STATISTICAL ANALYSIS PLAN

An Open-Label Safety Study of USL261 in the Outpatient Treatment of Subjects with Seizure Clusters

Protocol Number P261-402

Upsher-Smith Laboratories, Inc.
6701 Evenstad Drive
Maple Grove, MN 55369

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CONFIDENTIAL

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TABLE OF CONTENTS

LIST OF ABBREVIATIONS

Abbreviation	Definition
µL	Microliter
AE	Adverse event
AED	Antiepileptic Drugs
ATC	Anatomic Therapeutic Chemical
B-SIT	Brief Smell Identification Test
C-SSRS	Columbia-Suicide Severity Rating Scale
CI	Confidence interval
CRO	Contract Research Organization
DSMB	Data and Safety Monitoring Board
EMS	Emergency Medical Services
ER	Emergency Room
ET	Early Termination
IN	Intranasal
IRT	Interactive Response Technology
ITI	Intranasal Therapeutics, Inc.
ITIQ	Intranasal Therapy Impact Questionnaire
IV	Intravenous
LAR	Legally acceptable representative
MCS	Mental Health Component Score (SF-12v2)
Mg	Milligram
MedDRA	Medical Dictionary for Regulatory Activities
PCI	Potentially clinically important
PCS	Potentially clinically significant
PHCS	Physical Health Component Score (SF-12v2)
PK	Pharmacokinetic
PMP	Patient Management Plan
PT	Preferred Term in MedDRA
SF-12v2	SF-12v2 Health Survey
SAS	Statistical Analysis Software
SD	Standard deviation
USL	Upsher-Smith Laboratories, Inc.
USL261	Intranasal midazolam, study drug (formerly ITI-111)
SOC	System Organ Class in MedDRA
TEAE	Treatment-emergent adverse event
TSQM	Treatment Satisfaction Questionnaire for Medication
VNS	Vagus Nerve Stimulator
WHO	World Health Organization

1. INTRODUCTION

Acute repetitive seizures and seizure clusters occur in a subset of epilepsy patients. Seizure clusters have distinguishable characteristics that are easily recognized by patients, caregivers, and physicians and include a consistent onset (auras, prodrome) that may be indicative of convulsive or non-convulsive symptoms. Although patients typically recover between seizures, these seizure can last anywhere from minutes to hours.[1] When a cluster of seizures occurs outside a hospital, the patient must often be transported to an acute care facility so medical personnel can administer intravenous (IV) therapy to stop the seizure(s).[2]

The primary goals of seizure cluster treatment are seizure cessation and prevention of seizure recurrence.[1] Acute benzodiazepine treatment is effective for seizure control and often results in rapid seizure cluster termination; however, most treatment options rely on intervention by emergency medical personnel and therefore delay treatment while the patient is transported to a medical facility.[3] The development of an easily administered outpatient treatment of seizure clusters may reduce the need for emergency medical intervention and decrease seizure cluster duration.

This statistical analysis plan covers the detailed procedures for performing statistical analyses and producing tables, listings, and figures in the Phase III study described in Upsher-Smith Laboratories, Inc. Protocol P261-402 (Fifth Issue, Amendment 4, 20 May 2015).

2. STUDY DESIGN

2.1. General Study Design and Plan

This is an open-label, multicenter, safety extension study of USL261 in subjects with seizure clusters who have completed study P261-401. However if study P261-401 is terminated, subjects who have completed the Test Dose Visit (Visit 2) of study P261-401 will also be eligible to enter this study (P261-402). Each seizure cluster episode will be treated with a single dose of 5.0 mg USL261. A second dose of 5.0 mg USL261 may be given if the seizure cluster has not terminated within 10 minutes after initial study drug administration or if another seizure occurs between 10 minutes and 6 hours after administration of study drug. However, the second dose will not be administered if the subject has a respiratory rate < 8 breaths per minute, requires emergency rescue treatment with assisted breathing or intubation, or has excessive, uncharacteristic sedation (as defined by the investigator in the Patient Management Plan [PMP]). After each USL261-treated seizure cluster episode, the caregiver will call the study center as soon as possible, but no later than 24 hours after USL261 administration.

After obtaining informed consent and determining that the subject meets the eligibility requirements for this study, the subject/caregiver will be provided with enough study drug to treat one seizure cluster episode (1 treatment kit containing two 5.0 mg doses of USL261) at Visit 1. After one USL261-treated seizure cluster, the subject and caregiver will return to the study center for Visit 2 within 120 hours (5 days) of USL261 administration. At Visit 2, the

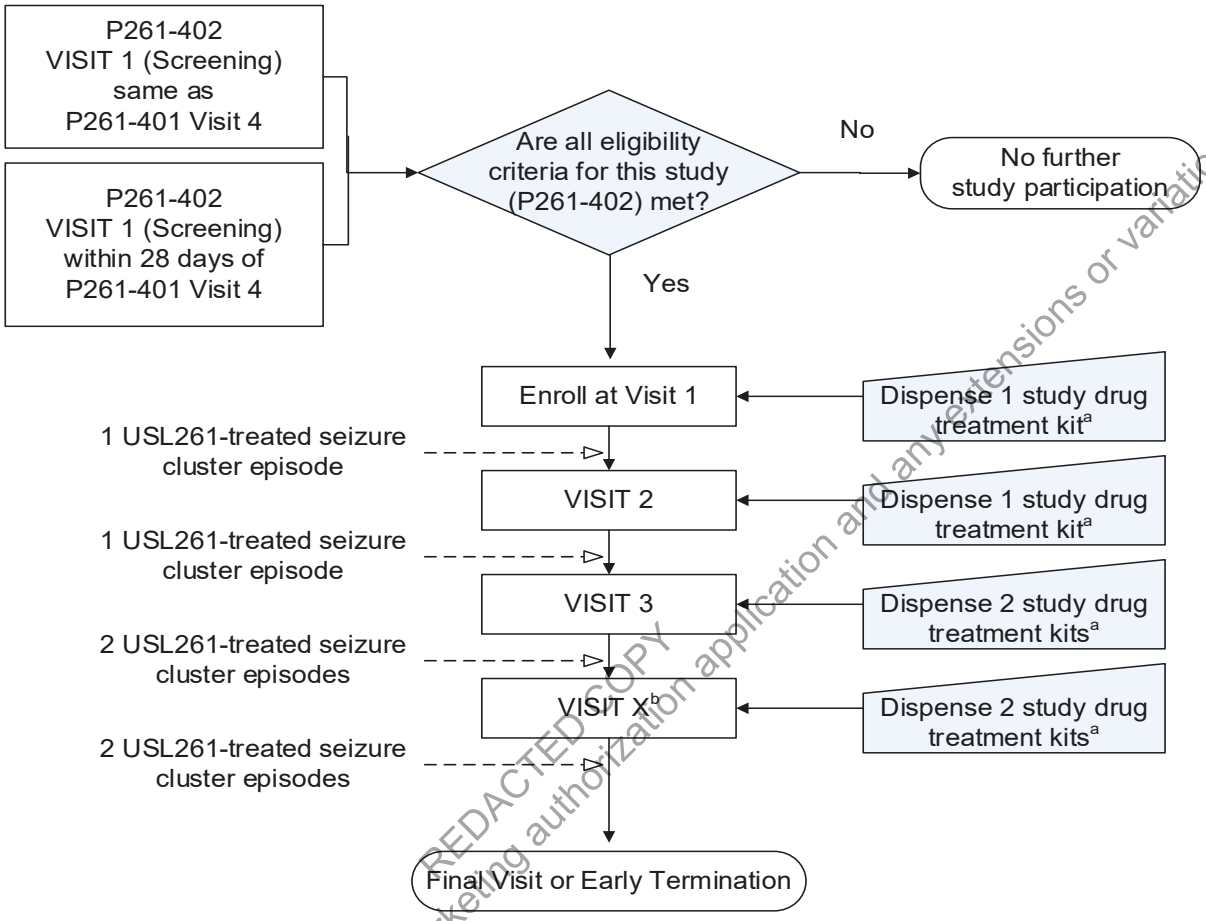
subject/caregiver will again be provided with enough study drug to treat 1 seizure cluster episode (1 treatment kit containing two 5.0 mg doses of USL261). After one USL261-treated seizure cluster, the subject and caregiver will return to the study center for Visit 3 within 120 hours (5 days) of USL261 administration. At Visit 3 and all subsequent visits (except for the Final Visit or Early Termination Visit) the subject/caregiver will be provided with enough study drug to treat 2 seizure cluster episodes (2 treatment kits, each containing two 5.0 mg doses of USL261). After Visit 3, subjects and caregivers will return to the study center after every second USL261-treated seizure cluster episode. Each of these visits will occur within 120 hours (5 days) after the last USL261 administration. A minimum of 3 days (72 hours) is required between treatments (1 treatment is defined as the use of one or two 5.0 mg doses of USL261 from one study drug treatment kit to treat a single seizure cluster episode). There is no limitation on the total number of seizure cluster episodes treated during the subject's participation in the study.

The duration of each subject's participation will vary and will be up to approximately 4 years from the date of enrollment (Visit 1). After this period, the study duration may be extended until marketing approval or a time period as approved by the Heath Authority where the study is being conducted. The study will be reviewed on an ongoing basis and immediate discontinuation of the study may occur if: a) safety concerns/issues are noted or have arisen during the conduct of the P261-402 study or other USL261 studies, b) USL261 does not demonstrate efficacy in controlled clinical studies, c) a regulatory authority (regardless of country) requests that clinical studies be interrupted or discontinued, or d) USL discontinues or will discontinue development of USL261.

Before any subject is enrolled in this open-label extension study, he/she must have completed study P261-401, or, if Study P261-401 has been terminated, subjects must have completed the Test Dose Visit (Visit 2) of study P261-401. Subjects must meet all other eligibility criteria for this study. Since enrollment is limited to subjects who have participated in study P261-401, a maximum of 240 subjects (the planned number of subjects completing the Comparative Phase in P261-401) are expected to enroll into this extension study.

Figure 1 of study flow chart on next page shows the overall study scheme.

Figure 1 Study Flow Chart



[a] Each study drug treatment kit contains two 5.0 mg doses of USL261
[b] Visits will continue until the Final Visit or Early Termination

Screening

After subjects and their caregivers have provided informed consent (and, when appropriate, assent), subjects will undergo screening procedures at Visit 1 (which may occur at the same time as or up to 28 days after Visit 4 of the preceding double-blind study P261-401). If Visit 1 of this study (P261-402) is on the same day as Visit 4 of study P261-401, the procedures performed at Visit 4 of study P261-401 that are common to Visit 1 will be used for both studies. If Visit 1 for this study (P261-402) is not on the same day as Visit 4 of P261-401, all necessary procedures will be repeated, except for physical exam, neurological exam, nasal exam, and clinical laboratory testing (hematology, serum chemistry and urinalysis). The time between Visit 4 of study P261-401 and Visit 1 of study P261-402 will be a maximum of 28 days. The time between Visit 4 of study P261-401 and Visit 1 of study P261-402 may be extended in certain cases; however, the extension must be approved by the Sponsor or Contract Research Organization (CRO) designee. If an extension is granted for a given

subject, that subject may have to undergo repeat screening laboratory assessments within 28 days prior to dispensing study drug.

Treatment Phase

Caregivers will administer the first 5.0 mg dose of USL261 at the time of recognition of a seizure cluster that meets study criteria (according to the subject's PMP). A second dose of USL261 5.0 mg may be administered if (a) the treated seizure cluster has not terminated within 10 minutes after the first dose, or (b) another seizure occurs between 10 minutes and 6 hours after administration of the study drug, AND (in both a and b) the subject does not have a respiratory rate < 8 breaths per minute, does not require emergency rescue treatment with assisted breathing or intubation, and does not have excessive, uncharacteristic sedation (as defined by the investigator in the PMP). The caregiver will monitor the subject for 24 hours after study drug administration to record safety and efficacy assessments. The caregiver will call the study center as soon as possible, but no later than 24 hours, after each USL261-treated seizure cluster episode. If seizure cluster activity persists or recurs following the administration of the second dose, caregivers will initiate the rescue protocol as outlined in the subject's PMP.

For Visits 2 and 3, which occur after each of the first 2 USL261-treated seizure cluster episodes, the subject and caregiver will return to the study center within 120 hours (5 days) of study drug administration.

After Visit 3, if the study drug has successfully treated the subject's seizure cluster episodes, the subject has tolerated the study drug treatment well in the judgment of the investigator, and the subject and caregiver have been compliant with the study procedures including completion of the Subject Workbooks and return of the study drug (used and unused), the subject and caregiver will be instructed to return to the study center after every second seizure cluster episode treated with USL261 until the Final Visit or Early Termination. A minimum of 3 days (72 hours) is required between treatments with study drug.

All study drug containers dispensed, whether used or unused, and Subject Workbooks are to be returned at the next study visit throughout the study. The study center will make monthly telephone calls between visits to caregiver(s) and subject (if subject is able to communicate adequately as determined by the investigator) when visits are more than 1 month apart. If 6 months pass without the subject having a seizure cluster episode, the subject and caregiver will be asked to come to the study center for re-training on study procedures.

The subject or caregiver will immediately report to the investigator (or his/her designee) as soon as possible any significant medical event (including events that are life-threatening or that result in death, hospitalization or prolonged hospitalization, persistent or significant disability, or incapacity of the subject) that occurs to the subject from the time written informed consent is obtained until completion of the final study visit or 7 days after last administration of study drug , whichever is later. The subject or caregiver may also call the study center at any time during the study for help or advice regarding study procedures.

2.2. Randomization and Method of Treatment Assignment

Randomization and treatment assignment are not needed for this study as all subjects will receive open-label USL261. Each subject will retain the study identification number from the P261-401 study for use in this study.

2.3. Study Procedures

The schedule of study procedures and evaluations is summarized in Table 1.

Table 1 Schedule of the Study Procedures

Phase	Screening	Treatment Phase			Study Termination
Visit Number	**Visit 1[a]**	**Visits 2 and 3 [b]**	**Visit X [c]**	**Treatment [d]**	**Final Visit or Early Termination**
Study Assessment					
Obtain Informed Consent[e]	X				
Contact IRT System	X	X	X		X
Confirm Inclusion/Exclusion Criteria	X				
Caregiver training[f]	X	X	X		
Medical / Surgical / Medication History[g]	X				
Concomitant therapy review[g]	X	X	X		X
ER and EMS Visit Review [h]		X	X		X
Update PMP[i]	X				
Physical Examination	X[j]	X	X		X
Neurological Examination	X[j,k]	X[l]	X[l]		X[k]
Nasal Examination	X[j]	X	X		X
B-SIT		X	X		X
Pregnancy Test – Urine[m]	X	X	X		X
Clinical Laboratory Testing[n]	X	X	X		X
Height	X				X
Body weight	X	X	X		X
Vital Sign measurements[o]	X	X	X		X
Study drug administration				X	
Caregiver call to study center				X	
Record seizure activity for 24 hours after study drug administration in the subject workbook				X[p]	
Evaluate subject's return to baseline functionality[q]				X	
Caregiver-recorded respiration rate[r]				X	
C-SSRS[s]	X	X	X		X
Outcome questionnaires[t]	X	X	X		X
Dispense Study Materials Kit[u]	X[v]				
Study Drug Kit [v]		X	X		
Drug Accountability		X	X		X
Collect and review Subject Workbook		X	X		X
AE Assessment	X	X	X	X	X

Telephone Follow-Up [w]		Approximately every 30 days (between visits that are at least 30 days apart)

[a] Procedures at Visit 1 may occur at the same time as Visit 4 of the preceding double-blind study (P261-401) or up to 28 days after Visit 4 of study P261-401. If Visit 1 of this study (P261-402) is on the same day as Visit 4 of study P261-401, the procedures performed at Visit 4 of study P261-401 that are common to Visit 1 will be used for both studies. If Visit 1 for this study (P261-402) is not on the same day as Visit 4 of P261-401, all necessary procedures will be repeated, except for physical exam, neurological exam, nasal exam, and clinical laboratory testing (hematology, serum chemistry and urinalysis).
[b] Visits 2 and 3 will take place within 120 hours (5 days) following each of the first 2 USL261-treated seizure cluster episodes.
[c] After Visit 3, each subject will return to the study center for a visit after every second USL261-treated episode. There is no limit on the number of seizure cluster episodes treated.
[d] These assessments are to be completed by the caregiver(s) outside of the study center.
[e] Informed consent provided by the subject (or subject's LAR) and caregiver before any other study-specific procedures; assent may also be required for some subjects and subjects with LARs (see protocol Section 5.4 informed consent).
[f] Caregiver training for P261-402 is required before study drug is dispensed at Visit 1. Review and re-instruct subjects and caregivers on the information provided in the training at all subsequent visits, except Final Visit or Early Termination Visit. Caregivers are also required to have a current CPR training certificate throughout the entire study.
[g] Update from Study P261-401.
[h] Collect number of calls to EMS and ER visits for a seizure cluster or other seizure emergency since last visit or follow-up phone call
[i] PMP from P261-401 will be updated for this study (see protocol Section 9.3.1). PMP updates should be completed before a subject receives the study materials kit at Visit 1.
[j] The physical, nasal, and neurological examinations performed at Visit 4 of Study P261-401 will be used for Visit 1 of this study.
[k] Complete neurological examination.
[l] Brief neurological examination.
[m] Pregnancy tests required only for females of childbearing potential as described in protocol Section 6.2.2.4.
[n]Hematology, serum chemistry, and urinalysis for all subjects; phenobarbital screen/levels for subjects taking phenobarbital and in subjects for which the investigator deems it necessary.
[o] Blood pressure (BP), heart rate (HR), respiration rate, and body temperature.
[p] For the first 2 years of participation in the study the date, start, and stop time of each seizure within 24 hours after any study drug administration will be recorded. After the first 2 years participation in the study, the date and start time of next seizure within 10 minutes to 24 hours after administration of the first and second dose of study drug will be recorded.
[q] Caregiver will evaluate the subject's return to baseline functionality after each treated seizure cluster episode and record the time when the subject was able to return to what he/she was doing.
[r]Caregiver counts the number of breaths taken by the subject during a 30-second interval. Caregivers will measure respiration rate at approximately 10, 15 and 30 minutes and 1, 2, and 4 hours after USL261 administration (see protocol Section 6.1.3).
[s] The Since Last Visit version is administered at all visits.
[t] The outcome questionnaires SF-12v2, TSQM, ITIQ and Caregiver Questionnaire are optional (see protocol Section 6.2.3)
[u] The study materials kit will include at a minimum: Individualized PMP, summary of the PMP, Subject Workbook (used for collecting and recording seizure activity information, study drug administration, respiration rate, and other observations made by the caregiver), study drug kit, and dosing instructions.
[v] One study drug kit will be dispensed at Visit 1 and Visit 2. Two study drug kits will be dispensed at Visit 3 and each Visit X.
[w] After Visit 1, telephone follow-up calls with the caregiver(s) and subject (if subject is able to communicate adequately as determined by the investigator) are to occur at least once each month (every 30 days) between visits that are at least 1 month apart until the subject has completed or prematurely discontinued from the study.

Abbreviations: B-SIT = Brief Smell Identification Test; BP = blood pressure; C-SSRS = Columbia-Suicide Severity Rating Scale; HR = heart rate; IRT = Interactive Response Technology system; LAR = legally acceptable representative; PMP = Patient Management Plan; TSQM = Treatment Satisfaction Questionnaire for Medication ; ITIQ = Intranasal Therapy Impact Questionnaire

3. STUDY OBJECTIVES AND CLINICAL ENDPOINTS

3.1. Study Objectives

The study objectives are to evaluate the long-term safety and tolerability of USL-261 in the treatment of seizure clusters using the following safety endpoints:

- Caregiver-recorded respiration rate at approximately 10 minutes, 15 minutes, 30 minutes, 1 hour, 2 hours and 4 hours after study drug administration
- Adverse events (AEs)
- Clinical laboratory tests
- Physical, nasal, and neurological examinations
- Vital sign measurements (systolic and diastolic blood pressure, pulse rate, respiration rate, and temperature) as recorded by the study center personnel
- Brief Smell Identification Test (B-SIT)
- Columbia-Suicide Severity Rating Scale (C-SSRS)
- Requirement for unscheduled emergency room (ER) or emergency medical service (EMS) visits within 24 hours after study drug administration

3.2. Clinical Endpoints

3.2.1. Safety Endpoints

The safety endpoints are listed above under Section 3.1, study objectives.

3.2.2. Efficacy Endpoints

- Treatment Success (defined in Section 6.7.1)
- Time to return to full baseline functionality (as determined by the caregiver)

3.2.3. Exploratory Efficacy Endpoints

- Proportion of subjects with recurrence of seizure(s) beginning 10 minutes after study drug administration to 4 hours after study drug administration
- Time to next seizure with a start time >10 minutes after study drug administration
- Proportion of subjects with recurrence of seizure(s) beginning 10 minutes after study drug administration to 24 hours after study drug administration
- Time from administration of the first open-label dose of study drug to the second open-label dose of study drug (for subjects receiving the second dose)

3.2.4. Outcome Endpoints

- SF-12v2 Health Survey (SF-12v2)
- Treatment Satisfaction Questionnaire for Medication (TSQM)
- Intranasal Therapy Impact Questionnaire (ITIQ)
- Caregiver Questionnaire

4. ANALYSIS POPULATIONS

4.1. Enrolled Population

The Enrolled Population includes subjects who completed study P261-401, or if Study P261-401 had been terminated, also subjects who completed the Test Dose Visit (Visit 2) of Study P261-401 will also be eligible to enter this study (P261-402). All subjects must meet all the eligibility criteria in P261-402.

4.2. Safety Population

The Safety Population includes all subjects who are enrolled in this open-label study (P261-402) and received at least one dose of open-label study drug during this open-label study (P261-402).

4.3. Efficacy Evaluable Population

The Efficacy Evaluable Population includes all subjects in the Safety Population who have any post-treatment efficacy assessment in Study P261-402.

5. GENERAL STATISTICAL CONSIDERATIONS

5.1. General Consideration

All datasets and output will be produced using SAS® Version 9.2 or higher (SAS Institute, Inc., Cary, North Carolina, USA).

5.2. Baseline

This study (P261-402) serves as an open-label extension for subjects who have completed study P261-401, or at least completed the test dose, if study P261-401 is terminated. The data presentations for study P261-402 will include, but are not limited to, summary of the change from baseline for the continuous safety endpoints and the outcome questionnaires (when applicable). In order to facilitate data summarization relative to exposure to active study medication, baseline endpoints will be defined as the latest non-missing value prior to Test Dose administration of USL261 from Study P261-401. Detailed baseline definitions of each endpoint of interest are presented in Table 2.

