALYSIS

All exploratory efficacy analyses will be carried out on the Safety Analysis Set, and be performed as follows:

- In the overall population.
- By age cohort.
- By body weight group

The main exploratory analysis will be based on observed data, with no imputation rules. Sensitivity analyses will be performed by imputing missing values as appropriate.

5.1. The Exploratory Endpoints

The exploratory endpoints are the following:

- Change from Baseline/Enrollment up to each time point of assessment in modified New York Heart Association / WHO FC.
- Change from baseline up to each time point of assessment in exercise capacity, as measured by the 6-minute walk distance (6MWD).

- Change from baseline in Panama FC up to each time point of assessment.
- Percent of baseline in plasma NT pro-BNP at each time point of assessment.
- Change from baseline up to each time point of assessment in Echo variables (imaging and Doppler evaluation):
    - Right ventricular systolic pressure.
    - Tricuspid annular plane systolic excursion.
    - Pulmonary artery acceleration time.
    - Left ventricular eccentricity index.
    - Right atrial area index (from apical 4 chamber view).
    - Tricuspid annular diameter (from apical 4 chamber view).
- Time to first of the following disease progression events occurring between first study drug dose and EOT + 7 days:
    - Death (all causes)
    - Atrial septostomy or Potts' anastomosis, or registration on lung transplant list
    - Hospitalization due to worsening PAH[§]
    - Clinical worsening* of PAH defined as: Need for, or initiation of new PAH-specific therapy[#] or i.v. diuretics or continuous oxygen use AND at least one of the following:
        - Worsening in WHO FC, or
        - New occurrence or worsening of syncope (in frequency or severity as per medical judgment), or
        - New occurrence or worsening of at least two PAH symptoms (i.e., shortness of breath/dyspnea, chest pain, cyanosis, dizziness/ near syncope, or fatigue), or
        - New occurrence or worsening of signs of right heart failure not responding to oral diuretics

[§]excluding hospitalizations that are elective, routine or clearly attributable to appearance/worsening of comorbidities (e.g., pneumonia).

*worsening from baseline.

[#]e.g., ERA, PDE-5 inhibitor, prostanoids, prostacyclin receptor (IP receptor) agonist, soluble guanylate cyclase stimulator.

5.2. Analysis of the Exploratory Efficacy Variables

5.2.1. Modified NYHA/WHO FC and Panama FC

At each time point, change from Baseline of assessment in modified NYHA/WHO FC and Panama FC will be classified as worsened (> baseline value), unchanged (= baseline value) or improved (< baseline value) and be summarized by age cohort and body weight group.

All data will be listed too by age cohort, site ID, participant ID and body weight group.

5.2.2. 6MWD

The change from baseline will be summarized at each time point of assessment up to the timepoint, using descriptive statistics for continuous variables. Two-sided 95% CIs of the mean and median will also be provided.

All exercise capacity data as measured by 6MWD test will be listed.

5.2.3. Plasma NT pro-BNP

The percent of baseline (defined as (NT pro-BNP value at the timepoint / NT pro-BNP at baseline [Day 1]) x 100) will be summarized at each time point of assessment and up to the timepoint with at least 10 participants in the age cohort, using descriptive statistics for continuous variables. The resulting mean and two-sided 95% CIs will be inversely transformed using the exponential function to provide the geometric mean and corresponding two-sided 95% CIs.

All data will be listed for each participant.

5.2.4. Echo/Doppler (assessed & transferred centrally)

The following Echo/Doppler variables, analyzed centrally, will be listed.

- Right ventricular systolic pressure (RVSP)
- Tricuspid annular plane systolic excursion (TAPSE)
- Pulmonary artery acceleration time)
- Left ventricular eccentricity index (LVEI)
- Right atrial area index (RAI)
- Tricuspid annular diameter

For each variable the change from baseline to each time point assessment will be summarized. Descriptive statistics for continuous variables will be displayed and the two-sided 95% CIs of the mean will also be provided.

5.2.5. Disease Progression/Clinical Worsening

Predefined signs and symptoms of PAH evaluated post baseline by the investigator to standardize the assessment of clinical worsening/disease progression and recorded in the eCRF will be listed.

In case of syncope or at least 2 new or worsening signs/symptoms the investigator must report disease progression in the eCRF and perform further exams to determine the cause.

Based on ‘Disease progression event summary’ the following time to event endpoint will be determined: time to disease progression/clinical worsening from first study drug dose up to EOT + 7 days.

All events (reasons) are considered:

- Death (all causes).

- Atrial septostomy or Potts' anastomosis, or registration on lung transplant list
- Hospitalization due to worsening PAH (excluding hospitalizations that are elective, routine or clearly attributable to appearance/worsening of comorbidities (e.g., pneumonia))
- Clinical worsening (from baseline) of PAH is defined as: need for, or the initiation of new PAH-specific therapy (e.g., ERA, PDE-5 inhibitor, prostanoids, prostacyclin receptor (IP receptor) agonist, soluble guanylate cyclase stimulator) or i.v. diuretics or continuous oxygen use AND at least one of the following:
    - Worsening in WHO FC, or
    - New occurrence or worsening of syncope (in frequency or severity as per medical judgment), or
    - New occurrence or worsening of at least two PAH symptoms (i.e., shortness of breath/dyspnea, chest pain, cyanosis, dizziness/ near syncope, or fatigue), or
    - New occurrence or worsening of signs of right heart failure not responding to oral diuretic

Deaths (all causes) not reported in "disease progression event summary" by the investigators will also be included in this analysis.

Event time is defined as the time elapsed from the first study drug administration to the day of the first occurrence of the event.

If the date of onset of the event is incomplete it is set to the lower limit, unless the lower limit is before the study treatment start date in which case it is set to the study treatment start date.

The number (and percentage) of participants reporting each type of event will be tabulated by age cohort, weight group and overall, for first event and for all events.

Participants who did not experience an event will have their event time censored at EOT + 7 days. The number of participants at risk, the number of participants censored and the number of participants with event will be displayed together with Kaplan Meier estimates.

This time to event endpoint will be also graphically presented as Kaplan Meier estimates with 2-sided 95% CIs at relevant time points (where the number of participants at risk is at least 10% of the total number of participants in the analysis set).

The type and date of disease progression event, as well as time to event, will be listed for all participants; as for the event type of "clinical worsening", components of worsening will also be included in the listing, based on "clinical worsening of PAH".

6. OTHER ENDPOINTS

Palatability and Acceptability of selexipag

Palatability and Acceptability of selexipag formulation will be assessed.

Answers for each question in the palatability questionnaire for Caregivers/Site Personnel, assessed via 5-point facial hedonic scale, will be summarized with counts and percentages by timepoint.

Acceptability of the selexipag formulation will be assessed through a 3-point categorical scale as to whether the child swallowed the medication at visits indicated in the assessment schedule: for all participants, parent(s) or LAR(s) or study site personnel will be asked following the drug intake whether the child swallowed the medication:

- a. fully,
- b. partially,
- c. not at all.

Answers for each question in acceptability questionnaire will be summarized with counts and percentages by timepoint.

Palatability and acceptability will also be listed.

7. STATISTICAL METHODS, CONVENTIONS FOR DISPLAYS AND DECIMAL PRECISION

Unless otherwise specified, all listings will be provided by center and participant number within each age cohort. They will be sorted then by assessment date as appropriate.

Descriptive summary statistics will be provided in the overall population, by age cohort and body weight group.

In summaries for categorical data all participants in the analysis set will be accounted for with tables displaying the number of participants with missing data. The number and percentage of participants in each category will be tabulated by visit as a shift table against baseline.

Summaries for continuous variables will include basic descriptive statistics: mean, median, first and third quartiles, standard deviation and range (minimum and maximum). Mean and median will be displayed as 1 decimal place more than the individual values. The standard deviations (SDs) will be displayed as 1 additional decimal place beyond that of the mean. If a count is 0, the percentage (0%) should not be displayed. The 0 count will be displayed, but the corresponding percentage should be omitted. If the corresponding denominator for the count is also 0, a hyphen (-) should be displayed rather than a 0 count or NA, and the corresponding percentage should be omitted.

- The participant percentages (%) presented in tables will be 1 decimal place unless the sample sizes for the percentages are small enough to warrant presenting as integers. The standard SAS rounding option will be used. For those percentages that rounds to 0.0, along with the count > 0, we will display < 0.1. For those percentages that would round to 100.0, where the count is less than the denominator, we will display > 99.9.
- All dates to be presented in Date9. format, along with time, wherever applicable.

Handling of Missing or Incomplete Date and Time Fields

Conventions for handling incomplete and missing dates are provided below. 'Lower limit' and 'upper limit' refer to the minimum or maximum, respectively, of a possible date. For example, if the day is missing, the lowest limit is the first day of the given month and the upper limit is the last day of the given month. If the day and month are missing, the lower limit refers to the 1st January of the given year and the upper limit to the 31st December of the given year.

Type of Date	Date is incomplete	Date is missing
Date of PAH diagnosis	Lower limit	No replacement
AE resolution date	The earlier of the Upper limit and the end of study date	No replacement, considered ongoing at end of study
AE onset date	If the end date of the AE is not before the start of study drug, and if the study drug start falls in the range of possible dates, it is the study drug start date. In all the other cases, it is the lower limit	The earlier of the end date of the AE and the start of study drug
Concomitant medication start date	Lower limit	No replacement, the medication is considered to have started before the study
Concomitant medication end date	The earlier of the Upper limit and the end of treatment date	No replacement, considered ongoing at end of treatment
Death date	Last of the Lower limit and recorded study assessment dates	Last of the recorded study assessment dates

Anomalous information for a date will be handled using the following rules prior to using the imputations mentioned above:

If the day part of a date is non-numeric or has an invalid value, then day will be considered as missing. For example, if date = 44Nov2000 then, as it isn't possible to have a 44th day of the month, the day will be considered missing.

If the month part of a date does not match that of the possible months, then it will be considered missing, and so will the accompanying day. For example, if date = 21ND99 then both day and month will be considered as missing.

If the year part of a date is non-numeric or has an invalid value, then the whole date will be considered as missing.

General Conventions:

- Study treatments start date is the first day of intake of study treatment. It is derived as the first 'Treatment start date' after sorting in chronological order all records. It coincides with Study Day 1.
- Study treatment end date (EOT) is the last day of intake of study treatment. It is derived as the last 'Treatment end date' after sorting in chronological order all records.
- Starting dose is the dose given on study treatment start date.

Study Day refers to the number of days elapsed since the day of study treatment start, plus 1 (i.e., Study Day 1 is the day of study treatment start). For dates prior to treatment start, it is the negative number of days elapsed between the date under consideration and the day of study treatment start. Therefore, the study day is always different from 0

8. SUPPORTING DOCUMENTATION

8.1. Appendix 1 List of Abbreviations

6MWD	6-minute walk distance
AUC	Area under the plasma concentration-time curve
$AUC_{\tau,ss}$	Area under the plasma concentration-time curve over one dosing interval at steady-state
$AUC_{\tau,ss,combined}$	Combined exposure over one dosing interval at steady-state
C_{max}	Maximum plasma concentration
$C_{max,ss}$	Maximum concentration at steady state
CHD	Congenital heart disease
CSR	Clinical Study Report
ECG	Electrocardiogram
Echo	Echocardiography
eCRF	electronic Case Report Form
EOS	End-of-Study
EOT	End-of-Treatment
EU	European Union
FAS	Full analysis set
FC	Functional class
GRIPHON	Prostacyclin (PGI2G) receptor agonist in Pulmonary arterial Hypertension
i.v.	Intravenous(ly)
ICF	Informed Consent Form
IDMC	Independent Data Monitoring Committee
iMTD	Individual maximum tolerated dose
LAP	Left atrium pressure
LAR	Legally authorized representative
LVEDP	Left ventricular end-diastolic pressure
MedDRA	Medical Dictionary for Regulatory Activities
mPAP	Mean pulmonary arterial pressure
NT pro-BNP	N-terminal pro b-type natriuretic peptide
NYHA	New York Heart Association
PAH	Pulmonary arterial hypertension
PAWP	Pulmonary arterial wedge pressure
PDE-5	Phosphodiesterase type-5
PK	Pharmacokinetic(s)
PKS	Pharmacokinetic Analysis Set
PT	Preferred term
PVOD	Pulmonary veno-occlusive disease
PVR	Pulmonary vascular resistance
PVRi	Pulmonary vascular resistance index
rhc	Right heart catheterization
SAE	serious adverse event
SAP	Statistical Analysis Plan
SBP	Systolic blood pressure
SD	Standard deviation
SIV	Site initiation visit
SOC	System Organ Class
TEAE	Treatment-emergent adverse event
TESAE	Treatment-emergent serious adverse event
T_{max}	Time at which C_{max} is observed
TSH	Thyroid-stimulating hormone
WHO	World Health Organization

8.2. Appendix 2 Definitions of Adverse Events of Special Interest

Definitions of Adverse Events of Special Interest

TABLE OF CONTENTS

Overview

This appendix defines the Adverse Events of Special Interest (AESI) used in the tables and listings produced for study AC-065A203.

