TITLE PAGE

Division: Worldwide Development
Information Type: Worldwide Epidemiology Study Protocol

Title:	PRJ2282 / 201491: CHESS: CPRD-COPD Hawthorne Effect Study in Salford: A UK cohort study to characterise patients enrolled in the Salford Lung Study and to evaluate a potential Hawthorne effect

Compound Number:	GW685698 / GW642444
Development Phase	IV
Effective Date:	23 October 2015
Subject:	COPD in the UK general population and comparison with the Salford Lung Study
Author(s):	**University of Manchester:** PPD **GlaxoSmithKline:** PPD **Clinical Practice Research Datalink:** PPD

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1. LIST OF ABBREVIATIONS

AIC	Akaike Information Criterion
CHESS	CPRD-COPD Hawthorne Effect Study in Salford
CPRD	Clinical Practice Research Datalink
COPD	Chronic Obstructive Pulmonary Disease
EHR	Electronic Health Record
EMR	Electronic Medical Record
FEV1	Forced expiratory volume in 1 second
FF	Fluticasone furoate
FVC	Forced vital capacity
GOLD	Global Initiative for Chronic Obstructive Lung Disease
GPRD	General Practice Research Database
GP	General Practitioner
GSK	GlaxoSmithKline
HCU	Health Care Utilisation
HES	Hospital Episode Statistics
ICS	Inhaled Corticosteroid
ISAC	CPRD Independent Scientific Advisory Committee
LABA	Long Acting Bronchodilator
LAMA	Long Acting Muscarinic Antagonist
MHRA	Medicines and Healthcare Products Regulatory Agency
MPR	Medication Possession Ratio
MRC	Medical Research Council
NICE	National Institute for Health and Care Excellence
NWeH	North West eHealth
ONS	Office for National Statistics
PDC	Percent Days Covered
SAS	Statistical Analysis System
SES	Socio-Economic Status
SIR	Salford Integrated Record
SLS	Salford Lung Study
SOC	Standard of Care

SOP	Standard Operating Procedure
UoM	University of Manchester
VI	Vilanterol

Trademark Information

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2. RESPONSIBLE PARTIES

The study will be led by University of Manchester (UoM) who will collaborate with North West eHealth (NWeH), Clinical Practice Research Datalink (CPRD) and GSK.

Study Task	Responsible group(s)
Protocol finalization	UoM
Develop specifications for data sets	UoM, GSK, CPRD, NWeH
Data extraction for SLS Standard of Care arm	NWeH
Creation of CPRD cohort dataset	UoM, CPRD
Analyses (using SAS) comparing SLS and CPRD	UoM
QC/QA of analysis	GSK (Observational Data Analytics)
Final study report	Drafting: UoM Review, comment, and edits: Scientific Committee Reporting to regulatory agency and web-based register: GSK
Manuscripts	Drafting: medical writer Review and edits: study team, scientific committee members

A Scientific Committee (see section below) will be assembled and will be required to review and input into study design and major study documents (final study protocol, final research analysis plan, final study report, peer-review publications).

CONFIDENTIAL

WWEpi Project number: PRJ2282

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Jeanne M. Pimenta
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INVESTIGATOR PROTOCOL AGREEMENT PAGE

- I confirm agreement to conduct the study in compliance with the protocol.
- I acknowledge that I am responsible for overall study conduct. I agree to personally conduct or supervise the described clinical study.
- I agree to ensure that all associates, colleagues and employees assisting in the conduct of the study are informed about their obligations. Mechanisms are in place to ensure that site staff receives the appropriate information throughout the study.

Investigator Name: **Matthew Sperrin**

PPD

23/10/15

Investigator Signature

Date

WWEpi Project number: PRJ2282

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GSK Members:

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Senior Director, Worldwide Epidemiology, Respiratory Therapeutic Area Lead, Worldwide Epidemiology GlaxoSmithKline

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Global Medical Advisory Lead, Respiratory Franchise, GlaxoSmithKline

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Director, Clinical Statistics, GlaxoSmithKline

3. ABSTRACT

Background: The Salford Lung Study (SLS) is a unique Phase IIIB pragmatic trial evaluating the effectiveness of a novel medicine – RELVAR (fluticasone furoate [FF], GW685698) and vilanterol [VI] GW642444) – compared with standard of care (SOC) among patients with Chronic Obstructive Pulmonary Disease (COPD). The trial is taking place in Salford, England. While the pragmatic nature of the trial is designed to test effectiveness in routine care, there are at least two possible concerns: 1) Salford may not be representative of the wider population in which the medicine may be used, and 2) there may be differences in local practice or changes to local practice caused by the study (the Hawthorne effect), which may artificially inflate the benefits of both RELVAR and SOC.

Objectives: The aim of the study is to evaluate the representativeness of Salford, and the potential Hawthorne effect, to place the SLS in wider context. The objectives are:

Co-primary objectives:

- **PO1**: To characterize the patients enrolled in the Standard of Care (SOC) arm of SLS COPD compared with the UK population of COPD patients (using the Clinical Practice Research Datalink (CPRD)), including distribution of SES/deprivation level, to evaluate the extent to which the SLS participants are representative of the UK patient population targeted for RELVAR. The comparator set will be specified on two bases: firstly, overall, and secondly, the subset fulfilling the protocol inclusion/exclusion criteria.

- **PO2**: To compare the rate of COPD exacerbation over the 12 months in Standard of Care arm of the SLS compared with the Standard of Care (SOC) recorded in the CPRD, in order to detect a potential Hawthorne effect.

- **PO3**: To compare the rate of serious pneumonia (defined by hospitalisation) over the 12 months in Standard of Care arm of the SLS compared with the Standard of Care recorded in the CPRD.

Secondary objectives:

- **SO1**: To make comparisons between the SLS SOC and the CPRD cohort on the following health care utilisation (HCU) endpoints: GP visits, hospital admissions, mortality and adherence.

- **SO2**: To evaluate other definitions of COPD exacerbations in SOC from CPRD.
.

- **SO3**: Self-controlled comparison of COPD and HCU endpoints in Salford before and after SLS commenced, using data from the SLS.

Study Design: Observational COPD cohort study, comparing Salford, UK (data source: SLS) with rest of UK (data source: CPRD) over a 12 month period.

Population: The setting is Salford, UK compared with rest of UK. The study population is, in Salford, participants recruited to the SLS and randomised to the SOC arm. In the rest of the UK, the comparison group is persons with COPD recorded in the CPRD who meet the eligibility criteria of the SLS.

Study Size: The target sample size for the SLS is 2,800. Study size in the CPRD will be based on the prevalence of COPD diagnosis codes; this will be a minimum 2,800 to match but is expected to be considerably larger (x5-10).

Analysis: Data analysis will use descriptive statistics for PO1. PO2 and PO3 will be addressed using multilevel modelling.

4. AMENDMENTS AND UPDATES

None.

5. MILESTONES

Deliverable	Timelines
Contract signed	November, 2014
Agreed Protocol for GSK protocol-review forum	November, 2014†
Completion of Statistical analyses plan. Development of programs for analyses.	November 2014 – 1st October 2015
"Data look" SLS data and CPRD data to UoM (Interim 1).	Jan 2016
Analyses of primary objectives (PO1 only) on subset of data using "data look" data (start working on PO2/3)	Feb-March 2016
Final SLS data (one year FU for all subjects) to UoM	1st-8th April 2016
Analyses of PO2 (COPD exacerbation data) using final SLS data: First report with P01/P02 to GSK	By 29th April 2016
Share output from Primary Objectives with SLS Scientific Committee; and CHESS Steering Committee	9-10th May 2016†
First manuscript developed and ready for submission with SLS paper to Thorax based PO1 and PO2 data	June-July 2016†
Programming for secondary objectives and PO3	May-October 2016
100% CPRD-HES data available to UoM (required for PO3 analyses).	Estimated at October 2016
Analysis for PO3 and draft tables circulated	November 2016
Draft complete study report with PO1/PO2/PO3 to GSK	December 2016†
Regulatory reporting of PO3	Q1 2017
Final follow-up manuscript	Q1-2 2017†

† Milestone payment

6. RATIONALE AND BACKGROUND

6.1. Background

Chronic Obstructive Pulmonary Disease (COPD) is a chronic obstructive disease of the airways associated with a significant social and healthcare burden [1, 2, 3]. Most patients with COPD are managed in primary care, as reflected in recent UK guidelines, which are specifically targeted at primary care physicians [4]. The major goals of treatment are to relieve symptoms, improve activity/exercise tolerance, prevent and treat exacerbations, reduce mortality risk and improve health status. However, despite such guidelines, COPD remains under-diagnosed and under-treated; variations in treatments, standards of care and adherence to guidelines have been reported across different geographical regions [2, 5, 6, 7, 8].

Large computerised patient databases provide a useful source of real life observational data, and the General Practice Research Database (GPRD) has been successfully used to generate descriptive epidemiology data in COPD [9, 10, 11, 12] from a large group of UK primary care practices. Historically, the limitations of the GPRD were a time gap between data capture and availability for the researcher and limited links to other healthcare databases, although these are currently being addressed with the development of the Clinical Practice Research Datalink (CPRD) and in recent Phase 4 pragmatic clinical trials [12]. The use of electronic medical record (EMR) data in health research is a key objective in the Department of Health's national research strategy [13].

The Salford Lung Study (SLS) is an ongoing Ph IIIB pragmatic trial comparing a new once daily ICS/LABA fixed dose combination (RELVAR: fluticasone furorate + vilanterol) in which patients are identified by EMR, enrolled in their GP office, randomized to RELVAR or Standard of Care (SOC) maintenance therapy and followed for safety and effectiveness via linked primary care/secondary routine care with primary endpoint of COPD moderate/severe exacerbations over 12 months [14]. MHRA and NICE provided joint advice for the SLS protocol and were supportive of the design to generate "real world" evidence which will demonstrate the value and safety of the medicine against the most relevant standard of care.

6.2. Rationale

Although the SLS will give evidence on the relative effectiveness of RELVAR compared with SOC, the SOC may be prone to the Hawthorne effect, which may distort the effect size.

The Hawthorne effect (also referred to as the observer effect) is a type of reactivity in which individuals improve or modify an aspect of their behaviour in response to their awareness of being observed. The original "Hawthorne effect" studies at the Hawthorne Works in Chicago, USA between 1924 and 1933 suggested that the novelty of being research subjects and the increased attention from such could lead to temporary increases in workers' productivity [15].

In the situation of this study, a potential Hawthorne effect may be a result of potentially different behaviours and decision making of GPs and nurses in their practices of caring for patients with COPD during the SLS study period.

Salford may not be representative of general UK population; hence the prognostic profiles, and potential effect of RELVAR in terms of the outcomes may differ in the general target COPD population compared with Salford.

Both of these issues mean that extrapolation of the results of the SLS to the wider UK population would be subject to major caveats. This proposal aims to explore, and assess how severe the caveats need to be.

7. RESEARCH QUESTION AND OBJECTIVE(S)

Co-primary objectives:

PO1: To characterize the patients enrolled in the Standard of Care (SOC) arm of the SLS compared with the UK population of COPD patients (using the Clinical Practice Research Datalink (CPRD)), including distribution of SES/deprivation level, to evaluate the extent to which the SLS participants are representative of the UK patient population targeted for RELVAR. The comparator set will be specified on two bases: firstly, overall, and secondly, the subset fulfilling the protocol inclusion/exclusion criteria.

PO2: To compare the rate of COPD exacerbation over the 12 months in Standard of Care arm of the SLS compared with the Standard of Care (SOC) recorded in the CPRD, in order to detect a potential Hawthorne effect or other differences.

PO3: To compare the rate of serious pneumonia (defined by hospitalisation) over the 12 months in Standard of Care arm of the SLS compared with the Standard of Care recorded in the CPRD.

Secondary objectives:

SO1: To make comparisons between the SLS Standard of Care and the CPRD cohort on the following health care utilisation (HCU) endpoints: GP visits, hospital admissions mortality and adherence.

SO2: To evaluate other definitions of COPD exacerbation in SOC from CPRD.

SO3: Self-controlled comparison of COPD and other HCU endpoints in Salford before and after SLS commenced.

8. RESEARCH METHODS

8.1. Study Design

This will be an observational COPD cohort study that will utilize the CPRD and the Salford EHR system – to compare selected cohorts with SLS.

For SLS, reference/index date is study entry. This will be matched in CPRD by the following algorithm:

1. Draw up a long-list of potentially eligible individuals in CPRD (patients who would be eligible at some point during the SLS recruitment phase).
2. For each individual:
    a. Randomly sample an entry date from full list of SLS entry dates.
    b. If patient is eligible at that entry date, then they will be included, accounting for relevant immortal time biases up to that entry date, otherwise, they will be excluded. Further details on methods of reducing immortal time bias (i.e left truncated at the entry date and survival modelling) will be outlined in the SAP.

First, the COPD populations in both Salford and in the wider CPRD (excluding Greater Manchester area) will be compared. Second, we will focus on comparisons between all patients enrolled in the SLS SOC arm versus a CPRD cohort that would have been eligible for SLS as per the inclusion and exclusion criteria.