Table 2 Baseline Definitions

Endpoint	Baseline defined as:
Efficacy	Data displays not dependent on defining baseline
Vital Signs	The last non-missing value prior to the first dose of study drug administration at Visit 2 in study P261-401 (note the data displays for ITIQ and Caregiver Questionnaire are not dependent on defining baseline)
Weight	
Laboratory Parameters	
B-SIT	
Outcome Questionnaires (SF12-V2, TSQM)	
Physical Exam	Data displays not dependent on defining baseline
Neurological Exam	
Nasal Exam	
AEs/SAEs	
C-SSRS	

5.3. Handling of Missing Data

Any specific imputation procedures for missing or incomplete data will be discussed in the section describing analytic or summary methods for the corresponding variable in question. Unless otherwise stated, observed data will be presented in tables and listings without imputation of missing values.

AEs with missing start dates will be considered treatment-emergent if the stop date has been recorded and is after the first dose date (first dose date refers to the first treatment with active study drug during study P261-402).

Missing AE relationship will be presented as 'related' in tables and as missing in listings. Missing AE intensity will be considered as 'severe' in tables but will be reported as missing in listings.

5.4. Interim Analysis

Although no interim analysis is planned for decision making regarding this study, a snapshot of the data contained in the clinical database will be taken at the appropriate times in order for the safety data accrued in this study to be included in any regulatory submissions for this compound.

5.5. Data and Safety Monitoring Board (DSMB)

The DSMB constituted for the P261-401 study will have access to the data from this study, if requested by the DSMB, for informational purposes and as supportive data during their review of the P261-401 study.

Details of the DSMB membership, meeting schedule, and data review and analysis will be documented in the DSMB Charter for the P261-401 study.

5.6. Multiple Comparisons and Multiplicity

Since this is an open-label extension study, there is no formal hypothesis testing. Where 95% confidence intervals are presented, there is no adjustment for multiple times of testing.

6. STATISTICAL ANALYSIS

All analyses will be descriptive with p-values presented for the change from baseline for selected outcome assessments.

Data will be listed and tabulated overall. Continuous variables, including the change from baseline (when appropriate), will be summarized using descriptive statistics [n, mean, standard deviation (SD), minimum, median, maximum]. Categorical variables will be summarized using counts and percentages. Time to event variables will be summarized using Kaplan-Meier estimates.

Baseline is defined in Section 5.2 above, or if not included in 5.2, as the last data point prior to the first dose of study P261-402 open-label study drug administration, unless otherwise stated.

Data listings will include all subjects with at least one applicable value. Listings will be sorted by site, subject number, and date/time (if applicable).

6.1. Subject Disposition

Individual subject disposition data will be listed by investigator site for the enrolled population.

A summary of subject disposition will display the number of subjects who completed study P261-401 and were screened for the open-label study P261-402, enrolled in the open-label study P261-402, and received open-label study drug. The number of subjects who discontinued study participation will be summarized according to the primary reason for early withdrawal.

6.2. Treatment Exposure and Treated Seizure Clusters

Treatment exposure will include exposure to USL261 in study P261-402. Exposure to active study treatment will be summarized descriptively by the total number of milligrams of USL261 received per subject. Exposure data (comparative dose assignment and open-label dose usage) from study P261-401 will only be presented in listing.

The total number of seizure cluster episodes treated with USL261 will be summarized descriptively as well as categorically (number of single 5.0 mg dose [no second 5.0 mg dose] administrations of USL261, number of repeat [5.0 mg + 5.0 mg] administrations of USL261, number of total 5.0 mg administrations of USL261). For the total number of seizure cluster episodes less than or equal to 5,

categorical variables will be summarized as 1, 2 - 3 , 4 - 5. For the total number of seizure cluster episodes greater than 5, categorical variables will be summarized in groups of 5, i.e. 6 - 10, 11 - 15, 16 - 20 and so on, until the maximum number based on the data.

The time on study (number of days from informed consent to the last completion / early termination visit) in study P261-402 will be summarized descriptively as well as categorically (0 – 6 months, 6 – 12 months, 12 – 24 months, and > 24 months).

The frequency of treated seizure clusters (average per year) will be summarized descriptively as well as categorically (<2 years, 2 - <4 years, 4 - <12 years, 12 - <26 years, 26 - <52 years, >52 years).

The time between successive treated seizure clusters will be summarized descriptively as well as categorically (<=7 days, >7 - <=14 days, >14 - <=30 days, >30 - <=90 days, >90 - <=180 days, >180 days).

6.3. Protocol Deviations

All instances of protocol non-compliance in study P261-402 will be tracked during the study and CSR reportable protocol deviations will be finalized by a Sponsor review prior to database lock. Protocol deviation categories will be presented in a data listing and summarized using counts and percentages. Deviations that may materially affect the evaluation of efficacy or safety will be identified as CSR Reportable. CSR Reportable protocol deviations may include, but are not limited to:

- Failure to obtain informed consent
- Failure to report a Serious Adverse Event (SAE)
- Enrolling patients outside of inclusion/exclusion criteria
- Drug dispensing/dosing errors

6.4. Demographics and Baseline Characteristics

Demographics and baseline characteristics for subjects continuing in this P261-402 open-label extension study (unless otherwise specified, based on the data as collected in the preceding P261-401 study) will be presented for the Enrolled, Safety and Efficacy Evaluable Populations. Subject demographics include age (calculated as the integer number of years between date of birth and informed consent date of P261-402), age group, gender, race, ethnicity, clinical site region, height, weight, weight category, BMI, BMI category, and inducer status (based on AED exposure in P261-402). Weight recorded in pounds will be converted to kilograms and height recorded in inches will be converted to centimeters. BMI will be calculated based on weight and height using below formula:

$$\text{BMI (kg/cm}^2\text{)} = \text{Weight/Height}^2$$

In addition subject age (years) will be categorized as follows:

- < 18 years
- ≥ 18 - < 65 years
- ≥ 65 years

Subject baseline characteristics include: IQ (if available), developmentally delayed status, EEG history, CT scan and/or MRI history, previous and current seizure types, seizure etiology including primary cause of epilepsy, and seizure cluster episode history.

6.5. Medical and Surgical History

Updates to medical and surgical history after the end of P261-401 study will be collected. Medical and surgical history will be coded using the MedDRA coding dictionary version 16.1. SOC will be sorted alphabetically and then preferred term will be sorted in order of frequency of the total column within each SOC. At each level of summarization, a subject will be counted only once for each medical and surgical history he/she has within that level. Subject listings of coded medical history terms will be provided.

6.6. Prior and Concomitant Medications

Prior medications are defined as medications in study P261-401 and P261-402 which started prior to the inform consent date in study P261-402. Concomitant drug therapy will include all medications (prescription or non-prescription), nutritional supplement, herbal preparation or devices (e.g., VNS) in study P261-401 and P261-402 taken/used from the inform consent date in the P261-402 open-label study through the Final Visit or ET Visit, including any with missing stop dates (or with partial missing stop dates that allow for the possibility the medication was taken after the inform consent date in study P261-402).

The World Health Organization Drug Dictionary (WHO Drug) of version December 2011 will be used to classify prior and concomitant by therapeutic class and preferred name based on ATC code level 4.

Concomitant medications will be summarized for the Safety population. Levels of summarization will include global, WHO Anatomic Therapeutic Chemical (ATC) Classification System level 3 drug class, ATC level 4 drug class, and WHO preferred name.

At each level of summarization, a subject will be counted only once for each concurrent medication he/she has within that level. The percentage of subjects having had at least one medication at each level will be calculated.

Concomitant medications excluding AEDs, prior AEDs, concomitant AEDs, concomitant AEDs used for epilepsy, and concomitant AEDs used for indications other than epilepsy will be summarized separately and similar to all concomita6nt medications.

Both Prior and Concomitant AEDs will be further broken down into enzyme-inducing and non-inducing AEDs.

Separate listings will be provided for all medications and AEDs for all subjects, with medications classified as prior flagged in the listings. AEDs collected from AED page on CRF will be presumed to have 'Epilepsy' as indication. AEDs collected from concomitant medication page will be listed by indication captured on CRF.

6.7. Analyses of Efficacy and Outcome Endpoints

Information recorded by the caregiver in the Subject Workbook will be used for analysis of the efficacy endpoints. Any seizures occurring within 24 hours after administration of study drug will be recorded.

6.7.1. Efficacy Endpoint

All analyses of the efficacy endpoints will be conducted for the Efficacy Evaluable Population.

6.7.1.1. Treatment Success

Treatment Success is a composite measure of efficacy that is defined as achieving both of the following criteria:

- Termination of seizure(s) within 10 minutes after study drug administration, and
- No recurrence of seizure(s) beginning 10 minutes after study drug administration to 6 hours after study drug administration.

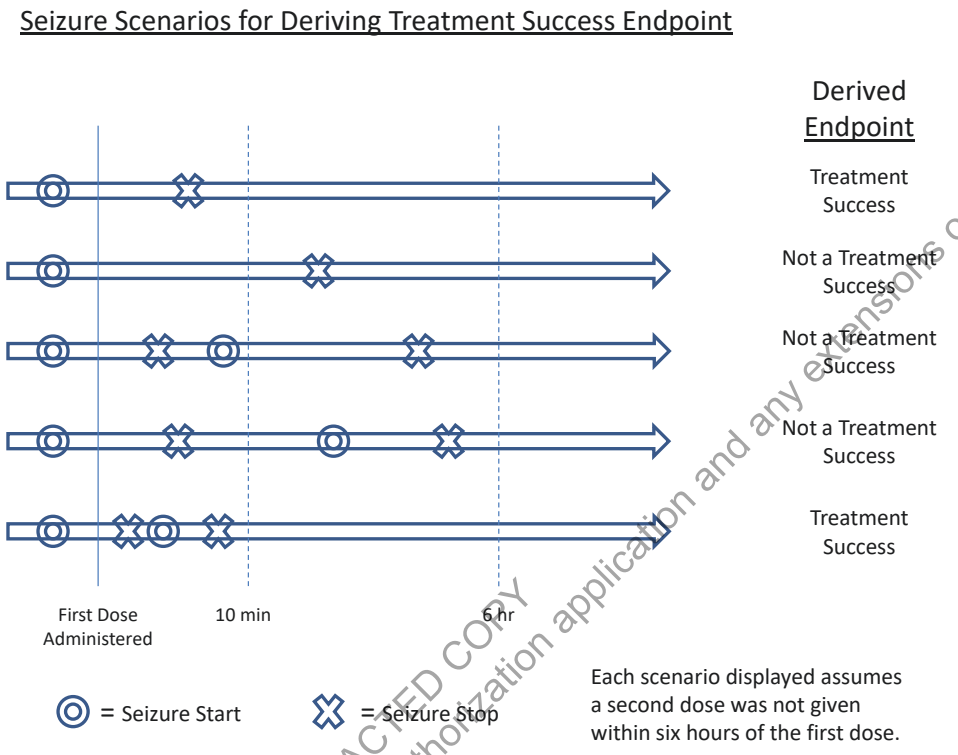
6.7.1.1.1. Derivation of Treatment Success Endpoint

Treatment Success will be determined based on data reported in the CRFs and derived programmatically for each treated seizure cluster. There are three components to be assessed in the programmatic derivation:

1. Termination of seizure(s) within 10 minutes: The initial seizure stopped within (≤) 10 minutes from the time of dosing and any subsequent seizures also stopped within 10 minutes of dosing.
2. No recurrence of seizure(s) beginning 10 minutes after study drug administration to 6 hours after study drug administration. The times of reported seizures will be used to assess if there are any seizures with start time from >10 minutes up to (≤) 6 hours after the first dose of study drug.
3. No second dose given within 6 hours of the first dose of study drug administration as receiving the second dose within (≤) 6 hours confounds the efficacy evaluation of the first dose.

For each treated seizure cluster, subjects who meet all three of these components will be defined as a "Treatment Success" for that seizure cluster. If a subject does not meet all three of these components, (which may or may not be due to missing data), they will be defined as "Not a Treatment Success" for that particular seizure cluster. As subjects may be treated for multiple seizure clusters, it is possible they could meet the criteria for "Treatment Success" for some seizure clusters, but not for all.

Possible scenarios for seizure data start and stop times within the 6 hour period following the first dose of study drug are displayed below, along with the treatment success endpoint derivation (assuming no second dose was given):



The percentage of subjects achieving Treatment Success and its components (seizure termination and recurrence) will be summarized for each USL261-treated seizure cluster (first, second, etc.). Additionally, all treated seizure clusters will be pooled (across all subjects) with the proportion of Treatment Successes (this data presentation may be broken down by the number of within-subject treated seizure clusters, based on the data observed; for example, presented by subjects treated for 1-2 seizure clusters, 2-5 clusters, 5-10 clusters, etc.). Descriptive statistics for the percentage of each subject's USL261-treated seizure clusters that met the criteria for Treatment Success will also be presented.

6.7.1.2. Time to Return to Full Baseline Functionality (as Determined by the Caregiver)

Time to return to full baseline functionality after study P261-402 open-label study drug administration will be summarized and plotted using Kaplan-Meier estimates for each successive seizure episode (first, second, etc.) and also pooled across all treated seizure clusters. Subjects who have no records on time of return to baseline functionality within 24 hours of study drug administration and have not been administered the 2nd dose of study drug will be censored at the end of the observation period. For each seizure cluster episode, subjects who were administered the 2nd dose of open-label study drug prior to returning to baseline functionality will be censored at the time that the 2nd open-label dose was administered.

6.7.2. Exploratory Efficacy Endpoints

All exploratory efficacy analyses will be based on the Efficacy Evaluable Population.

6.7.2.1. Proportion of Subjects with Recurrence of Seizure(s) Beginning 10 Minutes after Administration of Open-Label Study Drug to 4 Hours after

Subjects who have been administered the second dose of the study drug (ie, 5.0 mg dose of USL261) within 4 hours of the first dose for the episode will be assumed to have had a recurrent seizure. The proportion of subjects with recurrence of seizure(s) recorded in the diary with start time >10 minutes and ≤4 hours after the administration of study P261-402 open-label study drug will be summarized for each successive seizure cluster (first, second, etc.) and also pooled across all treated seizure clusters. Subjects who do not have a seizure recorded, or whose next seizure occurs > 4 hours after study drug administration, will be counted as not having a seizure in this particular analysis.

6.7.2.2. Time to Next Seizure with a Start Time >10 Minutes after Open-label Study Drug Administration

Kaplan-Meier estimates and plots will be used to summarize the time-to-next seizure after study P261-402 open-label study drug administration for each successive seizure episode (first, second, etc.) and also pooled across all treated seizure clusters. Subjects who do not have another seizure before the end of the 24-hour observation period, and have not been administered the second dose of open-label study drug will be censored at the end of the observation period. Subjects who have been administered the second dose of open-label study drug and did not have a seizure before the administration of the second dose will be censored at the time of the second dose administration. The time-to-next seizure percentiles (defined based on the data) with associated 95% confidence intervals (CIs) will be displayed. The probabilities of experiencing the next seizure after open-label study drug administration at each hour up to 24 hours with associated standard error and 95% confidence intervals will be presented.

6.7.2.3. Proportion of Subjects with Recurrence of Seizure(s) Beginning 10 Minutes after Study Drug Administration to 24 Hours after Study Drug Administration

The proportion of subjects with recurrence of seizure(s) with a start time >10 minutes and ≤24 hours after study P261-402 open-label study drug administration will be summarized for each successive seizure episode (first, second, etc.) and also pooled across all treated seizure clusters. Subjects who have been administered the second dose of open-label study drug within 24 hours will be assumed to have had a seizure. Subjects who do not have a seizure recorded with a start time >10 minutes and ≤24 hours after the administration of open-label study drug will be counted as not having a seizure in this particular analysis.

6.7.2.4. Data Presentations / Analyses When a Second Dose is Administered

Seizure cluster episodes where both the first and second (provided if the seizure cluster has not terminated within 10 minutes after initial study drug administration or if another seizure occurs between 10 minutes and 6 hours after administration of the study drug) administrations of USL261 are given are included in the following data presentations.

6.7.2.4.1. Treatment Success of the Second Dose of Study Drug (5.0 mg of USL261)

Treatment Success of the second dose for subjects receiving the second dose of USL261 will be presented for each successive seizure episode (first, second, etc.) and also pooled across all treated seizure clusters.

For this analysis, Treatment Success of the second dose is defined as achieving the following:

- Termination of seizure(s) within 10 minutes after the second dose of study drug (5.0 mg of USL261)
- No recurrence of seizure(s) beginning 10 minutes after administration of the second dose of study drug (ie, 5.0 mg of USL261) to 6 hours after the second dose of study drug (5.0 mg of USL261)

Subjects whose Subject Workbook indicates seizure termination within 10 minutes of the second dose and who have no seizures recorded with start time >10 minutes and ≤6 hours after the second dose of study drug will be considered a Treatment Success of the second dose. Subjects who do not meet either of these criteria will not be considered a Treatment Success of the second dose. Similar derivation rules as used for Section 6.7.1.1 Treatment Success endpoint will be used for defining Treatment Success of the second dose, with the exception of not including the rule pertaining to the second dose.

Number and percentage will be presented for Treatment Success of the second dose and each component (seizure termination and recurrence) for subjects who received two doses of study drug. The 95% CIs for the proportions will also be presented.

6.7.2.4.2. Time from Administration of the First Dose of Open-Label Study Drug to the 2nd Dose

For each successive seizure episode (first, second, etc.) and also pooled across all treated seizure clusters, time (in hours) from the administration of the first dose of study P261-402 open-label study drug to the 2nd dose (provided if the seizure cluster has not terminated within 10 minutes after initial study drug administration or if another seizure occurs between 10 minutes and 6 hours after administration of the study drug) will be descriptively summarized. In addition to the total number of subjects receiving this second dose, counts of subjects receiving the second dose in specific time categories post first dose (0 to ≤20 minutes, >20 minutes to ≤1 hr, > 1 hr) will also be presented. For each seizure cluster episode, only subjects who received both doses of open-label study drug will be included in this data presentation.

Kaplan-Meier estimates will be used to summarize the time-to-second dose for each successive seizure episode (first, second, etc.) and also pooled across all treated seizure clusters. Subjects who do not receive the second dose of study drug within 6 hours of the initial study drug administration will be censored at the end of this 6 hour period. The time-to-second dose percentiles (defined based on the data) with associated 95% CIs will be displayed. Kaplan-Meier curves by treatment group will also be presented.

Kaplan-Meier estimates will also be used to summarize the time-to-next seizure following the second dose for each successive seizure episode (first, second, etc.) and also pooled across all treated seizure clusters. Subjects who do not have another seizure before the end of the 24-hour observation period following the second dose of study drug will be censored at the end of this observation period. The

time-to-next seizure following the second dose percentiles (defined based on the data) with associated 95% CIs will be displayed. The probabilities of experiencing the next seizure following the second dose at each hour with associated standard error and 95% confidence intervals will be presented. Kaplan-Meier curves by treatment group will also be presented.

6.7.2.4.3. Treatment Success for all Doses of Study Drug

An analysis similar to that in Section 6.7.2.4.1 Treatment Success of the Second Dose of Study Drug, will be performed including all study drug administrations (regardless of 1st dose or 2nd dose).

6.7.3. Subject and Caregiver Outcome Assessments

The subjects and caregiver outcome assessments will be summarized using the efficacy evaluable population.

6.7.3.1. SF-12v2

The SF-12v2 is a 12-item questionnaire which will be administered to both the subject and caregiver at Visit 1 and Final/ET Visit in study P261-402. All summaries will be presented separately for the subject and caregiver. Eight domains make up the SF-12v2: physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. In addition, the Physical Health Component Score (PHCS) and the Mental Health Component Score (MCS) will be calculated. The scores for each domain, the PHCS and the MCS range from 0 to 100, where zero indicates the lowest level of health by the scales and 100 indicates the highest level of health.[4]

Summary scores for PHCS and MCS for each subject will be computed using published algorithms.[4] Each summary measure is scored and standardized using a t-score transformation, such that a higher score represents better health status, with a mean score of 50 and a standard deviation of 10 in the general population.[5] Missing data on the SF-12v2 will be handled as follows: domain scores will not be calculated for domains in which data are missing. Subsequently, component scores in which domain scores are missing will not be calculated.

The domain and component scores will be summarized descriptively at Baseline (defined as the last data point prior to the first dose of study drug administration at Visit 2 in study P261-401) and for Visit 1 and Final/ET Visit for study P261-402. Change from baseline will be summarized at Visit 1 and Final/ET Visit for study P261-402. For each domain and component score a paired t-test will be used to assess the within-group mean change from baseline.

6.7.3.2. Treatment Satisfaction Questionnaire for Medication (TSQM)

The TSQM is a 14-item questionnaire that will be administered to the subject. The four TSQM scale scores calculated from the questionnaire are: effectiveness, side-effects, convenience, and global satisfaction. The TSQM scale scores are computed by adding the items loading on each factor. The lowest possible score is subtracted from the composite score and divided by the greatest possible score minus the lowest possible score. This will provide a transformed score between 0 and 1 that is then multiplied by 100. If more than one item is missing from each scale, the scale will not be calculated. Calculation of each scale score is provided below.[6]

Effectiveness

([Q1 + Q2 + Q3) – 3]/18) * 100

If one item is missing then, ([Qx + Qy – 2]/12) * 100 where x and y = 1, 2, or 3, with x≠y.

Side-Effects

If Q4 is 'No' then score = 100

Else, ([Q5 + Q6 + Q7 + Q8 – 4]/16) * 100

If one item is missing then, ([Qx + Qy + Qz – 3]/12) * 100 where x, y, and z = 5, 6, 7, or 8, with x≠y≠z.

Convenience

([Q9 + Q10 + Q11) – 3]/18) * 100

If one item is missing then, ([Qx + Qy – 2]/12) * 100 where x and y = 9, 10, or 11.

Global Satisfaction

([Q12 + Q13 + Q14) – 3]/14) * 100

If one item is missing then, ([Qx + Qy – 2]/8) * 100 where x and y = 12, 13, or 14.

The 4 scale scores will be summarized descriptively for all visits and change from baseline (baseline is defined as the last data point prior to the first dose of study drug administration at Visit 2 in study P261-401) will be summarized for all post baseline visits. For each domain and component score a paired t-test will be used to assess the within-group mean change from baseline to each post baseline visits.