The MedDRA coding dictionary version used is 22.1 for Canada Submission and a later version will be used for final CSR.

1 Definition for each category of AESI

1.1 Anaemia

Cases reporting events of anaemia are retrieved from the safety database for analysis if they contain an event Preferred Term (PT) within the 'Haematopoietic erythropenia' Standardised MedDRA Query (SMQ) (broad scope), or the 'Haematopoietic cytopenias affecting more than one type of blood cell' SMQ (broad scope, with the exception of 2 unspecific PTs: 'blood disorder', 'blood count abnormal'), or if they contain an event with any MedDRA PT containing the text 'anaemia', i.e., any of the following MedDRA PTs:

ANAEMIA
ANAEMIA FOLATE DEFICIENCY
ANAEMIA HEINZ BODY
ANAEMIA MACROCYTIC
ANAEMIA MEGALOBLASTIC
ANAEMIA NEONATAL
ANAEMIA OF CHRONIC DISEASE
ANAEMIA OF MALIGNANT DISEASE
ANAEMIA OF PREGNANCY
ANAEMIA POSTOPERATIVE
ANAEMIA PROPHYLAXIS
ANAEMIA SPLENIC
ANAEMIA VITAMIN B12 DEFICIENCY
ANAEMIA VITAMIN B6 DEFICIENCY
APLASIA PURE RED CELL
APLASTIC ANAEMIA
ASPIRATION BONE MARROW ABNORMAL
AUTOIMMUNE ANAEMIA
AUTOIMMUNE APLASTIC ANAEMIA
AUTOIMMUNE HAEMOLYTIC ANAEMIA
AUTOSOMAL RECESSIVE MEGALOBLASTIC ANAEMIA
BICYTOPENIA
BIOPSY BONE MARROW ABNORMAL
BLOOD INCOMPATIBILITY HAEMOLYTIC ANAEMIA OF NEWBORN
BLOOD LOSS ANAEMIA
BLOOD LOSS ANAEMIA NEONATAL
BONE MARROW DISORDER
BONE MARROW FAILURE
BONE MARROW INFILTRATION
BONE MARROW MYELOGRAM ABNORMAL

BONE MARROW NECROSIS
CARDIAC HAEMOLYTIC ANAEMIA
COLD TYPE HAEMOLYTIC ANAEMIA
CONGENITAL ANAEMIA
CONGENITAL APLASTIC ANAEMIA
CONGENITAL DYSERYTHROPOIETIC ANAEMIA
COOMBS NEGATIVE HAEMOLYTIC ANAEMIA
COOMBS POSITIVE HAEMOLYTIC ANAEMIA
CYTOPENIA
DEFICIENCY ANAEMIA
ERYTHROBLAST COUNT ABNORMAL
ERYTHROBLAST COUNT DECREASED
ERYTHROID MATURATION ARREST
ERYTHROPENIA
ERYTHROPOIESIS ABNORMAL
ERYTHROPOIETIN DEFICIENCY ANAEMIA
FEBRILE BONE MARROW APLASIA
FOETAL ANAEMIA
FULL BLOOD COUNT DECREASED
GELATINOUS TRANSFORMATION OF THE BONE MARROW
HAEMATOCRIT ABNORMAL
HAEMATOCRIT DECREASED
HAEMATOTOXICITY
HAEMOGLOBIN ABNORMAL
HAEMOGLOBIN DECREASED
HAEMOLYTIC ANAEMIA
HAEMOLYTIC ANAEMIA ENZYME SPECIFIC
HAEMOLYTIC ICTEROANAEMIA
HAND AND FOOT SYNDROME SECONDARY TO SICKLE CELL ANAEMIA
HEREDITARY HAEMOLYTIC ANAEMIA
HEREDITARY SIDEROBLASTIC ANAEMIA
HEXOKINASE DEFICIENCY ANAEMIA
HYPERCHROMIC ANAEMIA
HYPOCHROMIC ANAEMIA
HYPOPLASTIC ANAEMIA
IMMUNE-MEDIATED CYTOPENIA
IRON DEFICIENCY ANAEMIA
LEUKOERYTHROBLASTIC ANAEMIA
MELANAEMIA
MICROANGIOPATHIC HAEMOLYTIC ANAEMIA
MICROCYTIC ANAEMIA
MYELODYSPLASTIC SYNDROME
MYELODYSPLASTIC SYNDROME TRANSFORMATION
MYELOFIBROSIS

MYELOID METAPLASIA
MYELOSUPPRESSION
NEPHROGENIC ANAEMIA
NORMOCHROMIC ANAEMIA
NORMOCHROMIC NORMOCYTIC ANAEMIA
NORMOCYTIC ANAEMIA
PANCYTOPENIA
PANMYELOPATHY
PERNICIOUS ANAEMIA
PLASMABLAST COUNT DECREASED
PRIMARY MYELOFIBROSIS
PROERYTHROBLAST COUNT ABNORMAL
PROERYTHROBLAST COUNT DECREASED
PROTEIN DEFICIENCY ANAEMIA
PYRUVATE KINASE DEFICIENCY ANAEMIA
RED BLOOD CELL COUNT ABNORMAL
RED BLOOD CELL COUNT DECREASED
REFRACTORY ANAEMIA WITH AN EXCESS OF BLASTS
REFRACTORY ANAEMIA WITH RINGED SIDEROBLASTS
RETICULOCYTE COUNT ABNORMAL
RETICULOCYTE COUNT DECREASED
RETICULOCYTE PERCENTAGE DECREASED
RETICULOCYTOPENIA
SCAN BONE MARROW ABNORMAL
SICKLE CELL ANAEMIA
SICKLE CELL ANAEMIA WITH CRISIS
SIDEROBLASTIC ANAEMIA
SPHEROCYTIC ANAEMIA
SPUR CELL ANAEMIA
WARM TYPE HAEMOLYTIC ANAEMIA

1.2 Bleeding events

Cases including events denoting haemorrhage or GI haemorrhage are retrieved from the safety database for analysis if they contain an event PT within either of the following MedDRA SMQs(narrow scope): ‘Haemorrhage terms (excl. laboratory terms)’, or ‘Gastrointestinal haemorrhage’, i.e., any of the following MedDRA PTs:

ABDOMINAL WALL HAEMATOMA
ABDOMINAL WALL HAEMORRHAGE
ABNORMAL UTERINE BLEEDING
ABNORMAL WITHDRAWAL BLEEDING
ACHENBACH SYNDROME
ACUTE HAEMORRHAGIC LEUKOENCEPHALITIS
ACUTE HAEMORRHAGIC ULCERATIVE COLITIS
ADMINISTRATION SITE BRUISE

ADMINISTRATION SITE HAEMATOMA
ADMINISTRATION SITE HAEMORRHAGE
ADRENAL HAEMATOMA
ADRENAL HAEMORRHAGE
ANAL FISSURE HAEMORRHAGE
ANAL HAEMORRHAGE
ANAL ULCER HAEMORRHAGE
ANASTOMOTIC HAEMORRHAGE
ANASTOMOTIC ULCER HAEMORRHAGE
ANEURYSM RUPTURED
ANGINA BULLOSA HAEMORRHAGICA
ANORECTAL VARICES HAEMORRHAGE
ANTICOAGULANT-RELATED NEPHROPATHY
ANTIPLATELET REVERSAL THERAPY
AORTIC ANEURYSM RUPTURE
AORTIC DISSECTION RUPTURE
AORTIC INTRAMURAL HAEMATOMA
AORTIC PERFORATION
AORTIC RUPTURE
APONEUROSIS CONTUSION
APPLICATION SITE BRUISE
APPLICATION SITE HAEMATOMA
APPLICATION SITE HAEMORRHAGE
APPLICATION SITE PURPURA
ARTERIAL HAEMORRHAGE
ARTERIAL INTRAMURAL HAEMATOMA
ARTERIAL PERFORATION
ARTERIAL RUPTURE
ARTERIOVENOUS FISTULA SITE HAEMATOMA
ARTERIOVENOUS FISTULA SITE HAEMORRHAGE
ARTERIOVENOUS GRAFT SITE HAEMATOMA
ARTERIOVENOUS GRAFT SITE HAEMORRHAGE
ASTRINGENT THERAPY
ATRIAL RUPTURE
AURICULAR HAEMATOMA
BASAL GANGLIA HAEMATOMA
BASAL GANGLIA HAEMORRHAGE
BASILAR ARTERY PERFORATION
BLADDER TAMPONADE
BLEEDING VARICOSE VEIN
BLOOD BLISTER

BLOOD LOSS ANAEMIA
BLOOD URINE
BLOOD URINE PRESENT
BLOODY DISCHARGE
BLOODY PERITONEAL EFFLUENT
BONE CONTUSION
BONE MARROW HAEMORRHAGE
BRAIN CONTUSION
BRAIN STEM HAEMATOMA
BRAIN STEM HAEMORRHAGE
BRAIN STEM MICROHAEMORRHAGE
BREAST HAEMATOMA
BREAST HAEMORRHAGE
BROAD LIGAMENT HAEMATOMA
BRONCHIAL HAEMORRHAGE
BRONCHIAL VARICES HAEMORRHAGE
BULLOUS HAEMORRHAGIC DERMATOSIS
BURSAL HAEMATOMA
CARDIAC CONTUSION
CAROTID ANEURYSM RUPTURE
CAROTID ARTERY PERFORATION
CATHETER SITE BRUISE
CATHETER SITE HAEMATOMA
CATHETER SITE HAEMORRHAGE
CENTRAL NERVOUS SYSTEM HAEMORRHAGE
CEPHALHAEMATOMA
CEREBELLAR HAEMATOMA
CEREBELLAR HAEMORRHAGE
CEREBELLAR MICROHAEMORRHAGE
CEREBRAL ANEURYSM PERFORATION
CEREBRAL ANEURYSM RUPTURED SYPHILITIC
CEREBRAL ARTERIOVENOUS MALFORMATION HAEMORRHAGIC
CEREBRAL ARTERY PERFORATION
CEREBRAL CYST HAEMORRHAGE
CEREBRAL HAEMATOMA
CEREBRAL HAEMORRHAGE
CEREBRAL HAEMORRHAGE FOETAL
CEREBRAL HAEMORRHAGE NEONATAL
CEREBRAL MICROHAEMORRHAGE
CERVIX HAEMATOMA UTERINE
CERVIX HAEMORRHAGE UTERINE

CHEST WALL HAEMATOMA
CHOROIDAL HAEMATOMA
CHOROIDAL HAEMORRHAGE
CHRONIC GASTROINTESTINAL BLEEDING
CHRONIC PIGMENTED PURPURA
CILIARY BODY HAEMORRHAGE
COITAL BLEEDING
COLONIC HAEMATOMA
CONJUNCTIVAL HAEMORRHAGE
CONTUSION
CORNEAL BLEEDING
CULLEN'S SIGN
CYSTITIS HAEMORRHAGIC
DEEP DISSECTING HAEMATOMA
DIARRHOEA HAEMORRHAGIC
DISSEMINATED INTRAVASCULAR COAGULATION
DIVERTICULITIS INTESTINAL HAEMORRHAGIC
DIVERTICULUM INTESTINAL HAEMORRHAGIC
DUODENAL OPERATION
DUODENAL ULCER HAEMORRHAGE
DUODENAL VASCULAR ECTASIA
DUODENITIS HAEMORRHAGIC
EAR HAEMORRHAGE
ECCHYMOSIS
ENCEPHALITIS HAEMORRHAGIC
ENTEROCOLITIS HAEMORRHAGIC
EPIDURAL HAEMORRHAGE
EPISTAXIS
EXSANGUINATION
EXTRA-AXIAL HAEMORRHAGE
EXTRADURAL HAEMATOMA
EXTRADURAL HAEMATOMA EVACUATION
EXTRAVASATION BLOOD
EYE CONTUSION
EYE HAEMATOMA
EYE HAEMORRHAGE
EYELID BLEEDING
EYELID CONTUSION
EYELID HAEMATOMA
FEMORAL ARTERY PERFORATION
FEMORAL VEIN PERFORATION