8.2. Setting

In terms of geography, Salford, UK, and surrounding areas within Greater Manchester, for the SLS group; UK-wide, excluding Greater Manchester, for the CPRD group. In terms of health settings, general practice – restricted to practices in Salford and to practices that contribute to CPRD (~10%).

8.2.1. Inclusion Criteria

Two cohorts will be produced. First, a CPRD cohort, using linked primary care, medication, Hospital Episode Statistics, and socio-economic data, according to the following inclusion criteria:

1. Diagnosis of COPD before index date (time period will be defined in the SAP)
2. Aged ≥40 at index date.
3. Alive, and registered with a GP, at index date.
4. Not registered with a GP in the Greater Manchester area.

Second, a Salford cohort will be constructed using the Salford Integrated Record (SIR), according to the inclusion criteria:

1. Diagnosis of COPD before index date.
2. Aged ≥40 at index date.

3. Alive, and registered with a GP, at index date.

Restricted cohorts will then be constructed in both the Salford and CPRD populations, based on the inclusion/exclusion criteria and study period for the SLS:

1. Patients with documented GP diagnosis of COPD, and currently receiving maintenance therapy
2. Male or female subjects aged ≥40 years of age at index date
3. Patients who have a history of treatment with systemic/oral corticosteroids, antibiotics (in association with GP contact) and/or hospitalisation for at least one COPD exacerbation in the 3 years prior to index date.
4. Current COPD Therapy

   All patients currently receiving either:

   - inhaled corticosteroid (ICS) alone or in combination with a long acting bronchodilator (this could be a fixed dose combination or an ICS/LABA provided in two separate inhalers, or ICS and LAMA),
   - or long-acting bronchodilator therapy alone (e.g. tiotropium or salmeterol, or the use of two bronchodilators i.e. LABA/LAMA),
   - or "triple therapy" i.e. ICS/LABA plus a Long Acting Muscarinic Antagonist (LAMA)

Finally, the third data source, the SLS, will be used as-is.

8.2.2. Exclusion Criteria

Subjects meeting any of the following criteria must not be included in the restricted cohorts:

1. Patients with any life threatening condition or uncontrolled/clinically significant disease (code list to be specified in the Study Analysis Plan)
2. Patients with unstable COPD: Patients with an exacerbation (defined by treatment with oral corticosteroids and/or antibiotic or hospital discharge listing COPD) with an onset within 2 weeks of index date. Delay index date until at least 2 weeks after the onset of an exacerbation and until the exacerbation has resolved.
3. Chronic user of oral corticosteroids: Subjects who are considered to be a chronic user of oral corticosteroids for respiratory or other indications (Algorithm to be specified in the Study Analysis Plan).
4. In the Salford population only, those patients who are entered in the SLS and randomised to the RELVAR arm.

8.3. Variables

8.3.1. Outcome definitions

Primary outcomes/endpoint:

- **Rate of COPD exacerbation:** The definition of a COPD exacerbation to be informed by the ongoing study being conducted by PPD et al. (collaborative project between London School of Hygiene and Tropical Medicine and GSK; GSK study number WEUSKOP5893).

  Moderate/severe COPD exacerbations will be identified using an algorithm combining GP visits, prescriptions for oral corticosteroids and/or antibiotics, or hospital admission, as defined using information from study WEUSKOP5893. Rate of exacerbation during the 12 month follow-up will be calculated and compared with the SLS rate in the standard of care arm; if technically possible, exacerbation rates for the 12 months prior to index date (matched enrolment date) would also be compared.

- **Pneumonia:** To be defined as per the codelist in Table 1 (see 13.1).

Secondary outcomes/endpoints:

- **Healthcare utilisation:** All GP visits/encounters and all hospital admissions during the 12 month study period.
- **Adherence to index prescription:** Defined as percent days covered (PDC) and medication possession ratio (MPR) will also be calculated for the matched cohort, as well as discontinuation, switching medicine or adding on other medicines, to be compared with the SLS SOC arm.
- **Deaths:** All cause, pneumonia death, COPD-attributed death during the 12 month follow-up. For the CPRD, deaths will be determined using Office of National Statistics (ONS) linked mortality data.
- **Other definitions of COPD exacerbation:** Other definitions will be described as per the outputs of study WEUSKOP5893.

8.3.2. Exposure definitions

This is a binary comparison of COPD patients enrolled in the SLS and COPD patients in the CPRD. Hence the primary exposure of interest is whether a patient is enrolled in SLS (yes/no). A third grouping, COPD patients in Salford (who are not in SLS) will also be examined.

8.3.3. Confounders and effect modifiers

- Sex
- Age
- Socio-economic status (SES)
- Current/SOC COPD Medication group:

- LAMA or LABA only
- LAMA+LABA
- LABA+ICS (combination product or two inhalers)
- LABA+ICS+LAMA

- Comorbidities
  - Cardio-and cerebrovascular diseases (heart failure, myocardial infarction, stroke)
  - Depression
  - Anxiety
  - Asthma
  - History of pneumonia
  - Gastro-oesophageal reflux and peptic ulcer disease
  - Diabetes
  - Charlson score (COPD will be removed from score)
- Markers of COPD severity
  - Previous COPD exacerbation
  - FEV1 % predicted
  - FEV1/FVC ratio
  - GOLD stage
  - MRC Dyspnoea score
- Comedications: major medication classes for each comorbidity of interest
- Smoking
- BMI
- Vaccinations
- Disability status

Further information on the definitions for the variables above will be provided in the SAP.

8.4. Data sources

The three main data sources are SLS, CPRD and SIR.

The Salford Lung Study (SLS) is described in [14]. In brief, it is a pragmatic trial, carried out in Salford, UK, to evaluate the relative effectiveness and safety of RELVAR compared with SOC. There are two separate studies within the SLS; one for COPD and the other for asthma. For this protocol, the SLS data refers to SLS for COPD only.

The CPRD is a primary care database consisting of a subset of GP practices across the UK. This will be linked to Hospital Episode Statistics (HES), socio-economic status (SES) and Office of National Statistics (ONS) datasets. For brevity, the linked dataset will henceforth be referred to as CPRD.

The SIR is a comprehensive primary and secondary care database detailing healthcare contacts, diagnostic tests and prescriptions of all patients registered with a GP in Salford, UK.

There are a range of subsets and derivations of the data sources that will be considered for this study, listed here for clarity.

CPRD: CPRD – all practices, all COPD patients

CPRD-GM: CPRD – practices/patients in Greater Manchester only, all COPD patients

CPRD-xGM: CPRD – excluding practices/patients in Greater Manchester, all COPD patients

CPRD-GM-IC: CPRD – practices/patients in Greater Manchester only, COPD patients meeting SLS inclusion criteria only

CPRD-xGM-IC: CPRD – excluding practices/patients in Greater Manchester, COPD patients meeting SLS inclusion criteria only

SLS-E: SLS – all eligible. Not all of these are enrolled (some decline)

SLS: SLS – all enrolled

SLS-SOC: SLS – SOC arm only

SIR: SIR – all COPD patients

SIR-IC: SIR - COPD patients meeting SLS inclusion criteria only

In the CPRD, data linkage will be subject to a lag due to the delayed availability of HES and ONS data. Fully linked data will only be available up to a certain date when analyses are undertaken, and as such, primary analyses will be restricted to include SLS enrolled patients up to that date. Subsequent analyses will be conducted once linkage is available for the entire recruitment period. As capture of events of serious pneumonia (as defined in the context of this study) is dependent on records of hospitalisation, PO3 will be analysed when fully linked CPRD-HES data are available.

8.5. Study size

The target sample size for the number of COPD patients enrolled in the SLS is 2,800. Study size in CPRD will be based on the prevalence of COPD diagnosis codes; this will be a minimum 2,800 to match but is expected to be considerably larger (x5-10).

8.6. Data management

8.6.1. Data handling conventions

Data handling within University of Manchester will be governed by the System Level Security Policy for the study (see Annex 1a). Quality control programming will be conducted by within GSK, following data handling SOPs.

8.6.2. Resourcing needs

Staff resources required for the project are outlined in section 2 (responsible parties).

8.6.3. Timings of Assessment during follow-up

As per SLS protocol for SLS patients. CPRD and SIR patients are observational only.

8.7. Data analysis

8.7.1. Essential analysis

All analyses will be conducted using SAS.

For PO1, distributions of the confounders and effect modifiers (as listed in Section 8.3.3) will be tabulated – summarised as proportions in each category for binary and categorical variables, and means/medians and standard deviations for continuous variables. Graphical visualisations will also be produced to aid interpretation (for example, boxplots to characterise age distributions in each population, stacked bar charts to visualise SES by population). This will be done for a series of the derived populations to separate out true differences in demographics in Salford and differences that arise as a consequence of data quality issues etc. The following comparisons will be of interest:

- CPRD-GM v CPRD-xGM: to give an indication of true demographic difference from the same data source.
- CPRD-GM-IC v CPRD-xGM-IC: as above, but restricted to patients meeting the inclusion criteria.
- SIR v CPRD-GM: to give an indication of differences arising as a consequence of selection bias of CPRD practices, and through data quality issues etc.
- SIR-IC v CPRD-GM-IC: as above, but restricted to patients meeting the inclusion criteria.
- SIR-IC v SLS-E: to give an indication of recruitment bias and physician researcher bias (at the approach stage).
- SIR-IC v SLS: to give an indication of recruitment bias (at recruitment stage).
- **SLS v CPRD-xGM-IC**: to indicate the difference between trial recruited, and those meeting the inclusion criteria outside of Salford. This is the key comparison for addressing PO1.

We will then move on to explicit modelling of regional variation of the characteristics within CPRD for the emboldened comparison (**SLS v CPRD-xGM-IC)** to ascertain whether the characteristics observed within Salford are unusual by comparison with CPRD-xGM-IC. We will take local authority regional level (anonymised) as the comparable unit to the study region for SLS. SLS will be considered unusual on a given demographic if an appropriately chosen summary statistic for that demographic (mean for continuous variables) falls outside the 2.5-97.5 percentile range.

For PO2, we will commence with exploratory analyses, similar to described above, to explore the distributions of the primary and secondary endpoints.

Hawthorne effect will be evaluated in two different ways.

Firstly, for descriptive purposes, we will measure the prevalence of the endpoints in a series of subgroups. For example, we will compare the COPD exacerbations in CPRD-xGM-IC with SLS, stratified by SES, gender, etc.

Secondly, we will take a multilevel modelling approach. For this we will combine the SLS and CPRD into one dataset (retaining an indicator of SLS membership). The hierarchies of the model will be patient -> GP practice -> local authority region (with SLS members being treated as a single distinct region) -> strategic health authority region. Strategic health authorities (population threshold of 1 million) are non-anonymised (named) regions. Local authority regions are below the population threshold so an anonymised LA marker will be available.

We will include all confounders and effect modifiers as covariates, with outcomes corresponding to the primary and secondary study outcomes (a separate model for each). Important fixed effects at the local authority level (for example, existence of community teams) will be incorporated into the model if these can be ascertained.

A final model will be selected via backward selection using AIC (Akaike Information Criterion). We will then examine the random effect of the SLS region in the context of the random effects for the other regions. Similar to the above, if the random effect of the SLS region falls outside the 2.5-97.5 percentile range, we will conclude that SOC SLS behaves unusually compared with the rest of the UK, and hence evidence of a Hawthorne effect.

PO3 will be carried out using the same approach as for PO2.

SO1 and SO2 (which pertain to comparing other endpoints, and sensitivity analyses of endpoint definition) will be carried out in the same way as PO2.

SO3 makes explicit the possible change in outcomes at commencement of SLS. We will compare outcome rates within Salford before and after the commencement of SLS, in a self-controlling case design. We will do the same thing within CPRD to control for UK-wide secular trends. This acts as sensitivity analysis to support PO2 (using controls distinct in time rather than in geography).

Additional work will take place exploring the development of methods for a framework of measuring representativeness; this is not within scope of this protocol and is described in Annex 2.1.

8.7.2. Exploratory analysis

8.7.3. General considerations for data analyses

The main identified risks are:

- How linkable the SLS and CPRD datasets are – e.g. can variables be extracted from both with the same (or very similar) definitions for all outcomes and potential confounders.
- Linkage of CPRD to HES and SES is not possible over the calendar dates that SLS has run as there is a lag time until these are released. Hence it may be necessary to restrict some analyses to data from earlier time periods.

8.8. Quality control

CPRD-GOLD has been used previously for descriptive drug utilization studies for prescription medications in respiratory diseases [16, 17, 18].

The standard operating procedures of University of Manchester will guide the conduct of the study, and will include internal quality audits; following rules for secure storage and backup of confidential data and study documentation; quality control procedures for programming, and requirements for senior scientific review.

The QC of analysis will be performed by GSK, in accordance with GSK Standard Operating Procedures (SOPs) and Guidance Documents, specifically the SOP_52213 (4.0) : Conducting Quality Control Review of Worldwide Epidemiology Study Results . The common data model will allow the use of one set of programming following creation of a standardized structure. Wherever feasible, all statistical programming will be independently reviewed by a second analyst, with oversight by a senior statistician. Key study documents, such as the ISAC Protocol, statistical analysis plan, and study reports will undergo quality-control checks and review by the Scientific Steering Committee. Archiving of the project materials will be performed in accordance with GSK SOPs for documentation and archiving of observational studies.