6.7.3.3. Intranasal Therapy Impact Questionnaire (ITIQ)

The ITIQ is a two item questionnaire that is completed by both the subject and caregiver at all Visits. The level of anxiety change since subject received intranasal therapy is a scale with a range from -7 to 7, and confidence about travelling having a spray the subject can take with them is a scale from 1 to 5. The change in level of anxiety and change since subject received intranasal therapy will be summarized descriptively. Counts and percentages will be used to summarize the confidence about travelling having a spray the subject can take with them at each visit.

6.7.3.4. Caregiver's Questionnaire

The Caregiver Questionnaire is self-administered by the primary caregiver and consists of caregiver demographics (completed at Visit 1 or if there is a change in primary caregiver during the study) and resource utilization (completed at all visits).

All caregiver's questionnaire resource utilization data collected during the study will be presented in the listings. In addition, utilization endpoints will be summarized, including all treated seizure clusters (that is, pooled), by the categories "treatment success" and "not a treatment success" as derived for each treated seizure cluster.

6.8. Safety Analyses

All safety analyses will be presented based on the Safety Population unless otherwise specified.

6.8.1. Adverse Events (AEs)

Adverse events will be coded using the Medical Dictionary for Regulatory Activities (MedDRA). The actual MedDRA version used will be noted in the footnote of each corresponding output. Coding includes system organ class (SOC) and preferred term (PT). All verbatim descriptions and coded terms will be listed for all AEs.

Pre-treatment AEs

Pre-treatment AEs will be defined as any AE that was ongoing at the end of study P261-401, or that started after the completion of study P261-401, and either ended before or did not increase in severity following open label study drug administration in P261-402. Pre-treatment AEs will be presented in a listing separate from treatment-emergent AEs (TEAEs). All summaries of AEs will be based only on TEAEs, excluding pre-treatment AEs.

Treatment-emergent AEs (TEAEs)

The following AEs will be defined as TEAEs:

- Any AE that begins after the first study P261-402 open-label study drug administration;
- Any AE that begins prior to the first study P261-402 open-label study drug administration and worsens in severity following open-label study drug administration;

All AEs will be listed by subject and by MedDRA SOC and PT.

The number of events and the frequency and percentage of subjects with TEAEs/SAEs will be summarized for the Safety Population. Summary tables of TEAEs and SAEs will be presented by SOC and PT. At each summary level, a subject will be counted only once for each AE he/she experienced within that level, regardless of how many occurrences of that AE that subject experienced. The percentage of subjects having had at least one TEAE/SAE at each level will be calculated. All the TEAE analyses will also be repeated for the subset of all TEAEs that started within two days of study drug administration.

Tabular summaries will include all TEAEs, TEAEs by age group (< 18 years, ≥18 - <65 years, ≥65 years), TEAEs by severity (mild, moderate, severe), TEAEs by relationship to study drug, TEAEs related to study drug by severity (mild, moderate, severe), TEAEs of special interest (AESIs), serious TEAEs (SAEs) with SAEs leading to permanent discontinuation and death, SAEs by severity, and SAEs by relationship to study drug. If there are any deaths while on the study, they will be presented in a listing that includes the AE leading to death, demographic data, details of study treatment, and relationship of the AE leading to death to the study drug. In addition, listings of all TEAEs, SAEs, TEAEs of special interest (AESIs), and AEs leading to discontinuation will be presented.

The following AEs of special interest (AESIs) are discussed in this section by AESI category.

- Taste and smell disorders
- Acute central respiratory depression
- Route of administration
- Depression and suicidality/self-injury
- Abuse-related AEs

Abuse-related TEAEs will be further broken out by the following categories:

- Drug Abuse, Dependence, Withdrawal and Substance-Related Disorders, Including Diversion
- Euphoria-related Term
- CNS Depressant Effects
- Stimulation and Anxiety Symptoms
- Perceptual Disturbances/Psychotomimetic Effects
- Mood Disorders and Disturbances
- Mental and Cognitive Impairment

SMQs and/or a USL-defined algorithm will be used to search AESIs. Search strategies are described in Table 3.

Table 3 Search Strategy for AESI

AESI category	Search Strategy
Taste and smell disorders	Modified Taste and Smell Disorders SMQ - broad
Acute central respiratory depression	Modified Acute Central Respiratory Depression SMQ - broad
Depression and Suicidality/Self-Injury	Modified Depression and Suicidality/Self-Injury SMQ – broad
Route of administration	USL-defined [Oral Soft Tissue Conditions HLT (Gastrointestinal Disorders SOC); Respiratory Disorders NEC (Respiratory, Thoracic and Mediastinal Disorders SOC); Upper Respiratory Tract Disorders (Exclude Infections) (Respiratory, Thoracic and Mediastinal Disorders SOC)] – excluding overlapping terms with Acute Central Respiratory Depression SMQ and terms unrelated to MDZ NS's nasal route of administration, e.g., terms for conditions in the respiratory tract below the larynx or terms with defined causes
Abuse-related AEs	USL-defined algorithm

Abbreviations: HLT=High Level Term; SMQ=Standardized MedDRA Queries; NEC=Not Elsewhere Classified.

Standard MedDRA Queries (SMQs) defined by the CIOMS Working Group are groupings of terms from one or more MedDRA SOCs that relate to a defined medical condition or area of interest. Modifications of SMQs will be documented. For hierarchical SMQs, the portion of the hierarchy to be used will be that part or those parts determined to be most relevant. A list of AEs in each category is presented in Appendix 2. Summary tables will be presented by SOC and preferred term.

In addition, "potentially clinically important" AESI will be presented for each category of AESI. AE which meets at least one of the following criteria is defined as a potentially clinically important AE:

- AE is an SAE
- AE led to discontinuation

- AE is severe in intensity and related to study drug
- AE required intervention and is related to study drug

In instances where a subject may have multiple TEAEs with differing levels of severity or relatedness, the most severe or most related event, respectively, will be reported for the severity and relatedness tables. For the purpose of summary, TEAEs with a reported relatedness of "Related", "Possibly Related", "Unlikely Related", or missing the relationship will be classified as related to study drug. TEAEs assessed as "Not Related" will be classified as not related to study drug. TEAEs with missing severity will be presented as severe in the tables but will be listed as missing.

6.8.2. Requirement for Unscheduled ER or EMS Visit

The number and percent of subjects requiring an unscheduled ER or EMS visit within 24 hours after study drug administration will be presented for each successive treated seizure cluster episode (first, second, etc.). In addition, the number of subjects requiring an unscheduled ER or EMS visit for any seizure cluster episode or other seizure emergency (treated or untreated) will be summarized (separately, for ER or EMS visit at any time, or visit within 24 hours after study drug administration). The total number of unscheduled ER or EMS visits will also be presented in a data listing.

6.8.3. Columbia-Suicide Severity Rating Scale (C-SSRS)

The C-SSRS is collected at all visits using the 'Since Last Visit' version.

Suicidal Ideation

The number and percent of subjects with each of the following suicidal ideation scores will be summarized for each visit. The highest score for suicide ideation will be used for each subject by visit.

Suicidal Ideation Scores

Suicidal ideation	Score
Wish to be dead	1
Non-specific active suicidal thoughts	2
Active suicidal ideation with any methods (not planned) without intent to act	3
Active suicidal ideation with some intent to act, without specific plan	4
Active suicidal ideation with specific plan and intent	5

Any suicidal ideation regardless of type will also be presented.

Each suicidal ideation severity rating will range from 0 (no ideation present) to 5 (active ideation with plan of intent). Descriptive statistics will be presented for suicidal ideation severity rating at each visit.

Descriptive statistics will also be presented for suicidal ideation intensity at each visit. The five intensity items (frequency, duration, controllability, deterrents, and reason for ideation) will be combined to create a total, sum score ranging between 0 and 25. If the subject did not have any suicidal ideation, the total score will be 0. If the subject had suicidal ideation and if one intensity item is missing, the total score will not be calculated.

Suicidal Behavior

The number and percent of the following suicidal behaviors will be summarized for each visit.

- Actual attempt
- Engaged in non-suicidal self-injurious behavior
- Aborted attempt
- Interrupted attempts
- Preparatory acts or behavior
- Suicidal behavior
- Any suicidal behavior regardless of type
- Completed suicide

Descriptive statistics will be presented for the following suicidal behaviors for each visit.

- Number of attempts
- Aborted attempts
- Interrupted attempts

The number and percent of subjects with any suicidal ideation or behavior will be presented for each visit.

6.8.4. Physical, Nasal, and Neurological Examinations

The number and percent of patients having normal and abnormal findings (clinically significant vs. not clinically significant) for each body system or assessment will be presented by visit for each of these exams.

6.8.5. Olfactory testing with Brief Smell Identification Test (B-SIT)

Descriptive statistics for the summary score and changes from baseline for olfactory testing with B-SIT over time will be presented by visit. All B-SIT data will be presented in a listing.

6.8.6. Laboratory Parameters

Clinical laboratory parameters for serum chemistry, hematology, and urinalysis will be summarized descriptively at baseline and each study P261-402 visit. Mean and mean change from baseline values will be presented at each study visit. Change from baseline will be calculated at each post baseline visit as the value at that visit minus the baseline value. If either the baseline or post baseline visit value is missing, the observation will not be included in the change from baseline summary at that visit. Baseline is defined as the latest non-missing value prior to Test Dose administration of USL261 from Study P261-401.

Each laboratory result will be classified as low (L), normal (N), and high (H) at each visit according to the laboratory-supplied normal range. The shift from baseline (as defined in Section 5.2) will be presented.

Potentially clinically significant (PCS) laboratory abnormalities will be identified using standardized criteria in Appendix 1 prior to database lock and will be presented using counts and percentages. Additional displays of PCS may be presented.

6.8.7. Vital Signs / Weight

Vital sign measurements, including body weight, performed by study site staff will be presented using descriptive statistics. Vital signs, including systolic and diastolic blood pressure (mmHg), pulse (beats/min), respiration rate (breaths/min), and temperature (degrees Celsius [° C]), along with body weight, will be summarized descriptively at baseline and each study P261-402 visit. Change from baseline will be calculated as post-baseline measurement minus baseline measurement. If either the baseline or post-baseline value is missing, the observation will not be included in the change from baseline summary at that visit. Baseline is defined as the latest non-missing value prior to Test Dose administration of USL261 from Study P261-401.

The number of subjects meeting the following criteria will be presented by visit, and by time point:

- < 8 breaths per minute after study drug administration
- > 24 breaths per minute after study drug administration
- systolic blood pressure < 85 mm Hg
- a change from baseline in systolic pressure ≥ 40 mm Hg
- diastolic blood pressure < 50 mm Hg
- a change from baseline in diastolic pressure ≥ 30 mm Hg
- pulse > 120 beats per minute
- pulse < 50 beats per minute
- a change from baseline in pulse ≥ 40 beats per minute

6.8.8. Caregiver-Recorded Respiration Rate

The caregiver-recorded respiration rate will be presented using descriptive statistics at the scheduled collection times of (approximately) 10 minutes, 15 minutes, 30 minutes, 1 hour, 2 hours, and 4 hours after the first dose of study P261-402 open-label study drug for each successive seizure cluster episode (first, second, etc.). The number of subjects who have <8 and >24 breaths per minute will be presented by time point, across time points for each seize cluster, and across all treated seizure clusters.

7. DEVIATIONS FROM THE PROTOCOL SPECIFIED ANALYSIS

The subjects and caregiver outcome assessments (detailed in Section 6.7.3) will be summarized using the efficacy evaluable population, instead of the safety population as specified in the protocol.

8. MOCK TABLES, FIGURES, AND DATA LISTINGS

The mock TLGs will be provided in a separate document.

9. REFERENCES

1. Cereghino JJ. Identification and treatment of acute repetitive seizures in children and adults. *Curr Treat Options Neurol*. 2007;9:249-255.
2. Lowenstein DH, Alldredge BK. Status epilepticus. *N Engl J Med.* 1988;338:970-976.
3. Glauser TA. Designing practical evidence-based treatment plans for children with prolonged seizures and status epilepticus. *J Child Neurol.* 2007;22:38S-46S.
4. Utah Department of Health. Interpreting the SF12. *2001 Utah Health Status Survey*. 2001: 1-17.
5. Web. < http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1434659/>
6. Web. <www.qualitymeasures.ahrq.gov>

Appendix 1 Potentially Clinically Significant Laboratory Values

Variable	Units	Values	
		Low	High
Haematology			
Haemoglobin	g/L	< 10	Not applicable
	g/L	> 2 decrease from baseline	> 2 increase above ULN*
Lymphocytes (Absolute)	10^9/L	< 0.8	Not applicable
Neutrophils (Absolute)	10^9/L	< 1.5	Not applicable
Platelet count	10^9/L	< 75	Not applicable
White blood cell (WBC) count	10^9/L	< 3	Not applicable
Serum Chemistry			
Albumin	g/L	< 30	Not applicable
Alkaline phosphotase (AP)	U/L	Not applicable	> 2.5xULN
Alanine aminotransferase (ALT) Grade 1	U/L	Not applicable	> ULN & ≤ 3xULN
Alanine aminotransferase (ALT) Grade 2	U/L	Not applicable	> 3xULN & ≤ 5xULN
Alanine aminotransferase (ALT) Grade 3	U/L	Not applicable	> 5xULN & ≤ 20xULN
Alanine aminotransferase (ALT) Grade 4	U/L	Not applicable	> 20xULN
Aspartate aminotransferase (AST) Grade 1	U/L	Not applicable	> ULN & ≤ 3xULN
Aspartate aminotransferase (AST) Grade 2	U/L	Not applicable	> 3xULN & ≤ 5xULN
Aspartate aminotransferase (AST) Grade 3	U/L	Not applicable	> 5xULN & ≤ 20xULN
Aspartate aminotransferase (AST) Grade 4	U/L	Not applicable	> 20xULN
Bicarbonate	mmol/L	≤ 15.9	Not applicable
Calcium	mmol/L	< 2	> 2.9
Cholesterol (Total)	mmol/L	Not applicable	> 7.75
Creatinine	umol/L	Not applicable	> 1.5xULN
	umol/L	Not applicable	> 2x baseline
Gamma glutamyl transferase (GGT)	U/L	Not applicable	> 2.5xULN
Glucose	mmol/L	< 3.0	> 8.9
Phosphorus	mmol/L	< 0.8	Not applicable
Potassium	mmol/L	< 3.0	> 5.5
Sodium	mmol/L	< 130	> 150
Total Bilirubin	umol/L	Not applicable	> 1.5xULN
Triglycerides	mmol/L	Not applicable	> 3.42

*ULN=Upper Limit of Normal

Appendix 2 List of AEs of special interest

(1) Abuse-related AEs (MedDRA Preferred Term):

Drug Abuse, Dependence, Withdrawal and Substance-Related Disorders, Including Diversion	
Accidental death	Multiple drug overdose intentional
Accidental overdose	Nasal necrosis
Accidental poisoning	Nasal septum perforation
Dependence	Nasal septum ulceration
Drug abuser	Needle track marks
Drug administered at inappropriate site	Neonatal complications of substance abuse
Drug dependence	Overdose
Drug detoxification	Poisoning
Drug diversion	Polysubstance dependence
Drug tolerance	Prescription form tampering
Drug tolerance increased	Product tampering
Drug toxicity	Product used for unknown indication
Drug Withdrawal	Rebound effect
Drug withdrawal convulsions	Substance abuse
Drug withdrawal headache	Substance abuser
Drug withdrawal syndrome	Substance use
Intentional drug misuse	Substance-induced mood disorder
Intentional overdose	Substance-induced psychotic disorder
Multiple drug overdose	Treatment noncompliance
Multiple drug overdose accidental	Withdrawal Syndrome
Euphoria-related Terms	
Dizziness	Feeling drunk
Elevated mood	Feeling of relaxation
Euphoric mood	Inappropriate affect
Feeling abnormal	
CNS Depressant Effects	
Fatigue	Sluggishness
Lethargy	Somnolence
Sedation	Stupor
Stimulation and Anxiety Symptoms	
Agitation	Hypervigilance

Anxiety	Nervousness
Energy increased	Psychomotor hyperactivity
Feeling jittery	Restlessness
Perceptual Disturbances/Psychotomimetic Effects	
Abnormal dreams	Hallucinations, mixed
Acute psychosis	Hostility
Aggression	Hypoaesthesia
Alice in wonderland syndrome	Ideas of reference
Altered state of consciousness	Illogical thinking
Altered visual depth perception	Illusion
Anger	Incoherent
Communication disorder	Indifference
Confusional state	Jamais vu
Consciousness fluctuating	Loose associations
Déjà vu	Magical thinking
Delirium	Muscle rigidity
Delusion	Nightmare
Depersonalisation	Paraesthesia
Derailment	Paranoia
Derealisation	Paroxysmal perceptual alteration
Disinhibition	Psychotic disorder
Disorientation	Reactive psychosis
Dissociation	Sensory disturbance
Dissociative disorder	Sensory level abnormal
Dissociative identity disorder	Somatic delusion
Dysarthria	Somatic hallucination
Fear	Staring
Flashback	Suspiciousness
Flight of ideas	Tangentiality
Formication	Thinking abnormal
Hallucination	Thought blocking
Hallucination, auditory	Thought broadcasting
Hallucination, olfactory	Thought insertion
Hallucination, synaesthetic	Thought withdrawal

Hallucination, tactile	Transient psychosis
Hallucination, visual	
Mood Disorders and Disturbances	
Abnormal behaviour	Asocial behaviour
Affective disorder	Attention-seeking behaviour
Affect lability	Belligerence
Depressed mood	Blunted affect
Depression	Compulsions
Emotional disorder	Confusional arousal
Emotional distress	Disturbance in social behaviour
Impatience	Feeling of despair
Mood altered	Flat effect
Mood swings	Impulsive behaviour
Personality change	Mania
Anhedonia	Panic attack
Antisocial behaviour	Panic reaction
Apathy	Parasomnia
Mental and Cognitive Impairment	
Amnesia	Mental disorder
Cognitive disorder	Mental status changes
Disturbance in attention	Paramnesia
Memory impairment	Psychomotor retardation
Mental impairment	Retrograde amnesia
Psychomotor skills impaired	Transient global amnesia
Amnestic disorder	Impaired driving ability
Anterograde amnesia	Impaired reasoning
Balance disorder	Dyslogia
Coordination abnormal	Bradyphrenia
Executive dysfunction	Confabulation
Judgement impaired	

(2) AEs related to acute central respiratory depression:

System Organ Class	Preferred Term	Lowest Level Term
Acute central respiratory depression (SMQ)		
Cardiac disorders	Cyanosis	Acrocyanosis

System Organ Class	Preferred Term	Lowest Level Term
Acute central respiratory depression (SMQ)		
Cardiac disorders	Cardiac arrest	Arrest cardiac
Cardiac disorders	Cardiac arrest	Asystole
Cardiac disorders	Cardiac arrest	Asystolia
Cardiac disorders	Cardiac arrest	Asystolic
Cardiac disorders	Cyanosis	Blue lips
Cardiac disorders	Cardiac arrest	Cardiac arrest
Cardiac disorders	Cardiac arrest	Cardiac arrest transient
Cardiac disorders	Cardio-respiratory arrest	Cardio-respiratory arrest
Cardiac disorders	Cardio-respiratory arrest	Cardiopulmonary arrest
Cardiac disorders	Cardiac arrest	Congestive cardioplegia
Cardiac disorders	Cyanosis	Cyanosed
Cardiac disorders	Cyanosis	Cyanosis
Cardiac disorders	Cyanosis	Cyanosis NOS
Cardiac disorders	Cyanosis	Cyanosis of lip
Cardiac disorders	Cyanosis	Cyanosis peripheral
Cardiac disorders	Cyanosis	Cyanotic
Cardiac disorders	Cardiac arrest	Heart arrest
Cardiac disorders	Cardiac arrest	Hypoxic arrest
Cardiac disorders	Cyanosis	Lips cyanosed
Cardiac disorders	Cyanosis	Nails cyanosed
Cardiac disorders	Cardiac arrest	Standstill cardiac
Cardiac disorders	Cardiopulmonary failure	Cardio-respiratory failure
Cardiac disorders	Cardio-respiratory distress	Cardio-respiratory distress
Cardiac disorders	Cardiopulmonary failure	Cardiopulmonary insufficiency
Cardiac disorders	Cardiopulmonary failure	Cardiopulmonary failure
Cardiac disorders	Cyanosis	Circumoral cyanosis
Cardiac disorders	Cyanosis	Cyanosis aggravated
Infections and infestations	Severe acute respiratory syndrome	Severe acute respiratory syndrome
Infections and infestations	Severe acute respiratory syndrome	SARS
Injury, poisoning and procedural complications	Respiratory fume inhalation disorder	Respiratory fume inhalation disorder NOS
Injury, poisoning and procedural complications	Respiratory fume inhalation disorder	Upper respiratory inflammation due to fumes and vapors
Injury, poisoning and procedural	Respiratory fume inhalation disorder	Upper respiratory inflammation due

System Organ Class	Preferred Term	Lowest Level Term
Acute central respiratory depression (SMQ)		
complications		to fumes and vapours
Injury, poisoning and procedural complications	Respiratory fume inhalation disorder	Smoke inhalation
Injury, poisoning and procedural complications	Respiratory fume inhalation disorder	Respiratory fume inhalation disorder
Injury, poisoning and procedural complications	Postoperative respiratory failure	Postoperative respiratory failure
Investigations	Blood gases abnormal	ABGs abnormal
Investigations	Blood gases abnormal	Abnormal arterial blood gases
Investigations	Breath sounds abnormal	Abnormal chest sounds
Investigations	Breath sounds abnormal	Abnormal chest sounds NOS
Investigations	Blood gases abnormal	Blood gases abnormal
Investigations	Blood gases abnormal	Blood gases NOS abnormal
Investigations	Blood pH abnormal	Blood pH abnormal
Investigations	Blood pH decreased	Blood pH decreased
Investigations	Breath sounds abnormal	Breath sounds decreased
Investigations	Respiratory rate decreased	Breathing rate slowed
Investigations	Respiratory rate decreased	Breathing slowed
Investigations	Breath sounds abnormal	Diminished lung sounds
Investigations	Blood pH decreased	Low pH
Investigations	Oxygen saturation abnormal	Oxygen saturation abnormal
Investigations	Oxygen saturation decreased	Oxygen saturation decreased
Investigations	Oxygen saturation decreased	Oxygen saturation low
Investigations	PO2 abnormal	Oxygen tension abnormal NOS
Investigations	PO2 decreased	Oxygen tension decreased
Investigations	PCO2 decreased	Partial pressure CO2 decreased
Investigations	PO2 abnormal	Partial pressure O2 abnormal NOS
Investigations	PO2 decreased	Partial pressure O2 decreased
Investigations	PCO2 decreased	PCO2 decreased
Investigations	Blood pH decreased	pH decreased
Investigations	Blood pH decreased	pH reduced
Investigations	Blood pH decreased	Plasma pH decreased
Investigations	PO2 abnormal	PO2 abnormal NOS
Investigations	PO2 decreased	PO2 decreased