FOETAL-MATERNAL HAEMORRHAGE
FOTHERGILL SIGN POSITIVE
GASTRIC ANTRAL VASCULAR ECTASIA
GASTRIC HAEMANGIOMA
GASTRIC HAEMORRHAGE
GASTRIC OCCULT BLOOD POSITIVE
GASTRIC ULCER HAEMORRHAGE
GASTRIC ULCER HAEMORRHAGE, OBSTRUCTIVE
GASTRIC VARICES HAEMORRHAGE
GASTRITIS ALCOHOLIC HAEMORRHAGIC
GASTRITIS HAEMORRHAGIC
GASTRODUODENAL HAEMORRHAGE
GASTROINTESTINAL ANASTOMOTIC LEAK
GASTROINTESTINAL ANGIECTASIA
GASTROINTESTINAL HAEMORRHAGE
GASTROINTESTINAL POLYP HAEMORRHAGE
GASTROINTESTINAL ULCER HAEMORRHAGE
GASTROINTESTINAL VASCULAR MALFORMATION HAEMORRHAGIC
GENITAL CONTUSION
GENITAL HAEMORRHAGE
GINGIVAL BLEEDING
GRAFT HAEMORRHAGE
GREY TURNER'S SIGN
HAEMANGIOMA RUPTURE
HAEMARTHROSIS
HAEMATEMESIS
HAEMATOCHEZIA
HAEMATOCOELE
HAEMATOMA
HAEMATOMA EVACUATION
HAEMATOMA INFECTION
HAEMATOMA MUSCLE
HAEMATOSALPINX
HAEMATOSPERMIA
HAEMATOTYMPANUM
HAEMATURIA
HAEMATURIA TRAUMATIC
HAEMOBILIA
HAEMOPERITONEUM
HAEMOPHILIC ARTHROPATHY
HAEMOPHILIC PSEUDOTUMOUR

HAEMOPTYSIS
HAEMORRHAGE
HAEMORRHAGE CORONARY ARTERY
HAEMORRHAGE FOETAL
HAEMORRHAGE IN PREGNANCY
HAEMORRHAGE INTRACRANIAL
HAEMORRHAGE NEONATAL
HAEMORRHAGE SUBCUTANEOUS
HAEMORRHAGE SUBEPIDERMAL
HAEMORRHAGE URINARY TRACT
HAEMORRHAGIC ADRENAL INFARCTION
HAEMORRHAGIC ARTERIOVENOUS MALFORMATION
HAEMORRHAGIC ASCITES
HAEMORRHAGIC BREAST CYST
HAEMORRHAGIC CEREBRAL INFARCTION
HAEMORRHAGIC CYST
HAEMORRHAGIC DIATHESIS
HAEMORRHAGIC DISEASE OF NEWBORN
HAEMORRHAGIC DISORDER
HAEMORRHAGIC EROSIVE GASTRITIS
HAEMORRHAGIC GASTROENTERITIS
HAEMORRHAGIC HEPATIC CYST
HAEMORRHAGIC INFARCTION
HAEMORRHAGIC NECROTIC PANCREATITIS
HAEMORRHAGIC OCCLUSIVE RETINAL VASCULITIS
HAEMORRHAGIC OVARIAN CYST
HAEMORRHAGIC STROKE
HAEMORRHAGIC THYROID CYST
HAEMORRHAGIC TRANSFORMATION STROKE
HAEMORRHAGIC TUMOUR NECROSIS
HAEMORRHAGIC URTICARIA
HAEMORRHAGIC VASCULITIS
HAEMORRHOIDAL HAEMORRHAGE
HAEMOSTASIS
HAEMOTHORAX
HEAVY MENSTRUAL BLEEDING
HENOCH-SCHONLEIN PURPURA
HEPATIC HAEMANGIOMA RUPTURE
HEPATIC HAEMATOMA
HEPATIC HAEMORRHAGE
HEREDITARY HAEMORRHAGIC TELANGIECTASIA

HYPERFIBRINOLYSIS
HYPHAEMA
ILIAC ARTERY PERFORATION
ILIAC ARTERY RUPTURE
ILIAC VEIN PERFORATION
IMMUNE THROMBOCYTOPENIA
IMPLANT SITE BRUISING
IMPLANT SITE HAEMATOMA
IMPLANT SITE HAEMORRHAGE
INCISION SITE HAEMATOMA
INCISION SITE HAEMORRHAGE
INCREASED TENDENCY TO BRUISE
INDUCED ABORTION HAEMORRHAGE
INFERIOR VENA CAVA PERFORATION
INFUSION SITE BRUISING
INFUSION SITE HAEMATOMA
INFUSION SITE HAEMORRHAGE
INJECTION SITE BRUISING
INJECTION SITE HAEMATOMA
INJECTION SITE HAEMORRHAGE
INSTILLATION SITE BRUISE
INSTILLATION SITE HAEMATOMA
INSTILLATION SITE HAEMORRHAGE
INTERMENSTRUAL BLEEDING
INTERNAL HAEMORRHAGE
INTESTINAL HAEMATOMA
INTESTINAL HAEMORRHAGE
INTESTINAL VARICES HAEMORRHAGE
INTRA-ABDOMINAL HAEMATOMA
INTRA-ABDOMINAL HAEMORRHAGE
INTRACEREBRAL HAEMATOMA EVACUATION
INTRACRANIAL HAEMATOMA
INTRACRANIAL TUMOUR HAEMORRHAGE
INTRAOCULAR HAEMATOMA
INTRAPARTUM HAEMORRHAGE
INTRATUMOURAL HAEMATOMA
INTRAVENTRICULAR HAEMORRHAGE
INTRAVENTRICULAR HAEMORRHAGE NEONATAL
IRIS HAEMORRHAGE
JOINT MICROHAEMORRHAGE
JUGULAR VEIN HAEMORRHAGE

KIDNEY CONTUSION
LACRIMAL HAEMORRHAGE
LARGE INTESTINAL HAEMORRHAGE
LARGE INTESTINAL ULCER HAEMORRHAGE
LARYNGEAL HAEMATOMA
LARYNGEAL HAEMORRHAGE
LIP HAEMATOMA
LIP HAEMORRHAGE
LIVER CONTUSION
LOWER GASTROINTESTINAL HAEMORRHAGE
LOWER LIMB ARTERY PERFORATION
LYMPH NODE HAEMORRHAGE
MALLORY-WEISS SYNDROME
MEDIASTINAL HAEMATOMA
MEDIASTINAL HAEMORRHAGE
MEDICAL DEVICE SITE BRUISE
MEDICAL DEVICE SITE HAEMATOMA
MEDICAL DEVICE SITE HAEMORRHAGE
MELAENA
MELAENA NEONATAL
MENINGORRHAGIA
MENOMETRORRHAGIA
MESENTERIC HAEMATOMA
MESENTERIC HAEMORRHAGE
MOUTH HAEMORRHAGE
MUCOCUTANEOUS HAEMORRHAGE
MUCOSAL HAEMORRHAGE
MUSCLE CONTUSION
MUSCLE HAEMORRHAGE
MYOCARDIAL HAEMORRHAGE
MYOCARDIAL RUPTURE
NAEVUS HAEMORRHAGE
NAIL BED BLEEDING
NASAL SEPTUM HAEMATOMA
NEONATAL GASTROINTESTINAL HAEMORRHAGE
NEPHRITIS HAEMORRHAGIC
NIPPLE EXUDATE BLOODY
OCCULT BLOOD POSITIVE
OCULAR RETROBULBAR HAEMORRHAGE
OESOPHAGEAL HAEMORRHAGE
OESOPHAGEAL INTRAMURAL HAEMATOMA

OESOPHAGEAL ULCER HAEMORRHAGE
OESOPHAGEAL VARICES HAEMORRHAGE
OESOPHAGITIS HAEMORRHAGIC
OMENTAL HAEMORRHAGE
OPTIC DISC HAEMORRHAGE
OPTIC NERVE SHEATH HAEMORRHAGE
ORAL BLOOD BLISTER
ORAL CONTUSION
ORAL MUCOSA HAEMATOMA
ORAL PURPURA
ORBITAL HAEMATOMA
ORBITAL HAEMORRHAGE
OSTEORRHAGIA
OVARIAN HAEMATOMA
OVARIAN HAEMORRHAGE
PALPABLE PURPURA
PANCREATIC HAEMORRHAGE
PANCREATIC PSEUDOCYST HAEMORRHAGE
PANCREATITIS HAEMORRHAGIC
PAPILLARY MUSCLE HAEMORRHAGE
PARANASAL SINUS HAEMATOMA
PARANASAL SINUS HAEMORRHAGE
PARATHYROID HAEMORRHAGE
PAROTID GLAND HAEMORRHAGE
PELVIC HAEMATOMA
PELVIC HAEMATOMA OBSTETRIC
PELVIC HAEMORRHAGE
PENILE CONTUSION
PENILE HAEMATOMA
PENILE HAEMORRHAGE
PEPTIC ULCER HAEMORRHAGE
PERICARDIAL HAEMORRHAGE
PERINEAL HAEMATOMA
PERIORBITAL HAEMATOMA
PERIORBITAL HAEMORRHAGE
PERIOSTEAL HAEMATOMA
PERIPARTUM HAEMORRHAGE
PERIPHERAL ARTERY ANEURYSM RUPTURE
PERIPHERAL ARTERY HAEMATOMA
PERITONEAL HAEMATOMA
PERIVENTRICULAR HAEMORRHAGE NEONATAL

PETECHIAE
PHARYNGEAL CONTUSION
PHARYNGEAL HAEMATOMA
PHARYNGEAL HAEMORRHAGE
PITUITARY APOPLEXY
PITUITARY HAEMORRHAGE
PLACENTA PRAEVIA HAEMORRHAGE
POLYMENORRHAGIA
POST ABORTION HAEMORRHAGE
POST PROCEDURAL CONTUSION
POST PROCEDURAL HAEMATOMA
POST PROCEDURAL HAEMATURIA
POST PROCEDURAL HAEMORRHAGE
POST TRANSFUSION PURPURA
POST-TRAUMATIC PUNCTATE INTRAEPIDERMAL HAEMORRHAGE
POSTMENOPAUSAL HAEMORRHAGE
POSTPARTUM HAEMORRHAGE
PREMATURE SEPARATION OF PLACENTA
PROCEDURAL HAEMORRHAGE
PROCTITIS HAEMORRHAGIC
PROSTATIC HAEMORRHAGE
PULMONARY ALVEOLAR HAEMORRHAGE
PULMONARY CONTUSION
PULMONARY HAEMATOMA
PULMONARY HAEMORRHAGE
PULMONARY HAEMORRHAGE NEONATAL
PUNCTURE SITE BRUISE
PUNCTURE SITE HAEMATOMA
PUNCTURE SITE HAEMORRHAGE
PURPURA
PURPURA FULMINANS
PURPURA NEONATAL
PURPURA NON-THROMBOCYTOPENIC
PURPURA SENILE
PUTAMEN HAEMORRHAGE
RADIATION ASSOCIATED HAEMORRHAGE
RECTAL HAEMORRHAGE
RECTAL ULCER HAEMORRHAGE
RENAL ARTERY PERFORATION
RENAL CYST HAEMORRHAGE
RENAL HAEMATOMA