8.9. Limitations of the research methods

Hawthorne effect can only be evaluated for the SOC comparison. This does not give definite evidence about whether the prognostic or predictive effect of RELVAR would differ in the general population. This information could only truly be obtained following use of RELVAR in the general population.

There is no direct metric by which 'representativeness' of the Salford cohort can be measured. Early explorations of this will be made in a companion project – see Annex 2.1.

While both the SLS and CPRD use GP data, some data (hospital validated COPD diagnoses, pneumonia data, pharmacy data) for participants in SLS are collected using a different mechanism to CPRD. In this study protocol, only serious pneumonia defined by hospitalization will be assessed, which is a subset of total pneumonia cases recorded in the SLS. Hence any differences (either in representativeness or treatment response) observed between the SLS and non-SLS cohorts could be attributed to differences in data quality and the data collection mechanism. This will be mitigated by an additional comparison of SLS data with CPRD data from within Greater Manchester.

8.9.1. Study closure/uninterpretability of results

Not applicable.

9. PROTECTION OF HUMAN SUBJECTS

9.1. Ethical approval and subject consent

Individual subject consent is not required as this work is using research data. Internal ethical approval will be sought from the University of Manchester.

Linkage of the CPRD to other datasets such as HES is undertaken by a trusted third party (the Health and Social Care Information Centre). The identifiers (date of birth, gender, NHS number, postcode of residence) required for linkage are sent directly from the originating general practice to the trusted third party. CPRD holds only a local patient identifier which is meaningful only at the patients' registered general practice. This identifier is pseudonymised a second time before being made available to researchers and analysts with access to the database.

CPRD's processes have been reviewed by the Confidentiality Advisory Group (CAG) and approved by the Health Research Authority (HRA) and Secretary of State to process patient identifiable information without consent under Regulation 5 of the Health Service (Control of Patient Information) Regulations 2002. This effectively removes the obligation to obtain patient consent for the use of confidential patient information for conducting purely observational research using CPRD databases, and associated linked datasets. This approval is conditional on approval of a study protocol by the CPRD Independent Scientific Advisory Committee (ISAC). In addition to ISAC approval, the protocol will be reviewed by GSK Worldwide Epidemiology Protocol Review Forum.

9.2. Subject confidentiality

The SLS data will be anonymised at source by the SLS team, before this is passed to University of Manchester.

The CPRD only contains fully de-identified patient data. No patient identifiable information will be available to the study team, or to GSK. All data held and processed by CPRD and any other study partners will be done so in compliance with the relevant legal obligations including the Data Protection Act 1998.

All data will be held on a secure computer network, with access restricted to authorised users.

10. MANAGEMENT AND REPORTING OF ADVERSE EVENTS/ADVERSE REACTIONS

This is a retrospective study. From the CPRD, free text data will not be available to allow causality determination of any potential adverse events. Adverse events arising from the SLS trial will have previously been reported appropriately during the trial period.

11. PLANS FOR DISSEMINATING AND COMMUNICATING STUDY RESULTS

11.1. Target Audience

This work is targeted 1) internally at GSK, 2) regulators and 3) the wider scientific community; in order to understand the SLS in wider context. Results will be disseminated externally primarily by manuscripts.

11.2. Study reporting and publications

Reporting and publications according to the following table:

Deliverable	Timelines
Agreed Protocol for GSK protocol-review forum	November, 2014
Completion of Statistical analyses plan. Development of programs for analyses.	November 2014 – 1st October 2015
Analyses of PO2 (COPD exacerbation data) using final SLS data: First report with PO1/PO2 to GSK	By 29th April 2016
Share output from Primary Objectives with SLS Scientific Committee; and CHESS Steering Committee	9-10th May 2016
First manuscript developed and ready for submission with SLS paper to Thorax based PO1 and PO2 data	June-July 2016
Analysis for P03 and draft tables circulated	November 2016
Draft complete study report with PO1/PO2/PO3 to GSK	December 2016
Regulatory reporting of PO3	Q1 2017

Final follow-up manuscript	Q1-2 2017

In addition, we will present the results of the study at international respiratory conferences as appropriate. The study protocol and results will be posted to GSK Clinical Study Register as per GSK SOPs.

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ANNEX 1. LIST OF STAND-ALONE DOCUMENTS

Annex 1a: System Level Security Policy (SLSP) for Study

System Details

1. **The System shall be known as**

   CHESS: CPRD-COPD Hawthorne Effect Study in Salford: A UK cohort study to characterise patients enrolled in the Salford Lung Study and to evaluate a potential Hawthorne effect

2. **The System's responsible owner shall be** PPD

3. **The System's Caldicott Guardian or Data Controller shall be** PPD PPD

System Security

4. **Security of the system shall be governed by the corporate security policy of University of Manchester**

   http://documents.manchester.ac.uk/display.aspx?DocID=6525 (policy)

   http://documents.manchester.ac.uk/display.aspx?DocID=8039 (responsibilities)

5. **The System's responsible security manager shall be:**

   PPD University IT Security Coordinator

6. **The security manager duties shall include**:

   Devise, implement, enforce and review the University's IT security and data handling policies.
   Being the first point of contact for any security related queries or concerns.
   Being consulted on and providing the final sign-off for any requests for change to any aspects of IT security for the system.

7. **The System shall incorporate the following security countermeasures**:

   - **Physical Security – Data Processing**: The researchers are based within Vaughan House which is swipe card access only from reception into the building. Staff and Postgraduate students must have their University swipe cards enabled for access to the building. The offices are also locked when vacant.
   - **Physical Security – Data Hosting**: The data will be stored within Personal Drives (P: Drives) hosted on the University's network storage infrastructure which is the recommended location for storing sensitive or critical University

data. The storage infrastructure is hosted across two data centres (approx. 2KM apart) for resilience and disaster recovery purposes. Physical access to the data centres is strictly limited to data centre staff and a limited number of authorised IT Services staff. The data centres are protected by physical and electronic access security systems, swipe card access in and out of the data centres and CCTV coverage. The data centres are locked down out of hours and access is discouraged, but can be arranged by prior agreement with the data centre manager.

- **Access Control and Privilege Management:** The data will be hosted on authorised system user's P: drives which are strictly controlled data shares within the University's network storage infrastructure to which only the owner of the P: Drive has access permissions. The data share will only be accessed via a mapped network drive from PCs identified for research data processing.
- **Network Security Measures:** Network access control lists prevent PCs outside of the campus LAN from accessing the network storage infrastructure.
- **Other – Data Processing:** Four PCs have been identified for processing the research data. Once the PC has loaded the operating system a local, password protected computer account is required to login to the PC. This account is unique to the primary user of the computer and only the account owner knows the password. The PC has the Windows firewall enabled and configured to prevent remote access. The PCs have been configured to automatically update their antivirus signatures daily and have been configured to download and install any Microsoft operating system and application security patches automatically from the Microsoft update service.

System Management

8. **The System shall be developed / provided by:**

   University of Manchester, Faculty of Medical & Human Sciences, Information Services
   University of Manchester, IT Services Division

9. **The System shall be implemented & maintained by:**

   University of Manchester, Faculty of Medical & Human Sciences, Information Services will configure and maintain the security aspects of the PC, user accounts and access controls for the data share on the network storage infrastructure.

   University of Manchester, IT Services Division (ITSD) will be responsible for providing secure, reliable data hosting on the network storage infrastructure.

   Servers procured by ITSD include maintenance on either 3 or 5 year agreements depending on the Service requirements. Supplier engineers replace any defectives items and may request access to the Data Centre. In addition Data centre staff are trained and able to carry out component replacements on behalf of the suppliers.

Storage arrays are procured with support and maintenance included as part of a 3 year package. The SAN Arrays in the central ITS Data Centres are supplied by EMC and have allocated engineers who are familiar with our site configuration and conversant in maintaining the equipment and advising on future changes.

To ensure the security of University hosted infrastructure systems, all system changes must be authorised via the change management process. Any proposed system changes are recorded as requests for change (RFC's) and authorised by the change advisory board (CAB).

10. **The System shall be shared or used by the following organisations:**

GSK will have direct access to the system for quality checking purposes.

System Design

11. **The System shall comprise:**

The research PCs connect to the University's network via access switches which are located in data cabinets within secure, dedicated comms rooms. The switches are logically segregated into separate VLAN's for network efficiency and security. The access switches then connect to the University's core router and onto perimeter routers via multiple paths for resilient access to the data centres where the network storage infrastructure is hosted. The perimeter routers connect onto the JANET network and the wider internet. The perimeter routers are configured with access control lists which provide security for incoming network traffic. A network diagram can be found at the end of this SLSP.

The operating system on the PCs identified for data processing require local username and password authentication for access. The P: drives on the network require username and password authentication also.

Operational Processes

12. **The patient identifiable / sensitive data will be collected:**

Datasets will be pseudonymised at source by providers. No patient identifiable or sensitive information will be processed.

13. **The data will be stored:**

The data will be stored electronically in R and SAS file formats. The data will be made available to authorised members of research staff via P: drives hosted on the University's network storage infrastructure housed in the University's data centres.

14. **The data will be processed**:

Four University approved desktop PCs will be used to process the data. The PCs will not cache copies of the data and all data will be stored on the network storage infrastructure.

The University's Information Handling Policy sets out how digital information should be handled. This includes confidentiality, integrity and availability and the use of encryption tools for the protection of sensitive information and communications.

http://www.itservices.manchester.ac.uk/medialibrary/pdf/secureguidance/GP-InformationHandling.pdf

15. **The System's authorised users shall be** :

University of Manchester:

- PPD
- 1 x Research Associate, to be appointed.

GSK

- TBA by GSK.

The system's authorised users are all University members of staff and individuals designated by GSK. The data will not be accessible by any other third party organisations

16. **When the system or its data has completed its purpose / has become redundant or is no longer needed, the following methods will be adopted to dispose of equipment, back-up media or other stored data**:

Sensitive material on removable media are deleted as soon as possible. Printed materials and CD/DVDs containing sensitive information are shredded when no longer required. When the analysis is completed the researcher will delete files. All items of equipment containing storage media shall be checked to ensure that any sensitive data and licensed software has been removed or securely overwritten.

Desktop PCs are disposed of when replaced via a recognised disposal company, Computer Disposals LTD (CDL). CDL erase the hard drives to Government Restricted Standard SEAP (UK), which is three overwrites plus an additional verification pass. A certificate is produced for every successfully data erased hard drive to include the make, model and serial number of the hard drive. Any hard drive that fails the data erase process is degaussed on site at CDL using the latest CESG approved degausses and forwarded for recycling.

University IT Services has a policy of securely wiping network storage infrastructure arrays onsite prior to disposal. Disks are securely erased by software aligned to the DoD5220-22M standard and are then disposed of via CDL who also wipe the disks as per their procedure outlined above.

System Audit

17. **The System shall benefit from the following internal / external audit arrangements:**

In 2006, the University's IT Services undertook (in conjunction with KPMG) a comprehensive IT Risk Management Benchmarking exercise to appraise the University's approach to the management of IT-related risks. The review was intended to provide a benchmark upon which to build the maturity of IT Services activities over a number of years. Whilst the exercise found a number of positive areas within IT, it also identified a number of areas for development and agreed management action plans to address the issues raised.

A follow-up review was conducted during 2009 by UNIAC, the University's internal auditing body. This review: (i) revisited each original recommendation, ascertaining progress to date (supported by testing where appropriate) and its ongoing relevance; (ii) commented on the adequacy of the actions to date; (iii) proposed revised action plans for previous actions remaining outstanding; (iv) made additional suggestions over and above the agreed action.

The original KPMG report contained over thirty high and medium level recommendations and, realistically, a number of them would take a considerable period to fully implement. The follow-up review in 2009 concluded that: (i) recommendations had been fully implemented with no further action required in seven areas; (ii) good progress had been made towards implementing a further fifteen recommendations; (iii) some progress had been made towards implementing a further six recommendations; (iv) limited progress had been made towards implementing a final four recommendations.

Overall, the report concluded that progress has been encouraging and indicated that IT Services management had provided adequate focus to improving the management of IT risks.

Future auditing arrangements include regular audits agreed with internal and external auditors. The Director of IT Services meets the UNIAC Director annually to agree the internal programme; the external programme is agreed via the University's Audit Committee.

18. **The System shall be risk assessed every 12 months**

The University's Compliance and Risk Officer (CRO) is responsible for ensuring that the University is meeting its many statutory and regulatory compliance obligations. The CRO is responsible for supporting the University's risk management process, all aspects of risk management and has developed a risk management framework.

All major University functional areas (including IT Services) are required to conduct annual risk assessments and to review risk registers on a quarterly basis. Risk registers are submitted to the University's CRO for reporting to the

University's Risk Management Committee. Risk management is a specific responsibility of heads of operational areas.

System Protection

19. **The System shall benefit from the following resilience / contingency / disaster recovery arrangements:**

    The University's storage infrastructure is hosted and replicated across two data centres (approx. 2KM apart) for resilience and disaster recovery purposes.

    The University's IT Services Division (ITSD) utilises Legato Networker Backup domains. Supporting infrastructure comprises disk libraries and both physical and virtual tape libraries. Cross data centre backup is performed, so services hosted within data centre 1 (Kilburn) are backed up to data centre 2 (Reynold) and vice versa.