System Organ Class	Preferred Term	Lowest Level Term
Acute central respiratory depression (SMQ)		
Investigations	PCO2 decreased	Reduced CO2 tension
Investigations	Respiratory rate decreased	Respiration rate decreased
Investigations	Respiratory rate decreased	Respiratory rate decreased
Investigations	Respiratory rate decreased	Respiratory rate low
Investigations	Breath sounds abnormal	Respiratory sounds decreased
Investigations	Blood pH decreased	Serum pH decreased
Investigations	Oxygen saturation abnormal	Oximetry abnormal
Investigations	Oxygen saturation decreased	Oximetry decreased
Investigations	Blood pH decreased	Arterial blood pH decreased
Investigations	Blood pH decreased	Venous blood pH decreased
Investigations	PCO2 abnormal	PCO2 abnormal
Investigations	Breath sounds abnormal	Abnormal chest sound
Investigations	PO2 abnormal	PO2 abnormal
Investigations	Breath sounds absent	Breath sounds absent
Investigations	Breath sounds abnormal	Breath sounds abnormal
Investigations	Breath sounds abnormal	Vesicular breathing abnormal
Investigations	Venous oxygen saturation decreased	Mixed venous blood saturation decreased
Investigations	Venous oxygen saturation abnormal	Mixed venous blood saturation abnormal
Investigations	Venous oxygen saturation decreased	SvO2 decreased
Investigations	Venous oxygen saturation abnormal	SvO2 abnormal
Investigations	Capnogram abnormal	Capnogram abnormal
Investigations	End-tidal CO2 abnormal	End-tidal CO2 abnormal
Investigations	End-tidal CO2 decreased	End-tidal CO2 decreased
Investigations	Alveolar oxygen partial pressure decreased	Alveolar oxygen partial pressure decreased
Investigations	Alveolar oxygen partial pressure abnormal	Alveolar oxygen partial pressure abnormal
Investigations	Venous oxygen partial pressure decreased	Venous oxygen partial pressure decreased
Investigations	Venous oxygen partial pressure abnormal	Venous oxygen partial pressure abnormal
Investigations	Venous oxygen saturation decreased	Venous oxygen saturation decreased
Investigations	Venous oxygen saturation abnormal	Venous oxygen saturation abnormal

System Organ Class	Preferred Term	Lowest Level Term
Acute central respiratory depression (SMQ)		
Investigations	Oxygen saturation decreased	Arterial oxygen saturation decreased
Investigations	Oxygen saturation abnormal	Arterial oxygen saturation abnormal
Investigations	PO2 decreased	Arterial oxygen partial pressure decreased
Investigations	PO2 abnormal	Arterial oxygen partial pressure abnormal
Investigations	PO2 decreased	PaO2 decreased
Investigations	PO2 abnormal	PaO2 abnormal
Investigations	Breath sounds abnormal	Coarse breath sounds
Nervous system disorders	Central-alveolar hypoventilation	Central-alveolar hypoventilation
Nervous system disorders	Hypercapnic coma	Hypercapnic coma
Psychiatric disorders	Breath holding	Breath holding
Psychiatric disorders	Breath holding	Breath holding attack
Psychiatric disorders	Breath holding	Breath holding spells
Respiratory, thoracic and mediastinal disorders	Acute respiratory distress syndrome	A.R.D.S.
Respiratory, thoracic and mediastinal disorders	Respiratory acidosis	Acidosis respiratory
Respiratory, thoracic and mediastinal disorders	Acute respiratory failure	Acute on chronic respiratory failure
Respiratory, thoracic and mediastinal disorders	Acute respiratory distress syndrome	Acute respiratory distress syndrome
Respiratory, thoracic and mediastinal disorders	Acute respiratory failure	Acute respiratory failure
Respiratory, thoracic and mediastinal disorders	Acute respiratory distress syndrome	Adult RDS
Respiratory, thoracic and mediastinal disorders	Acute respiratory distress syndrome	Adult respiratory distress syndrome
Respiratory, thoracic and mediastinal disorders	Acute respiratory distress syndrome	Adult respiratory stress syndrome
Respiratory, thoracic and mediastinal disorders	Dyspnoea	Air hunger
Respiratory, thoracic and mediastinal disorders	Anoxia	Anoxia
Respiratory, thoracic and mediastinal disorders	Apnoea	Apnea
Respiratory, thoracic and mediastinal disorders	Apnoea	Apnoea

System Organ Class	Preferred Term	Lowest Level Term
Acute central respiratory depression (SMQ)		
Respiratory, thoracic and mediastinal disorders	Apnoeic attack	Apnoea attack
Respiratory, thoracic and mediastinal disorders	Apnoeic attack	Apnoeic attack
Respiratory, thoracic and mediastinal disorders	Acute respiratory distress syndrome	ARDS
Respiratory, thoracic and mediastinal disorders	Respiratory arrest	Arrest pulmonary
Respiratory, thoracic and mediastinal disorders	Respiratory arrest	Arrest respiratory
Respiratory, thoracic and mediastinal disorders	Asphyxia	Asphyxia
Respiratory, thoracic and mediastinal disorders	Asphyxia	Asphyxiation
Respiratory, thoracic and mediastinal disorders	Bradypnoea	Bradypnea
Respiratory, thoracic and mediastinal disorders	Bradypnoea	Bradypnoea
Respiratory, thoracic and mediastinal disorders	Dyspnoea	Breath shortness
Respiratory, thoracic and mediastinal disorders	Hypopnoea	Breathing abnormally shallow
Respiratory, thoracic and mediastinal disorders	Respiratory arrest	Breathing arrested
Respiratory, thoracic and mediastinal disorders	Dyspnoea	Breathing difficult
Respiratory, thoracic and mediastinal disorders	Hypopnoea	Breathing shallow
Respiratory, thoracic and mediastinal disorders	Dyspnoea	Breathlessness
Respiratory, thoracic and mediastinal disorders	Hypercapnia	Carbon dioxide narcosis
Respiratory, thoracic and mediastinal disorders	Sleep apnoea syndrome	Central sleep apnoea syndrome
Respiratory, thoracic and mediastinal disorders	Cheyne-Stokes respiration	Cheyne-Stokes respiration
Respiratory, thoracic and mediastinal disorders	Cyanosis central	Cyanosis central
Respiratory, thoracic and mediastinal disorders	Respiratory depression	Depression respiratory

System Organ Class	Preferred Term	Lowest Level Term
Acute central respiratory depression (SMQ)		
Respiratory, thoracic and mediastinal disorders	Dyspnoea	Difficulty breathing
Respiratory, thoracic and mediastinal disorders	Respiratory distress	Distress respiratory
Respiratory, thoracic and mediastinal disorders	Dyspnoea	Dyspnea
Respiratory, thoracic and mediastinal disorders	Dyspnoea	Dyspnea exacerbated
Respiratory, thoracic and mediastinal disorders	Dyspnoea	Dyspnoea
Respiratory, thoracic and mediastinal disorders	Dyspnoea	Dyspnoea exacerbated
Respiratory, thoracic and mediastinal disorders	Dyspnoea	Dyspnoea NOS
Respiratory, thoracic and mediastinal disorders	Respiratory failure	Failure respiratory
Respiratory, thoracic and mediastinal disorders	Dyspnoea	Gasping
Respiratory, thoracic and mediastinal disorders	Dyspnoea	Hunger air
Respiratory, thoracic and mediastinal disorders	Hypercapnia	Hypercapnia
Respiratory, thoracic and mediastinal disorders	Hypercapnia	Hypercapnic
Respiratory, thoracic and mediastinal disorders	Hypercapnia	Hypercarbia
Respiratory, thoracic and mediastinal disorders	Hypopnoea	Hypopnea
Respiratory, thoracic and mediastinal disorders	Hypopnoea	Hypopnoea
Respiratory, thoracic and mediastinal disorders	Hypoventilation	Hypoventilation
Respiratory, thoracic and mediastinal disorders	Hypoxia	Hypoxaemia
Respiratory, thoracic and mediastinal disorders	Hypoxia	Hypoxemia
Respiratory, thoracic and mediastinal disorders	Hypoxia	Hypoxia
Respiratory, thoracic and mediastinal disorders	Hypoxia	Hypoxic

System Organ Class	Preferred Term	Lowest Level Term
Acute central respiratory depression (SMQ)		
Respiratory, thoracic and mediastinal disorders	Dyspnoea	Increased shortness of breath
Respiratory, thoracic and mediastinal disorders	Dyspnoea	Increased work of breathing
Respiratory, thoracic and mediastinal disorders	Dyspnoea	Labored breathing
Respiratory, thoracic and mediastinal disorders	Dyspnoea	Laboured breathing
Respiratory, thoracic and mediastinal disorders	Dyspnoea	Laboured respiration
Respiratory, thoracic and mediastinal disorders	Dyspnoea	Marked inactivity of chest wall on inspiratory effort
Respiratory, thoracic and mediastinal disorders	Hypercapnia	Narcosis carbon dioxide
Respiratory, thoracic and mediastinal disorders	Sleep apnoea syndrome	Obstructive sleep apnoea syndrome
Respiratory, thoracic and mediastinal disorders	Orthopnoea	Orthopnea
Respiratory, thoracic and mediastinal disorders	Orthopnoea	Orthopnoea
Respiratory, thoracic and mediastinal disorders	Respiratory arrest	Pulmonary arrest
Respiratory, thoracic and mediastinal disorders	Respiratory gas exchange disorder	Resp gas exchange disorder NOS
Respiratory, thoracic and mediastinal disorders	Respiration abnormal	Respiration abnormal
Respiratory, thoracic and mediastinal disorders	Cheyne-Stokes respiration	Respiration biot-type
Respiratory, thoracic and mediastinal disorders	Cheyne-Stokes respiration	Respiration Cheyne-Stokes-type
Respiratory, thoracic and mediastinal disorders	Respiratory depression	Respiration depressed
Respiratory, thoracic and mediastinal disorders	Respiratory failure	Respiration failure
Respiratory, thoracic and mediastinal disorders	Respiratory disorder	Respiration irregularity
Respiratory, thoracic and mediastinal disorders	Dyspnoea	Respiration labored
Respiratory, thoracic and mediastinal disorders	Dyspnoea	Respiration labored

System Organ Class	Preferred Term	Lowest Level Term
Acute central respiratory depression (SMQ)		
Respiratory, thoracic and mediastinal disorders	Hypopnoea	Respiration spontaneous decreased
Respiratory, thoracic and mediastinal disorders	Respiratory disorder	Respiratory abnormality, unspecified
Respiratory, thoracic and mediastinal disorders	Respiratory acidosis	Respiratory acidosis
Respiratory, thoracic and mediastinal disorders	Respiratory arrest	Respiratory arrest
Respiratory, thoracic and mediastinal disorders	Respiratory depression	Respiratory depression
Respiratory, thoracic and mediastinal disorders	Respiratory depth decreased	Respiratory depth decreased
Respiratory, thoracic and mediastinal disorders	Respiratory disorder	Respiratory disorder
Respiratory, thoracic and mediastinal disorders	Respiratory disorder	Respiratory disorder NOS
Respiratory, thoracic and mediastinal disorders	Respiratory distress	Respiratory distress
Respiratory, thoracic and mediastinal disorders	Acute respiratory distress syndrome	Respiratory distress syndrome adult
Respiratory, thoracic and mediastinal disorders	Respiratory disorder	Respiratory dysfunction NOS
Respiratory, thoracic and mediastinal disorders	Respiratory failure	Respiratory failure
Respiratory, thoracic and mediastinal disorders	Respiratory gas exchange disorder	Respiratory gas exchange disorder NOS
Respiratory, thoracic and mediastinal disorders	Respiratory failure	Respiratory insufficiency
Respiratory, thoracic and mediastinal disorders	Respiratory paralysis	Respiratory paralysis
Respiratory, thoracic and mediastinal disorders	Respiratory disorder	Respiratory rhythm disorder
Respiratory, thoracic and mediastinal disorders	Respiratory disorder	Respiratory system disorder
Respiratory, thoracic and mediastinal disorders	Hypercapnia	Retention carbon dioxide
Respiratory, thoracic and mediastinal disorders	Hypopnoea	Shallow breathing
Respiratory, thoracic and mediastinal disorders	Acute respiratory distress syndrome	Shock lung

System Organ Class	Preferred Term	Lowest Level Term
Acute central respiratory depression (SMQ)		
Respiratory, thoracic and mediastinal disorders	Dyspnoea	Short of breath
Respiratory, thoracic and mediastinal disorders	Dyspnoea	Shortness of breath
Respiratory, thoracic and mediastinal disorders	Sleep apnoea syndrome	Sleep apnea
Respiratory, thoracic and mediastinal disorders	Sleep apnoea syndrome	Sleep apnea syndrome
Respiratory, thoracic and mediastinal disorders	Sleep apnoea syndrome	Sleep apnoea
Respiratory, thoracic and mediastinal disorders	Sleep apnoea syndrome	Sleep apnoea syndrome
Respiratory, thoracic and mediastinal disorders	Sleep apnoea syndrome	Sleep apnoea syndromes
Respiratory, thoracic and mediastinal disorders	Asphyxia	Strangulation
Respiratory, thoracic and mediastinal disorders	Asphyxia	Suffocation
Respiratory, thoracic and mediastinal disorders	Acute respiratory distress syndrome	Surfactant deficiency syndrome adult
Respiratory, thoracic and mediastinal disorders	Acute respiratory distress syndrome	Syndrome adult respiratory distress
Respiratory, thoracic and mediastinal disorders	Acute respiratory distress syndrome	Syndrome respiratory distress adult
Respiratory, thoracic and mediastinal disorders	Respiratory disorder	Unspecified disease of respiratory system
Respiratory, thoracic and mediastinal disorders	Hypoventilation	Ventilation difficult
Respiratory, thoracic and mediastinal disorders	Respiratory failure	Ventilatory failure
Respiratory, thoracic and mediastinal disorders	Respiration abnormal	Respiratory sighs
Respiratory, thoracic and mediastinal disorders	Acute respiratory failure	Acute respiratory decompensation
Respiratory, thoracic and mediastinal disorders	Respiration abnormal	Respiration abnormal NOS
Respiratory, thoracic and mediastinal disorders	Respiratory failure	Pulmonary failure
Respiratory, thoracic and mediastinal disorders	Asphyxia	Injury asphyxiation

System Organ Class	Preferred Term	Lowest Level Term
Acute central respiratory depression (SMQ)		
Respiratory, thoracic and mediastinal disorders	Sleep apnoea syndrome	Apnoea syndrome
Respiratory, thoracic and mediastinal disorders	Dyspnoea	Labored respiration
Respiratory, thoracic and mediastinal disorders	Apnoeic attack	Apnea attack
Respiratory, thoracic and mediastinal disorders	Sleep apnoea syndrome	Apnea syndrome
Respiratory, thoracic and mediastinal disorders	Sleep apnoea syndrome	Central sleep apnea syndrome
Respiratory, thoracic and mediastinal disorders	Sleep apnoea syndrome	Obstructive sleep apnea syndrome
Respiratory, thoracic and mediastinal disorders	Orthopnoea	Supine dyspnea
Respiratory, thoracic and mediastinal disorders	Orthopnoea	Supine dyspnea
Respiratory, thoracic and mediastinal disorders	Respiratory failure	Hypercapnic respiratory failure
Respiratory, thoracic and mediastinal disorders	Respiratory gas exchange disorder	Respiratory gas exchange disorder
Respiratory, thoracic and mediastinal disorders	Respiratory failure	Restrictive respiratory insufficiency
Respiratory, thoracic and mediastinal disorders	Apnoeic attack	Apneic attack
Respiratory, thoracic and mediastinal disorders	Dyspnoea	Acute dyspnea
Respiratory, thoracic and mediastinal disorders	Dyspnoea	Acute dyspnea
Respiratory, thoracic and mediastinal disorders	Cyanosis central	Cyanosis central aggravated
Respiratory, thoracic and mediastinal disorders	Respiratory failure	Respiratory failure aggravated
Respiratory, thoracic and mediastinal disorders	Acute respiratory failure	Acute respiratory insufficiency
Respiratory, thoracic and mediastinal disorders	Sleep apnoea syndrome	Hypopnea syndrome
Respiratory, thoracic and mediastinal disorders	Sleep apnoea syndrome	Hypopnoea syndrome
Respiratory, thoracic and mediastinal disorders	Hypoventilation	Alveolar hypoventilation

System Organ Class	Preferred Term	Lowest Level Term
Acute central respiratory depression (SMQ)		
Surgical and medical procedures	Oxygen supplementation	Oxygen supplementation

(3) AEs related to route of administration:

System Organ Class	Preferred Term	Lowest Level Term
Route of Administration : Oral Soft Tissue Conditions (HLT)		
Gastrointestinal disorders	Angina bullosa haemorrhagica	Angina bullosa haemorrhagica
Gastrointestinal disorders	Angina bullosa haemorrhagica	Angina bullosa hemorrhagica
Gastrointestinal disorders	Aphthous stomatitis	Aphthous stoma
Gastrointestinal disorders	Aphthous stomatitis	Aphthous stomatitis
Gastrointestinal disorders	Aphthous stomatitis	Aphthous ulcer
Gastrointestinal disorders	Aphthous stomatitis	Buccal mucosa aphthous ulceration
Gastrointestinal disorders	Aphthous stomatitis	Canker sores oral
Gastrointestinal disorders	Aphthous stomatitis	Oral aphthae
Gastrointestinal disorders	Aphthous stomatitis	Stomatitis aphthous
Gastrointestinal disorders	Aphthous stomatitis	Stomatitis ulcerative aphthous
Gastrointestinal disorders	Aphthous stomatitis	Ulcer aphthous
Gastrointestinal disorders	Aphthous stomatitis	Ulcer aphthous oral
Gastrointestinal disorders	Aphthous stomatitis	Ulcers aphthous oral
Gastrointestinal disorders	Aphthous stomatitis	Canker sore lip
Gastrointestinal disorders	Aphthous stomatitis	Aphthous ulcer recurrent
Gastrointestinal disorders	Aphthous stomatitis	Aphtha
Gastrointestinal disorders	Buccal mucosal roughening	Roughness oral
Gastrointestinal disorders	Buccal mucosal roughening	Buccal mucosal roughening
Gastrointestinal disorders	Buccal mucosal roughening	Rough mouth
Gastrointestinal disorders	Burning mouth syndrome	Burning mouth syndrome
Gastrointestinal disorders	Chapped lips	Lip rough
Gastrointestinal disorders	Chapped lips	Chapped lips
Gastrointestinal disorders	Chapped lips	Cracked lips
Gastrointestinal disorders	Cheilitis	Angular cheilitis
Gastrointestinal disorders	Cheilitis	Angular stomatitis
Gastrointestinal disorders	Cheilitis	Cheilitis
Gastrointestinal disorders	Cheilitis	Lip redness
Gastrointestinal disorders	Cheilitis	Desquamative cheilitis

System Organ Class	Preferred Term	Lowest Level Term
Route of Administration : Oral Soft Tissue Conditions (HLT)		
Gastrointestinal disorders	Cheilitis	Rash lips
Gastrointestinal disorders	Cheilitis	Irritation lips
Gastrointestinal disorders	Cheilitis	Raw lips
Gastrointestinal disorders	Cheilitis	Redness corner of mouth
Gastrointestinal disorders	Cheilitis	Inflammation lips
Gastrointestinal disorders	Cheilitis	Soreness corner mouth
Gastrointestinal disorders	Cheilitis	Sores lip
Gastrointestinal disorders	Cheilitis	Perleche
Gastrointestinal disorders	Cheilitis	Angular cheilosis
Gastrointestinal disorders	Cheilitis granulomatosa	Cheilitis granulomatosa
Gastrointestinal disorders	Cheilosis	Cheilosis
Gastrointestinal disorders	Contact stomatitis	Contact stomatitis
Gastrointestinal disorders	Enlarged uvula	Enlarged uvula
Gastrointestinal disorders	Gingival blister	Gingival blister
Gastrointestinal disorders	Gingival blister	Blisters gum
Gastrointestinal disorders	Gingival oedema	Gingival oedema
Gastrointestinal disorders	Gingival oedema	Oedema gum
Gastrointestinal disorders	Gingival oedema	Gingival edema
Gastrointestinal disorders	Gingival oedema	Edema gum
Gastrointestinal disorders	Gingival pruritus	Gingival pruritus
Gastrointestinal disorders	Gingival pruritus	Itching gum
Gastrointestinal disorders	Gingival swelling	Gingival swelling
Gastrointestinal disorders	Gingival swelling	Gum swelling
Gastrointestinal disorders	Hypoaesthesia oral	Anaesthesia lip
Gastrointestinal disorders	Hypoaesthesia oral	Anaesthesia mouth
Gastrointestinal disorders	Hypoaesthesia oral	Anaesthesia oral mucosa
Gastrointestinal disorders	Hypoaesthesia oral	Anaesthesia tongue
Gastrointestinal disorders	Hypoaesthesia oral	Hypoaesthesia oral NOS
Gastrointestinal disorders	Hypoaesthesia oral	Hypoaesthesia tongue
Gastrointestinal disorders	Hypoaesthesia oral	Numbness circumoral
Gastrointestinal disorders	Hypoaesthesia oral	Numbness of mouth angular
Gastrointestinal disorders	Hypoaesthesia oral	Numbness of tongue
Gastrointestinal disorders	Hypoaesthesia oral	Numbness oral