RENAL HAEMORRHAGE
RESPIRATORY TRACT HAEMORRHAGE
RESPIRATORY TRACT HAEMORRHAGE NEONATAL
RETINAL ANEURYSM RUPTURE
RETINAL HAEMORRHAGE
RETINOPATHY HAEMORRHAGIC
RETROPERITONEAL HAEMATOMA
RETROPERITONEAL HAEMORRHAGE
RETROPLACENTAL HAEMATOMA
RUPTURED CEREBRAL ANEURYSM
SCLERAL HAEMATOMA
SCLERAL HAEMORRHAGE
SCROTAL HAEMATOCOELE
SCROTAL HAEMATOMA
SCROTAL HAEMORRHAGE
SHOCK HAEMORRHAGIC
SKIN HAEMORRHAGE
SKIN NEOPLASM BLEEDING
SKIN ULCER HAEMORRHAGE
SMALL INTESTINAL HAEMORRHAGE
SMALL INTESTINAL ULCER HAEMORRHAGE
SOFT TISSUE HAEMORRHAGE
SPERMATIC CORD HAEMORRHAGE
SPINAL CORD HAEMATOMA
SPINAL CORD HAEMORRHAGE
SPINAL EPIDURAL HAEMATOMA
SPINAL EPIDURAL HAEMORRHAGE
SPINAL SUBARACHNOID HAEMORRHAGE
SPINAL SUBDURAL HAEMATOMA
SPINAL SUBDURAL HAEMORRHAGE
SPLEEN CONTUSION
SPLENIC ARTERY PERFORATION
SPLENIC HAEMATOMA
SPLENIC HAEMORRHAGE
SPLENIC VARICES HAEMORRHAGE
SPLINTER HAEMORRHAGES
SPONTANEOUS HAEMATOMA
SPONTANEOUS HAEMORRHAGE
STOMA SITE HAEMORRHAGE
STOMATITIS HAEMORRHAGIC
SUBARACHNOID HAEMATOMA

SUBARACHNOID HAEMORRHAGE
SUBARACHNOID HAEMORRHAGE NEONATAL
SUBCAPSULAR HEPATIC HAEMATOMA
SUBCAPSULAR RENAL HAEMATOMA
SUBCAPSULAR SPLENIC HAEMATOMA
SUBCHORIONIC HAEMATOMA
SUBCHORIONIC HAEMORRHAGE
SUBCLAVIAN ARTERY PERFORATION
SUBCLAVIAN VEIN PERFORATION
SUBCUTANEOUS HAEMATOMA
SUBDURAL HAEMATOMA
SUBDURAL HAEMATOMA EVACUATION
SUBDURAL HAEMORRHAGE
SUBDURAL HAEMORRHAGE NEONATAL
SUBENDOCARDIAL HAEMORRHAGE
SUBGALEAL HAEMATOMA
SUBGALEAL HAEMORRHAGE
SUBRETINAL HAEMATOMA
SUPERIOR VENA CAVA PERFORATION
TESTICULAR HAEMORRHAGE
THALAMUS HAEMORRHAGE
THIRD STAGE POSTPARTUM HAEMORRHAGE
THORACIC HAEMORRHAGE
THROMBOCYTOPENIC PURPURA
THROMBOTIC THROMBOCYTOPENIC PURPURA
THYROID HAEMORRHAGE
TONGUE HAEMATOMA
TONGUE HAEMORRHAGE
TONSILLAR HAEMORRHAGE
TOOTH PULP HAEMORRHAGE
TOOTH SOCKET HAEMORRHAGE
TRACHEAL HAEMORRHAGE
TRAUMATIC HAEMATOMA
TRAUMATIC HAEMORRHAGE
TRAUMATIC HAEMOTHORAX
TRAUMATIC INTRACRANIAL HAEMATOMA
TRAUMATIC INTRACRANIAL HAEMORRHAGE
TUMOUR HAEMORRHAGE
ULCER HAEMORRHAGE
UMBILICAL CORD HAEMORRHAGE
UMBILICAL HAEMATOMA

UMBILICAL HAEMORRHAGE
UPPER GASTROINTESTINAL HAEMORRHAGE
URETERIC HAEMORRHAGE
URETHRAL HAEMORRHAGE
URINARY BLADDER HAEMATOMA
URINARY BLADDER HAEMORRHAGE
URINARY OCCULT BLOOD
URINARY OCCULT BLOOD POSITIVE
UROGENITAL HAEMORRHAGE
UTERINE HAEMATOMA
UTERINE HAEMORRHAGE
VACCINATION SITE BRUISING
VACCINATION SITE HAEMATOMA
VACCINATION SITE HAEMORRHAGE
VAGINAL HAEMATOMA
VAGINAL HAEMORRHAGE
VARICOSE VEIN RUPTURED
VASCULAR ACCESS SITE BRUISING
VASCULAR ACCESS SITE HAEMATOMA
VASCULAR ACCESS SITE HAEMORRHAGE
VASCULAR ACCESS SITE RUPTURE
VASCULAR ANASTOMOTIC HAEMORRHAGE
VASCULAR GRAFT HAEMORRHAGE
VASCULAR PSEUDOANEURYSM RUPTURED
VASCULAR PURPURA
VASCULAR RUPTURE
VEIN RUPTURE
VENOUS HAEMORRHAGE
VENOUS PERFORATION
VENTRICLE RUPTURE
VERTEBRAL ARTERY PERFORATION
VESSEL PUNCTURE SITE BRUISE
VESSEL PUNCTURE SITE HAEMATOMA
VESSEL PUNCTURE SITE HAEMORRHAGE
VITREOUS HAEMATOMA
VITREOUS HAEMORRHAGE
VULVAL HAEMATOMA
VULVAL HAEMATOMA EVACUATION
VULVAL HAEMORRHAGE
WHITE NIPPLE SIGN
WITHDRAWAL BLEED

WOUND HAEMATOMA
WOUND HAEMORRHAGE

1.3 Gastrointestinal disturbances denoting intestinal intussusception (manifested as ileus or obstruction)

Cases including events denoting GI disturbances are retrieved from the safety database for analysis if they contain an event with any MedDRA PT containing the text ‘ileus’, ‘intestinal obstruction’, ‘intestinal pseudo-obstruction’, ‘intussusception’, or ‘volvulus’, with the exception of unspecific PT: ‘keratomileusis’, i.e., any of the following MedDRA PTs:

CONGENITAL INTESTINAL OBSTRUCTION
DISTAL INTESTINAL OBSTRUCTION SYNDROME
GALLBLADDER VOLVULUS
GALLSTONE ILEUS
GASTRIC ILEUS
GASTRIC VOLVULUS
GASTROINTESTINAL OBSTRUCTION
ILEUS
ILEUS PARALYTIC
ILEUS SPASTIC
INTESTINAL OBSTRUCTION
INTESTINAL PSEUDO-OBSTRUCTION
INTUSSUSCEPTION
LARGE INTESTINAL OBSTRUCTION
LARGE INTESTINAL OBSTRUCTION REDUCTION
MALIGNANT GASTROINTESTINAL OBSTRUCTION
MECHANICAL ILEUS
MECONIUM ILEUS
NEONATAL INTESTINAL OBSTRUCTION
POSTOPERATIVE ILEUS
SMALL INTESTINAL INTUSSUSCEPTION REDUCTION
SMALL INTESTINAL OBSTRUCTION
SMALL INTESTINAL OBSTRUCTION REDUCTION
SUBILEUS
VOLVULUS
VOLVULUS OF SMALL BOWEL
VOLVULUS REPAIR

1.4 Hyperthyroidism

Cases including events of hyperthyroidism are retrieved from the safety database for analysis if they contain an event PT within the ‘Hyperthyroidism’ SMQ (broad scope), i.e., any of the following MedDRA PTs:

ANTI-THYROID ANTIBODY
ANTI-THYROID ANTIBODY DECREASED
ANTI-THYROID ANTIBODY POSITIVE
ANTITHYROID ARTHRITIS SYNDROME
AUTOIMMUNE THYROID DISORDER
AUTOIMMUNE THYROIDITIS

BASEDOW'S DISEASE
BIOPSY THYROID GLAND ABNORMAL
BLOOD THYROID STIMULATING HORMONE ABNORMAL
BLOOD THYROID STIMULATING HORMONE DECREASED
BLOOD THYROID STIMULATING HORMONE INCREASED
BUTANOL-EXTRACTABLE IODINE DECREASED
BUTANOL-EXTRACTABLE IODINE INCREASED
CONGENITAL THYROID DISORDER
ENDOCRINE OPHTHALMOPATHY
EUTHYROID SICK SYNDROME
EXOPHTHALMOS
FREE THYROXINE INDEX ABNORMAL
FREE THYROXINE INDEX DECREASED
FREE THYROXINE INDEX INCREASED
GAMMA RADIATION THERAPY TO THYROID
GOITRE
HASHIMOTO'S ENCEPHALOPATHY
HASHITOXICOSIS
HYPERTHYROIDISM
IMMUNE-MEDIATED HYPERTHYROIDISM
IMMUNE-MEDIATED THYROIDITIS
INAPPROPRIATE THYROID STIMULATING HORMONE SECRETION
INFECTIOUS THYROIDITIS
IODINE UPTAKE ABNORMAL
IODINE UPTAKE DECREASED
IODINE UPTAKE INCREASED
MALIGNANT EXOPHTHALMOS
MARINE LENHART SYNDROME
ORBITAL DECOMPRESSION
PHOTON RADIATION THERAPY TO THYROID
POLYGLANDULAR AUTOIMMUNE SYNDROME TYPE II
POLYGLANDULAR AUTOIMMUNE SYNDROME TYPE III
PRIMARY HYPERTHYROIDISM
PROTEIN BOUND IODINE DECREASED
PROTEIN BOUND IODINE INCREASED
RADIOACTIVE IODINE THERAPY
RADIOTHERAPY TO THYROID
REVERSE TRI-IODOTHYRONINE DECREASED
REVERSE TRI-IODOTHYRONINE INCREASED
SECONDARY HYPERTHYROIDISM
SILENT THYROIDITIS

THYREOSTATIC THERAPY
THYROGLOBULIN ABSENT
THYROGLOBULIN DECREASED
THYROGLOBULIN INCREASED
THYROGLOBULIN PRESENT
THYROID AUTOTRANSPLANTATION
THYROID DERMATOPATHY
THYROID DISORDER
THYROID DYSFUNCTION IN PREGNANCY
THYROID ELECTRON RADIATION THERAPY
THYROID FUNCTION TEST ABNORMAL
THYROID GLAND SCAN ABNORMAL
THYROID HEMIAGENESIS
THYROID HORMONE REPLACEMENT THERAPY
THYROID HORMONES INCREASED
THYROID OPERATION
THYROID PAIN
THYROID RELEASING HORMONE CHALLENGE TEST ABNORMAL
THYROID STIMULATING IMMUNOGLOBULIN INCREASED
THYROID THERAPY
THYROID TUBERCULOSIS
THYROIDECTOMY
THYROIDITIS
THYROIDITIS ACUTE
THYROIDITIS CHRONIC
THYROIDITIS FIBROUS CHRONIC
THYROIDITIS SUBACUTE
THYROTOXIC CARDIOMYOPATHY
THYROTOXIC CRISIS
THYROTOXIC MYOPATHY
THYROTOXIC PERIODIC PARALYSIS
THYROXIN BINDING GLOBULIN ABNORMAL
THYROXIN BINDING GLOBULIN DECREASED
THYROXIN BINDING GLOBULIN INCREASED
THYROXINE ABNORMAL
THYROXINE DECREASED
THYROXINE FREE ABNORMAL
THYROXINE FREE DECREASED
THYROXINE FREE INCREASED
THYROXINE INCREASED
THYROXINE THERAPY

TOXIC GOITRE
TOXIC NODULAR GOITRE
TRI-IODOTHYRONINE ABNORMAL
TRI-IODOTHYRONINE DECREASED
TRI-IODOTHYRONINE FREE ABNORMAL
TRI-IODOTHYRONINE FREE DECREASED
TRI-IODOTHYRONINE FREE INCREASED
TRI-IODOTHYRONINE FREE NORMAL
TRI-IODOTHYRONINE INCREASED
TRI-IODOTHYRONINE UPTAKE ABNORMAL
TRI-IODOTHYRONINE UPTAKE DECREASED
TRI-IODOTHYRONINE UPTAKE INCREASED
ULTRASOUND THYROID ABNORMAL
X-RAY THERAPY TO THYROID

1.5 Hypotension

"The case will be included in this subgroup if it contains an event with any of the following MedDRA Preferred Terms:

BLOOD PRESSURE AMBULATORY DECREASED
BLOOD PRESSURE DECREASED
BLOOD PRESSURE DIASTOLIC DECREASED
BLOOD PRESSURE IMMEASURABLE
BLOOD PRESSURE ORTHOSTATIC DECREASED
BLOOD PRESSURE SYSTOLIC DECREASED
BLOOD PRESSURE SYSTOLIC INSPIRATORY DECREASED
CT HYPOTENSION COMPLEX
DIALYSIS HYPOTENSION
DIASTOLIC HYPOTENSION
HYPOTENSION
HYPOTENSIVE CRISIS
MEAN ARTERIAL PRESSURE DECREASED
NEONATAL HYPOTENSION
ORTHOSTATIC HYPOTENSION
POST PROCEDURAL HYPOTENSION
PROCEDURAL HYPOTENSION