    Backup/recovery plans are documented as part of the service install process during the commissioning of a specific service. Each Service is responsible for its business continuity and disaster recovery plans, to which ITSD feed in its technical recovery plans

    ITSD operates a change management process. All proposed changes to infrastructure hosted, maintained and administered by ITSD are recorded via the RFC process with changes being authorised by a Change Advisory Board (CAB).

20. **In the event of serious disruption or total system failure, business continuity shall be provided by the following means:**

    The University's geographically dispersed, replicated, twin data centre approach with cross site backup has been designed to be as fault tolerant as possible and to provide business continuity in the event of a data centre failure. Should a situation arise where both data centres became unavailable then the University's disaster recovery plans relating to the failed system would be implemented.

21. **In the event of a security or confidentiality breach occurring the following procedure shall be followed:**

    Information on the procedure for reporting a security or confidentiality breach is available from the following link on the University's Secure-IT website:
    http://www.itservices.manchester.ac.uk/secure-it/reporting/

SSP Ownership

22. **This SLSP shall be the responsibility of:**

    PPD

22.1 - Shall be reviewed on an annual basis for its completeness and for relevant update.

23. **The SLSP shall be available / distributed to:**

Authorised GSK and University of Manchester staff involved in research activities or members of IT staff assisting with the completion of SLSP forms.

- Through which secure means:

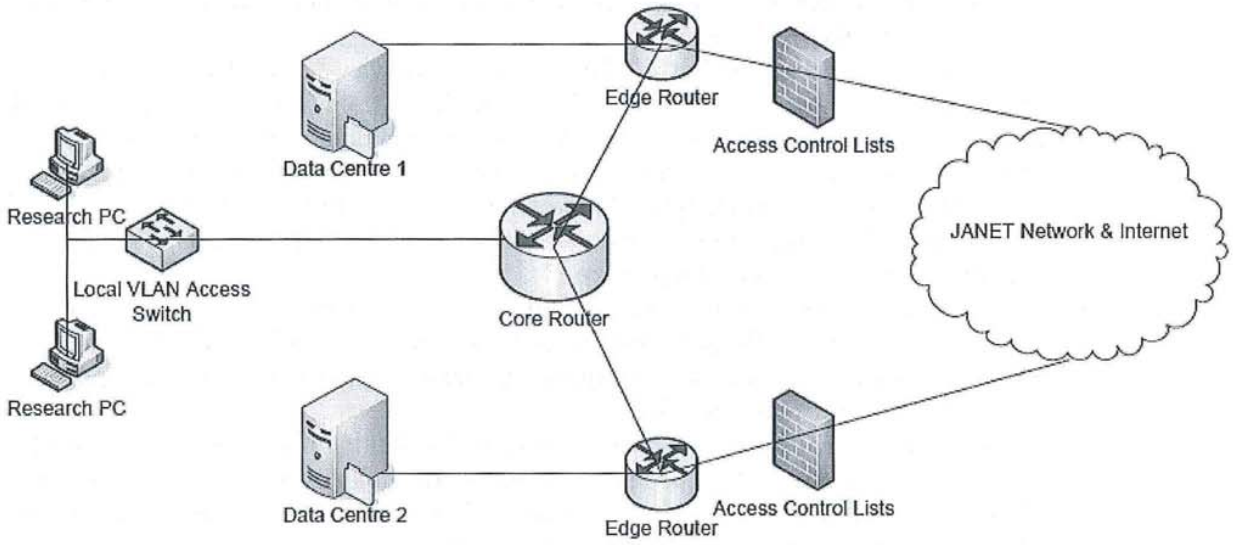
The SLSP document will be distributed to authorised GSK and University of Manchester staff via the internal email system.

Data Protection Registration

24. **Please confirm that your organisation has Data Protection Registration to cover the purposes of analysis and for the classes of data requested.**

http://www.ico.gov.uk/ESDWebPages/search.asp - . Registration No: Z6787610

Network diagram as referenced in the System Design section of the SLSP



ANNEX 2. ADDITIONAL INFORMATION

A2.1 Development of methods for the measurements of representativeness

This part of the project will deal with the development of methods for measuring representativeness of trials and evaluating potential effects of non-representativeness. It will be explorative and focused on methods. The concept of representativeness of trials is widely known but it is less known how to actually measure representativeness. This project will evaluate RELVAR use as an exemplar case study. These results will be compared to a historic case study of selective Cox-2 inhibitors (comparing the registration trials); the Cox-2 analyses will be conducted and funded as part of the GetReal IMI project. The RELVAR project will include the following activities:

(i) Review of literature for methods that can measure level of representativeness and evaluate the effects of non-representativeness. These methods may include multilevel models (including levels of clinician, practice, patient, disease and exposure characteristics.

(ii) Risk prediction models will be developed in CPRD for the outcomes of interest (to be defined). This analysis will determine the risk factors for the outcomes of interest. In addition, experts will be asked to provide likely effect modifiers of RELVAR. The analyses will focus on risk factors and effect modifiers.

(iii) Three populations will be identified in CPRD:

a. the first population will be based on the inclusion and exclusion criteria of the SLS trial. In case that information is missing in the EHR, methods will be evaluated to possibly impute these criteria.

b. the second population will be based on expert views of the likely possible use of RELVAR, and will be compared to Cox-2 inhibitors (from GetReal) in actual clinical practice. As an example, the trials for selective Cox-2 inhibitors were conducted in narrowly defined populations while later used in very broad population (replacing traditional NSAIDs). Any analysis of representativeness would have showed a considerable difference between the populations potentially eligible for a trial and potential users in actual clinical practice.

c. the third population will consist of all COPD patients aged 40 years or older alive at the index date. The propensity score for recruitment into SLS (as based on the Salford data) will be applied to this population, estimating the probability that a patient could have been recruited into SLS.

(iv) The analyses will include comparisons of the distribution of risk factors and effect modifiers between these three populations and the trial populations. Also, a comparison of incidence rates for the outcomes of interest will be conducted across these populations. Methods will be developed to integrate these results.

This project will be conducted in collaboration with GetReal partners, including NICE.

13. TABLES

13.1. Table 1: Pneumonia definition/codes used in SLS

Within the SLS, these codes are used assess pneumonia from hospital discharge records.

ICD-10 code	ICD-10 description	Comment
B67.1	Other B67.1 Echinococcus granulosus infection of lung	Other
J17.3	Other J17.3 Pneumonia in parasitic diseases	Other
J16	Pneumonia due to other infectious organisms NEC	unspecified
J16.8	Pneumonia due to other specified infectious organisms	unspecified
J17	Pneumonia in diseases classified elsewhere	unspecified
J17.8	Pneumonia in other diseases classified elsewhere	unspecified
J18	Pneumoniaorganism unspecified	unspecified
J18.0	Bronchopneumonia, unspecified	unspecified
J18.1	Lobar pneumonia, unspecified	unspecified
J18.8	Other pneumonia, organism unspecified	unspecified
J18.9	Pneumonia, unspecified	unspecified
A06.5	Amoebic lung abscess	Lung abscess
J85	Abscess of lung and mediastinum	Lung abscess
J85.0	Gangrene and necrosis of lung	Lung abscess
J85.1	Abscess of lung with pneumonia	Lung abscess
J85.2	Abscess of lung without pneumonia	Lung abscess
B20.6	HIV disease resulting in Pneumocystis carinii pneumonia	Fungal
B37.1	Pulmonary candidiasis	Fungal
B38.0	Acute pulmonary coccidioidomycosis	Fungal
B38.1	Chronic pulmonary coccidioidomycosis	Fungal
B38.2	Pulmonary coccidioidomycosis, unspecified	Fungal
B39.0	Acute pulmonary histoplasmosis capsulation	Fungal
B39.2	Pulmonary histoplasmosis capsulati, unspecified	Fungal
B40.0	Acute pulmonary blastomycosis	Fungal
B40.2	Pulmonary blastomycosis, unspecified	Fungal
B41.0	Pulmonary paracoccidioidomycosis	Fungal
B42.0	Pulmonary sporotrichosis	Fungal
B44.0	Invasive pulmonary aspergillosis	Fungal

B44.1	Other pulmonary aspergillosis	Fungal
B45.0	Pulmonary cryptococcosis	Fungal
B46.0	Pulmonary mucormycosis	Fungal
B58.3	Pulmonary toxoplasmosis	Fungal
B59.X	Pneumocystosis	Fungal
J17.2	Pneumonia in mycoses	Fungal
A15	Respiratory TB bacteriologically and histologically confirmed	Mycobacterial
A15.0	TB lung confirm sputum microscopy with or without culture	Mycobacterial
A15.1	Tuberculosis of lung, confirmed by culture only	Mycobacterial
A15.2	Tuberculosis of lung, confirmed histologically	Mycobacterial
A15.3	Tuberculosis of lung, confirmed by unspecified means	Mycobacterial
A15.4	TB intrathoracic lymph nodes confirm bact histologically	Mycobacterial
A15.5	Tuberculosis of larynx, trachea & bronchus conf bact/hist'y	Mycobacterial
A15.6	Tuberculous pleurisy, conf bacteriologically/his'y	Mycobacterial
A15.7	Primary respiratory TB confirm bact and histologically	Mycobacterial
A15.8	Other respiratory TB confirm bact and histologically	Mycobacterial
A15.9	Respiratory TB unspec confirm bact and histologically	Mycobacterial
A16	Respiratory TB not confirmed bacteriologically or histologically	Mycobacterial
A16.0	Tuberculosis of lung, bacteriologically & histolog'y neg	Mycobacterial
A16.1	Tuberculosis lung bact and histological examin not done	Mycobacterial
A16.2	TB lung without mention of bact or histological confirm	Mycobacterial
A16.5	TB pleurisy without mention of bact or histological confirm	Mycobacterial
A16.7	Prim respiratory TB without mention of bact or hist confirm	Mycobacterial
A16.8	Oth respiratory TB without mention of bact or hist confirm	Mycobacterial
A16.9	Resp TB unspec without mention of bact or hist confirm	Mycobacterial
A19	Miliary tuberculosis	Mycobacterial
A19.0	Acute miliary tuberculosis of a single specified site	Mycobacterial

A19.1	Acute miliary tuberculosis of multiple sites	Mycobacterial
A19.2	Acute miliary tuberculosis, unspecified	Mycobacterial
A19.8	Other miliary tuberculosis	Mycobacterial
A19.9	Miliary tuberculosis, unspecified	Mycobacterial
A31.0	Pulmonary mycobacterial infection	Mycobacterial
B01.2	Varicella pneumonia	Viral
B05.2	Measles complicated by pneumonia	Viral
J10.0	Influenza with pneumonia, influenza virus identified	Viral
J11.0	Influenza with pneumonia, virus not identified	Viral
J12	Viral pneumonia, not elsewhere classified	Viral
J12.0	Adenoviral pneumonia	Viral
J12.1	Respiratory syncytial virus pneumonia	Viral
J12.2	Parainfluenza virus pneumonia	Viral
J12.8	Other viral pneumonia	Viral
J12.9	Viral pneumonia, unspecified	Viral
J17.1	Pneumonia in viral diseases classified elsewhere	Viral
A20.2	Pneumonic plague	Bacterial
A21.2	Pulmonary tularaemia	Bacterial
A22.1	Pulmonary anthrax	Bacterial
A42.0	Pulmonary actinomycosis	Bacterial
A43.0	Pulmonary nocardiosis	Bacterial
A48.1	Legionnaires' disease	Bacterial
J13	Pneumonia due to Streptococcus pneumoniae	Bacterial
J13.0	Pneumonia due to Streptococcus pneumoniae	Bacterial
J13X	Pneumonia due to Streptococcus pneumoniae	Bacterial
J14	Pneumonia due to Haemophilus influenzae	Bacterial
J14.0	Pneumonia due to Haemophilus influenzae	Bacterial
J14X	Pneumonia due to Haemophilus influenzae	Bacterial
J15	Bacterial pneumonianot elsewhere classified	Bacterial
J15.0	Pneumonia due to Klebsiella pneumoniae	Bacterial
J15.1	Pneumonia due to Pseudomonas	Bacterial
J15.2	Pneumonia due to staphylococcus	Bacterial
J15.3	Pneumonia due to streptococcus, group	Bacterial

	B	
J15.4	Pneumonia due to other streptococci	Bacterial
J15.5	Pneumonia due to Escherichia coli	Bacterial
J15.6	Pneumonia due to other aerobic Gram-negative bacteria	Bacterial
J15.7	Pneumonia due to Mycoplasma pneumoniae	Bacterial
J15.8	Other bacterial pneumonia	Bacterial
J15.9	Bacterial pneumonia, unspecified	Bacterial
J16.0	Chlamydial pneumonia	Bacterial
J17.0	Pneumonia in bacterial diseases classified elsewhere	Bacterial
B25.0	Cytomegaloviral pneumonitis	No
B38	Coccidioidomycosis	No
B38.9	Coccidioidomycosis, unspecified	No
B39	Histoplasmosis	No
B39.4	Histoplasmosis capsulati, unspecified	No
B39.5	Histoplasmosis duboisii	No
B39.9	Histoplasmosis, unspecified	No
B40	Blastomycosis	No
B409	Blastomycosis, unspecified	No
B44	Aspergillosis	No
B44.9	Aspergillosis, unspecified	No
J18.2	Hypostatic pneumonia, unspecified	No
J86.0	Pyothorax with fistula	No
J86.9 Pyothorax without fistula	Pyothorax without fistula	No
'X' denotes that all subcodes under the 3-digit main number are included		
"No" in category denotes not assigned to a major category		