System Organ Class	Preferred Term	Lowest Level Term
Route of Administration : Oral Soft Tissue Conditions (HLT)		
Gastrointestinal disorders	Hypoaesthesia oral	Numbness perioral
Gastrointestinal disorders	Hypoaesthesia oral	Oral mucosal anaesthesia
Gastrointestinal disorders	Hypoaesthesia oral	Perioral numbness
Gastrointestinal disorders	Hypoaesthesia oral	Tongue sensation loss of
Gastrointestinal disorders	Hypoaesthesia oral	Tongue tip numbness of
Gastrointestinal disorders	Hypoaesthesia oral	Hypoaesthesia lips
Gastrointestinal disorders	Hypoaesthesia oral	Hypoaesthesia gingival
Gastrointestinal disorders	Hypoaesthesia oral	Numbness mouth
Gastrointestinal disorders	Hypoaesthesia oral	Numb mouth
Gastrointestinal disorders	Hypoaesthesia oral	Numb lips
Gastrointestinal disorders	Hypoaesthesia oral	Numbness lips
Gastrointestinal disorders	Hypoaesthesia oral	Hypoaesthesia gum
Gastrointestinal disorders	Hypoaesthesia oral	Numbness gum
Gastrointestinal disorders	Hypoaesthesia oral	Numbness gingival
Gastrointestinal disorders	Hypoaesthesia oral	Hypoesthesia gingival
Gastrointestinal disorders	Hypoaesthesia oral	Hypoesthesia lips
Gastrointestinal disorders	Hypoaesthesia oral	Hypoesthesia oral
Gastrointestinal disorders	Hypoaesthesia oral	Hypoesthesia tongue
Gastrointestinal disorders	Hypoaesthesia oral	Hypoaesthesia oral
Gastrointestinal disorders	Hypoaesthesia oral	Hypoesthesia gum
Gastrointestinal disorders	Hypoaesthesia oral	Anesthesia lip
Gastrointestinal disorders	Hypoaesthesia oral	Anesthesia mouth
Gastrointestinal disorders	Hypoaesthesia oral	Anesthesia oral mucosa
Gastrointestinal disorders	Hypoaesthesia oral	Anesthesia tongue
Gastrointestinal disorders	Leukoplakia oral	Leukoplakia of mouth
Gastrointestinal disorders	Leukoplakia oral	Leukoplakia of oral mucosa, including tongue
Gastrointestinal disorders	Leukoplakia oral	Leukoplakia oral
Gastrointestinal disorders	Leukoplakia oral	Leukoplakia oral NOS
Gastrointestinal disorders	Leukoplakia oral	Oral leukoplakia NOS
Gastrointestinal disorders	Leukoplakia oral	Leukoplakia buccalis
Gastrointestinal disorders	Leukoplakia oral	Leukoplakia labialis
Gastrointestinal disorders	Leukoplakia oral	Leukoplakia lingualis

System Organ Class	Preferred Term	Lowest Level Term
Route of Administration : Oral Soft Tissue Conditions (HLT)		
Gastrointestinal disorders	Leukoplakia oral	Leukoplakia of oral mucosa, incl tongue
Gastrointestinal disorders	Leukoplakia oral	Leukoplakia tongue
Gastrointestinal disorders	Lip blister	Blister of lip
Gastrointestinal disorders	Lip blister	Lip blister
Gastrointestinal disorders	Lip blister	Blister lip
Gastrointestinal disorders	Lip discolouration	Lip colour altered
Gastrointestinal disorders	Lip discolouration	Lip discolouration
Gastrointestinal disorders	Lip discolouration	Lip color altered
Gastrointestinal disorders	Lip discolouration	Lip discoloration
Gastrointestinal disorders	Lip disorder	Lip disorder NOS
Gastrointestinal disorders	Lip disorder	Lip disorder
Gastrointestinal disorders	Lip disorder	Bumps lip
Gastrointestinal disorders	Lip erosion	Lip erosion
Gastrointestinal disorders	Lip exfoliation	Lip sloughing
Gastrointestinal disorders	Lip exfoliation	Peeling lips
Gastrointestinal disorders	Lip exfoliation	Lip exfoliation
Gastrointestinal disorders	Lip haematoma	Lip haematoma
Gastrointestinal disorders	Lip haematoma	Lip hematoma
Gastrointestinal disorders	Lip haemorrhage	Lip haemorrhage
Gastrointestinal disorders	Lip haemorrhage	Hemorrhage lips
Gastrointestinal disorders	Lip haemorrhage	Bleeding lips
Gastrointestinal disorders	Lip haemorrhage	Lip hemorrhage
Gastrointestinal disorders	Lip haemorrhage	Haemorrhage lips
Gastrointestinal disorders	Lip haemorrhage	Lip bleeding
Gastrointestinal disorders	Lip oedema	Edema lip
Gastrointestinal disorders	Lip oedema	Lip edema
Gastrointestinal disorders	Lip oedema	Lip oedema
Gastrointestinal disorders	Lip oedema	Oedema lip
Gastrointestinal disorders	Lip pain	Lip pain
Gastrointestinal disorders	Lip pain	Lip sore
Gastrointestinal disorders	Lip pain	Lip soreness
Gastrointestinal disorders	Lip pain	Tender lips

System Organ Class	Preferred Term	Lowest Level Term
Route of Administration : Oral Soft Tissue Conditions (HLT)		
Gastrointestinal disorders	Lip pain	Stinging lips
Gastrointestinal disorders	Lip pain	Sensitive lips
Gastrointestinal disorders	Lip pruritus	Lip pruritus
Gastrointestinal disorders	Lip swelling	Lip swelling
Gastrointestinal disorders	Lip swelling	Lips swelling non-specific
Gastrointestinal disorders	Lip swelling	Swelling lips
Gastrointestinal disorders	Lip swelling	Swelling of lips
Gastrointestinal disorders	Lip swelling	Swollen lips
Gastrointestinal disorders	Lip ulceration	Lip ulcer
Gastrointestinal disorders	Lip ulceration	Lip ulceration
Gastrointestinal disorders	Lip ulceration	Ulcer lip
Gastrointestinal disorders	Melanoplakia oral	Melanoplakia oral
Gastrointestinal disorders	Mouth haemorrhage	Hemorrhage mouth
Gastrointestinal disorders	Mouth haemorrhage	Hemorrhage of mouth
Gastrointestinal disorders	Mouth haemorrhage	Hemorrhage oral
Gastrointestinal disorders	Mouth haemorrhage	Mouth haemorrhage
Gastrointestinal disorders	Mouth haemorrhage	Mouth hemorrhage
Gastrointestinal disorders	Mouth haemorrhage	Oral haemorrhage
Gastrointestinal disorders	Mouth haemorrhage	Oral hemorrhage
Gastrointestinal disorders	Mouth haemorrhage	Oral mucosa bleeding
Gastrointestinal disorders	Mouth haemorrhage	Oral mucosa ecchymosis
Gastrointestinal disorders	Mouth haemorrhage	Oral mucosal petechiae
Gastrointestinal disorders	Mouth haemorrhage	Petechiae oral mucosa
Gastrointestinal disorders	Mouth haemorrhage	Bleeding mouth
Gastrointestinal disorders	Mouth haemorrhage	Haemorrhage mouth
Gastrointestinal disorders	Mouth haemorrhage	Haemorrhage of mouth
Gastrointestinal disorders	Mouth haemorrhage	Haemorrhage oral
Gastrointestinal disorders	Mouth haemorrhage	Mouth bleeding
Gastrointestinal disorders	Mouth ulceration	Buccal mucosa ulceration
Gastrointestinal disorders	Mouth ulceration	Buccal ulceration
Gastrointestinal disorders	Mouth ulceration	Mouth ulcer
Gastrointestinal disorders	Mouth ulceration	Mouth ulceration
Gastrointestinal disorders	Mouth ulceration	Oral ulceration

System Organ Class	Preferred Term	Lowest Level Term
Route of Administration : Oral Soft Tissue Conditions (HLT)		
Gastrointestinal disorders	Mouth ulceration	Stomatitis ulcerative
Gastrointestinal disorders	Mouth ulceration	Ulcer buccal
Gastrointestinal disorders	Mouth ulceration	Ulcer mouth
Gastrointestinal disorders	Mouth ulceration	Ulceration mouth
Gastrointestinal disorders	Mouth ulceration	Ulceration of mouth
Gastrointestinal disorders	Mouth ulceration	Ulcerative stomatitis
Gastrointestinal disorders	Mouth ulceration	Ulcerative stomatitis, acute
Gastrointestinal disorders	Mouth ulceration	Mouth ulceration aggravated
Gastrointestinal disorders	Odynophagia	Odynophagia
Gastrointestinal disorders	Odynophagia	Swallowing painful
Gastrointestinal disorders	Oedema mouth	Edema of mouth
Gastrointestinal disorders	Oedema mouth	Oedema mouth
Gastrointestinal disorders	Oedema mouth	Oral mucosa swollen
Gastrointestinal disorders	Oedema mouth	Swollen mouth
Gastrointestinal disorders	Oedema mouth	Edema mouth
Gastrointestinal disorders	Oedema mouth	Oedema of mouth
Gastrointestinal disorders	Oral discharge	Oral discharge
Gastrointestinal disorders	Oral discomfort	Burning oral sensation
Gastrointestinal disorders	Oral discomfort	Discomfort in mouth
Gastrointestinal disorders	Oral discomfort	Lip burning sensation of
Gastrointestinal disorders	Oral discomfort	Oral cavity discomfort
Gastrointestinal disorders	Oral discomfort	Oral discomfort
Gastrointestinal disorders	Oral discomfort	Oral hot feeling
Gastrointestinal disorders	Oral discomfort	Burning corner of mouth
Gastrointestinal disorders	Oral discomfort	Burning lips
Gastrointestinal disorders	Oral discomfort	Burning mouth
Gastrointestinal disorders	Oral disorder	Oral soft tissue disorder NOS
Gastrointestinal disorders	Oral disorder	Oral mucosal disorder
Gastrointestinal disorders	Oral disorder	Oral lesion
Gastrointestinal disorders	Oral disorder	Oral soft tissue disorder
Gastrointestinal disorders	Oral disorder	Oral disorder
Gastrointestinal disorders	Oral disorder	Mouth bump
Gastrointestinal disorders	Oral dysaesthesia	Dysesthesia of lips

System Organ Class	Preferred Term	Lowest Level Term
Route of Administration : Oral Soft Tissue Conditions (HLT)		
Gastrointestinal disorders	Oral dysaesthesia	Dysesthesia of tongue
Gastrointestinal disorders	Oral dysaesthesia	Oral dysaesthesia
Gastrointestinal disorders	Oral dysaesthesia	Oral dysesthesia
Gastrointestinal disorders	Oral dysaesthesia	Dysaesthesia of lips
Gastrointestinal disorders	Oral dysaesthesia	Dysaesthesia of tongue
Gastrointestinal disorders	Oral dysaesthesia	Vincent's symptom
Gastrointestinal disorders	Oral leukoedema	Oral leukoedema
Gastrointestinal disorders	Oral lichen planus	Oral lichen planus
Gastrointestinal disorders	Oral mucosa atrophy	Oral mucosa atrophy
Gastrointestinal disorders	Oral mucosa erosion	Oral mucosa erosion
Gastrointestinal disorders	Oral mucosal blistering	Blistering of mouth
Gastrointestinal disorders	Oral mucosal blistering	Oral mucosa blister
Gastrointestinal disorders	Oral mucosal blistering	Oral mucosa blistering
Gastrointestinal disorders	Oral mucosal blistering	Oral mucosal blistering
Gastrointestinal disorders	Oral mucosal discolouration	Oral mucosa discolouration
Gastrointestinal disorders	Oral mucosal discolouration	Oral mucosal discolouration
Gastrointestinal disorders	Oral mucosal discolouration	Oral mucosal discoloration
Gastrointestinal disorders	Oral mucosal eruption	Oral mucosal eruption
Gastrointestinal disorders	Oral mucosal erythema	Oral mucosa redness
Gastrointestinal disorders	Oral mucosal erythema	Oral redness
Gastrointestinal disorders	Oral mucosal erythema	Redness mouth
Gastrointestinal disorders	Oral mucosal erythema	Oral mucosal erythema
Gastrointestinal disorders	Oral mucosal erythema	Palatal erythema
Gastrointestinal disorders	Oral mucosal exfoliation	Oral mucosal sloughing
Gastrointestinal disorders	Oral mucosal exfoliation	Sloughing of buccal mucosa
Gastrointestinal disorders	Oral mucosal exfoliation	Sloughing of mouth
Gastrointestinal disorders	Oral mucosal exfoliation	Gingival sloughing
Gastrointestinal disorders	Oral mucosal exfoliation	Peeling mouth
Gastrointestinal disorders	Oral mucosal exfoliation	Desquamation mouth
Gastrointestinal disorders	Oral mucosal exfoliation	Sloughing gums
Gastrointestinal disorders	Oral mucosal exfoliation	Sloughing gingival
Gastrointestinal disorders	Oral mucosal exfoliation	Peeling gingival
Gastrointestinal disorders	Oral mucosal exfoliation	Peeling gum

System Organ Class	Preferred Term	Lowest Level Term
Route of Administration : Oral Soft Tissue Conditions (HLT)		
Gastrointestinal disorders	Oral mucosal exfoliation	Desquamation gum
Gastrointestinal disorders	Oral mucosal exfoliation	Desquamation gingival
Gastrointestinal disorders	Oral mucosal exfoliation	Oral mucosal exfoliation
Gastrointestinal disorders	Oral mucosal hypertrophy	Oral mucosal hypertrophy
Gastrointestinal disorders	Oral pain	Mouth pain
Gastrointestinal disorders	Oral pain	Oral angular pain
Gastrointestinal disorders	Oral pain	Oral mucosa pain
Gastrointestinal disorders	Oral pain	Oral pain
Gastrointestinal disorders	Oral pain	Pain mouth
Gastrointestinal disorders	Oral pain	Pain oral
Gastrointestinal disorders	Oral pain	Sore mouth
Gastrointestinal disorders	Oral pain	Sensitive mouth
Gastrointestinal disorders	Oral pain	Tender mouth
Gastrointestinal disorders	Oral pain	Stinging mouth
Gastrointestinal disorders	Oral pain	Soreness roof of mouth
Gastrointestinal disorders	Oral papule	Oral papule
Gastrointestinal disorders	Oral pruritus	Intraoral pruritus
Gastrointestinal disorders	Oral pruritus	Itching mouth
Gastrointestinal disorders	Oral pruritus	Oral pruritus
Gastrointestinal disorders	Oral submucosal fibrosis	Oral submucosal fibrosis
Gastrointestinal disorders	Oral submucosal fibrosis	Oral submucous fibrosis, including of tongue
Gastrointestinal disorders	Oral submucosal fibrosis	Oral submucous fibrosis, incl of tongue
Gastrointestinal disorders	Oral toxicity	Oral toxicity
Gastrointestinal disorders	Palatal disorder	Palatal disorder
Gastrointestinal disorders	Palatal disorder	Palatal lesion
Gastrointestinal disorders	Palatal disorder	Palatal nodule
Gastrointestinal disorders	Palatal disorder	Soft palate disorder
Gastrointestinal disorders	Palatal dysplasia	Palatal dysplasia
Gastrointestinal disorders	Palatal oedema	Palatine arch swollen
Gastrointestinal disorders	Palatal oedema	Oedema uvula
Gastrointestinal disorders	Palatal oedema	Edema uvula
Gastrointestinal disorders	Palatal oedema	Palatal oedema

System Organ Class	Preferred Term	Lowest Level Term
Route of Administration : Oral Soft Tissue Conditions (HLT)		
Gastrointestinal disorders	Palatal oedema	Palatal edema
Gastrointestinal disorders	Palatitis	Palatitis
Gastrointestinal disorders	Paraesthesia oral	Circumoral paresthesia
Gastrointestinal disorders	Paraesthesia oral	Mouth paresthesia
Gastrointestinal disorders	Paraesthesia oral	Paraesthesia circumoral
Gastrointestinal disorders	Paraesthesia oral	Paraesthesia mouth
Gastrointestinal disorders	Paraesthesia oral	Paraesthesia oral NOS
Gastrointestinal disorders	Paraesthesia oral	Paraesthesia tongue
Gastrointestinal disorders	Paraesthesia oral	Paresthesia circumoral
Gastrointestinal disorders	Paraesthesia oral	Paresthesia mouth
Gastrointestinal disorders	Paraesthesia oral	Tongue abnormal feeling of
Gastrointestinal disorders	Paraesthesia oral	Paraesthesia lips
Gastrointestinal disorders	Paraesthesia oral	Paraesthesia gingival
Gastrointestinal disorders	Paraesthesia oral	Tingling mouth
Gastrointestinal disorders	Paraesthesia oral	Tingling lips
Gastrointestinal disorders	Paraesthesia oral	Paresthesia lips
Gastrointestinal disorders	Paraesthesia oral	Tingling tongue
Gastrointestinal disorders	Paraesthesia oral	Tingling gum
Gastrointestinal disorders	Paraesthesia oral	Tingling gingival
Gastrointestinal disorders	Paraesthesia oral	Paraesthesia gum
Gastrointestinal disorders	Paraesthesia oral	Paresthesia gingival
Gastrointestinal disorders	Paraesthesia oral	Paresthesia gum
Gastrointestinal disorders	Paraesthesia oral	Paresthesia oral
Gastrointestinal disorders	Paraesthesia oral	Paresthesia tongue
Gastrointestinal disorders	Paraesthesia oral	Paraesthesia oral
Gastrointestinal disorders	Paraesthesia oral	Perioral tingling
Gastrointestinal disorders	Paraesthesia oral	Perioral paraesthesia
Gastrointestinal disorders	Paraesthesia oral	Perioral paresthesia
Gastrointestinal disorders	Pigmentation buccal	Pigmentation buccal
Gastrointestinal disorders	Pigmentation lip	Lip pigmental spot
Gastrointestinal disorders	Pigmentation lip	Lip pigmentation
Gastrointestinal disorders	Pigmentation lip	Pigmentation lip
Gastrointestinal disorders	Pyostomatitis vegetans	Pyostomatitis vegetans

System Organ Class	Preferred Term	Lowest Level Term
Route of Administration : Oral Soft Tissue Conditions (HLT)		
Gastrointestinal disorders	Stomatitis	Buccal inflammation
Gastrointestinal disorders	Stomatitis	Mouth irritation
Gastrointestinal disorders	Stomatitis	Mucositis oral
Gastrointestinal disorders	Stomatitis	Stomatitis
Gastrointestinal disorders	Stomatitis	Sores mouth
Gastrointestinal disorders	Stomatitis	Sores roof of mouth
Gastrointestinal disorders	Stomatitis	Raw mouth
Gastrointestinal disorders	Stomatitis	Irritation roof of mouth
Gastrointestinal disorders	Stomatitis	Chapped mouth
Gastrointestinal disorders	Stomatitis	Inflammation of mouth
Gastrointestinal disorders	Stomatitis	Mouth broke out
Gastrointestinal disorders	Stomatitis	Inflammation under tongue
Gastrointestinal disorders	Stomatitis	Oral mucosal irritation
Gastrointestinal disorders	Stomatitis	Vesicular stomatitis
Gastrointestinal disorders	Stomatitis	Gingivostomatitis
Gastrointestinal disorders	Stomatitis	Pseudomembranous stomatitis
Gastrointestinal disorders	Stomatitis haemorrhagic	Stomatitis haemorrhagic
Gastrointestinal disorders	Stomatitis haemorrhagic	Stomatitis hemorrhagic
Gastrointestinal disorders	Stomatitis necrotising	Cancrum oris
Gastrointestinal disorders	Stomatitis necrotising	Mouth necrosis
Gastrointestinal disorders	Stomatitis necrotising	Necrosis mouth
Gastrointestinal disorders	Stomatitis necrotising	Noma
Gastrointestinal disorders	Stomatitis necrotising	Stomatitis necrotising
Gastrointestinal disorders	Stomatitis necrotising	Stomatitis necrotizing
Gastrointestinal disorders	Uvulitis	Uvulitis

System Organ Class	Preferred Term	Lowest Level Term
Route of Administration: Respiratory Disorders NEC (HLT)		
Respiratory, thoracic and mediastinal disorders	Allergic cough	Allergic cough
Respiratory, thoracic and mediastinal disorders	Choking	Choked on food
Respiratory, thoracic and mediastinal disorders	Choking	Choking

System Organ Class	Preferred Term	Lowest Level Term
Route of Administration: Respiratory Disorders NEC (HLT)		
Respiratory, thoracic and mediastinal disorders	Choking	Choke on medication
Respiratory, thoracic and mediastinal disorders	Choking sensation	Choking sensation
Respiratory, thoracic and mediastinal disorders	Choking sensation	Choking sensation (excl psychogenic and dysphagia)
Respiratory, thoracic and mediastinal disorders	Choking sensation	Pharynx closed sensation of
Respiratory, thoracic and mediastinal disorders	Choking sensation	Pharynx strangled sensation of
Respiratory, thoracic and mediastinal disorders	Cough	Cough
Respiratory, thoracic and mediastinal disorders	Cough	Cough increased
Respiratory, thoracic and mediastinal disorders	Cough	Cough nonproductive
Respiratory, thoracic and mediastinal disorders	Cough	Cough resembling asthma
Respiratory, thoracic and mediastinal disorders	Cough	Coughing
Respiratory, thoracic and mediastinal disorders	Cough	Dry cough
Respiratory, thoracic and mediastinal disorders	Cough	Irritant cough
Respiratory, thoracic and mediastinal disorders	Cough	Irritative cough
Respiratory, thoracic and mediastinal disorders	Cough	Nocturnal cough
Respiratory, thoracic and mediastinal disorders	Cough	Persistent dry cough
Respiratory, thoracic and mediastinal disorders	Cough	Persistent non-productive cough
Respiratory, thoracic and mediastinal disorders	Cough	Cough aggravated
Respiratory, thoracic and mediastinal disorders	Cough	Coughing after drug inhalation
Respiratory, thoracic and mediastinal disorders	Cough	Drug-induced cough
Respiratory, thoracic and mediastinal disorders	Cough	Smoker's cough

System Organ Class	Preferred Term	Lowest Level Term
Route of Administration: Respiratory Disorders NEC (HLT)		
Respiratory, thoracic and mediastinal disorders	Cough	Paroxysmal cough
Respiratory, thoracic and mediastinal disorders	Cough	Acute cough
Respiratory, thoracic and mediastinal disorders	Cough	Chronic cough
Respiratory, thoracic and mediastinal disorders	Cough	Persistent cough
Respiratory, thoracic and mediastinal disorders	Cough	Painful cough
Respiratory, thoracic and mediastinal disorders	Cough	Cough ineffective
Respiratory, thoracic and mediastinal disorders	Cough	Cough weak
Respiratory, thoracic and mediastinal disorders	Cough decreased	Cough decreased
Respiratory, thoracic and mediastinal disorders	Dry throat	Dry throat
Respiratory, thoracic and mediastinal disorders	Dry throat	Pharynx dry
Respiratory, thoracic and mediastinal disorders	Dry throat	Throat dry
Respiratory, thoracic and mediastinal disorders	Dysphonia	Distorted voice
Respiratory, thoracic and mediastinal disorders	Dysphonia	Disturbance in loudness
Respiratory, thoracic and mediastinal disorders	Dysphonia	Dysphonia
Respiratory, thoracic and mediastinal disorders	Dysphonia	Hoarse voice
Respiratory, thoracic and mediastinal disorders	Dysphonia	Hoarseness
Respiratory, thoracic and mediastinal disorders	Dysphonia	Hoarseness of voice
Respiratory, thoracic and mediastinal disorders	Dysphonia	Phonation difficulty
Respiratory, thoracic and mediastinal disorders	Dysphonia	Resonance disorder
Respiratory, thoracic and mediastinal disorders	Dysphonia	Vocal tone disorder