1.6 Light-dependent non-melanoma skin malignancies

Cases including events denoting non-melanoma skin malignancies are retrieved from the safety database for analysis if they contain an event PT within the MedDRA High Level Term ‘Skin neoplasms malignant and unspecified (excl. melanoma)’, or if they contain the MedDRA PT ‘Squamous cell carcinoma’, i.e., any of the following MedDRA PTs:

ATYPICAL FIBROXANTHOMA

BASAL CELL CARCINOMA
BASAL CELL CARCINOMA METASTATIC
BASAL CELL NAEVUS SYNDROME
BASOSQUAMOUS CARCINOMA OF SKIN
BOWEN'S DISEASE
CARCINOMA IN SITU OF SKIN
DYSPLASTIC NAEVUS SYNDROME
ECCRINE CARCINOMA
EPIDERMAL NAEVUS SYNDROME
EXTRAMAMMARY PAGET'S DISEASE
HIDRADENOCARCINOMA
KERATOACANTHOMA
MALIGNANT SWEAT GLAND NEOPLASM
MARJOLIN'S ULCER
MASTOCYTOMA
NEOPLASM SKIN
NEUROENDOCRINE CARCINOMA OF THE SKIN
PILOMATRIX CARCINOMA
POROCARCINOMA
SEBACEOUS CARCINOMA
SKIN ANGIOSARCOMA
SKIN CANCER
SKIN CANCER METASTATIC
SKIN NEOPLASM BLEEDING
SKIN SQUAMOUS CELL CARCINOMA METASTATIC
SKIN SQUAMOUS CELL CARCINOMA RECURRENT
SQUAMOUS CELL CARCINOMA
SQUAMOUS CELL CARCINOMA OF SKIN
TRICHOBLASTIC CARCINOMA

1.7 Major adverse cardiovascular events

Cases including major adverse cardiovascular events (MACE) are retrieved from the safety database for analysis if they contain an event PT within any of the following MedDRA SMQs: ‘Conditions associated with central nervous system haemorrhages and cerebrovascular accidents’ (broad scope), ‘Haemorrhagic central nervous system vascular conditions’ (narrow scope), ‘Ischaemic central nervous system vascular conditions’ (narrow scope), or ‘Myocardial infarction’ (narrow scope), or an event with any of the following MedDRA PTs: ‘Cardiac arrest’, ‘Cardiac death’, ‘Cardio-respiratory arrest’, ‘Coronary artery disease’, ‘Coronary artery insufficiency’, ‘Coronary vein stenosis’, ‘Myocardial ischaemia’, ‘Pseudostroke’, ‘Sudden cardiac death’, and ‘Sudden death’, i.e., any of the following MedDRA PTs:

ACUTE CARDIAC EVENT
ACUTE CORONARY SYNDROME

ACUTE MYOCARDIAL INFARCTION
AGNOSIA
AMAUROSIS FUGAX
ANGINA UNSTABLE
ANGIOGRAM CEREBRAL ABNORMAL
APHASIA
BALINT'S SYNDROME
BASAL GANGLIA HAEMATOMA
BASAL GANGLIA HAEMORRHAGE
BASAL GANGLIA INFARCTION
BASAL GANGLIA STROKE
BASILAR ARTERY ANEURYSM
BASILAR ARTERY OCCLUSION
BASILAR ARTERY PERFORATION
BASILAR ARTERY STENOSIS
BASILAR ARTERY THROMBOSIS
BENEDIKT'S SYNDROME
BLOOD CREATINE PHOSPHOKINASE MB ABNORMAL
BLOOD CREATINE PHOSPHOKINASE MB INCREASED
BRACHIOCEPHALIC ARTERIOSCLEROSIS
BRACHIOCEPHALIC ARTERY OCCLUSION
BRACHIOCEPHALIC ARTERY STENOSIS
BRAIN HYPOXIA
BRAIN INJURY
BRAIN STEM EMBOLISM
BRAIN STEM HAEMATOMA
BRAIN STEM HAEMORRHAGE
BRAIN STEM INFARCTION
BRAIN STEM ISCHAEMIA
BRAIN STEM MICROHAEMORRHAGE
BRAIN STEM STROKE
BRAIN STEM THROMBOSIS
BRAIN STENT INSERTION
CADASIL
CAPSULAR WARNING SYNDROME
CARASIL SYNDROME
CARDIAC ARREST
CARDIAC DEATH
CARDIO-RESPIRATORY ARREST
CAROTID ANEURYSM RUPTURE
CAROTID ANGIOPLASTY

CAROTID ARTERIAL EMBOLUS
CAROTID ARTERIOSCLEROSIS
CAROTID ARTERY ANEURYSM
CAROTID ARTERY BYPASS
CAROTID ARTERY DISEASE
CAROTID ARTERY DISSECTION
CAROTID ARTERY INSUFFICIENCY
CAROTID ARTERY OCCLUSION
CAROTID ARTERY PERFORATION
CAROTID ARTERY RESTENOSIS
CAROTID ARTERY STENOSIS
CAROTID ARTERY STENT INSERTION
CAROTID ARTERY STENT REMOVAL
CAROTID ARTERY THROMBOSIS
CAROTID ENDARTERECTOMY
CAROTID REVASCULARISATION
CENTRAL NERVOUS SYSTEM HAEMORRHAGE
CENTRAL PAIN SYNDROME
CEREBELLAR ARTERY OCCLUSION
CEREBELLAR ARTERY THROMBOSIS
CEREBELLAR ATHEROSCLEROSIS
CEREBELLAR EMBOLISM
CEREBELLAR HAEMATOMA
CEREBELLAR HAEMORRHAGE
CEREBELLAR INFARCTION
CEREBELLAR ISCHAEMIA
CEREBELLAR MICROHAEMORRHAGE
CEREBELLAR STROKE
CEREBRAL ANEURYSM PERFORATION
CEREBRAL ANEURYSM RUPTURED SYPHILITIC
CEREBRAL ARTERIOSCLEROSIS
CEREBRAL ARTERIOVENOUS MALFORMATION HAEMORRHAGIC
CEREBRAL ARTERY EMBOLISM
CEREBRAL ARTERY OCCLUSION
CEREBRAL ARTERY PERFORATION
CEREBRAL ARTERY RESTENOSIS
CEREBRAL ARTERY STENOSIS
CEREBRAL ARTERY STENT INSERTION
CEREBRAL ARTERY THROMBOSIS
CEREBRAL CAVERNOUS MALFORMATION
CEREBRAL CYST HAEMORRHAGE

CEREBRAL ENDOVASCULAR ANEURYSM REPAIR
CEREBRAL GAS EMBOLISM
CEREBRAL HAEMATOMA
CEREBRAL HAEMORRHAGE
CEREBRAL HAEMORRHAGE FOETAL
CEREBRAL HAEMORRHAGE NEONATAL
CEREBRAL HAEMOSIDERIN DEPOSITION
CEREBRAL INFARCTION
CEREBRAL INFARCTION FOETAL
CEREBRAL ISCHAEMIA
CEREBRAL MICROEMBOLISM
CEREBRAL MICROHAEMORRHAGE
CEREBRAL MICROINFARCTION
CEREBRAL REPERFUSION INJURY
CEREBRAL REVASCULARISATION
CEREBRAL SEPTIC INFARCT
CEREBRAL SMALL VESSEL ISCHAEMIC DISEASE
CEREBRAL THROMBOSIS
CEREBRAL VASCULAR OCCLUSION
CEREBRAL VASOCONSTRICTION
CEREBRAL VENOUS THROMBOSIS
CEREBRAL VENTRICULAR RUPTURE
CEREBROVASCULAR ACCIDENT
CEREBROVASCULAR ACCIDENT PROPHYLAXIS
CEREBROVASCULAR DISORDER
CEREBROVASCULAR INSUFFICIENCY
CEREBROVASCULAR PSEUDOANEURYSM
CEREBROVASCULAR STENOSIS
CHARCOT-BOUCHARD MICROANEURYSMS
CLAUDE'S SYNDROME
CONGENITAL HEMIPARESIS
CORONARY ARTERY DISEASE
CORONARY ARTERY EMBOLISM
CORONARY ARTERY INSUFFICIENCY
CORONARY ARTERY OCCLUSION
CORONARY ARTERY REOCCLUSION
CORONARY ARTERY THROMBOSIS
CORONARY BYPASS THROMBOSIS
CORONARY VASCULAR GRAFT OCCLUSION
CORONARY VEIN STENOSIS
CSF BILIRUBIN POSITIVE

CSF RED BLOOD CELL COUNT POSITIVE
DELAYED ISCHAEMIC NEUROLOGICAL DEFICIT
DIPLEGIA
DYSARTHRIA
EMBOLIC CEREBELLAR INFARCTION
EMBOLIC CEREBRAL INFARCTION
EMBOLIC STROKE
EPIDURAL HAEMORRHAGE
EXTRA-AXIAL HAEMORRHAGE
EXTRADURAL HAEMATOMA
EXTRADURAL HAEMATOMA EVACUATION
EXTRAISCHAEMIC CEREBRAL HAEMATOMA
FOVILLE SYNDROME
HAEMORRHAGE INTRACRANIAL
HAEMORRHAGIC CEREBRAL INFARCTION
HAEMORRHAGIC STROKE
HAEMORRHAGIC TRANSFORMATION STROKE
HEMIANAESTHESIA
HEMIASOMATOGNOSIA
HEMIATAXIA
HEMIDYSAESTHESIA
HEMIHYPERAESTHESIA
HEMIPARAESTHESIA
HEMIPARESIS
HEMIPLEGIA
HUNT AND HESS SCALE
HYPOXIC-ISCHAEMIC ENCEPHALOPATHY
INNER EAR INFARCTION
INTERNAL CAPSULE INFARCTION
INTERNAL CAROTID ARTERY DEFORMITY
INTRA-CEREBRAL ANEURYSM OPERATION
INTRACEREBRAL HAEMATOMA EVACUATION
INTRACRANIAL ANEURYSM
INTRACRANIAL ARTERY DISSECTION
INTRACRANIAL HAEMATOMA
INTRACRANIAL TUMOUR HAEMORRHAGE
INTRAVENTRICULAR HAEMORRHAGE
INTRAVENTRICULAR HAEMORRHAGE NEONATAL
ISCHAEMIC CEREBRAL INFARCTION
ISCHAEMIC STROKE
KOUNIS SYNDROME

LACUNAR INFARCTION
LACUNAR STROKE
LATERAL MEDULLARY SYNDROME
LATEROPULSION
MENINGORRHAGIA
MIGRAINOUS INFARCTION
MILLARD-GUBLER SYNDROME
MODIFIED RANKIN SCORE DECREASED
MODIFIED RANKIN SCORE INCREASED
MONOPARESIS
MONOPLEGIA
MOYAMOYA DISEASE
MYOCARDIAL INFARCTION
MYOCARDIAL ISCHAEMIA
MYOCARDIAL NECROSIS
MYOCARDIAL REPERFUSION INJURY
MYOCARDIAL STUNNING
NIH STROKE SCALE ABNORMAL
NIH STROKE SCALE SCORE DECREASED
NIH STROKE SCALE SCORE INCREASED
PAPILLARY MUSCLE INFARCTION
PARALYSIS
PARAPARESIS
PARAPLEGIA
PARESIS
PERINATAL STROKE
PERIPROCEDURAL MYOCARDIAL INFARCTION
PERIVENTRICULAR HAEMORRHAGE NEONATAL
PITUITARY APOPLEXY
PITUITARY HAEMORRHAGE
POST CARDIAC ARREST SYNDROME
POST PROCEDURAL MYOCARDIAL INFARCTION
POST PROCEDURAL STROKE
POST STROKE DEPRESSION
POSTHAEMORRHAGIC HYDROCEPHALUS
POSTINFARCTION ANGINA
PRECEREBRAL ARTERIOSCLEROSIS
PRECEREBRAL ARTERY EMBOLISM
PRECEREBRAL ARTERY OCCLUSION
PRECEREBRAL ARTERY THROMBOSIS
PSEUDOSTROKE