Annex 2: Code lists for key definitions using in study PRJ2282/201491

1. Medical codes considered to identify those with COPD in the CPRD
2. Code lists for moderate/severe COPD exacerbation used in CPRD and SLS-EHR
3. Code list to define Hospitalised pneumonia (PO3 and SO2) in CPRD

1. COPD: MEDICAL CODES CONSIDERED TO IDENTIFY THOSE WITH COPD IN THE CPRD

Description	CPRD Medcode	Read Code
Airways obstructn irreversible	4084	663K.00
COPD accident and emergency attendance since last visit	19106	66Yd.00
COPD follow-up	18476	66YL.11
COPD patient unsuitable for pulmonary rehab - enh serv admin	99948	9kf0.00
COPD self-management plan agreed	104117	661M300
COPD self-management plan review	104169	661N300
Centrilobular emphysema	10980	H322.00
Chronic bullous emphysema	26306	H320.00
Chronic bullous emphysema NOS	23492	H320z00
Chronic obstructiv pulmonary disease medication optimisation	103678	8BMa000
Chronic obstructive airways disease	998	H3...11
Chronic obstructive airways disease NOS	5710	H3z..00
Chronic obstructive pulmonary disease	1001	H3...00
Chronic obstructive pulmonary disease 3 monthly review	102685	66YB000
Chronic obstructive pulmonary disease 6 monthly review	103007	66YB100
Chronic obstructive pulmonary disease NOS	37247	H3z..11
Chronic obstructive pulmonary disease annual review	11287	66YM.00
Chronic obstructive pulmonary disease clini management plan	45777	8CR1.00
Chronic obstructive pulmonary disease disturbs sleep	45770	66Yg.00
Chronic obstructive pulmonary disease does not disturb sleep	45771	66Yh.00
Chronic obstructive pulmonary disease follow-up	18621	66YL.00
Chronic obstructive pulmonary disease monitor phone invite	38074	9Oi4.00
Chronic obstructive pulmonary disease monitoring	9520	66YB.00
Chronic obstructive pulmonary disease monitoring 1st letter	28755	9Oi0.00
Chronic obstructive pulmonary disease monitoring 2nd letter	34202	9Oi1.00
Chronic obstructive pulmonary disease monitoring 3rd letter	34215	9Oi2.00
Chronic obstructive pulmonary disease monitoring admin	18792	9Oi..00

Description	CPRD Medcode	Read Code
Chronic obstructive pulmonary disease monitoring by doctor	45998	66YT.00
Chronic obstructive pulmonary disease monitoring by nurse	26018	66YS.00
Chronic obstructive pulmonary disease monitoring due	37371	66YD.00
Chronic obstructive pulmonary disease monitoring verb invite	42258	9Oi3.00
Emergency COPD admission since last appointment	19003	66Ye.00
Emphysema	794	H32..00
Emphysema NOS	33450	H32z.00
Emphysematous bronchitis	14798	H312100
End stage chronic obstructive airways disease	104608	H3A..00
Has chronic obstructive pulmonary disease care plan	104481	8CMV.00
Health education - chronic obstructive pulmonary disease	42313	679V.00
Issue of chronic obstructive pulmonary disease rescue pack	101042	8BMW.00
Mild chronic obstructive pulmonary disease	10863	H36..00
Moderate chronic obstructive pulmonary disease	10802	H37..00
Multiple COPD emergency hospital admissions	46036	66Yi.00
Number of COPD exacerbations in past year	28743	66Yf.00
Obstructive chronic bronchitis	27819	H312.00
Obstructive chronic bronchitis NOS	44525	H312z00
Other specified chronic obstructive airways disease	12166	H3y..00
Referred for COPD structured smoking assessment	103400	9kf1.11
Severe chronic obstructive pulmonary disease	9876	H38..00
Very severe chronic obstructive pulmonary disease	93568	H39..00
Acute exacerbation of chronic obstructive airways disease	1446	H312200
Admit COPD emergency	11019	8H2R.00
Chron obstruct pulmonary dis wth acute exacerbation, unspec	7884	H3y1.00
Chronic obstruct pulmonary dis with acute lower resp infectn	21061	H3y0.00

2. CODE LISTS FOR MODERATE/SEVERE COPD EXACERBATION

The definition of a COPD exacerbation was identified using a validated algorithm based on medical and treatment codes in primary care data that have been shown to result in a positive predictive value of 86% and 63% ([1]). The algorithm defined any of the following as exacerbation events:

- (1) Prescription of pre-specified antibiotics (ABx) and oral corticosteroid (OCS) for 5-14 days both on the same day,
- (2) Exacerbation symptom definition (Exacerbation symptoms are codes suggesting increase in two or more of: breathlessness, cough, or sputum volume and/or purulence) and use of pre-specified antibiotics, where medical code is on the same day as prescription, OR
  Exacerbation symptom definition and oral corticosteroids, where medical code is on the same day as prescription,
- (3) Lower respiratory tract infection (LRTI) code (not including pneumonia codes, but including acute bronchitis and other lower respiratory tract infection diagnosis codes),
- (4) Definite Acute Exacerbation of COPD (AECOPD) medical diagnosis code.

When secondary care episode data was available the following notes from secondary care were also considered as representing exacerbations.

- (5) "Probable" AECOPD as the primary diagnosis within a Hospital Episode OR
- (6) "Definite" AECOPD recorded as any diagnosis within a Hospital Episode

Events of type (1) or (2) were not considered as exacerbations when the date of prescribing coincided with the issue of a rescue pack for AECOPD or a formal review of the patient's COPD status by the GP.

Events of type (3) or (4) were not considered as exacerbations when the events were recorded on the same data as a formal review of the patient's COPD status.

For the analyses comparing CPRD to the Salford EHR were only primary care data was used, events of type (1) were identified by the following relaxed definition:

- (1) Prescription of pre-specified antibiotics (ABx) and oral corticosteroid (OCS) both on the same day

The sets of codes used to identify prescription for ABx or OCS, exacerbation symptoms, LRTIs, AECOPDs, rescue packs for COPD exacerbations and reviews for COPD are listed.

[1] Rothnie KJ, Müllerová H, Hurst JR, Smeeth L, Davis K, Thomas SL, Quint JK. Validation of the Recording of Acute Exacerbations of COPD in UK Primary Care Electronic Healthcare Records. PLoS One. 2016 Mar 9;11(3):e0151357.

Moderate/severe COPD exacerbation coding definition

Prescriptions of pre-specified antibiotics (ABx)

CPRD Prodcode	Description
18685	achromycin 125mg/5ml oral solution (wyeth pharmaceuticals)
4579	achromycin 250mg capsules (wyeth pharmaceuticals)
15513	achromycin 250mg tablet (wyeth pharmaceuticals)
32233	achromycin powder (wyeth pharmaceuticals)
15407	achromycin v 250mg capsule (wyeth pharmaceuticals)
54152	acnamino mr 100mg capsules (almus pharmaceuticals ltd)
14984	acnamino mr 100mg capsules (dexcel-pharma ltd)
18728	aknemin 100mg capsules (almirall ltd)
18684	aknemin 50 capsules (almirall ltd)
22016	almodan 125mg/5ml oral solution (berk pharmaceuticals ltd)
17282	almodan 125mg/5ml syrup (teva uk ltd)
21799	almodan 250mg capsule (berk pharmaceuticals ltd)
21845	almodan 250mg/5ml oral solution (berk pharmaceuticals ltd)
21963	almodan 250mg/5ml oral solution (berk pharmaceuticals ltd)
21827	almodan 500mg capsule (berk pharmaceuticals ltd)
22029	amiclav 250mg/125mg tablets (ashbourne pharmaceuticals ltd)
11634	amix 125 oral suspension (ashbourne pharmaceuticals ltd)
11613	amix 250 capsules (ashbourne pharmaceuticals ltd)
21844	amix 250 oral suspension (ashbourne pharmaceuticals ltd)
18786	amix 500 capsules (ashbourne pharmaceuticals ltd)
29697	amopen 125mg/5ml liquid (yorkshire pharmaceuticals ltd)
30498	amopen 250mg capsule (yorkshire pharmaceuticals ltd)
31423	amopen 250mg/5ml liquid (yorkshire pharmaceuticals ltd)
17711	amopen 500mg capsule (yorkshire pharmaceuticals ltd)
12378	amoram 125mg/5ml oral suspension (lpc medical (uk) ltd)
9243	amoram 250mg capsules (lpc medical (uk) ltd)
22438	amoram 250mg/5ml oral suspension (lpc medical (uk) ltd)
22415	amoram 500mg capsules (lpc medical (uk) ltd)
8906	amoxicillin 125mg / clavulanic acid 31mg/5ml oral suspension
13285	amoxicillin 125mg / clavulanic acid 31mg/5ml oral suspension
53942	amoxicillin 125mg / clavulanic acid 62.5mg/5ml oral suspension
41835	amoxicillin 125mg powder (ivax pharmaceuticals uk ltd)
3742	amoxicillin 125mg sugar free chewable tablets
13848	amoxicillin 125mg sugar free powder
485	amoxicillin 125mg/1.25ml oral suspension paediatric
42822	amoxicillin 125mg/5ml mixture (celltech pharma europe ltd)
28872	amoxicillin 125mg/5ml mixture (crosspharma ltd)
41818	amoxicillin 125mg/5ml oral solution (berk pharmaceuticals ltd)
42240	amoxicillin 125mg/5ml oral solution (co-pharma ltd)
29337	amoxicillin 125mg/5ml oral solution (neo laboratories ltd)
62	amoxicillin 125mg/5ml oral suspension
33690	amoxicillin 125mg/5ml oral suspension (a a h pharmaceuticals ltd)

CPRD Prodcode	Description
34857	amoxicillin 125mg/5ml oral suspension (actavis uk ltd)
42545	amoxicillin 125mg/5ml oral suspension (almus pharmaceuticals ltd)
50002	amoxicillin 125mg/5ml oral suspension (bristol laboratories ltd)
32622	amoxicillin 125mg/5ml oral suspension (generics (uk) ltd)
23238	amoxicillin 125mg/5ml oral suspension (ivax pharmaceuticals uk ltd)
48038	amoxicillin 125mg/5ml oral suspension (kent pharmaceuticals ltd)
52685	amoxicillin 125mg/5ml oral suspension (phoenix healthcare distribution ltd)
28875	amoxicillin 125mg/5ml oral suspension (ranbaxy (uk) ltd)
43229	amoxicillin 125mg/5ml oral suspension (sandoz ltd)
55047	amoxicillin 125mg/5ml oral suspension (sandoz ltd)
28870	amoxicillin 125mg/5ml oral suspension (teva uk ltd)
56561	amoxicillin 125mg/5ml oral suspension (waymade healthcare plc)
503	amoxicillin 125mg/5ml oral suspension sugar free
33696	amoxicillin 125mg/5ml oral suspension sugar free (a a h pharmaceuticals ltd)
34679	amoxicillin 125mg/5ml oral suspension sugar free (actavis uk ltd)
53078	amoxicillin 125mg/5ml oral suspension sugar free (alliance healthcare (distribution) ltd)
36054	amoxicillin 125mg/5ml oral suspension sugar free (almus pharmaceuticals ltd)
52122	amoxicillin 125mg/5ml oral suspension sugar free (bristol laboratories ltd)
31014	amoxicillin 125mg/5ml oral suspension sugar free (generics (uk) ltd)
24150	amoxicillin 125mg/5ml oral suspension sugar free (ivax pharmaceuticals uk ltd)
34384	amoxicillin 125mg/5ml oral suspension sugar free (kent pharmaceuticals ltd)
52857	amoxicillin 125mg/5ml oral suspension sugar free (phoenix healthcare distribution ltd)
29858	amoxicillin 125mg/5ml oral suspension sugar free (sandoz ltd)
34638	amoxicillin 125mg/5ml oral suspension sugar free (teva uk ltd)
55626	amoxicillin 125mg/5ml oral suspension sugar free (waymade healthcare plc)
1391	amoxicillin 250mg / clavulanic acid 125mg tablets
7636	amoxicillin 250mg / clavulanic acid 62mg/5ml oral suspension
13262	amoxicillin 250mg / clavulanic acid 62mg/5ml oral suspension
42809	amoxicillin 250mg capsule (c p pharmaceuticals ltd)
31661	amoxicillin 250mg capsule (co-pharma ltd)
28882	amoxicillin 250mg capsule (crosspharma ltd)
34435	amoxicillin 250mg capsule (ddsa pharmaceuticals ltd)
33222	amoxicillin 250mg capsule (lagap)
32872	amoxicillin 250mg capsule (mepra-pharm)
34714	amoxicillin 250mg capsule (neo laboratories ltd)
45267	amoxicillin 250mg capsule (regent laboratories ltd)
9	amoxicillin 250mg capsules
25484	amoxicillin 250mg capsules (a a h pharmaceuticals ltd)
33343	amoxicillin 250mg capsules (actavis uk ltd)
54796	amoxicillin 250mg capsules (boston healthcare ltd)
54491	amoxicillin 250mg capsules (bristol laboratories ltd)
30745	amoxicillin 250mg capsules (generics (uk) ltd)
34042	amoxicillin 250mg capsules (ivax pharmaceuticals uk ltd)