System Organ Class	Preferred Term	Lowest Level Term
Route of Administration: Respiratory Disorders NEC (HLT)		
Respiratory, thoracic and mediastinal disorders	Dysphonia	Vocal volume disorder
Respiratory, thoracic and mediastinal disorders	Dysphonia	Voice alteration
Respiratory, thoracic and mediastinal disorders	Dysphonia	Voice disturbance
Respiratory, thoracic and mediastinal disorders	Dysphonia	Voice disturbance, unspecified
Respiratory, thoracic and mediastinal disorders	Dysphonia	Voice lowered
Respiratory, thoracic and mediastinal disorders	Dysphonia	Hypophonia
Respiratory, thoracic and mediastinal disorders	Dysphonia	Rhinolalia
Respiratory, thoracic and mediastinal disorders	Haemoptysis	Blood streaked sputum
Respiratory, thoracic and mediastinal disorders	Haemoptysis	Coughing blood
Respiratory, thoracic and mediastinal disorders	Haemoptysis	Haemoptysis
Respiratory, thoracic and mediastinal disorders	Haemoptysis	Hemoptysis
Respiratory, thoracic and mediastinal disorders	Haemoptysis	Sputum bloody
Respiratory, thoracic and mediastinal disorders	Hiccups	Hiccough
Respiratory, thoracic and mediastinal disorders	Hiccups	Hiccup
Respiratory, thoracic and mediastinal disorders	Hiccups	Hiccups
Respiratory, thoracic and mediastinal disorders	Hiccups	Singultation
Respiratory, thoracic and mediastinal disorders	Hiccups	Singultous
Respiratory, thoracic and mediastinal disorders	Hiccups	Singultus
Respiratory, thoracic and mediastinal disorders	Hiccups	Intractable hiccups
Respiratory, thoracic and mediastinal disorders	Increased bronchial secretion	Airway secretion excessive

System Organ Class	Preferred Term	Lowest Level Term
Route of Administration: Respiratory Disorders NEC (HLT)		
Respiratory, thoracic and mediastinal disorders	Increased bronchial secretion	Bronchial secretion excessive
Respiratory, thoracic and mediastinal disorders	Increased bronchial secretion	Bronchorrhea
Respiratory, thoracic and mediastinal disorders	Increased bronchial secretion	Bronchorrhoea
Respiratory, thoracic and mediastinal disorders	Increased bronchial secretion	Excessive bronchial secretion
Respiratory, thoracic and mediastinal disorders	Increased bronchial secretion	Tracheo-bronchial secretion excess
Respiratory, thoracic and mediastinal disorders	Increased bronchial secretion	Increased bronchial secretion
Respiratory, thoracic and mediastinal disorders	Increased upper airway secretion	Throat secretion increased
Respiratory, thoracic and mediastinal disorders	Increased upper airway secretion	Phlegm
Respiratory, thoracic and mediastinal disorders	Increased upper airway secretion	Increased upper airway secretion
Respiratory, thoracic and mediastinal disorders	Increased viscosity of bronchial secretion	Sputum viscosity increased
Respiratory, thoracic and mediastinal disorders	Increased viscosity of bronchial secretion	Increased viscosity of bronchial secretion
Respiratory, thoracic and mediastinal disorders	Increased viscosity of nasal secretion	Increased viscosity of nasal secretion
Respiratory, thoracic and mediastinal disorders	Increased viscosity of nasal secretion	Thick nasal mucus
Respiratory, thoracic and mediastinal disorders	Laryngeal discomfort	Laryngeal discomfort
Respiratory, thoracic and mediastinal disorders	Laryngeal discomfort	Pharyngolaryngeal discomfort
Respiratory, thoracic and mediastinal disorders	Laryngeal pain	Laryngeal pain
Respiratory, thoracic and mediastinal disorders	Laryngeal pain	Larynx burning pain of
Respiratory, thoracic and mediastinal disorders	Laryngeal pain	Larynx pain
Respiratory, thoracic and mediastinal disorders	Laryngeal pain	Pharyngolaryngeal pain
Respiratory, thoracic and mediastinal disorders	Mouth breathing	Jaw breathing

System Organ Class	Preferred Term	Lowest Level Term
Route of Administration: Respiratory Disorders NEC (HLT)		
Respiratory, thoracic and mediastinal disorders	Mouth breathing	Mouth breathing
Respiratory, thoracic and mediastinal disorders	Nasal discharge discolouration	Nasal discharge discolouration
Respiratory, thoracic and mediastinal disorders	Nasal discharge discolouration	Nasal discharge discoloration
Respiratory, thoracic and mediastinal disorders	Nasal discomfort	Discomfort in nose
Respiratory, thoracic and mediastinal disorders	Nasal discomfort	Nasal burning
Respiratory, thoracic and mediastinal disorders	Nasal discomfort	Nasal cavity strange sensation of
Respiratory, thoracic and mediastinal disorders	Nasal discomfort	Nasal irritation
Respiratory, thoracic and mediastinal disorders	Nasal discomfort	Nasal itching
Respiratory, thoracic and mediastinal disorders	Nasal discomfort	Nasal passage irritation
Respiratory, thoracic and mediastinal disorders	Nasal discomfort	Nasal soreness
Respiratory, thoracic and mediastinal disorders	Nasal discomfort	Sore nose
Respiratory, thoracic and mediastinal disorders	Nasal discomfort	Nasal discomfort
Respiratory, thoracic and mediastinal disorders	Nasal flaring	Nasal flaring
Respiratory, thoracic and mediastinal disorders	Nasal obstruction	Nasal obstruction
Respiratory, thoracic and mediastinal disorders	Nasal obstruction	Nasal obstruction increased
Respiratory, thoracic and mediastinal disorders	Nasopharyngeal reflux	Nasopharyngeal reflux
Respiratory, thoracic and mediastinal disorders	Nocturnal dyspnoea	Nocturnal dyspnoea
Respiratory, thoracic and mediastinal disorders	Nocturnal dyspnoea	Nocturnal dyspnea
Respiratory, thoracic and mediastinal disorders	Oropharyngeal blistering	Oropharyngeal blistering
Respiratory, thoracic and mediastinal disorders	Oropharyngeal discomfort	Pharynx discomfort

System Organ Class	Preferred Term	Lowest Level Term
Route of Administration: Respiratory Disorders NEC (HLT)		
Respiratory, thoracic and mediastinal disorders	Oropharyngeal discomfort	Pharynx ill sensation of
Respiratory, thoracic and mediastinal disorders	Oropharyngeal discomfort	Pharynx strange sensation of
Respiratory, thoracic and mediastinal disorders	Oropharyngeal discomfort	Oropharyngeal discomfort
Respiratory, thoracic and mediastinal disorders	Oropharyngeal pain	Pain pharynx
Respiratory, thoracic and mediastinal disorders	Oropharyngeal pain	Pain throat
Respiratory, thoracic and mediastinal disorders	Oropharyngeal pain	Sore throat
Respiratory, thoracic and mediastinal disorders	Oropharyngeal pain	Sore throat NOS
Respiratory, thoracic and mediastinal disorders	Oropharyngeal pain	Throat pain
Respiratory, thoracic and mediastinal disorders	Oropharyngeal pain	Throat sore
Respiratory, thoracic and mediastinal disorders	Oropharyngeal pain	Chronic sore throat
Respiratory, thoracic and mediastinal disorders	Oropharyngeal pain	Oropharyngeal pain
Respiratory, thoracic and mediastinal disorders	Oropharyngeal plaque	Mouth plaque
Respiratory, thoracic and mediastinal disorders	Oropharyngeal plaque	Plaque mouth
Respiratory, thoracic and mediastinal disorders	Oropharyngeal plaque	Oropharyngeal plaque
Respiratory, thoracic and mediastinal disorders	Oropharyngeal scar	Oropharyngeal scar
Respiratory, thoracic and mediastinal disorders	Paranasal sinus discomfort	Paranasal sinus discomfort
Respiratory, thoracic and mediastinal disorders	Productive cough	Productive cough
Respiratory, thoracic and mediastinal disorders	Productive cough	Sputum
Respiratory, thoracic and mediastinal disorders	Productive cough	Expectoration
Respiratory, thoracic and mediastinal disorders	Respiratory tract oedema	Respiratory tract oedema

System Organ Class	Preferred Term	Lowest Level Term
Route of Administration: Respiratory Disorders NEC (HLT)		
Respiratory, thoracic and mediastinal disorders	Respiratory tract oedema	Airway oedema
Respiratory, thoracic and mediastinal disorders	Respiratory tract oedema	Airway edema
Respiratory, thoracic and mediastinal disorders	Respiratory tract oedema	Respiratory tract edema
Respiratory, thoracic and mediastinal disorders	Rhinalgia	Nasal stinging
Respiratory, thoracic and mediastinal disorders	Rhinalgia	Stinging of nose
Respiratory, thoracic and mediastinal disorders	Rhinalgia	Rhinalgia
Respiratory, thoracic and mediastinal disorders	Rhinalgia	Nasal pain
Respiratory, thoracic and mediastinal disorders	Rhinorrhoea	Nasal discharge
Respiratory, thoracic and mediastinal disorders	Rhinorrhoea	Nasal discharge watery excessive
Respiratory, thoracic and mediastinal disorders	Rhinorrhoea	Rhinorrhea
Respiratory, thoracic and mediastinal disorders	Rhinorrhoea	Rhinorrhoea
Respiratory, thoracic and mediastinal disorders	Rhinorrhoea	Runny nose
Respiratory, thoracic and mediastinal disorders	Rhinorrhoea	Nasal mucus increased
Respiratory, thoracic and mediastinal disorders	Rhinorrhoea	Mucus nasal increased
Respiratory, thoracic and mediastinal disorders	Rhinorrhoea	Gustatory rhinorrhoea
Respiratory, thoracic and mediastinal disorders	Rhinorrhoea	Sniffles
Respiratory, thoracic and mediastinal disorders	Rhinorrhoea	Gustatory rhinorrhea
Respiratory, thoracic and mediastinal disorders	Sneezing	Paroxysmal sneeze
Respiratory, thoracic and mediastinal disorders	Sneezing	Sneezing
Respiratory, thoracic and mediastinal disorders	Sneezing	Sneezing excessive

System Organ Class	Preferred Term	Lowest Level Term
Route of Administration: Respiratory Disorders NEC (HLT)		
Respiratory, thoracic and mediastinal disorders	Snoring	Snore
Respiratory, thoracic and mediastinal disorders	Snoring	Snoring
Respiratory, thoracic and mediastinal disorders	Sputum decreased	Sputum decreased
Respiratory, thoracic and mediastinal disorders	Sputum discoloured	Sputum discolored
Respiratory, thoracic and mediastinal disorders	Sputum discoloured	Sputum discoloured
Respiratory, thoracic and mediastinal disorders	Sputum increased	Sputum excretion increased
Respiratory, thoracic and mediastinal disorders	Sputum increased	Sputum increased
Respiratory, thoracic and mediastinal disorders	Sputum retention	Sputum excretion difficulty
Respiratory, thoracic and mediastinal disorders	Sputum retention	Sputum expectoration difficult
Respiratory, thoracic and mediastinal disorders	Sputum retention	Sputum sticking sensation of
Respiratory, thoracic and mediastinal disorders	Sputum retention	Sputum retention
Respiratory, thoracic and mediastinal disorders	Suffocation feeling	Suffocation feeling
Respiratory, thoracic and mediastinal disorders	Throat irritation	Burning in throat
Respiratory, thoracic and mediastinal disorders	Throat irritation	Local throat irritation
Respiratory, thoracic and mediastinal disorders	Throat irritation	Pharyngo-oral irritation
Respiratory, thoracic and mediastinal disorders	Throat irritation	Pharynx burning sensation of
Respiratory, thoracic and mediastinal disorders	Throat irritation	Pharynx irritated sensation of
Respiratory, thoracic and mediastinal disorders	Throat irritation	Pharynx itchy sensation of
Respiratory, thoracic and mediastinal disorders	Throat irritation	Throat burning sensation of
Respiratory, thoracic and mediastinal disorders	Throat irritation	Throat irritation

System Organ Class	Preferred Term	Lowest Level Term
Route of Administration: Respiratory Disorders NEC (HLT)		
Respiratory, thoracic and mediastinal disorders	Throat irritation	Itchy throat
Respiratory, thoracic and mediastinal disorders	Throat lesion	Throat lesion
Respiratory, thoracic and mediastinal disorders	Throat tightness	Constriction throat
Respiratory, thoracic and mediastinal disorders	Throat tightness	Throat constriction
Respiratory, thoracic and mediastinal disorders	Throat tightness	Throat tightness
Respiratory, thoracic and mediastinal disorders	Upper airway necrosis	Upper airway necrosis
Respiratory, thoracic and mediastinal disorders	Upper airway obstruction	Upper airway obstruction
Respiratory, thoracic and mediastinal disorders	Upper airway resistance syndrome	Upper airway resistance syndrome
Respiratory, thoracic and mediastinal disorders	Upper respiratory tract congestion	Upper respiratory tract congestion
Respiratory, thoracic and mediastinal disorders	Upper respiratory tract inflammation	Upper respiratory tract inflammation
Respiratory, thoracic and mediastinal disorders	Upper respiratory tract inflammation	Acute upper respiratory tract inflammation
Respiratory, thoracic and mediastinal disorders	Upper respiratory tract irritation	Upper respiratory tract irritation
Respiratory, thoracic and mediastinal disorders	Upper-airway cough syndrome	Posterior nasal drip
Respiratory, thoracic and mediastinal disorders	Upper-airway cough syndrome	Postnasal drip
Respiratory, thoracic and mediastinal disorders	Upper-airway cough syndrome	Chronic post nasal drip
Respiratory, thoracic and mediastinal disorders	Upper-airway cough syndrome	Upper-airway cough syndrome
Respiratory, thoracic and mediastinal disorders	Yawning	Yawn
Respiratory, thoracic and mediastinal disorders	Yawning	Yawning
Respiratory, thoracic and mediastinal disorders	Yawning	Yawning excessive

System Organ Class	Preferred Term	Lowest Level Term

Route of Administration: Upper Respiratory Tract Disorders (HLT) (Exclude Infections)		
Respiratory, thoracic and mediastinal disorders	Adductor vocal cord weakness	Adductor vocal cord weakness
Respiratory, thoracic and mediastinal disorders	Adenoidal disorder	Adenoidal disorder
Respiratory, thoracic and mediastinal disorders	Adenoidal hypertrophy	Adenoid vegetations
Respiratory, thoracic and mediastinal disorders	Adenoidal hypertrophy	Adenoidal hypertrophy
Respiratory, thoracic and mediastinal disorders	Allergic pharyngitis	Allergic pharyngitis
Respiratory, thoracic and mediastinal disorders	Allergic sinusitis	Allergic sinusitis
Respiratory, thoracic and mediastinal disorders	Allergic sinusitis	Seasonal sinusitis
Respiratory, thoracic and mediastinal disorders	Chronic eosinophilic rhinosinusitis	Chronic eosinophilic rhinosinusitis
Respiratory, thoracic and mediastinal disorders	Chronic hyperplastic eosinophilic sinusitis	Chronic hyperplastic eosinophilic sinusitis
Respiratory, thoracic and mediastinal disorders	Croup noninfectious	Croup noninfectious
Respiratory, thoracic and mediastinal disorders	Dysaesthesia pharynx	Dysaesthesia pharynx
Respiratory, thoracic and mediastinal disorders	Dysaesthesia pharynx	Dysesthesia pharynx
Respiratory, thoracic and mediastinal disorders	Dysaesthesia pharynx	Laryngopharyngeal dysesthesia
Respiratory, thoracic and mediastinal disorders	Dysaesthesia pharynx	Laryngopharyngeal dysaesthesia
Respiratory, thoracic and mediastinal disorders	Eosinophilic rhinitis	Eosinophilic rhinitis
Respiratory, thoracic and mediastinal disorders	Epiglottic cyst	Epiglottic cyst
Respiratory, thoracic and mediastinal disorders	Epiglottic erythema	Epiglottic erythema
Respiratory, thoracic and mediastinal disorders	Epiglottic mass	Epiglottic mass
Respiratory, thoracic and mediastinal disorders	Epiglottic oedema	Epiglottic oedema
Respiratory, thoracic and mediastinal disorders	Epiglottic oedema	Epiglottic edema
Respiratory, thoracic and	Epiglottis ulcer	Epiglottis ulcer

System Organ Class	Preferred Term	Lowest Level Term
Route of Administration: Upper Respiratory Tract Disorders (HLT) (Exclude Infections)		
mediastinal disorders		
Respiratory, thoracic and mediastinal disorders	Epistaxis	Bleeding nose
Respiratory, thoracic and mediastinal disorders	Epistaxis	Epistaxis
Respiratory, thoracic and mediastinal disorders	Epistaxis	Haemorrhage nasal
Respiratory, thoracic and mediastinal disorders	Epistaxis	Hemorrhage nasal
Respiratory, thoracic and mediastinal disorders	Epistaxis	Nasal bleeding
Respiratory, thoracic and mediastinal disorders	Epistaxis	Nasal mucus blood tinged
Respiratory, thoracic and mediastinal disorders	Epistaxis	Nose bleed
Respiratory, thoracic and mediastinal disorders	Epistaxis	Nose bleeds
Respiratory, thoracic and mediastinal disorders	Epistaxis	Nosebleed
Respiratory, thoracic and mediastinal disorders	Epistaxis	Chronic epistaxis
Respiratory, thoracic and mediastinal disorders	Intranasal hypoaesthesia	Intranasal numbness
Respiratory, thoracic and mediastinal disorders	Intranasal hypoaesthesia	Intranasal hypoaesthesia
Respiratory, thoracic and mediastinal disorders	Intranasal hypoaesthesia	Intranasal hypoesthesia
Respiratory, thoracic and mediastinal disorders	Intranasal paraesthesia	Intranasal paraesthesia
Respiratory, thoracic and mediastinal disorders	Intranasal paraesthesia	Intranasal paresthesia
Respiratory, thoracic and mediastinal disorders	Laryngeal cyst	Laryngeal cyst
Respiratory, thoracic and mediastinal disorders	Laryngeal disorder	Laryngeal disorder NOS
Respiratory, thoracic and mediastinal disorders	Laryngeal disorder	Unspecified disease of larynx
Respiratory, thoracic and mediastinal disorders	Laryngeal disorder	Laryngeal disorder
Respiratory, thoracic and	Laryngeal dyspnoea	Laryngeal dyspnoea

System Organ Class	Preferred Term	Lowest Level Term
Route of Administration: Upper Respiratory Tract Disorders (HLT) (Exclude Infections)		
mediastinal disorders		
Respiratory, thoracic and mediastinal disorders	Laryngeal dyspnoea	Laryngeal dyspnea
Respiratory, thoracic and mediastinal disorders	Laryngeal erythema	Laryngeal erythema
Respiratory, thoracic and mediastinal disorders	Laryngeal haematoma	Laryngeal haematoma
Respiratory, thoracic and mediastinal disorders	Laryngeal haematoma	Laryngeal hematoma
Respiratory, thoracic and mediastinal disorders	Laryngeal haematoma	Glottic haematoma
Respiratory, thoracic and mediastinal disorders	Laryngeal haematoma	Glottic hematoma
Respiratory, thoracic and mediastinal disorders	Laryngeal haemorrhage	Laryngeal haemorrhage
Respiratory, thoracic and mediastinal disorders	Laryngeal haemorrhage	Laryngeal hemorrhage
Respiratory, thoracic and mediastinal disorders	Laryngeal haemorrhage	Laryngeal bleeding
Respiratory, thoracic and mediastinal disorders	Laryngeal hypertrophy	Laryngeal hypertrophy
Respiratory, thoracic and mediastinal disorders	Laryngeal infiltration	Laryngeal infiltration NOS
Respiratory, thoracic and mediastinal disorders	Laryngeal infiltration	Laryngeal infiltration
Respiratory, thoracic and mediastinal disorders	Laryngeal inflammation	Laryngeal inflammation
Respiratory, thoracic and mediastinal disorders	Laryngeal inflammation	Laryngeal mucositis
Respiratory, thoracic and mediastinal disorders	Laryngeal leukoplakia	Laryngeal leukoplakia
Respiratory, thoracic and mediastinal disorders	Laryngeal leukoplakia	Laryngeal leucoplakia
Respiratory, thoracic and mediastinal disorders	Laryngeal mass	Laryngeal mass
Respiratory, thoracic and mediastinal disorders	Laryngeal necrosis	Laryngeal necrosis
Respiratory, thoracic and mediastinal disorders	Laryngeal necrosis	Laryngeal chondronecrosis
Respiratory, thoracic and	Laryngeal obstruction	Laryngeal obstruction

System Organ Class	Preferred Term	Lowest Level Term
Route of Administration: Upper Respiratory Tract Disorders (HLT) (Exclude Infections)		
mediastinal disorders		
Respiratory, thoracic and mediastinal disorders	Laryngeal obstruction	Subglottic obstruction
Respiratory, thoracic and mediastinal disorders	Laryngeal oedema	Edema glottis
Respiratory, thoracic and mediastinal disorders	Laryngeal oedema	Edema larynx
Respiratory, thoracic and mediastinal disorders	Laryngeal oedema	Edema of larynx
Respiratory, thoracic and mediastinal disorders	Laryngeal oedema	Edema vocal cord
Respiratory, thoracic and mediastinal disorders	Laryngeal oedema	Glottic edema
Respiratory, thoracic and mediastinal disorders	Laryngeal oedema	Glottic oedema
Respiratory, thoracic and mediastinal disorders	Laryngeal oedema	Laryngeal edema
Respiratory, thoracic and mediastinal disorders	Laryngeal oedema	Laryngeal oedema
Respiratory, thoracic and mediastinal disorders	Laryngeal oedema	Larynx edema
Respiratory, thoracic and mediastinal disorders	Laryngeal oedema	Larynx oedema
Respiratory, thoracic and mediastinal disorders	Laryngeal oedema	Oedema of larynx
Respiratory, thoracic and mediastinal disorders	Laryngeal oedema	Subglottic edema
Respiratory, thoracic and mediastinal disorders	Laryngeal oedema	Subglottic oedema
Respiratory, thoracic and mediastinal disorders	Laryngeal oedema	Vocal cord edema
Respiratory, thoracic and mediastinal disorders	Laryngeal oedema	Vocal cord oedema
Respiratory, thoracic and mediastinal disorders	Laryngeal oedema	Oedema glottis
Respiratory, thoracic and mediastinal disorders	Laryngeal oedema	Oedema larynx
Respiratory, thoracic and mediastinal disorders	Laryngeal oedema	Oedema vocal cord
Respiratory, thoracic and	Laryngeal oedema	Aryepiglottis edema