PUTAMEN HAEMORRHAGE
QUADRIPARESIS
QUADRIPLEGIA
REVERSIBLE CEREBRAL VASOCONSTRICTION SYNDROME
REVERSIBLE ISCHAEMIC NEUROLOGICAL DEFICIT
RIGHT HEMISPHERE DEFICIT SYNDROME
RUPTURED CEREBRAL ANEURYSM
SILENT MYOCARDIAL INFARCTION
SPINAL ARTERY EMBOLISM
SPINAL ARTERY THROMBOSIS
SPINAL CORD HAEMATOMA
SPINAL CORD HAEMORRHAGE
SPINAL CORD INFARCTION
SPINAL CORD ISCHAEMIA
SPINAL EPIDURAL HAEMATOMA
SPINAL EPIDURAL HAEMORRHAGE
SPINAL STROKE
SPINAL SUBARACHNOID HAEMORRHAGE
SPINAL SUBDURAL HAEMATOMA
SPINAL SUBDURAL HAEMORRHAGE
STROKE IN EVOLUTION
SUBARACHNOID HAEMATOMA
SUBARACHNOID HAEMORRHAGE
SUBARACHNOID HAEMORRHAGE NEONATAL
SUBCLAVIAN STEAL SYNDROME
SUBDURAL HAEMATOMA
SUBDURAL HAEMATOMA EVACUATION
SUBDURAL HAEMORRHAGE
SUBDURAL HAEMORRHAGE NEONATAL
SUDDEN CARDIAC DEATH
SUDDEN DEATH
SUPERFICIAL SIDEROSIS OF CENTRAL NERVOUS SYSTEM
THALAMIC INFARCTION
THALAMUS HAEMORRHAGE
THROMBOTIC CEREBRAL INFARCTION
THROMBOTIC STROKE
TRANSIENT ISCHAEMIC ATTACK
TROPONIN I INCREASED
TROPONIN INCREASED
TROPONIN T INCREASED
VASCULAR ENCEPHALOPATHY

VASCULAR STENT OCCLUSION
VASCULAR STENT STENOSIS
VEIN OF GALEN ANEURYSMAL MALFORMATION
VERTEBRAL ARTERY ANEURYSM
VERTEBRAL ARTERY ARTERIOSCLEROSIS
VERTEBRAL ARTERY DISSECTION
VERTEBRAL ARTERY OCCLUSION
VERTEBRAL ARTERY PERFORATION
VERTEBRAL ARTERY STENOSIS
VERTEBRAL ARTERY THROMBOSIS
VERTEBROBASILAR INSUFFICIENCY
VERTEBROBASILAR STROKE
VISUAL AGNOSIA
VISUAL MIDLINE SHIFT SYNDROME
WEBER'S SYNDROME

1.8 Medication errors

Cases with events of medication errors are retrieved from the safety database for analysis if they contain an event PT within the 'Medication errors' SMQ (narrow scope), i.e., any of the following MedDRA PTs:

ACCIDENTAL DEVICE INGESTION
ACCIDENTAL DEVICE INGESTION BY A CHILD
ACCIDENTAL EXPOSURE TO PRODUCT
ACCIDENTAL EXPOSURE TO PRODUCT BY CHILD
ACCIDENTAL EXPOSURE TO PRODUCT PACKAGING
ACCIDENTAL EXPOSURE TO PRODUCT PACKAGING BY CHILD
ACCIDENTAL OVERDOSE
ACCIDENTAL POISONING
ACCIDENTAL UNDERDOSE
ACCIDENTAL USE OF PLACEBO
BOOSTER DOSE MISSED
CIRCUMSTANCE OR INFORMATION CAPABLE OF LEADING TO DEVICE USE ERROR
CIRCUMSTANCE OR INFORMATION CAPABLE OF LEADING TO MEDICATION ERROR
CONTRAINDICATED DEVICE USED
CONTRAINDICATED PRODUCT ADMINISTERED
CONTRAINDICATED PRODUCT PRESCRIBED
DEPRESCRIBING ERROR
DEVICE DISPENSING ERROR
DEVICE MONITORING PROCEDURE NOT PERFORMED
DEVICE PROGRAMMING ERROR
DEVICE USE CONFUSION

DEVICE USE ERROR
DISCONTINUED PRODUCT ADMINISTERED
DOCUMENTED HYPERSENSITIVITY TO ADMINISTERED PRODUCT
DOSE CALCULATION ERROR
DRUG ADMINISTERED IN WRONG DEVICE
DRUG DISPENSED TO WRONG PATIENT
DRUG DOSE OMISSION BY DEVICE
DRUG DOSE TITRATION NOT PERFORMED
DRUG MONITORING PROCEDURE INCORRECTLY PERFORMED
DRUG MONITORING PROCEDURE NOT PERFORMED
DRUG TITRATION ERROR
DUPLICATE THERAPY ERROR
EXPIRED DEVICE USED
EXPIRED PRODUCT ADMINISTERED
EXPOSURE VIA DIRECT CONTACT
EXPOSURE VIA EYE CONTACT
EXPOSURE VIA SKIN CONTACT
EXTRA DOSE ADMINISTERED
FAILURE OF CHILD RESISTANT PRODUCT CLOSURE
FAILURE TO SUSPEND MEDICATION
INADEQUATE ASEPTIC TECHNIQUE IN USE OF PRODUCT
INAPPROPRIATE SCHEDULE OF PRODUCT ADMINISTRATION
INAPPROPRIATE SCHEDULE OF PRODUCT DISCONTINUATION
INCOMPLETE COURSE OF VACCINATION
INCORRECT DISPOSAL OF PRODUCT
INCORRECT DOSAGE ADMINISTERED
INCORRECT DOSE ADMINISTERED
INCORRECT DOSE ADMINISTERED BY DEVICE
INCORRECT DOSE ADMINISTERED BY PRODUCT
INCORRECT DRUG ADMINISTRATION RATE
INCORRECT PRODUCT ADMINISTRATION DURATION
INCORRECT PRODUCT DOSAGE FORM ADMINISTERED
INCORRECT PRODUCT FORMULATION ADMINISTERED
INCORRECT ROUTE OF PRODUCT ADMINISTRATION
INTERCEPTED ACCIDENTAL EXPOSURE TO PRODUCT BY CHILD
INTERCEPTED MEDICATION ERROR
INTERCEPTED PRODUCT ADMINISTRATION ERROR
INTERCEPTED PRODUCT DISPENSING ERROR
INTERCEPTED PRODUCT MONITORING ERROR
INTERCEPTED PRODUCT PREPARATION ERROR
INTERCEPTED PRODUCT PRESCRIBING ERROR

INTERCEPTED PRODUCT SELECTION ERROR
INTERCEPTED PRODUCT STORAGE ERROR
INTERCEPTED WRONG PATIENT SELECTED
LABELLED DRUG-DISEASE INTERACTION MEDICATION ERROR
LABELLED DRUG-DRUG INTERACTION MEDICATION ERROR
LABELLED DRUG-FOOD INTERACTION MEDICATION ERROR
LACK OF ADMINISTRATION SITE ROTATION
LACK OF APPLICATION SITE ROTATION
LACK OF INFUSION SITE ROTATION
LACK OF INJECTION SITE ROTATION
LACK OF VACCINATION SITE ROTATION
MEDICAL DEVICE MONITORING ERROR
MEDICATION ERROR
MULTIPLE USE OF SINGLE-USE PRODUCT
PARAVENOUS DRUG ADMINISTRATION
PRODUCT ADMINISTERED AT INAPPROPRIATE SITE
PRODUCT ADMINISTERED BY WRONG PERSON
PRODUCT ADMINISTERED TO PATIENT OF INAPPROPRIATE AGE
PRODUCT ADMINISTRATION ERROR
PRODUCT APPEARANCE CONFUSION
PRODUCT BARCODE ISSUE
PRODUCT CONFUSION
PRODUCT DESIGN CONFUSION
PRODUCT DISPENSING ERROR
PRODUCT DOSAGE FORM CONFUSION
PRODUCT DOSE OMISSION IN ERROR
PRODUCT LABEL CONFUSION
PRODUCT MONITORING ERROR
PRODUCT NAME CONFUSION
PRODUCT PACKAGING CONFUSION
PRODUCT PREPARATION ERROR
PRODUCT PRESCRIBING ERROR
PRODUCT SELECTION ERROR
PRODUCT STORAGE ERROR
PRODUCT SUBSTITUTION ERROR
RECALLED PRODUCT ADMINISTERED
SINGLE COMPONENT OF A TWO-COMPONENT PRODUCT ADMINISTERED
THERAPEUTIC DRUG MONITORING ANALYSIS INCORRECTLY PERFORMED
THERAPEUTIC DRUG MONITORING ANALYSIS NOT PERFORMED
TRANSCRIPTION MEDICATION ERROR
TRANSFUSION WITH INCOMPATIBLE BLOOD

UNINTENTIONAL USE FOR UNAPPROVED INDICATION
VACCINATION ERROR
WRONG DEVICE USED
WRONG DOSAGE FORM
WRONG DOSAGE FORMULATION
WRONG DOSE
WRONG DRUG
WRONG PATIENT
WRONG PATIENT RECEIVED PRODUCT
WRONG PRODUCT ADMINISTERED
WRONG PRODUCT PROCURED
WRONG PRODUCT STORED
WRONG RATE
WRONG ROUTE
WRONG SCHEDULE
WRONG STRENGTH
WRONG TECHNIQUE IN DEVICE USAGE PROCESS
WRONG TECHNIQUE IN PRODUCT USAGE PROCESS

1.9 Ophthalmological effects associated with retinal vascular system

Cases describing ophthalmological effects associated with the retinal vascular system are retrieved from the safety database for analysis if they contain an event PT within the 'Retinal disorders' SMQ (broad scope), i.e., any of the following MedDRA PTs:

ACQUIRED PIGMENTED RETINOPATHY
ACUTE MACULAR OUTER RETINOPATHY
ACUTE ZONAL OCCULT OUTER RETINOPATHY
AGE-RELATED MACULAR DEGENERATION
AIDS RETINOPATHY
AMAUROSIS FUGAX
ANGIOGRAM RETINA ABNORMAL
ARTERIOSCLEROTIC RETINOPATHY
AUTOIMMUNE EYE DISORDER
AUTOIMMUNE RETINOPATHY
BENIGN NEOPLASM OF RETINA
BIOPSY RETINA ABNORMAL
BIRDSHOT CHORIORETINOPATHY
BLINDNESS
BLINDNESS TRANSIENT
BLINDNESS UNILATERAL
CENTRAL VISION LOSS
CHOLESTEROLOSIS BULBI

CHORIORETINAL ATROPHY
CHORIORETINAL DISORDER
CHORIORETINAL SCAR
CHORIORETINITIS
CHORIORETINOPATHY
CHOROIDAL OSTEOMA
CHROMATOPSIA
CILIARY BODY MELANOMA
COLOUR BLINDNESS
COLOUR BLINDNESS ACQUIRED
COLOUR VISION TESTS ABNORMAL
COLOUR VISION TESTS ABNORMAL BLUE-YELLOW
COLOUR VISION TESTS ABNORMAL RED-GREEN
COMMOTIO RETINAE
CYSTOID MACULAR OEDEMA
DELAYED LIGHT ADAPTATION
DETACHMENT OF MACULAR RETINAL PIGMENT EPITHELIUM
DETACHMENT OF RETINAL PIGMENT EPITHELIUM
DIABETIC RETINAL OEDEMA
DIABETIC RETINOPATHY
DIFFUSE UVEAL MELANOCYTIC PROLIFERATION
DISRUPTION OF THE PHOTORECEPTOR INNER SEGMENT-OUTER SEGMENT
DRY AGE-RELATED MACULAR DEGENERATION
DYSCHROMATOPSIA
EXTRAOCULAR RETINOBLASTOMA
EXUDATIVE RETINOPATHY
EYE DISORDER
EYE HAEMATOMA
EYE HAEMORRHAGE
EYE INFARCTION
EYE NAEVUS
EYE OPACITY
FLUORESCENCE ANGIOGRAM ABNORMAL
FOVEAL DEGENERATION
FOVEAL REFLEX ABNORMAL
FUNDOSCOPY ABNORMAL
HAEMORRHAGIC OCCLUSIVE RETINAL VASCULITIS
HYPERAESTHESIA EYE
HYPERTENSIVE CEREBROVASCULAR DISEASE
HYPOTONY MACULOPATHY
IMMUNE RECOVERY UVEITIS