CPRD Prodcode	Description
30528	amoxicillin 250mg capsules (kent pharmaceuticals ltd)
54271	amoxicillin 250mg capsules (mawdsley-brooks & company ltd)
51536	amoxicillin 250mg capsules (milpharm ltd)
30743	amoxicillin 250mg capsules (ranbaxy (uk) ltd)
48006	amoxicillin 250mg capsules (sandoz ltd)
23967	amoxicillin 250mg capsules (teva uk ltd)
54185	amoxicillin 250mg capsules (wockhardt uk ltd)
870	amoxicillin 250mg sugar free chewable tablets
42815	amoxicillin 250mg/5ml mixture (celltech pharma europe ltd)
33570	amoxicillin 250mg/5ml mixture (crosspharma ltd)
40238	amoxicillin 250mg/5ml mixture (mepra-pharm)
45317	amoxicillin 250mg/5ml oral solution (neo laboratories ltd)
427	amoxicillin 250mg/5ml oral suspension
33165	amoxicillin 250mg/5ml oral suspension (a a h pharmaceuticals ltd)
34760	amoxicillin 250mg/5ml oral suspension (actavis uk ltd)
41090	amoxicillin 250mg/5ml oral suspension (almus pharmaceuticals ltd)
55018	amoxicillin 250mg/5ml oral suspension (bristol laboratories ltd)
33689	amoxicillin 250mg/5ml oral suspension (generics (uk) ltd)
32640	amoxicillin 250mg/5ml oral suspension (ivax pharmaceuticals uk ltd)
51382	amoxicillin 250mg/5ml oral suspension (phoenix healthcare distribution ltd)
55499	amoxicillin 250mg/5ml oral suspension (ranbaxy (uk) ltd)
37755	amoxicillin 250mg/5ml oral suspension (sandoz ltd)
56223	amoxicillin 250mg/5ml oral suspension (sandoz ltd)
53924	amoxicillin 250mg/5ml oral suspension (sigma pharmaceuticals plc)
27725	amoxicillin 250mg/5ml oral suspension (teva uk ltd)
585	amoxicillin 250mg/5ml oral suspension sugar free
34232	amoxicillin 250mg/5ml oral suspension sugar free (a a h pharmaceuticals ltd)
40243	amoxicillin 250mg/5ml oral suspension sugar free (actavis uk ltd)
54222	amoxicillin 250mg/5ml oral suspension sugar free (alliance healthcare (distribution) ltd)
42732	amoxicillin 250mg/5ml oral suspension sugar free (almus pharmaceuticals ltd)
49065	amoxicillin 250mg/5ml oral suspension sugar free (bristol laboratories ltd)
31535	amoxicillin 250mg/5ml oral suspension sugar free (generics (uk) ltd)
33699	amoxicillin 250mg/5ml oral suspension sugar free (ivax pharmaceuticals uk ltd)
34855	amoxicillin 250mg/5ml oral suspension sugar free (kent pharmaceuticals ltd)
34775	amoxicillin 250mg/5ml oral suspension sugar free (teva uk ltd)
17746	amoxicillin 375mg soluble tablets
1140	amoxicillin 3g oral powder sachets sugar free
33383	amoxicillin 3g oral powder sachets sugar free (a a h pharmaceuticals ltd)
40168	amoxicillin 3g oral powder sachets sugar free (kent pharmaceuticals ltd)
28130	amoxicillin 3g oral powder sachets sugar free (teva uk ltd)
41734	amoxicillin 3g powder (actavis uk ltd)
15192	amoxicillin 400mg / clavulanic acid 57mg/5ml sugar free oral suspension
13216	amoxicillin 500mg / clavulanic acid 125mg tablets
38684	amoxicillin 500mg capsule (c p pharmaceuticals ltd)

CPRD Prodcode	Description
35570	amoxicillin 500mg capsule (crosspharma ltd)
34885	amoxicillin 500mg capsule (ddsa pharmaceuticals ltd)
44854	amoxicillin 500mg capsule (lagap)
34912	amoxicillin 500mg capsule (neo laboratories ltd)
48	amoxicillin 500mg capsules
33692	amoxicillin 500mg capsules (a a h pharmaceuticals ltd)
53627	amoxicillin 500mg capsules (accord healthcare ltd)
26157	amoxicillin 500mg capsules (actavis uk ltd)
52820	amoxicillin 500mg capsules (alliance healthcare (distribution) ltd)
47640	amoxicillin 500mg capsules (almus pharmaceuticals ltd)
55527	amoxicillin 500mg capsules (boston healthcare ltd)
52771	amoxicillin 500mg capsules (bristol laboratories ltd)
23740	amoxicillin 500mg capsules (generics (uk) ltd)
29463	amoxicillin 500mg capsules (ivax pharmaceuticals uk ltd)
33706	amoxicillin 500mg capsules (kent pharmaceuticals ltd)
52058	amoxicillin 500mg capsules (medreich plc)
54725	amoxicillin 500mg capsules (milpharm ltd)
34852	amoxicillin 500mg capsules (ranbaxy (uk) ltd)
31801	amoxicillin 500mg capsules (sandoz ltd)
34001	amoxicillin 500mg capsules (teva uk ltd)
55394	amoxicillin 500mg capsules (wockhardt uk ltd)
1722	amoxicillin 500mg dispersible tablets
2281	amoxicillin 500mg sugar free chewable tablets
4582	amoxicillin 750mg soluble tablets
9343	amoxicillin 750mg sugar free powder
439	amoxicillin with clavulanic acid dispersible tablets
2171	amoxil 125mg/1.25ml paediatric oral suspension (glaxosmithkline uk ltd)
2153	amoxil 125mg/5ml syrup sucrose free (glaxosmithkline uk ltd)
133	amoxil 250mg capsules (glaxosmithkline uk ltd)
1812	amoxil 250mg/5ml syrup sucrose free (glaxosmithkline uk ltd)
2174	amoxil 3g oral powder sachets sucrose free (glaxosmithkline uk ltd)
847	amoxil 500mg capsules (glaxosmithkline uk ltd)
49590	amoxil 500mg capsules (lexon (uk) ltd)
51436	amoxil 500mg capsules (mawdsley-brooks & company ltd)
56700	amoxil 500mg capsules (necessity supplies ltd)
15148	amoxil 500mg dispersible tablet (smithkline beecham plc)
4010	amoxil 750mg sachets (glaxosmithkline uk ltd)
4154	amoxil fiztab 125mg tablet (bencard)
1637	amoxil fiztab 250mg tablet (bencard)
7737	amoxil fiztab 500mg tablet (bencard)
27897	amoxycillin
31571	amoxycillin
32505	amoxycillin
7592	amoxycillin 125 mg cap
22469	amoxycillin 125mg/31mg clavulanic acid

CPRD Prodcode	Description
25034	amoxycillin 125mg/62mg clavulanic acid
7581	amoxycillin 125mg/62mg clavulanic acid syr
27886	amoxycillin 250/clavulanic acid 125 disp
19795	amoxycillin 250mg/clavulanic acid 125mg
1570	amoxycillin 500 mg tab
2902	amoxycillin fiztab 125 mg tab
1393	amoxycillin fiztab 250 mg tab
21982	amoxycillin trihydrate sachet
22293	amoxycillin trihydrate sachet
31286	amoxymed 125mg/5ml oral solution (medipharma ltd)
3669	amoxymed 250mg capsule (medipharma ltd)
33109	amrit 125mg/5ml liquid (bhr pharmaceuticals ltd)
27714	amrit 250mg capsule (bhr pharmaceuticals ltd)
33110	amrit 250mg/5ml liquid (bhr pharmaceuticals ltd)
33112	amrit 500mg capsule (bhr pharmaceuticals ltd)
27495	arpimycin 125mg/5ml liquid (rosemont pharmaceuticals ltd)
36544	arpimycin 125mg/5ml oral suspension (rosemont pharmaceuticals ltd)
24220	arpimycin 250mg/5ml liquid (rosemont pharmaceuticals ltd)
36514	arpimycin 250mg/5ml oral suspension (rosemont pharmaceuticals ltd)
37022	arpimycin 500mg/5ml liquid (rosemont pharmaceuticals ltd)
415	augmentin 125/31 sf oral suspension (glaxosmithkline uk ltd)
50595	augmentin 125/31 sf oral suspension (mawdsley-brooks & company ltd)
51164	augmentin 125/31 sf oral suspension (waymade healthcare plc)
569	augmentin 250/62 sf oral suspension (glaxosmithkline uk ltd)
52666	augmentin 250/62 sf oral suspension (sigma pharmaceuticals plc)
2507	augmentin 375mg dispersible tablets (glaxosmithkline uk ltd)
49063	augmentin 375mg tablets (doncaster pharmaceuticals ltd)
399	augmentin 375mg tablets (glaxosmithkline uk ltd)
48683	augmentin 375mg tablets (lexon (uk) ltd)
49374	augmentin 375mg tablets (mawdsley-brooks & company ltd)
49048	augmentin 375mg tablets (waymade healthcare plc)
50279	augmentin 625mg tablets (doncaster pharmaceuticals ltd)
509	augmentin 625mg tablets (glaxosmithkline uk ltd)
49656	augmentin 625mg tablets (lexon (uk) ltd)
52207	augmentin 625mg tablets (mawdsley-brooks & company ltd)
49321	augmentin 625mg tablets (sigma pharmaceuticals plc)
49683	augmentin 625mg tablets (waymade healthcare plc)
5341	augmentin-duo 400/57 oral suspension (glaxosmithkline uk ltd)
56591	augmentin-duo 400/57 oral suspension (lexon (uk) ltd)
51194	augmentin-duo 400/57 oral suspension (sigma pharmaceuticals plc)
2127	aureomycin 250mg capsule (wyeth pharmaceuticals)
31007	aureomycin powder (wyeth pharmaceuticals)
25127	avelox 400mg tablets (bayer plc)
26289	bacticlor mr 375mg tablets (ranbaxy (uk) ltd)
4895	benzoyl peroxide 5% / erythromycin 3% gel

CPRD Prodcode	Description
21802	berkmycen 250mg tablet (berk pharmaceuticals ltd)
17093	bisolvomycin capsule (boehringer ingelheim ltd)
21978	blemix 100mg tablets (ashbourne pharmaceuticals ltd)
21865	blemix 50mg tablets (ashbourne pharmaceuticals ltd)
13910	cefaclor 125mg/5ml liquid (generics (uk) ltd)
14607	cefaclor 125mg/5ml liquid (lagap)
1038	cefaclor 125mg/5ml oral suspension
39703	cefaclor 125mg/5ml oral suspension (a a h pharmaceuticals ltd)
34913	cefaclor 125mg/5ml oral suspension (genus pharmaceuticals ltd)
32235	cefaclor 125mg/5ml oral suspension (ranbaxy (uk) ltd)
7526	cefaclor 125mg/5ml oral suspension sugar free
56610	cefaclor 125mg/5ml oral suspension sugar free (phoenix healthcare distribution ltd)
9520	cefaclor 250mg capsule (lagap)
366	cefaclor 250mg capsules
30772	cefaclor 250mg capsules (ranbaxy (uk) ltd)
20420	cefaclor 250mg/5ml liquid (generics (uk) ltd)
20409	cefaclor 250mg/5ml liquid (lagap)
3737	cefaclor 250mg/5ml oral suspension
46973	cefaclor 250mg/5ml oral suspension (genus pharmaceuticals ltd)
48025	cefaclor 250mg/5ml oral suspension (ranbaxy (uk) ltd)
9293	cefaclor 250mg/5ml oral suspension sugar free
3180	cefaclor 375mg modified-release tablets
34838	cefaclor 375mg modified-release tablets (a a h pharmaceuticals ltd)
20881	cefaclor 375mg modified-release tablets (ranbaxy (uk) ltd)
4689	cefaclor 500mg capsule (lagap)
2976	cefaclor 500mg capsules
43425	cefaclor 500mg capsules (a a h pharmaceuticals ltd)
55211	cefaclor 500mg capsules (kent pharmaceuticals ltd)
30771	cefaclor 500mg capsules (ranbaxy (uk) ltd)
8051	cefaclor 500mg modified-release tablets
12248	cefalexin 125mg/1.25ml paediatric drops
1693	cefalexin 125mg/5ml oral suspension
29748	cefalexin 125mg/5ml oral suspension (a a h pharmaceuticals ltd)
32181	cefalexin 125mg/5ml oral suspension (actavis uk ltd)
53945	cefalexin 125mg/5ml oral suspension (alliance healthcare (distribution) ltd)
39417	cefalexin 125mg/5ml oral suspension (generics (uk) ltd)
32642	cefalexin 125mg/5ml oral suspension (kent pharmaceuticals ltd)
36578	cefalexin 125mg/5ml oral suspension (ranbaxy (uk) ltd)
33329	cefalexin 125mg/5ml oral suspension (teva uk ltd)
6651	cefalexin 125mg/5ml oral suspension sugar free
19144	cefalexin 125mg/5ml oral suspension sugar free (teva uk ltd)
1384	cefalexin 125mg/5ml suspension
18451	cefalexin 1g tablets
33802	cefalexin 250mg capsule (berk pharmaceuticals ltd)