System Organ Class	Preferred Term	Lowest Level Term
Route of Administration: Upper Respiratory Tract Disorders (HLT) (Exclude Infections)		
mediastinal disorders		
Respiratory, thoracic and mediastinal disorders	Laryngeal oedema	Aryepiglottis oedema
Respiratory, thoracic and mediastinal disorders	Laryngeal oedema	Acute laryngeal edema
Respiratory, thoracic and mediastinal disorders	Laryngeal oedema	Acute laryngeal oedema
Respiratory, thoracic and mediastinal disorders	Laryngeal polyp	Laryngeal polyp
Respiratory, thoracic and mediastinal disorders	Laryngeal stenosis	Laryngeal stenosis
Respiratory, thoracic and mediastinal disorders	Laryngeal stenosis	Laryngeal stricture
Respiratory, thoracic and mediastinal disorders	Laryngeal stenosis	Stenosis of larynx
Respiratory, thoracic and mediastinal disorders	Laryngeal stenosis	Subglottic stenosis
Respiratory, thoracic and mediastinal disorders	Laryngeal stenosis	Supraglottic stenosis
Respiratory, thoracic and mediastinal disorders	Laryngeal ulceration	Laryngeal ulceration
Respiratory, thoracic and mediastinal disorders	Laryngeal ulceration	Larynx ulcer
Respiratory, thoracic and mediastinal disorders	Laryngeal ulceration	Larynx ulceration
Respiratory, thoracic and mediastinal disorders	Laryngeal ventricle prolapse	Laryngeal ventricle prolapse
Respiratory, thoracic and mediastinal disorders	Laryngitis allergic	Laryngitis allergic
Respiratory, thoracic and mediastinal disorders	Laryngospasm	Glottic spasm
Respiratory, thoracic and mediastinal disorders	Laryngospasm	Laryngeal spasm
Respiratory, thoracic and mediastinal disorders	Laryngospasm	Laryngismus
Respiratory, thoracic and mediastinal disorders	Laryngospasm	Laryngospasm
Respiratory, thoracic and mediastinal disorders	Laryngospasm	Larynx muscle hypersensitive
Respiratory, thoracic and	Laryngospasm	Spasm glottis

System Organ Class	Preferred Term	Lowest Level Term
Route of Administration: Upper Respiratory Tract Disorders (HLT) (Exclude Infections)		
mediastinal disorders		
Respiratory, thoracic and mediastinal disorders	Laryngospasm	Spasm larynx
Respiratory, thoracic and mediastinal disorders	Larynx irritation	Larynx irritation
Respiratory, thoracic and mediastinal disorders	Larynx irritation	Larynx itching
Respiratory, thoracic and mediastinal disorders	Maxillary sinus pseudocyst	Maxillary sinus pseudocyst
Respiratory, thoracic and mediastinal disorders	Nasal cavity mass	Nasal cavity mass
Respiratory, thoracic and mediastinal disorders	Nasal congestion	Congestion nasal
Respiratory, thoracic and mediastinal disorders	Nasal congestion	Nasal congestion
Respiratory, thoracic and mediastinal disorders	Nasal congestion	Nasal stuffiness
Respiratory, thoracic and mediastinal disorders	Nasal congestion	Nose congestion
Respiratory, thoracic and mediastinal disorders	Nasal congestion	Rhinitis medicamentosa
Respiratory, thoracic and mediastinal disorders	Nasal congestion	Rhinitis medicamentous
Respiratory, thoracic and mediastinal disorders	Nasal congestion	Nasal mucosal swelling
Respiratory, thoracic and mediastinal disorders	Nasal congestion	Chronic nasal congestion
Respiratory, thoracic and mediastinal disorders	Nasal congestion	Acute nasal congestion
Respiratory, thoracic and mediastinal disorders	Nasal cyst	Nasal cyst
Respiratory, thoracic and mediastinal disorders	Nasal cyst	Intranasal cyst
Respiratory, thoracic and mediastinal disorders	Nasal disorder	Nasal disorder NOS
Respiratory, thoracic and mediastinal disorders	Nasal disorder	Nasal disorder
Respiratory, thoracic and mediastinal disorders	Nasal dryness	Dry nose
Respiratory, thoracic and	Nasal dryness	Nasal dryness

System Organ Class	Preferred Term	Lowest Level Term
Route of Administration: Upper Respiratory Tract Disorders (HLT) (Exclude Infections)		
mediastinal disorders		
Respiratory, thoracic and mediastinal disorders	Nasal dryness	Nose dry feeling of
Respiratory, thoracic and mediastinal disorders	Nasal dryness	Nose dryness
Respiratory, thoracic and mediastinal disorders	Nasal inflammation	Nasal inflammation
Respiratory, thoracic and mediastinal disorders	Nasal inflammation	Nasal septal inflammation
Respiratory, thoracic and mediastinal disorders	Nasal inflammation	Nasal mucosal inflammation
Respiratory, thoracic and mediastinal disorders	Nasal mucosa atrophy	Nasal mucosa atrophy
Respiratory, thoracic and mediastinal disorders	Nasal mucosal discolouration	Nasal mucosal discolouration
Respiratory, thoracic and mediastinal disorders	Nasal mucosal discolouration	Nasal mucosal discoloration
Respiratory, thoracic and mediastinal disorders	Nasal mucosal discolouration	Nasal mucosal pallor
Respiratory, thoracic and mediastinal disorders	Nasal mucosal disorder	Nasal mucosal disorder NOS
Respiratory, thoracic and mediastinal disorders	Nasal mucosal disorder	Nasal mucosal disorder
Respiratory, thoracic and mediastinal disorders	Nasal mucosal disorder	Nasal mucosal erythema
Respiratory, thoracic and mediastinal disorders	Nasal mucosal disorder	Nasal mucosal hyperaemia
Respiratory, thoracic and mediastinal disorders	Nasal mucosal disorder	Nasal mucosal ulcer
Respiratory, thoracic and mediastinal disorders	Nasal mucosal disorder	Nasal mucosal hyperemia
Respiratory, thoracic and mediastinal disorders	Nasal mucosal hypertrophy	Nasal mucosal hypertrophy
Respiratory, thoracic and mediastinal disorders	Nasal necrosis	Nasal mucosal necrosis
Respiratory, thoracic and mediastinal disorders	Nasal necrosis	Nasal necrosis
Respiratory, thoracic and mediastinal disorders	Nasal necrosis	Necrosis nasal
Respiratory, thoracic and	Nasal necrosis	Nasal septal mucosa necrosis

System Organ Class	Preferred Term	Lowest Level Term
Route of Administration: Upper Respiratory Tract Disorders (HLT) (Exclude Infections)		
mediastinal disorders		
Respiratory, thoracic and mediastinal disorders	Nasal odour	Nasal odour
Respiratory, thoracic and mediastinal disorders	Nasal odour	Nasal odor
Respiratory, thoracic and mediastinal disorders	Nasal oedema	Nasal oedema
Respiratory, thoracic and mediastinal disorders	Nasal oedema	Nose edema
Respiratory, thoracic and mediastinal disorders	Nasal oedema	Nose oedema
Respiratory, thoracic and mediastinal disorders	Nasal oedema	Nasal turbinate edema
Respiratory, thoracic and mediastinal disorders	Nasal oedema	Nasal edema
Respiratory, thoracic and mediastinal disorders	Nasal oedema	Nasal turbinate oedema
Respiratory, thoracic and mediastinal disorders	Nasal polyps	Nasal polyp
Respiratory, thoracic and mediastinal disorders	Nasal polyps	Nasal polyps
Respiratory, thoracic and mediastinal disorders	Nasal polyps	Polyp of nasal cavity
Respiratory, thoracic and mediastinal disorders	Nasal polyps	Polyps nasal
Respiratory, thoracic and mediastinal disorders	Nasal polyps	Unspecified nasal polyp
Respiratory, thoracic and mediastinal disorders	Nasal polyps	Hyperplastic nasal polyp
Respiratory, thoracic and mediastinal disorders	Nasal polyps	Choanal polyp
Respiratory, thoracic and mediastinal disorders	Nasal septum disorder	Nasal septum disorder
Respiratory, thoracic and mediastinal disorders	Nasal septum disorder	Nasal septum disorder NOS
Respiratory, thoracic and mediastinal disorders	Nasal septum disorder	Nasal septal erythema
Respiratory, thoracic and mediastinal disorders	Nasal septum perforation	Nasal septum perforation
Respiratory, thoracic and	Nasal septum perforation	Perforation nasal septum

System Organ Class	Preferred Term	Lowest Level Term
Route of Administration: Upper Respiratory Tract Disorders (HLT) (Exclude Infections)		
mediastinal disorders		
Respiratory, thoracic and mediastinal disorders	Nasal septum ulceration	Nasal septum ulceration
Respiratory, thoracic and mediastinal disorders	Nasal turbinate abnormality	Nasal turbinate abnormality
Respiratory, thoracic and mediastinal disorders	Nasal turbinate hypertrophy	Hypertrophy of nasal turbinates
Respiratory, thoracic and mediastinal disorders	Nasal turbinate hypertrophy	Nasal turbinate hypertrophy
Respiratory, thoracic and mediastinal disorders	Nasal turbinate hypertrophy	Concha bullosa
Respiratory, thoracic and mediastinal disorders	Nasal ulcer	Nasal ulcer
Respiratory, thoracic and mediastinal disorders	Oropharyngeal spasm	Oropharyngeal spasm
Respiratory, thoracic and mediastinal disorders	Oropharyngeal spasm	Spasm oropharyngeal
Respiratory, thoracic and mediastinal disorders	Oropharyngeal swelling	Oropharyngeal swelling
Respiratory, thoracic and mediastinal disorders	Paranasal cyst	Paranasal sinus mucocoele
Respiratory, thoracic and mediastinal disorders	Paranasal cyst	Paranasal cyst
Respiratory, thoracic and mediastinal disorders	Paranasal cyst	Paranasal sinus mucocele
Respiratory, thoracic and mediastinal disorders	Paranasal sinus haematoma	Maxillary sinus haematoma
Respiratory, thoracic and mediastinal disorders	Paranasal sinus haematoma	Maxillary sinus hematoma
Respiratory, thoracic and mediastinal disorders	Paranasal sinus haematoma	Paranasal sinus haematoma
Respiratory, thoracic and mediastinal disorders	Paranasal sinus haematoma	Paranasal sinus hematoma
Respiratory, thoracic and mediastinal disorders	Paranasal sinus hypersecretion	Paranasal sinus hypersecretion
Respiratory, thoracic and mediastinal disorders	Paranasal sinus hypersecretion	Nasal sinus discharge
Respiratory, thoracic and mediastinal disorders	Paranasal sinus mucosal hypertrophy	Paranasal sinus mucosal hypertrophy
Respiratory, thoracic and	Paranasal sinus necrosis	Paranasal sinus necrosis

System Organ Class	Preferred Term	Lowest Level Term
Route of Administration: Upper Respiratory Tract Disorders (HLT) (Exclude Infections)		
mediastinal disorders		
Respiratory, thoracic and mediastinal disorders	Pharyngeal cyst	Pharyngeal cyst
Respiratory, thoracic and mediastinal disorders	Pharyngeal disorder	Pharyngeal disorder NOS
Respiratory, thoracic and mediastinal disorders	Pharyngeal disorder	Unspecified disease of pharynx
Respiratory, thoracic and mediastinal disorders	Pharyngeal disorder	Nasopharyngeal disorder
Respiratory, thoracic and mediastinal disorders	Pharyngeal disorder	Pharyngeal disorder
Respiratory, thoracic and mediastinal disorders	Pharyngeal dyskinesia	Pharyngeal dyskinesia
Respiratory, thoracic and mediastinal disorders	Pharyngeal enanthema	Pharyngeal enanthema
Respiratory, thoracic and mediastinal disorders	Pharyngeal erosion	Pharyngeal erosion
Respiratory, thoracic and mediastinal disorders	Pharyngeal erythema	Pharynx redness of
Respiratory, thoracic and mediastinal disorders	Pharyngeal erythema	Red throat
Respiratory, thoracic and mediastinal disorders	Pharyngeal erythema	Pharyngeal erythema
Respiratory, thoracic and mediastinal disorders	Pharyngeal erythema	Uvular erythema
Respiratory, thoracic and mediastinal disorders	Pharyngeal exudate	Pharyngeal exudate
Respiratory, thoracic and mediastinal disorders	Pharyngeal fistula	Pharyngeal fistula
Respiratory, thoracic and mediastinal disorders	Pharyngeal haematoma	Pharyngeal haematoma
Respiratory, thoracic and mediastinal disorders	Pharyngeal haematoma	Pharyngeal hematoma
Respiratory, thoracic and mediastinal disorders	Pharyngeal haemorrhage	Haemorrhage from throat
Respiratory, thoracic and mediastinal disorders	Pharyngeal haemorrhage	Haemorrhage pharyngeal
Respiratory, thoracic and mediastinal disorders	Pharyngeal haemorrhage	Hemorrhage from throat
Respiratory, thoracic and	Pharyngeal haemorrhage	Pharyngeal haemorrhage

System Organ Class	Preferred Term	Lowest Level Term
Route of Administration: Upper Respiratory Tract Disorders (HLT) (Exclude Infections)		
mediastinal disorders		
Respiratory, thoracic and mediastinal disorders	Pharyngeal haemorrhage	Hemorrhage pharyngeal
Respiratory, thoracic and mediastinal disorders	Pharyngeal haemorrhage	Pharyngeal hemorrhage
Respiratory, thoracic and mediastinal disorders	Pharyngeal haemorrhage	Oropharyngeal hemorrhage
Respiratory, thoracic and mediastinal disorders	Pharyngeal haemorrhage	Oropharyngeal haemorrhage
Respiratory, thoracic and mediastinal disorders	Pharyngeal haemorrhage	Pharyngeal bleeding
Respiratory, thoracic and mediastinal disorders	Pharyngeal hypertrophy	Pharyngeal hypertrophy
Respiratory, thoracic and mediastinal disorders	Pharyngeal hypoaesthesia	Pharyngeal hypoaesthesia
Respiratory, thoracic and mediastinal disorders	Pharyngeal hypoaesthesia	Numbness throat
Respiratory, thoracic and mediastinal disorders	Pharyngeal hypoaesthesia	Pharyngeal hypoesthesia
Respiratory, thoracic and mediastinal disorders	Pharyngeal inflammation	Pharyngeal inflammation
Respiratory, thoracic and mediastinal disorders	Pharyngeal inflammation	Pharyngeal mucositis
Respiratory, thoracic and mediastinal disorders	Pharyngeal lesion	Pharyngeal lesion
Respiratory, thoracic and mediastinal disorders	Pharyngeal leukoplakia	Pharyngeal leukoplakia
Respiratory, thoracic and mediastinal disorders	Pharyngeal mass	Pharyngeal mass
Respiratory, thoracic and mediastinal disorders	Pharyngeal mucosa atrophy	Pharyngeal mucosa atrophy
Respiratory, thoracic and mediastinal disorders	Pharyngeal necrosis	Pharyngeal necrosis
Respiratory, thoracic and mediastinal disorders	Pharyngeal oedema	Edema pharynx
Respiratory, thoracic and mediastinal disorders	Pharyngeal oedema	Oedema pharynx
Respiratory, thoracic and mediastinal disorders	Pharyngeal oedema	Pharyngeal oedema
Respiratory, thoracic and	Pharyngeal oedema	Pharynx edema

System Organ Class	Preferred Term	Lowest Level Term
Route of Administration: Upper Respiratory Tract Disorders (HLT) (Exclude Infections)		
mediastinal disorders		
Respiratory, thoracic and mediastinal disorders	Pharyngeal oedema	Throat edema
Respiratory, thoracic and mediastinal disorders	Pharyngeal oedema	Throat oedema
Respiratory, thoracic and mediastinal disorders	Pharyngeal oedema	Throat swelling
Respiratory, thoracic and mediastinal disorders	Pharyngeal oedema	Throat swelling non-specific
Respiratory, thoracic and mediastinal disorders	Pharyngeal oedema	Throat swelling NOS
Respiratory, thoracic and mediastinal disorders	Pharyngeal oedema	Pharyngeal edema
Respiratory, thoracic and mediastinal disorders	Pharyngeal oedema	Pharynx oedema
Respiratory, thoracic and mediastinal disorders	Pharyngeal polyp	Pharyngeal polyp
Respiratory, thoracic and mediastinal disorders	Pharyngeal stenosis	Pharyngeal stenosis
Respiratory, thoracic and mediastinal disorders	Pharyngeal ulceration	Pharyngeal ulceration
Respiratory, thoracic and mediastinal disorders	Reflux laryngitis	Laryngopharyngeal reflux
Respiratory, thoracic and mediastinal disorders	Reflux laryngitis	Reflux laryngitis
Respiratory, thoracic and mediastinal disorders	Rhinitis allergic	Allergic rhinitis
Respiratory, thoracic and mediastinal disorders	Rhinitis allergic	Allergic rhinitis (excl hay fever)
Respiratory, thoracic and mediastinal disorders	Rhinitis allergic	Atopic rhinitis
Respiratory, thoracic and mediastinal disorders	Rhinitis allergic	Rhinitis allergic
Respiratory, thoracic and mediastinal disorders	Rhinitis allergic	Rhinitis allergic atopic
Respiratory, thoracic and mediastinal disorders	Rhinitis allergic	Rhinitis allergic NOS
Respiratory, thoracic and mediastinal disorders	Rhinitis atrophic	Atrophic rhinitis
Respiratory, thoracic and	Rhinitis atrophic	Ozena

System Organ Class	Preferred Term	Lowest Level Term
Route of Administration: Upper Respiratory Tract Disorders (HLT) (Exclude Infections)		
mediastinal disorders		
Respiratory, thoracic and mediastinal disorders	Rhinitis atrophic	Rhinitis atrophic
Respiratory, thoracic and mediastinal disorders	Rhinitis atrophic	Dry rhinitis
Respiratory, thoracic and mediastinal disorders	Rhinitis hypertrophic	Rhinitis hypertrophic
Respiratory, thoracic and mediastinal disorders	Rhinitis perennial	Perennial allergic rhinitis
Respiratory, thoracic and mediastinal disorders	Rhinitis perennial	Perennial rhinitis
Respiratory, thoracic and mediastinal disorders	Rhinitis perennial	Rhinitis perennial
Respiratory, thoracic and mediastinal disorders	Rhinitis seasonal	Allergic rhinitis due to pollen
Respiratory, thoracic and mediastinal disorders	Rhinitis seasonal	Rhinitis seasonal
Respiratory, thoracic and mediastinal disorders	Rhinitis seasonal	Seasonal allergic rhinitis
Respiratory, thoracic and mediastinal disorders	Rhinitis seasonal	Seasonal rhinitis
Respiratory, thoracic and mediastinal disorders	Rhinitis ulcerative	Rhinitis ulcerative
Respiratory, thoracic and mediastinal disorders	Rhinolithiasis	Rhinolithiasis
Respiratory, thoracic and mediastinal disorders	Rhinolithiasis	Nasal calculus
Respiratory, thoracic and mediastinal disorders	Sinus congestion	Nasal sinus congestion
Respiratory, thoracic and mediastinal disorders	Sinus congestion	Sinus congestion
Respiratory, thoracic and mediastinal disorders	Sinus disorder	Sinus disorder NOS
Respiratory, thoracic and mediastinal disorders	Sinus disorder	Sinus disorder
Respiratory, thoracic and mediastinal disorders	Sinus perforation	Perforation of sinus
Respiratory, thoracic and mediastinal disorders	Sinus perforation	Sinus perforation
Respiratory, thoracic and	Sinus polyp	Antral polyp (of maxillary sinus)

System Organ Class	Preferred Term	Lowest Level Term
Route of Administration: Upper Respiratory Tract Disorders (HLT) (Exclude Infections)		
mediastinal disorders		
Respiratory, thoracic and mediastinal disorders	Sinus polyp	Maxillary sinus polyp
Respiratory, thoracic and mediastinal disorders	Sinus polyp	Sinus polyp
Respiratory, thoracic and mediastinal disorders	Sinus polyp degeneration	Polypoid sinus degeneration
Respiratory, thoracic and mediastinal disorders	Sinus polyp degeneration	Sinus polyp degeneration
Respiratory, thoracic and mediastinal disorders	Sinusitis noninfective	Sinusitis noninfective
Respiratory, thoracic and mediastinal disorders	Stridor	Stridor
Respiratory, thoracic and mediastinal disorders	Stridor	Stridor inspiratory
Respiratory, thoracic and mediastinal disorders	Tonsillar atrophy	Tonsillar atrophy
Respiratory, thoracic and mediastinal disorders	Tonsillar atrophy	Submerged tonsil
Respiratory, thoracic and mediastinal disorders	Tonsillar disorder	Chronic tonsillar disease
Respiratory, thoracic and mediastinal disorders	Tonsillar disorder	Tonsillar disorder
Respiratory, thoracic and mediastinal disorders	Tonsillar disorder	Cryptic tonsil
Respiratory, thoracic and mediastinal disorders	Tonsillar haemorrhage	Tonsillar haemorrhage
Respiratory, thoracic and mediastinal disorders	Tonsillar haemorrhage	Tonsillar hemorrhage
Respiratory, thoracic and mediastinal disorders	Tonsillar haemorrhage	Tonsillar bleeding
Respiratory, thoracic and mediastinal disorders	Tonsillar hypertrophy	Tonsillar hypertrophy
Respiratory, thoracic and mediastinal disorders	Tonsillar hypertrophy	Enlarged tonsils
Respiratory, thoracic and mediastinal disorders	Tonsillar inflammation	Tonsillar inflammation
Respiratory, thoracic and mediastinal disorders	Tonsillar ulcer	Tonsillar ulcer
Respiratory, thoracic and	Tonsillolith	Tonsillolith