IMMUNE-MEDIATED UVEITIS
INTERNAL LIMITING MEMBRANE PEELING
INTRA-OCULAR INJECTION COMPLICATION
INTRAOCULAR HAEMATOMA
INTRAVITREAL IMPLANT
IRVAN SYNDROME
LEUKAEMIC RETINOPATHY
LEUKOCORIA
LIPAEMIA RETINALIS
LOW LUMINANCE BEST-CORRECTED VISUAL ACUITY DECREASED
MACULAR CYST
MACULAR DEGENERATION
MACULAR DETACHMENT
MACULAR FIBROSIS
MACULAR HOLE
MACULAR ISCHAEMIA
MACULAR OEDEMA
MACULAR OPACITY
MACULAR PIGMENTATION
MACULAR PSEUDOHOLE
MACULAR REFLEX ABNORMAL
MACULAR RUPTURE
MACULAR SCAR
MACULAR TELANGIECTASIA
MACULAR THICKENING
MACULOPATHY
MALIGNANT NEOPLASM OF RETINA
METAMORPHOPSIA
MYOPIC CHORIORETINAL DEGENERATION
MYOPIC TRACTION MACULOPATHY
NECROTISING RETINITIS
NEOVASCULAR AGE-RELATED MACULAR DEGENERATION
NEUROPATHY, ATAXIA, RETINITIS PIGMENTOSA SYNDROME
NON-PROLIFERATIVE RETINOPATHY
NONINFECTIVE CHORIORETINITIS
NONINFECTIVE RETINITIS
OCULAR ISCHAEMIC SYNDROME
OCULAR LYMPHOMA
OCULAR STEM CELL TRANSPLANT
OPHTHALMIC ARTERY THROMBOSIS
OPHTHALMIC VEIN THROMBOSIS

OPTIC DISC TRACTION SYNDROME
OPTICAL COHERENCE TOMOGRAPHY ABNORMAL
ORBITAL HAEMATOMA
ORBITAL HAEMORRHAGE
PARANEOPLASTIC RETINOPATHY
PARS PLANA CYST
PATHOLOGIC MYOPIA
PERIPAPILLARY PIGMENTATION
PHOTOPHOBIA
PHOTOPSIA
POST THROMBOTIC RETINOPATHY
PUPILLARY LIGHT REFLEX TESTS ABNORMAL
PURTSCHER RETINOPATHY
RADIATION RETINOPATHY
RED REFLEX ABNORMAL
RETINAL ANEURYSM
RETINAL ANEURYSM RUPTURE
RETINAL ARTERIOVENOUS MALFORMATION
RETINAL ARTERY EMBOLISM
RETINAL ARTERY OCCLUSION
RETINAL ARTERY SPASM
RETINAL ARTERY STENOSIS
RETINAL ARTERY THROMBOSIS
RETINAL COLLATERAL VESSELS
RETINAL COLOBOMA
RETINAL CRYOABLATION
RETINAL CYST
RETINAL CYST EXCISION
RETINAL DEGENERATION
RETINAL DEPIGMENTATION
RETINAL DEPOSITS
RETINAL DETACHMENT
RETINAL DISORDER
RETINAL DRUSEN
RETINAL DYSTROPHY
RETINAL EXUDATES
RETINAL FIBROSIS
RETINAL FOVEA DISORDER
RETINAL FUNCTION TEST ABNORMAL
RETINAL HAEMORRHAGE
RETINAL IMPLANT

RETINAL INFARCTION
RETINAL INFILTRATES
RETINAL INJURY
RETINAL ISCHAEMIA
RETINAL LASER COAGULATION
RETINAL MELANOCYTOMA
RETINAL MELANOMA
RETINAL MIGRAINE
RETINAL NEOPLASM
RETINAL NEOVASCULARISATION
RETINAL OCCLUSIVE VASCULITIS
RETINAL OEDEMA
RETINAL OPERATION
RETINAL PALLOR
RETINAL PERIVASCULAR SHEATHING
RETINAL PHOTOTOXICITY
RETINAL PIGMENT EPITHELIAL TEAR
RETINAL PIGMENT EPITHELIOPATHY
RETINAL PIGMENTATION
RETINAL SCAR
RETINAL TEAR
RETINAL TELANGIECTASIA
RETINAL THICKENING
RETINAL TOXICITY
RETINAL TRANSPLANT
RETINAL TUMOUR EXCISION
RETINAL VASCULAR DISORDER
RETINAL VASCULAR OCCLUSION
RETINAL VASCULAR THROMBOSIS
RETINAL VASCULITIS
RETINAL VEIN OCCLUSION
RETINAL VEIN THROMBOSIS
RETINAL VEIN VARICES
RETINAL VESSEL AVULSION
RETINAL WHITE WITHOUT PRESSURE
RETINITIS
RETINITIS PIGMENTOSA
RETINOBLASTOMA
RETINOGRAM ABNORMAL
RETINOPATHY
RETINOPATHY HAEMORRHAGIC

RETINOPATHY HYPERTENSIVE
RETINOPATHY HYPERVISCOSITY
RETINOPATHY OF PREMATURITY
RETINOPATHY PROLIFERATIVE
RETINOPATHY SICKLE CELL
RETINOPATHY SOLAR
RETINOPEXY
RETINOSCHISIS
RHEGMATOGENOUS RETINAL DETACHMENT
SCINTILLATING SCOTOMA
SCLERAL BUCKLING SURGERY
SCLEROTOMY
SEROUS RETINAL DETACHMENT
SEROUS RETINOPATHY
SERPIGINOUS CHOROIDITIS
SUBRETINAL FIBROSIS
SUBRETINAL FLUID
SUBRETINAL HAEMATOMA
SUBRETINAL HYPERREFLECTIVE EXUDATION
SUSAC'S SYNDROME
TESSELLATED FUNDUS
TRACTIONAL RETINAL DETACHMENT
TRANSPUPILLARY THERMOTHERAPY
TUNNEL VISION
UVEAL MELANOMA
VASCULAR ENDOTHELIAL GROWTH FACTOR OVEREXPRESSION
VENOUS STASIS RETINOPATHY
VISION BLURRED
VISUAL ACUITY REDUCED
VISUAL ACUITY TESTS ABNORMAL
VISUAL FIELD DEFECT
VISUAL FIELD TESTS ABNORMAL
VISUAL IMPAIRMENT
VITREAL CELLS
VITRECTOMY
VITREOMACULAR INTERFACE ABNORMAL
VITREORETINAL TRACTION SYNDROME
VITREOUS ADHESIONS
VITREOUS DETACHMENT
VITREOUS DISORDER
VITREOUS FLOATERS

VITREOUS HAEMATOMA
VITREOUS HAEMORRHAGE
VITREOUS HAZE
VITRITIS
VOGT-KOYANAGI-HARADA DISEASE
XANTHOPSIA

1.10 Pregnancy

Cases referring to pregnancy are retrieved from the safety database for analysis if they meet any of the following conditions:

The case contains an event with a primary MedDRA System Organ Class containing the text: 'pregnancy' (but excluding the MedDRA PTs: 'Pregnancy test urine negative', 'Pregnancy test negative', or 'Pregnancy test false positive'),

OR

It contains an event with a MedDRA primary HLT or PT containing the following text: 'abortion', or 'pregnancy' (but excluding the PT 'Woman of childbearing potential').

OR

It contains an event with any of the following MedDRA PTs: 'Maternal drugs affecting foetus', 'Miscarriage of partner', or 'Paternal drugs affecting foetus', i.e., any of the following MedDRA PTs:

ABNORMAL CORD INSERTION
ABNORMAL LABOUR
ABNORMAL LABOUR AFFECTING FOETUS
ABNORMAL PRODUCT OF CONCEPTION
ABORTED PREGNANCY
ABORTION
ABORTION COMPLETE
ABORTION COMPLETE COMPLICATED
ABORTION COMPLICATED
ABORTION EARLY
ABORTION INCOMPLETE
ABORTION INCOMPLETE COMPLICATED
ABORTION INDUCED
ABORTION INDUCED COMPLETE
ABORTION INDUCED COMPLETE COMPLICATED
ABORTION INDUCED COMPLICATED
ABORTION INDUCED INCOMPLETE
ABORTION INDUCED INCOMPLETE COMPLICATED
ABORTION INFECTED
ABORTION LATE
ABORTION MISSED

ABORTION OF ECTOPIC PREGNANCY
ABORTION SPONTANEOUS
ABORTION SPONTANEOUS COMPLETE
ABORTION SPONTANEOUS COMPLETE COMPLICATED
ABORTION SPONTANEOUS COMPLICATED
ABORTION SPONTANEOUS INCOMPLETE
ABORTION SPONTANEOUS INCOMPLETE COMPLICATED
ABORTION THREATENED
ACUTE FATTY LIVER OF PREGNANCY
ADRENOCORTICAL INSUFFICIENCY NEONATAL
AFTERBIRTH PAIN
AMNIORRHEXIS
AMNIORRHOEA
AMNIOTIC CAVITY DISORDER
ANAEMIA OF PREGNANCY
ANAESTHETIC COMPLICATION NEONATAL
ANAPHYLACTOID SYNDROME OF PREGNANCY
ANEMBRYONIC GESTATION
ARRESTED LABOUR
ASYNCLITIC PRESENTATION
BACTERIURIA IN PREGNANCY
BIOCHEMICAL PREGNANCY
BIRTH TRAUMA
BIRTH WEIGHT NORMAL
BOTTLE FEEDING
BREAST ENGORGEMENT IN NEWBORN
BREAST FEEDING
BREECH DELIVERY
BREECH PRESENTATION
BROW PRESENTATION
CAPUT SUCCEDANEUM
CEPHALHAEMATOMA
CEPHALO-PELVIC DISPROPORTION
CERVICAL DILATATION
CERVICAL INCOMPETENCE
CERVIX DYSTOCIA
CHILD BORN TO UNMARRIED PARENTS
CHOLESTASIS OF PREGNANCY
CHORIOAMNIOTIC SEPARATION
CHRONIC VILLITIS OF UNKNOWN ETIOLOGY
COMPLICATION OF DELIVERY

COMPLICATION OF PREGNANCY
CRANIAL NERVE INJURY SECONDARY TO BIRTH TRAUMA
DECIDUAL CAST
DELAYED DELIVERY
DELIVERY
DELIVERY OUTSIDE HEALTH FACILITY
DIABETES COMPLICATING PREGNANCY
DISCORDANT TWIN
DRUG EXPOSURE BEFORE PREGNANCY
ECLAMPSIA
ECTOPIC PREGNANCY
ECTOPIC PREGNANCY TERMINATION
ECTOPIC PREGNANCY UNDER HORMONAL CONTRACEPTION
ECTOPIC PREGNANCY WITH CONTRACEPTIVE DEVICE
ELDERLY PRIMIGRAVIDA
EXPOSURE DURING PREGNANCY
EXPOSURE VIA BREAST MILK
EXPOSURE VIA FATHER
FACE PRESENTATION
FACIAL NERVE INJURY DUE TO BIRTH TRAUMA
FAILED INDUCTION OF LABOUR
FAILED TRIAL OF LABOUR
FALSE LABOUR
FALSE NEGATIVE PREGNANCY TEST
FEAR OF PREGNANCY
FIRST TRIMESTER PREGNANCY
FOETAL ACIDOSIS
FOETAL ARM PROLAPSE
FOETAL CARDIAC DISORDER
FOETAL COMPARTMENT FLUID COLLECTION
FOETAL DAMAGE
FOETAL DEATH
FOETAL DISORDER
FOETAL DISTRESS SYNDROME
FOETAL DYSTOCIA
FOETAL EXPOSURE DURING DELIVERY
FOETAL EXPOSURE DURING PREGNANCY
FOETAL EXPOSURE TIMING UNSPECIFIED
FOETAL GROWTH ABNORMALITY
FOETAL GROWTH RESTRICTION
FOETAL HYPOKINESIA