CPRD Prodcode	Description
155	cefalexin 250mg capsules
34253	cefalexin 250mg capsules (a a h pharmaceuticals ltd)
19152	cefalexin 250mg capsules (actavis uk ltd)
54864	cefalexin 250mg capsules (alliance healthcare (distribution) ltd)
52283	cefalexin 250mg capsules (arrow generics ltd)
19160	cefalexin 250mg capsules (generics (uk) ltd)
19133	cefalexin 250mg capsules (ivax pharmaceuticals uk ltd)
41736	cefalexin 250mg capsules (kent pharmaceuticals ltd)
52282	cefalexin 250mg capsules (milpharm ltd)
24090	cefalexin 250mg capsules (pliva pharma ltd)
36599	cefalexin 250mg capsules (ranbaxy (uk) ltd)
9690	cefalexin 250mg capsules (teva uk ltd)
40747	cefalexin 250mg chewable tablets
1146	cefalexin 250mg tablets
33334	cefalexin 250mg tablets (a a h pharmaceuticals ltd)
36330	cefalexin 250mg tablets (actavis uk ltd)
47163	cefalexin 250mg tablets (arrow generics ltd)
36701	cefalexin 250mg tablets (generics (uk) ltd)
31825	cefalexin 250mg tablets (ivax pharmaceuticals uk ltd)
9698	cefalexin 250mg tablets (teva uk ltd)
41825	cefalexin 250mg/5ml oral solution (c p pharmaceuticals ltd)
1860	cefalexin 250mg/5ml oral suspension
42008	cefalexin 250mg/5ml oral suspension (a a h pharmaceuticals ltd)
45221	cefalexin 250mg/5ml oral suspension (actavis uk ltd)
29464	cefalexin 250mg/5ml oral suspension (generics (uk) ltd)
41192	cefalexin 250mg/5ml oral suspension (ranbaxy (uk) ltd)
41968	cefalexin 250mg/5ml oral suspension (teva uk ltd)
6671	cefalexin 250mg/5ml oral suspension sugar free
34133	cefalexin 250mg/5ml oral suspension sugar free (teva uk ltd)
1713	cefalexin 250mg/5ml suspension
44755	cefalexin 500mg capsule (berk pharmaceuticals ltd)
400	cefalexin 500mg capsules
32643	cefalexin 500mg capsules (a a h pharmaceuticals ltd)
19138	cefalexin 500mg capsules (actavis uk ltd)
52851	cefalexin 500mg capsules (alliance healthcare (distribution) ltd)
19184	cefalexin 500mg capsules (generics (uk) ltd)
9664	cefalexin 500mg capsules (ivax pharmaceuticals uk ltd)
36569	cefalexin 500mg capsules (kent pharmaceuticals ltd)
54955	cefalexin 500mg capsules (milpharm ltd)
19161	cefalexin 500mg capsules (ranbaxy (uk) ltd)
29281	cefalexin 500mg capsules (teva uk ltd)
865	cefalexin 500mg tablets
29202	cefalexin 500mg tablets (a a h pharmaceuticals ltd)
22321	cefalexin 500mg tablets (generics (uk) ltd)
31827	cefalexin 500mg tablets (ivax pharmaceuticals uk ltd)

CPRD Prodcode	Description
9689	cefalexin 500mg tablets (teva uk ltd)
2227	cefalexin 500mg/5ml oral suspension
17150	ceporex 125mg/1.25ml drops (glaxo laboratories ltd)
7560	ceporex 125mg/5ml liquid (galen ltd)
3609	ceporex 125mg/5ml oral solution (galen ltd)
41106	ceporex 125mg/5ml syrup (co-pharma ltd)
12235	ceporex 1g tablet (galen ltd)
192	ceporex 250mg capsule (galen ltd)
40884	ceporex 250mg capsules (co-pharma ltd)
8019	ceporex 250mg tablet (galen ltd)
41049	ceporex 250mg tablets (co-pharma ltd)
8625	ceporex 250mg/5ml liquid (galen ltd)
8008	ceporex 250mg/5ml oral solution (galen ltd)
40945	ceporex 250mg/5ml syrup (co-pharma ltd)
2661	ceporex 500mg capsule (galen ltd)
40915	ceporex 500mg capsules (co-pharma ltd)
8085	ceporex 500mg tablet (galen ltd)
40914	ceporex 500mg tablets (co-pharma ltd)
5859	ceporex 500mg/5ml oral solution (galen ltd)
41230	ceporex 500mg/5ml syrup (co-pharma ltd)
7881	chlortetracycline 250mg capsules
36689	chlortetracycline hcl syr
17284	chlortetracycline hyd./demeclocycline hy 115.4 mg tab
738	chlortetracycline with demeclocycline with tetracycline tablets
27016	ciprofloxacin
498	ciprofloxacin 100mg tablets
42507	ciprofloxacin 100mg tablets (a a h pharmaceuticals ltd)
48031	ciprofloxacin 100mg tablets (almus pharmaceuticals ltd)
54555	ciprofloxacin 100mg tablets (doncaster pharmaceuticals ltd)
54674	ciprofloxacin 100mg tablets (phoenix healthcare distribution ltd)
39913	ciprofloxacin 100mg tablets (sandoz ltd)
52309	ciprofloxacin 100mg tablets (sigma pharmaceuticals plc)
52945	ciprofloxacin 200mg/100ml solution for infusion vials
56439	ciprofloxacin 200mg/100ml solution for infusion vials (a a h pharmaceuticals ltd)
34647	ciprofloxacin 250mg tablet (neo laboratories ltd)
281	ciprofloxacin 250mg tablets
29343	ciprofloxacin 250mg tablets (a a h pharmaceuticals ltd)
50601	ciprofloxacin 250mg tablets (accord healthcare ltd)
34308	ciprofloxacin 250mg tablets (actavis uk ltd)
51537	ciprofloxacin 250mg tablets (alliance healthcare (distribution) ltd)
54393	ciprofloxacin 250mg tablets (arrow generics ltd)
54701	ciprofloxacin 250mg tablets (bristol laboratories ltd)
56381	ciprofloxacin 250mg tablets (co-pharma ltd)
43814	ciprofloxacin 250mg tablets (dr reddy's laboratories (uk) ltd)

CPRD Prodcode	Description
33989	ciprofloxacin 250mg tablets (generics (uk) ltd)
41561	ciprofloxacin 250mg tablets (ivax pharmaceuticals uk ltd)
54302	ciprofloxacin 250mg tablets (medreich plc)
34448	ciprofloxacin 250mg tablets (niche generics ltd)
34694	ciprofloxacin 250mg tablets (pliva pharma ltd)
34559	ciprofloxacin 250mg tablets (sandoz ltd)
34478	ciprofloxacin 250mg tablets (teva uk ltd)
34655	ciprofloxacin 250mg tablets (wockhardt uk ltd)
4091	ciprofloxacin 250mg/5ml oral suspension
10304	ciprofloxacin 2mg/ml infusion
45341	ciprofloxacin 500mg tablet (neo laboratories ltd)
34322	ciprofloxacin 500mg tablet (niche generics ltd)
583	ciprofloxacin 500mg tablets
29458	ciprofloxacin 500mg tablets (a a h pharmaceuticals ltd)
52501	ciprofloxacin 500mg tablets (accord healthcare ltd)
34605	ciprofloxacin 500mg tablets (actavis uk ltd)
49445	ciprofloxacin 500mg tablets (almus pharmaceuticals ltd)
56789	ciprofloxacin 500mg tablets (apc pharmaceuticals & chemicals (europe) ltd)
52616	ciprofloxacin 500mg tablets (arrow generics ltd)
53641	ciprofloxacin 500mg tablets (co-pharma ltd)
50055	ciprofloxacin 500mg tablets (doncaster pharmaceuticals ltd)
53088	ciprofloxacin 500mg tablets (dr reddy's laboratories (uk) ltd)
30707	ciprofloxacin 500mg tablets (generics (uk) ltd)
42174	ciprofloxacin 500mg tablets (ivax pharmaceuticals uk ltd)
55917	ciprofloxacin 500mg tablets (medreich plc)
43557	ciprofloxacin 500mg tablets (pliva pharma ltd)
53878	ciprofloxacin 500mg tablets (ranbaxy (uk) ltd)
43797	ciprofloxacin 500mg tablets (sandoz ltd)
45285	ciprofloxacin 500mg tablets (teva uk ltd)
34494	ciprofloxacin 500mg tablets (wockhardt uk ltd)
34973	ciprofloxacin 750mg tablet (niche generics ltd)
1837	ciprofloxacin 750mg tablets
29472	ciprofloxacin 750mg tablets (a a h pharmaceuticals ltd)
43517	ciprofloxacin 750mg tablets (actavis uk ltd)
52099	ciprofloxacin 750mg tablets (bristol laboratories ltd)
56856	ciprofloxacin 750mg tablets (ranbaxy (uk) ltd)
28544	ciprofloxaxin 400mg/200ml in glucose 5% infusion
9154	ciproxin 100mg tablets (bayer plc)
1202	ciproxin 250mg tablets (bayer plc)
52353	ciproxin 250mg tablets (doncaster pharmaceuticals ltd)
53519	ciproxin 250mg tablets (lexon (uk) ltd)
163	ciproxin 250mg/5ml oral suspension (bayer plc)
728	ciproxin 500mg tablets (bayer plc)
52807	ciproxin 500mg tablets (mawdsley-brooks & company ltd)
52177	ciproxin 500mg tablets (sigma pharmaceuticals plc)

CPRD Prodcode	Description
49839	ciproxin 500mg tablets (waymade healthcare plc)
7752	ciproxin 750mg tablets (bayer plc)
45591	clarie xl 500mg tablets (teva uk ltd)
10326	clarithromycin 125mg granules straws
331	clarithromycin 125mg/5ml oral suspension
45795	clarithromycin 125mg/5ml oral suspension (a a h pharmaceuticals ltd)
54903	clarithromycin 125mg/5ml oral suspension (alliance healthcare (distribution) ltd)
51831	clarithromycin 125mg/5ml oral suspension (phoenix healthcare distribution ltd)
41453	clarithromycin 125mg/5ml oral suspension (ranbaxy (uk) ltd)
53168	clarithromycin 125mg/5ml oral suspension (sandoz ltd)
26059	clarithromycin 187.5mg granules straws
765	clarithromycin 250mg granules sachets
17645	clarithromycin 250mg granules straws
537	clarithromycin 250mg tablets
34650	clarithromycin 250mg tablets (a a h pharmaceuticals ltd)
54472	clarithromycin 250mg tablets (accord healthcare ltd)
48163	clarithromycin 250mg tablets (actavis uk ltd)
52158	clarithromycin 250mg tablets (alliance healthcare (distribution) ltd)
54882	clarithromycin 250mg tablets (almus pharmaceuticals ltd)
52719	clarithromycin 250mg tablets (apotex uk ltd)
53086	clarithromycin 250mg tablets (doncaster pharmaceuticals ltd)
34394	clarithromycin 250mg tablets (generics (uk) ltd)
51154	clarithromycin 250mg tablets (kent pharmaceuticals ltd)
53153	clarithromycin 250mg tablets (phoenix healthcare distribution ltd)
53688	clarithromycin 250mg tablets (ranbaxy (uk) ltd)
47582	clarithromycin 250mg tablets (sandoz ltd)
50946	clarithromycin 250mg tablets (sigma pharmaceuticals plc)
54269	clarithromycin 250mg tablets (somex pharma)
34533	clarithromycin 250mg tablets (teva uk ltd)
54897	clarithromycin 250mg tablets (tillomed laboratories ltd)
53144	clarithromycin 250mg tablets (wockhardt uk ltd)
5357	clarithromycin 250mg/5ml oral suspension
54241	clarithromycin 250mg/5ml oral suspension (a a h pharmaceuticals ltd)
55148	clarithromycin 250mg/5ml oral suspension (alliance healthcare (distribution) ltd)
34811	clarithromycin 250mg/5ml oral suspension (ranbaxy (uk) ltd)
53179	clarithromycin 250mg/5ml oral suspension (sandoz ltd)
54208	clarithromycin 250mg/5ml oral suspension (sigma pharmaceuticals plc)
55428	clarithromycin 250mg/5ml oral suspension (waymade healthcare plc)
54529	clarithromycin 500mg modified-release tablet (hillcross pharmaceuticals ltd)
6803	clarithromycin 500mg modified-release tablets
681	clarithromycin 500mg tablets
38163	clarithromycin 500mg tablets (a a h pharmaceuticals ltd)
51426	clarithromycin 500mg tablets (accord healthcare ltd)