System Organ Class	Preferred Term	Lowest Level Term
Route of Administration: Upper Respiratory Tract Disorders (HLT) (Exclude Infections)		
mediastinal disorders		
Respiratory, thoracic and mediastinal disorders	Vasomotor rhinitis	Vasomotor rhinitis
Respiratory, thoracic and mediastinal disorders	Velopharyngeal incompetence	Velopharyngeal incompetence
Respiratory, thoracic and mediastinal disorders	Vocal cord atrophy	Vocal cord atrophy
Respiratory, thoracic and mediastinal disorders	Vocal cord cyst	Vocal cord cyst
Respiratory, thoracic and mediastinal disorders	Vocal cord disorder	Vocal cord disorder NOS
Respiratory, thoracic and mediastinal disorders	Vocal cord disorder	Vocal cord dysfunction
Respiratory, thoracic and mediastinal disorders	Vocal cord disorder	Vocal cord disorder
Respiratory, thoracic and mediastinal disorders	Vocal cord inflammation	Vocal cord inflammation
Respiratory, thoracic and mediastinal disorders	Vocal cord leukoplakia	Vocal cord leukoplakia
Respiratory, thoracic and mediastinal disorders	Vocal cord polyp	Polyp of vocal cord
Respiratory, thoracic and mediastinal disorders	Vocal cord polyp	Vocal cord polyp
Respiratory, thoracic and mediastinal disorders	Vocal cord thickening	Singers nodules
Respiratory, thoracic and mediastinal disorders	Vocal cord thickening	Vocal cord thickening
Respiratory, thoracic and mediastinal disorders	Vocal cord thickening	Vocal cord nodule

(4) AEs related to taste and smell disorders:

System Organ Class	Preferred Term	Lowest Level Term
Taste and Smell Disorders (SMQ)		
Nervous system disorders	Dysgeusia	After taste
Nervous system disorders	Ageusia	Ageusia
Nervous system disorders	Parosmia	Altered smell sensation
Nervous system disorders	Anosmia	Anosmia
Nervous system disorders	Dysgeusia	Dysgeusia

System Organ Class	Preferred Term	Lowest Level Term
Taste and Smell Disorders (SMQ)		
Nervous system disorders	Parosmia	Dysosmia
Nervous system disorders	Parosmia	Dysosmia NOS
Nervous system disorders	Parosmia	Faint odor of sulfur
Nervous system disorders	Hypogeusia	Gustatory sense diminished
Psychiatric disorders	Hallucination, gustatory	Hallucination gustatory
Psychiatric disorders	Hallucination, olfactory	Hallucination olfactory
Psychiatric disorders	Hallucination, gustatory	Hallucination, gustatory
Psychiatric disorders	Hallucination, olfactory	Hallucination, olfactory
Nervous system disorders	Parosmia	Hyperosmia
Nervous system disorders	Hypogeusia	Hypogeusia
Nervous system disorders	Anosmia	Loss of smell
Nervous system disorders	Ageusia	Loss of taste
Psychiatric disorders	Hallucination, olfactory	Olfactory hallucination
Nervous system disorders	Dysgeusia	Parageusia
Nervous system disorders	Parosmia	Parosmia
Nervous system disorders	Parosmia	Perversion olfactory
Nervous system disorders	Parosmia	Smell alteration
Nervous system disorders	Parosmia	Smell change
Nervous system disorders	Anosmia	Smell loss
Nervous system disorders	Parosmia	Smell perversion
Nervous system disorders	Parosmia	Smelly sensation
Nervous system disorders	Parosmia	Strange smell sensation
Nervous system disorders	Dysgeusia	Taste abnormality
Nervous system disorders	Ageusia	Taste absent
Nervous system disorders	Dysgeusia	Taste alteration
Nervous system disorders	Dysgeusia	Taste altered
Nervous system disorders	Dysgeusia	Taste bitter
Nervous system disorders	Dysgeusia	Taste bitter-salty
Nervous system disorders	Dysgeusia	Taste changed
Nervous system disorders	Hypogeusia	Taste diminished
Nervous system disorders	Dysgeusia	Taste disturbance
Nervous system disorders	Dysgeusia	Taste garlic
Nervous system disorders	Ageusia	Taste loss

System Organ Class	Preferred Term	Lowest Level Term
Taste and Smell Disorders (SMQ)		
Nervous system disorders	Dysgeusia	Taste metallic
Nervous system disorders	Dysgeusia	Taste peculiar
Nervous system disorders	Dysgeusia	Taste perversion
Nervous system disorders	Dysgeusia	Taste salty
Nervous system disorders	Dysgeusia	Taste sour
Nervous system disorders	Dysgeusia	Taste sweet
Nervous system disorders	Dysgeusia	Bilious taste
Nervous system disorders	Parosmia	Cacosmia
Nervous system disorders	Hyposmia	Hyposmia
Nervous system disorders	Parosmia	Faint odour of sulfur
Nervous system disorders	Olfactory nerve disorder	Olfactory nerve disorder
Investigations	Olfactory test abnormal	Olfactory test abnormal
Investigations	Olfactory test abnormal	Olfactory acuity test abnormal
Nervous system disorders	Hyposmia	Diminished sense of smell
Investigations	Gustometry abnormal	Gustometry abnormal
General disorders and administration site conditions	Product taste abnormal	Medication after taste
Nervous system disorders	Parosmia	Phantosmia
Nervous system disorders	Parosmia	Olfactism
Nervous system disorders	Hypergeusia	Hypergeusia
Nervous system disorders	Dysgeusia	Chalky taste

(5) AEs related to depression and suicidality/self-injury:

Preferred Term	Lowest Level Term
Depression and Suicide/Self-Injury: Depression (SMQ) (Exclude Suicide/Self-Injury)	
Activation syndrome	Activation syndrome
Adjustment disorder with depressed mood	Adjustment disorder with depressed mood
Adjustment disorder with depressed mood	Adjustment reaction with brief depressive reaction
Adjustment disorder with depressed mood	Adjustment reaction with prolonged depressive reaction
Adjustment disorder with mixed anxiety and depressed mood	Adjustment disorder with mixed anxiety and depressed mood
Agitated depression	Agitated depression
Agitated depression	Depression agitated
Anhedonia	Anhedonia

Preferred Term	Lowest Level Term
Depression and Suicide/Self-Injury: Depression (SMQ) (Exclude Suicide/Self-Injury)	
Anhedonia	Loss of all pleasure
Antidepressant therapy	Antidepressant therapy
Childhood depression	Childhood depression
Decreased interest	Decreased interest
Decreased interest	Loss of all interest
Decreased interest	Loss of interest
Decreased interest	Reduced interest in usual activities
Depressed mood	Chronic depressive mood
Depressed mood	Dejection emotional
Depressed mood	Depressed mood
Depressed mood	Emotional dejection
Depressed mood	Feeling blue
Depressed mood	Feeling down
Depressed mood	Feeling sad
Depressed mood	Low mood
Depressed mood	Mood depression
Depressed mood	Mood depressions
Depressed mood	Unhappiness
Depression	Acute depression
Depression	Anxiety depression
Depression	Anxiodepressive syndrome
Depression	Anxious depression
Depression	Atypical depressive disorder
Depression	Brief depressive reaction
Depression	Chronic depression
Depression	Depressed reaction
Depression	Depressed state
Depression	Depression
Depression	Depression aggravated
Depression	Depression functional
Depression	Depression mental
Depression	Depression NOS
Depression	Depression reactive

Preferred Term	Lowest Level Term
Depression and Suicide/Self-Injury: Depression (SMQ) (Exclude Suicide/Self-Injury)	
Depression	Depression worsened
Depression	Depressive disorder
Depression	Depressive episode
Depression	Depressive illness
Depression	Depressive reaction
Depression	Depressive state
Depression	Depressive stupor
Depression	Exogenous depression
Depression	Mixed anxiety & depressive
Depression	Reactive depression
Depression	Recurrent depressive disorder
Depression	Unipolar depression
Depression	Unipolar depressive illness
Depression postoperative	Depression postoperative
Depression postoperative	Postoperative depression
Depressive symptoms	Depressive symptoms
Depressive symptoms	Depressive symptoms aggravvated
Dysphoria	Dysphoria
Dysthymic disorder	Chronic depressive personality disorder
Dysthymic disorder	Depression neurotic
Dysthymic disorder	Depressive neurosis
Dysthymic disorder	Depressive personality disorder
Dysthymic disorder	Dysthymia
Dysthymic disorder	Dysthymic disorder
Dysthymic disorder	Neurotic depression
Electroconvulsive therapy	Bilateral ECT
Electroconvulsive therapy	ECT
Electroconvulsive therapy	ECT (electro-convulsive therapy)
Electroconvulsive therapy	Electroconvulsive therapy
Electroconvulsive therapy	Modified ECT
Electroconvulsive therapy	Unilateral ECT
Electroconvulsive therapy	Unmodified ECT
Feeling guilty	Feeling guilty

Preferred Term	Lowest Level Term
Depression and Suicide/Self-Injury: Depression (SMQ) (Exclude Suicide/Self-Injury)	
Feeling guilty	Feeling remorse
Feeling of despair	Feeling of despair
Feelings of worthlessness	Feelings of worthlessness
Major depression	Depression endogenous
Major depression	Depression psychotic
Major depression	Depressive type psychosis
Major depression	Endogenous depression
Major depression	Involutional depression
Major depression	Involutional melancholia
Major depression	Major depression
Major depression	Major depressive disorder aggravated
Major depression	Major depressive disorder NOS
Major depression	Major depressive disorder with melancholic features
Major depression	Major depressive disorder, recurrent episode
Major depression	Major depressive disorder, recurrent episode, in full remission
Major depression	Major depressive disorder, single episode
Major depression	Major depressive disorder, single episode in full remission
Major depression	Major depressive illness
Major depression	Melancholia
Major depression	Melancholic depression
Major depression	Psychosis depressive
Major depression	Psychotic depression
Menopausal depression	Depression perimenopausal
Menopausal depression	Depression postmenopausal
Menopausal depression	Menopausal depression
Menopausal depression	Postmenopausal depression
Post stroke depression	Post stroke depression
Postictal depression	Postictal depression
Postpartum depression	Baby blues
Postpartum depression	Depression puerperal
Postpartum depression	Postnatal blues
Postpartum depression	Postnatal depression (excl psychosis)

Preferred Term	Lowest Level Term
Depression and Suicide/Self-Injury: Depression (SMQ) (Exclude Suicide/Self-Injury)	
Postpartum depression	Postpartum depression
Postpartum depression	Puerperal depression
Postpartum depression	Transitory postpartum mood disturbance
Affect lability	Affect lability
Affect lability	Affective incontinence
Affect lability	Emotional incontinence
Affect lability	Emotional instability
Affect lability	Emotional lability
Affect lability	Instability emotional
Affect lability	Labile affect
Affect lability	Lability emotional
Affect lability	Mental lability symptom
Affect lability	Pseudobulbar affect
Alcohol abuse	Alcohol abuse
Alcohol abuse	Alcohol abuse chronic
Alcohol abuse	Alcohol abuse, continuous drinking behavior
Alcohol abuse	Alcohol abuse, continuous drinking behaviour
Alcohol abuse	Alcohol abuse, episodic drinking behavior
Alcohol abuse	Alcohol abuse, episodic drinking behaviour
Alcohol abuse	Alcohol abuse, in remission
Alcohol abuse	Alcohol abuse, unspecified drinking behavior
Alcohol abuse	Alcohol abuse, unspecified drinking behaviour
Alcohol abuse	Nondependent abuse of alcohol
Alcohol poisoning	Acute alcoholic intoxication
Alcohol poisoning	Acute alcoholic intoxication in alcoholism, continuous drinking behavior
Alcohol poisoning	Acute alcoholic intoxication in alcoholism, continuous drinking behaviour
Alcohol poisoning	Acute alcoholic intoxication in alcoholism, episodic drinking behavior
Alcohol poisoning	Acute alcoholic intoxication in alcoholism, episodic drinking behaviour
Alcohol poisoning	Acute alcoholic intoxication in alcoholism, in remission
Alcohol poisoning	Acute alcoholic intoxication in alcoholism, unspecified drinking behavior

Preferred Term	Lowest Level Term
Depression and Suicide/Self-Injury: Depression (SMQ) (Exclude Suicide/Self-Injury)	
Alcohol poisoning	Acute alcoholic intoxication in alcoholism, unspecified drinking behaviour
Alcohol poisoning	Alcohol intoxication
Alcohol poisoning	Alcohol intoxication acute
Alcohol poisoning	Alcohol intoxication, acute
Alcohol poisoning	Alcohol poisoning
Alcohol poisoning	Drunkenness
Alcohol poisoning	Toxic effect of alcohol
Alcohol poisoning	Toxic effect of ethyl alcohol
Alcohol poisoning	Toxic effect of fusel oil
Alcohol poisoning	Toxic effect of isopropyl alcohol
Alcohol poisoning	Toxic effect of methyl alcohol
Alcohol poisoning	Toxic effect of unspecified alcohol
Alcohol problem	Alcohol problem
Alcohol problem	Alcohol problem NOS
Alcohol rehabilitation	Alcohol rehabilitation
Alcoholism	Alcohol addiction
Alcoholism	Alcohol craving
Alcoholism	Alcohol dependence syndrome
Alcoholism	Alcoholic relapse
Alcoholism	Alcoholism
Alcoholism	Alcoholism (excl psychosis)
Alcoholism	Chronic alcoholism
Alcoholism	Dipsomania
Apathy	Ambition loss of
Apathy	Apathy
Apathy	Avolition
Apathy	Initiative loss of
Apathy	Lack of motivation
Apathy	Loss of ambition
Apathy	Loss of initiative
Blunted affect	Affective blunting
Blunted affect	Blunted affect

Preferred Term	Lowest Level Term
Depression and Suicide/Self-Injury: Depression (SMQ) (Exclude Suicide/Self-Injury)	
Constricted affect	Constricted affect
Constricted affect	Restricted affect
Crying	Crying
Crying	Crying abnormal
Crying	Crying uncontrollable
Crying	High-pitched crying
Crying	Inconsolable crying
Crying	Persistent crying
Crying	Uncontrollable crying
Crying	Weeping
Crying	Weepy
Disturbance in attention	Attention concentration difficulty
Disturbance in attention	Attention impaired
Disturbance in attention	Attentiveness decreased
Disturbance in attention	Concentration (mental) abnormal
Disturbance in attention	Concentration ability impaired
Disturbance in attention	Concentration impaired
Disturbance in attention	Concentration impairment
Disturbance in attention	Concentration loss
Disturbance in attention	Disturbance in attention
Disturbance in attention	Impairment of attention
Disturbance in attention	Mental concentration decreased
Disturbance in attention	Mental concentration difficult
Disturbance in attention	Mental concentration difficulty
Disturbance in attention	Mental concentration impaired
Disturbance in attention	Poor concentration
Disturbance in attention	Simple disturbance of activity and attention
Disturbance in attention	Vigilance decreased
Dyssomnia	Dysfunctions associated with sleep stages or arousal from sleep
Dyssomnia	Dyssomnia
Dyssomnia	Dyssomnia NOS
Emotional distress	Embarrassment

Preferred Term	Lowest Level Term
Depression and Suicide/Self-Injury: Depression (SMQ) (Exclude Suicide/Self-Injury)	
Emotional distress	Emotional distress
Emotional distress	Humiliation
Emotional distress	Mental distress
Emotional distress	Suffering
Emotional poverty	Emotional poverty
Emotional poverty	Emotional withdrawal
Emotional poverty	Lack of feeling emotions
Emotional poverty	Poverty emotional
Emotional poverty	Withdrawal emotional
Hypersomnia	Hypersomnia
Hypersomnia	Idiopathic hypersomnia
Hypersomnia	Persistent disorder of initiating or maintaining wakefulness
Hypersomnia	Primary hypersomnia
Hypersomnia	Sleep excessive
Hypersomnia	Transient disorder of initiating or maintaining wakefulness
Hyposomnia	Hyposomnia
Impaired self-care	Impaired self-care
Initial insomnia	Initial insomnia
Initial insomnia	Trouble falling asleep
Intentional product misuse	Intentional drug misuse
Intentional product misuse	Intentional misuse
Intentional product misuse	Intentional misuse by dose change
Intentional product misuse	Intentional misuse in dosing frequency
Intentional product misuse	Intentional product misuse
Intentional product use issue	Intentional dose decrease
Intentional product use issue	Intentional dose increase
Intentional product use issue	Intentional product use issue
Intentional product use issue	Intentional use beyond labeled administration duration
Intentional product use issue	Intentional use beyond labeled duration
Intentional product use issue	Intentional use beyond labelled administration duration
Intentional product use issue	Intentional use beyond labelled duration
Intentional product use issue	Intentional use by incorrect route

Preferred Term	Lowest Level Term
Depression and Suicide/Self-Injury: Depression (SMQ) (Exclude Suicide/Self-Injury)	
Intentional product use issue	Intentional use for unlabeled indication
Intentional product use issue	Intentional use for unlabelled indication
Listless	Listless
Listless	Listlessness
Maternal use of illicit drugs	Maternal use of illicit drugs
Memory impairment	Forgetfulness
Memory impairment	Hypomnesia
Memory impairment	Memory deficit
Memory impairment	Memory disturbance
Memory impairment	Memory disturbance (excl dementia)
Memory impairment	Memory impaired
Memory impairment	Memory impairment
Memory impairment	Short-term memory impairment
Middle insomnia	Arousal night
Middle insomnia	Middle insomnia
Middle insomnia	Nocturnal awakening
Middle insomnia	Sleep maintenance insomnia
Mood altered	Affect alteration
Mood altered	Affect altered
Mood altered	Altered mood
Mood altered	Bad mood
Mood altered	Mood alteration NOS
Mood altered	Mood altered
Mood altered	Mood change
Mood swings	Mood swings
Mood swings	Mood variable
Morose	Morose
Morose	Moroseness
Negative thoughts	Negative thoughts
Neglect of personal appearance	Appearance personal neglect of
Neglect of personal appearance	Neglect of person appearance
Neglect of personal appearance	Neglect of personal appearance
Neglect of personal appearance	Personal appearance neglect of

Preferred Term	Lowest Level Term
Depression and Suicide/Self-Injury: Depression (SMQ) (Exclude Suicide/Self-Injury)	
Poor quality sleep	Light sleep
Poor quality sleep	Poor quality sleep
Poor quality sleep	Poor sleep
Poor quality sleep	Sleep restless
Poor quality sleep	Sleep unwell
Poor quality sleep	Wakefulness
Psychomotor hyperactivity	Activity motor exaggerated
Psychomotor hyperactivity	Behavior hyperactive
Psychomotor hyperactivity	Behaviour hyperactive
Psychomotor hyperactivity	Hyperactive
Psychomotor hyperactivity	Hyperactivity
Psychomotor hyperactivity	Increased activity
Psychomotor hyperactivity	Irritable hyperkinesis
Psychomotor hyperactivity	Motor activity exaggerated
Psychomotor hyperactivity	Muscular hyperactivity
Psychomotor hyperactivity	Overactive
Psychomotor hyperactivity	Overactivity
Psychomotor hyperactivity	Psychomotor agitation
Psychomotor hyperactivity	Psychomotor excitability
Psychomotor hyperactivity	Psychomotor hyperactivity
Psychomotor retardation	Psychomotor retardation
Psychosocial support	Psychosocial counseling
Psychosocial support	Psychosocial support
Psychotherapy	Art therapy
Psychotherapy	Cognitive psychotherapy
Psychotherapy	Couples psychotherapy
Psychotherapy	Family psychotherapy
Psychotherapy	Group psychotherapy
Psychotherapy	Hippotherapy
Psychotherapy	Interpersonal psychotherapy
Psychotherapy	Play therapy
Psychotherapy	Psychotherapy
Psychotherapy	Supportive psychotherapy

Preferred Term	Lowest Level Term
Depression and Suicide/Self-Injury: Depression (SMQ) (Exclude Suicide/Self-Injury)	
Self esteem decreased	Self esteem decreased
Substance-induced mood disorder	Stimulant-induced mood disorder
Substance-induced mood disorder	Substance-induced mood disorder
Tearfulness	Tearfulness
Terminal insomnia	Awakening early
Terminal insomnia	Early morning awakening
Terminal insomnia	Terminal insomnia

Preferred Term	Lowest Level Term
Depression and Suicide/Self-Injury: Suicide/Self-Injury (SMQ)	
Columbia suicide severity rating scale abnormal	Columbia suicide severity rating scale abnormal
Completed suicide	Accomplished suicide
Completed suicide	Completed suicide
Completed suicide	Suicide
Completed suicide	Suicide (accomplished)
Depression suicidal	Depression suicidal
Depression suicidal	Suicidal depression
Intentional overdose	Deliberate overdose
Intentional overdose	Drug overdose deliberate self-inflicted
Intentional overdose	Intentional overdose
Intentional overdose	Multiple drug overdose intentional
Intentional overdose	Non-accidental overdose
Intentional overdose	Overdose deliberate self-inflicted
Intentional overdose	Overdose intentional
Intentional self-injury	Deliberate self-harm
Intentional self-injury	Deliberate self-injury
Intentional self-injury	Intentional self-injury
Intentional self-injury	Parasuicide
Intentional self-injury	Repeated parasuicide
Intentional self-injury	Self inflicted laceration
Intentional self-injury	Self mutilation

Preferred Term	Lowest Level Term
Depression and Suicide/Self-Injury: Suicide/Self-Injury (SMQ)	
Attempted suicide	Deliberate poisoning
Attempted suicide	Poisoning deliberate
Poisoning deliberate	Poisoning deliberate
Poisoning deliberate	Poisoning deliberate self-inflicted
Self injurious behaviour	Self injurious behavior
Self injurious behaviour	Self injurious behavior without suicidal intent
Self injurious behaviour	Self injurious behaviour
Self injurious behaviour	Self injurious behaviour without suicidal intent
Self-injurious ideation	Self-injurious ideation
Self-injurious ideation	Thoughts of self harm
Suicidal behaviour	Preparatory actions toward imminent suicidal behavior
Suicidal behaviour	Preparatory actions toward imminent suicidal behaviour
Suicidal behaviour	Suicidal behavior
Suicidal behaviour	Suicidal behaviour
Suicidal behaviour	Suicide gesture
Suicidal ideation	Active suicidal ideation
Suicidal ideation	Death wishes
Suicidal ideation	Life weariness
Suicidal ideation	Passive suicidal ideation
Suicidal ideation	Suicidal ideation
Suicidal ideation	Suicidal intention
Suicidal ideation	Suicidal plans
Suicidal ideation	Suicidal tendency
Suicide attempt	Attempted suicide
Suicide attempt	Suicide attempt
Suicide attempt	Suicide attempt other than overdose
Suicide attempt	Unsuccessful suicide