FOETAL MACROSOMIA
FOETAL MALNUTRITION
FOETAL MALPOSITION
FOETAL MALPRESENTATION
FOETAL PLACENTAL THROMBOSIS
FOETAL-MATERNAL HAEMORRHAGE
GESTATIONAL DIABETES
GESTATIONAL HYPERTENSION
GESTATIONAL OEDEMA
GESTATIONAL TROPHOBLASTIC DETACHMENT
GLUCOSE TOLERANCE IMPAIRED IN PREGNANCY
GLYCOSURIA DURING PREGNANCY
HABITUAL ABORTION
HAEMORRHAGE FOETAL
HAEMORRHAGE IN PREGNANCY
HELLP SYNDROME
HETEROTOPIC PREGNANCY
HIGH FOETAL HEAD
HIGH RISK PREGNANCY
HYDROPS FOETALIS
HYPEREMESIS GRAVIDARUM
HYPOTHERMIA NEONATAL
IMMINENT ABORTION
INCOORDINATE UTERINE ACTION
INDETERMINATE PREGNANCY TEST RESULT
INDUCED ABORTION FAILED
INDUCED ABORTION HAEMORRHAGE
INDUCED ABORTION INFECTION
INDUCED LABOUR
INJURY TO SPINAL CORD SECONDARY TO BIRTH TRAUMA
INTRAPARTUM HAEMORRHAGE
JAUNDICE NEONATAL
LABOUR COMPLICATION
LABOUR PAIN
LACK OF PRENATAL CARE
LACTATION NORMAL
LARGE FOR DATES BABY
LEUKOPENIA NEONATAL
LITHOPEDION
LIVE BIRTH
LOCKED TWINS

LOW BIRTH WEIGHT BABY
MATERNAL CANCER IN PREGNANCY
MATERNAL CONDITION AFFECTING FOETUS
MATERNAL DEATH AFFECTING FOETUS
MATERNAL DEATH DURING CHILDBIRTH
MATERNAL DISTRESS DURING LABOUR
MATERNAL DRUGS AFFECTING FOETUS
MATERNAL EXPOSURE BEFORE PREGNANCY
MATERNAL EXPOSURE DURING BREAST FEEDING
MATERNAL EXPOSURE DURING DELIVERY
MATERNAL EXPOSURE DURING PREGNANCY
MATERNAL EXPOSURE TIMING UNSPECIFIED
MATERNAL EXPOSURE VIA PARTNER DURING PREGNANCY
MECONIUM ABNORMAL
MECONIUM IN AMNIOTIC FLUID
MECONIUM INCREASED
MECONIUM STAIN
MIRROR SYNDROME
MISCARRIAGE OF PARTNER
MISSED LABOUR
MOLAR ABORTION
MORNING SICKNESS
MULTIGRAVIDA
MULTIPAROUS
MULTIPLE PREGNANCY
NEONATAL DISORDER
NEONATAL THYROTOXICOSIS
NORMAL FOETUS
NORMAL LABOUR
NORMAL NEWBORN
NULLI GRAVIDA
NULLIPAROUS
OBLIQUE PRESENTATION
OBSTRUCTED LABOUR
OLIGOHYDRAMNIOS
OMPHALORRHEXIS
PARITY
PATERNAL DRUGS AFFECTING FOETUS
PATERNAL EXPOSURE BEFORE PREGNANCY
PATERNAL EXPOSURE DURING PREGNANCY
PATERNAL EXPOSURE TIMING UNSPECIFIED

PELVIC GIRDLE PAIN
PELVIC HAEMATOMA OBSTETRIC
PERINATAL BRAIN DAMAGE
PERINEAL REPAIR BREAKDOWN
PERIPARTUM CARDIOMYOPATHY
PERIPARTUM HAEMORRHAGE
PLACENTA ACCRETA
PLACENTA DUPLEX
PLACENTA PRAEVIA
PLACENTA PRAEVIA HAEMORRHAGE
PLACENTAL CALCIFICATION
PLACENTAL CYST
PLACENTAL DISORDER
PLACENTAL DYSPLASIA
PLACENTAL HYPERTROPHY
PLACENTAL INFARCTION
PLACENTAL INSUFFICIENCY
PLACENTAL LAKE
PLACENTAL NECROSIS
PLACENTAL POLYP
PLANNING TO BECOME INFERTILE
PLANNING TO BECOME PREGNANT
POLYHYDRAMNIOS
POLYMORPHIC ERUPTION OF PREGNANCY
POOR WEIGHT GAIN NEONATAL
POST ABORTION COMPLICATION
POST ABORTION HAEMORRHAGE
POST ABORTION INFECTION
POSTMATURE BABY
POSTNATAL GROWTH RESTRICTION
POSTPARTUM DISORDER
POSTPARTUM HAEMORRHAGE
POSTPARTUM STATE
POSTPARTUM UTERINE SUBINVOLUTION
PRE-ECLAMPSIA
PRECIPITATE LABOUR
PREGNANCY
PREGNANCY AFTER POST COITAL CONTRACEPTION
PREGNANCY IN HABITUAL ABORTER
PREGNANCY OF PARTNER
PREGNANCY OF UNKNOWN LOCATION

PREGNANCY ON CONTRACEPTIVE
PREGNANCY ON ORAL CONTRACEPTIVE
PREGNANCY TEST
PREGNANCY TEST POSITIVE
PREGNANCY TEST URINE
PREGNANCY TEST URINE POSITIVE
PREGNANCY WITH ADVANCED MATERNAL AGE
PREGNANCY WITH CONTRACEPTIVE DEVICE
PREGNANCY WITH CONTRACEPTIVE PATCH
PREGNANCY WITH IMPLANT CONTRACEPTIVE
PREGNANCY WITH INJECTABLE CONTRACEPTIVE
PREGNANCY WITH YOUNG MATERNAL AGE
PREMATURE BABY
PREMATURE DELIVERY
PREMATURE LABOUR
PREMATURE RUPTURE OF MEMBRANES
PREMATURE SEPARATION OF PLACENTA
PRETERM PREMATURE RUPTURE OF MEMBRANES
PREVIOUS CAESAREAN SECTION
PRIMIGRAVIDA
PRIMIPAROUS
PROLONGED LABOUR
PROLONGED PREGNANCY
PROLONGED RUPTURE OF MEMBRANES
PROPHYLAXIS OF ABORTION
PSEUDOMENSTRUATION NEONATAL
RENAL DISORDER IN PREGNANCY
RETAINED PLACENTA OR MEMBRANES
RETAINED PRODUCTS OF CONCEPTION
RETROPLACENTAL HAEMATOMA
RISK OF FUTURE PREGNANCY MISCARRIAGE
RUBELLA IN PREGNANCY
RUPTURED ECTOPIC PREGNANCY
SECOND TRIMESTER PREGNANCY
SELECTIVE ABORTION
SHORT INTERPREGNANCY INTERVAL
SHOULDER DYSTOCIA
SMALL FOR DATES BABY
SMALL SIZE PLACENTA
SOMATIC SYMPTOM DISORDER OF PREGNANCY
STILLBIRTH

SUBCHORIONIC HAEMATOMA
SUBCHORIONIC HAEMORRHAGE
SUPERIMPOSED PRE-ECLAMPSIA
TERM BABY
TERM BIRTH
THIRD STAGE POSTPARTUM HAEMORRHAGE
THIRD TRIMESTER PREGNANCY
THREATENED LABOUR
THYROID DYSFUNCTION IN PREGNANCY
TRANSVERSE PRESENTATION
TRAUMATIC DELIVERY
TUBAL RUPTURE
TWIN PREGNANCY
UMBILICAL CORD ABNORMALITY
UMBILICAL CORD AROUND NECK
UMBILICAL CORD COMPRESSION
UMBILICAL CORD CYST
UMBILICAL CORD HAEMORRHAGE
UMBILICAL CORD OCCLUSION
UMBILICAL CORD PROLAPSE
UMBILICAL CORD SHORT
UMBILICAL CORD THROMBOSIS
UMBILICAL CORD VASCULAR DISORDER
UMBILICAL GRANULOMA
UNINTENDED PREGNANCY
UNSTABLE FOETAL LIE
UNWANTED PREGNANCY
UTERINE ATONY
UTERINE CONTRACTIONS ABNORMAL
UTERINE CONTRACTIONS DURING PREGNANCY
UTERINE HYPERSTIMULATION
UTERINE HYPERTONUS
UTERINE HYPOKINESIA
UTERINE HYPOTONUS
UTERINE INVERSION
UTERINE IRRITABILITY
UTERINE TACHYSYSTOLE
VANISHING TWIN SYNDROME
VASA PRAEVIA
VENOUS THROMBOSIS IN PREGNANCY
WEIGHT DECREASE NEONATAL

1.11 Pulmonary venoocclusive disease associated with pulmonary oedema

The case will be included in this subgroup if it contains an event with the following MedDRA Preferred Term:

ACUTE LUNG INJURY
ACUTE PULMONARY OEDEMA
ACUTE RESPIRATORY DISTRESS SYNDROME
NEGATIVE PRESSURE PULMONARY OEDEMA
NON-CARDIOGENIC PULMONARY OEDEMA
PULMONARY CONGESTION
PULMONARY OEDEMA
PULMONARY OEDEMA NEONATAL
REEXPANSION PULMONARY OEDEMA

1.12 Renal function impairment / acute renal failure

Cases including events denoting renal function impairment / acute renal failure are retrieved from the safety database for analysis if they contain an event PT within the MedDRA SMQ 'Acute renal failure' (narrow scope) or it contains an event with any of the following MedDRA PTs: 'Blood creatinine abnormal', 'Blood creatinine increased', 'Creatinine renal clearance abnormal', 'Creatinine renal clearance decreased', 'Glomerular filtration rate abnormal', 'Glomerular filtration rate decreased', 'Renal function test abnormal', 'Renal transplant', 'Renal tubular injury', 'Renal tubular necrosis', and 'Urine output decreased', i.e., any of the following MedDRA PTs:

ACUTE KIDNEY INJURY
ACUTE PHOSPHATE NEPHROPATHY
ANURIA
AZOTAEMIA
BLOOD CREATININE ABNORMAL
BLOOD CREATININE INCREASED
CONTINUOUS HAEMODIAFILTRATION
CREATININE RENAL CLEARANCE ABNORMAL
CREATININE RENAL CLEARANCE DECREASED
DIALYSIS
FOETAL RENAL IMPAIRMENT
GLOMERULAR FILTRATION RATE ABNORMAL
GLOMERULAR FILTRATION RATE DECREASED
HAEMODIALYSIS
HAEMOFILTRATION
NEONATAL ANURIA
NEPHROPATHY TOXIC
OLIGURIA
PERITONEAL DIALYSIS
PRERENAL FAILURE
RENAL FAILURE

RENAL FAILURE NEONATAL
RENAL FUNCTION TEST ABNORMAL
RENAL IMPAIRMENT
RENAL IMPAIRMENT NEONATAL
RENAL TRANSPLANT
RENAL TUBULAR INJURY
RENAL TUBULAR NECROSIS
SUBACUTE KIDNEY INJURY
URINE OUTPUT DECREASED

1.13 Prostacyclin associated reactions

ARTHRALGIA
DIARRHOEA
DIZZINESS
FLUSHING
HEADACHE
MUSCULOSKELETAL PAIN
MYALGIA
NAUSEA
PAIN IN EXTREMITY
PAIN IN JAW
TEMPOROMANDIBULAR JOINT SYNDROME
VOMITING

1.14 COVID-19 Infection

ASYMPTOMATIC COVID-19
CONGENITAL COVID-19
CORONAVIRUS INFECTION
CORONAVIRUS TEST POSITIVE
COVID-19
COVID-19 IMMUNISATION
COVID-19 PNEUMONIA
COVID-19 PROPHYLAXIS
COVID-19 TREATMENT
EXPOSURE TO SARS-COV-2
MULTISYSTEM INFLAMMATORY SYNDROME IN CHILDREN
OCCUPATIONAL EXPOSURE TO SARS-COV-2
POST-ACUTE COVID-19 SYNDROME
SARS-COV-2 ANTIBODY TEST POSITIVE
SARS-COV-2 CARRIER
SARS-COV-2 RNA DECREASED
SARS-COV-2 RNA FLUCTUATION

SARS-COV-2 RNA INCREASED
SARS-COV-2 SEPSIS
SARS-COV-2 TEST FALSE NEGATIVE
SARS-COV-2 TEST POSITIVE
SARS-COV-2 VIRAEMIA
SUSPECTED COVID-19
VACCINE DERIVED SARS-COV-2 INFECTION