CPRD Prodcode	Description
48023	clarithromycin 500mg tablets (actavis uk ltd)
49939	clarithromycin 500mg tablets (alliance healthcare (distribution) ltd)
53715	clarithromycin 500mg tablets (almus pharmaceuticals ltd)
53776	clarithromycin 500mg tablets (doncaster pharmaceuticals ltd)
34608	clarithromycin 500mg tablets (generics (uk) ltd)
53703	clarithromycin 500mg tablets (kent pharmaceuticals ltd)
46488	clarithromycin 500mg tablets (ranbaxy (uk) ltd)
40784	clarithromycin 500mg tablets (sandoz ltd)
53109	clarithromycin 500mg tablets (somex pharma)
34974	clarithromycin 500mg tablets (teva uk ltd)
53875	clarithromycin 500mg tablets (tillomed laboratories ltd)
28349	clarosip 125mg granules for oral suspension straws (grunenthal ltd)
31689	clarosip 187.5mg granules for oral suspension straws (grunenthal ltd)
31690	clarosip 250mg granules for oral suspension straws (grunenthal ltd)
9925	clavulanic acid 125mg with amoxicillin 250mg tablets
13239	clavulanic acid 125mg with amoxicillin 500mg tablets
24006	clavulanic acid 31mg with amoxcillin 125mg/5ml oral suspension
21775	clavulanic acid 31mg with amoxicillin 125mg/5ml sugar free oral suspension
20432	clavulanic acid 57mg with amoxicillin 400mg/5ml sugar free suspension
42485	clavulanic acid 62mg with amoxicillin 250mg/5ml oral suspension
16612	clavulanic acid 62mg with amoxicillin 250mg/5ml sugar free suspension
24093	clavulanic acid with amoxicillin dispersible tablets
12504	clomocycline 170mg capsules
10200	co-amoxiclav 125mg/31mg/5ml oral suspension
54052	co-amoxiclav 125mg/31mg/5ml oral suspension (a a h pharmaceuticals ltd)
54732	co-amoxiclav 125mg/31mg/5ml oral suspension (generics (uk) ltd)
1638	co-amoxiclav 125mg/31mg/5ml oral suspension sugar free
43548	co-amoxiclav 125mg/31mg/5ml oral suspension sugar free (a a h pharmaceuticals ltd)
54324	co-amoxiclav 125mg/31mg/5ml oral suspension sugar free (actavis uk ltd)
54452	co-amoxiclav 125mg/31mg/5ml oral suspension sugar free (alliance healthcare (distribution) ltd)
54808	co-amoxiclav 125mg/31mg/5ml oral suspension sugar free (almus pharmaceuticals ltd)
28874	co-amoxiclav 125mg/31mg/5ml oral suspension sugar free (ivax pharmaceuticals uk ltd)
56884	co-amoxiclav 125mg/31mg/5ml oral suspension sugar free (phoenix healthcare distribution ltd)
34680	co-amoxiclav 125mg/31mg/5ml oral suspension sugar free (ranbaxy (uk) ltd)
34972	co-amoxiclav 125mg/31mg/5ml oral suspension sugar free (sandoz ltd)
829	co-amoxiclav 250mg/125mg dispersible tablets sugar free
545	co-amoxiclav 250mg/125mg tablets
30786	co-amoxiclav 250mg/125mg tablets (a a h pharmaceuticals ltd)
19209	co-amoxiclav 250mg/125mg tablets (actavis uk ltd)
51623	co-amoxiclav 250mg/125mg tablets (alliance healthcare (distribution) ltd)
48147	co-amoxiclav 250mg/125mg tablets (almus pharmaceuticals ltd)
34297	co-amoxiclav 250mg/125mg tablets (generics (uk) ltd)

CPRD Prodcode	Description
28871	co-amoxiclav 250mg/125mg tablets (ivax pharmaceuticals uk ltd)
33693	co-amoxiclav 250mg/125mg tablets (kent pharmaceuticals ltd)
50446	co-amoxiclav 250mg/125mg tablets (phoenix healthcare distribution ltd)
30783	co-amoxiclav 250mg/125mg tablets (ranbaxy (uk) ltd)
19414	co-amoxiclav 250mg/125mg tablets (sandoz ltd)
34734	co-amoxiclav 250mg/125mg tablets (teva uk ltd)
55312	co-amoxiclav 250mg/125mg tablets (waymade healthcare plc)
46915	co-amoxiclav 250mg/125mg tablets (zentiva)
7364	co-amoxiclav 250mg/62mg/5ml oral suspension
54708	co-amoxiclav 250mg/62mg/5ml oral suspension (a a h pharmaceuticals ltd)
54780	co-amoxiclav 250mg/62mg/5ml oral suspension (generics (uk) ltd)
524	co-amoxiclav 250mg/62mg/5ml oral suspension sugar free
42227	co-amoxiclav 250mg/62mg/5ml oral suspension sugar free (a a h pharmaceuticals ltd)
51678	co-amoxiclav 250mg/62mg/5ml oral suspension sugar free (almus pharmaceuticals ltd)
37304	co-amoxiclav 250mg/62mg/5ml oral suspension sugar free (ivax pharmaceuticals uk ltd)
40320	co-amoxiclav 250mg/62mg/5ml oral suspension sugar free (ranbaxy (uk) ltd)
46918	co-amoxiclav 250mg/62mg/5ml oral suspension sugar free (sandoz ltd)
34234	co-amoxiclav 250mg/62mg/5ml oral suspension sugar free (teva uk ltd)
56578	co-amoxiclav 250mg/62mg/5ml oral suspension sugar free (waymade healthcare plc)
6687	co-amoxiclav 400mg/57mg/5ml oral suspension sugar free
51637	co-amoxiclav 400mg/57mg/5ml oral suspension sugar free (a a h pharmaceuticals ltd)
641	co-amoxiclav 500mg/125mg tablets
33701	co-amoxiclav 500mg/125mg tablets (a a h pharmaceuticals ltd)
50742	co-amoxiclav 500mg/125mg tablets (actavis uk ltd)
50341	co-amoxiclav 500mg/125mg tablets (alliance healthcare (distribution) ltd)
53609	co-amoxiclav 500mg/125mg tablets (apc pharmaceuticals & chemicals (europe) ltd)
53996	co-amoxiclav 500mg/125mg tablets (aurobindo pharma ltd)
30705	co-amoxiclav 500mg/125mg tablets (generics (uk) ltd)
29356	co-amoxiclav 500mg/125mg tablets (ivax pharmaceuticals uk ltd)
40148	co-amoxiclav 500mg/125mg tablets (kent pharmaceuticals ltd)
49610	co-amoxiclav 500mg/125mg tablets (medreich plc)
54591	co-amoxiclav 500mg/125mg tablets (phoenix healthcare distribution ltd)
34493	co-amoxiclav 500mg/125mg tablets (ranbaxy (uk) ltd)
32910	co-amoxiclav 500mg/125mg tablets (sandoz ltd)
29353	co-amoxiclav 500mg/125mg tablets (teva uk ltd)
44154	co-amoxiclav 500mg/125mg tablets (zentiva)
21860	cyclodox 100mg capsule (berk pharmaceuticals ltd)
24245	cyclomin 100mg tablet (berk pharmaceuticals ltd)
21837	cyclomin 50mg tablet (berk pharmaceuticals ltd)
9131	demeclocycline 150mg capsules
8694	demeclocycline 300mg tablets

CPRD Prodcode	Description
50765	demeclocycline 300mg/5ml oral solution
24643	demeclocycline with chlortetracycline with tetracycline tablets
21878	demix 100 capsules (ashbourne pharmaceuticals ltd)
21828	demix 50 capsules (ashbourne pharmaceuticals ltd)
2256	deteclo 300mg tablet (wyeth pharmaceuticals)
13327	deteclo 300mg tablets (mercury pharma group ltd)
2428	distaclor 125mg/5ml liquid (dista products ltd)
25384	distaclor 125mg/5ml oral suspension (flynn pharma ltd)
4576	distaclor 250mg capsule (dista products ltd)
9219	distaclor 250mg/5ml liquid (dista products ltd)
22042	distaclor 250mg/5ml oral suspension (flynn pharma ltd)
7889	distaclor 375mg modified-release tablet (dista products ltd)
319	distaclor 500mg capsule (dista products ltd)
18243	distaclor 500mg capsules (flynn pharma ltd)
3523	distaclor 500mg modified-release tablet (dista products ltd)
20992	distaclor mr 375mg tablets (flynn pharma ltd)
21038	doxatet 100mg tablet (manufacturer unknown)
2884	doxycycline (as hyclate) 100mg dispersible tablets
970	doxycycline (as hyclate) 100mg tablets
12987	doxycycline (as hyclate) 50mg capsules with microgranules
23819	doxycycline (as hyclate) 50mg capsules with microgranules
8724	doxycycline (as hyclate) 50mg/5ml oral solution
41560	doxycycline 100mg capsule (ivax pharmaceuticals uk ltd)
34594	doxycycline 100mg capsule (neo laboratories ltd)
34423	doxycycline 100mg capsule (pliva pharma ltd)
41605	doxycycline 100mg capsule (sandoz ltd)
1046	doxycycline 100mg capsules
24149	doxycycline 100mg capsules (a a h pharmaceuticals ltd)
34300	doxycycline 100mg capsules (actavis uk ltd)
49737	doxycycline 100mg capsules (alliance healthcare (distribution) ltd)
46807	doxycycline 100mg capsules (almus pharmaceuticals ltd)
32066	doxycycline 100mg capsules (generics (uk) ltd)
24126	doxycycline 100mg capsules (ivax pharmaceuticals uk ltd)
33671	doxycycline 100mg capsules (kent pharmaceuticals ltd)
53310	doxycycline 100mg capsules (sigma pharmaceuticals plc)
30739	doxycycline 100mg capsules (teva uk ltd)
55519	doxycycline 100mg capsules (waymade healthcare plc)
6396	doxycycline 100mg dispersible tablets sugar free
26747	doxycycline 100mg tablet (neo laboratories ltd)
40796	doxycycline 40mg modified-release capsules
264	doxycycline 50mg capsules
34175	doxycycline 50mg capsules (a a h pharmaceuticals ltd)
48095	doxycycline 50mg capsules (actavis uk ltd)
53973	doxycycline 50mg capsules (alliance healthcare (distribution) ltd)
34765	doxycycline 50mg capsules (generics (uk) ltd)

CPRD Prodcode	Description
40391	doxycycline 50mg capsules (ivax pharmaceuticals uk ltd)
32419	doxycycline 50mg capsules (teva uk ltd)
23405	doxylar 100mg capsules (sandoz ltd)
23432	doxylar 50mg capsules (sandoz ltd)
17226	economycin 250mg capsule (ddsa pharmaceuticals ltd)
26111	economycin 250mg tablet (ddsa pharmaceuticals ltd)
40980	efracea 40mg modified-release capsules (galderma (uk) ltd)
4489	erycen 250mg tablet (berk pharmaceuticals ltd)
23017	erycen 500mg tablet (berk pharmaceuticals ltd)
318	erymax 250mg capsule (elan pharma)
10190	erymax 250mg gastro-resistant capsules (teva uk ltd)
14511	erymax sprinkle 125mg capsule (elan pharma)
9434	erymin 250mg/5ml oral suspension (elan pharma)
48017	erythoden 125mg/5ml liquid (stevenden healthcare)
41389	erythoden 250mg/5ml liquid (stevenden healthcare)
39616	erythrocin 250 tablets (amdipharm plc)
480	erythrocin 250mg tablet (abbott laboratories ltd)
1072	erythrocin 500 500mg tablet (abbott laboratories ltd)
39613	erythrocin 500 tablets (amdipharm plc)
53449	erythrocin 500 tablets (lexon (uk) ltd)
51984	erythrocin 500 tablets (mawdsley-brooks & company ltd)
53004	erythrocin 500 tablets (necessity supplies ltd)
50693	erythrocin 500 tablets (sigma pharmaceuticals plc)
50223	erythrocin 500 tablets (stephar (u.k.) ltd)
27768	erythrolar 250mg tablet (lagap)
50205	erythrolar 250mg tablets (ennogen pharma ltd)
4153	erythrolar 250mg/5ml liquid (lagap)
23954	erythrolar 500mg tablet (lagap)
49301	erythrolar 500mg tablets (ennogen pharma ltd)
3209	erythromid 250mg tablet (abbott laboratories ltd)
9148	erythromid ds 500mg tablet (abbott laboratories ltd)
1376	erythromycin 100 mg syr
7792	erythromycin 12 mg syr
14429	erythromycin 125mg sprinkle capsules
34231	erythromycin 125mg/5ml liquid (berk pharmaceuticals ltd)
33248	erythromycin 125mg/5ml liquid (ivax pharmaceuticals uk ltd)
397	erythromycin 125mg/5ml oral suspension
9656	erythromycin 2% gel
1969	erythromycin 250 mg mix
29154	erythromycin 250mg capsule (actavis uk ltd)
103	erythromycin 250mg gastro-resistant capsules
33686	erythromycin 250mg gastro-resistant capsules (a a h pharmaceuticals ltd)
50580	erythromycin 250mg gastro-resistant capsules (actavis uk ltd)
50694	erythromycin 250mg gastro-resistant capsules (alliance healthcare (distribution) ltd)

CPRD Prodcode	Description
55133	erythromycin 250mg gastro-resistant capsules (kent pharmaceuticals ltd)
49952	erythromycin 250mg gastro-resistant capsules (phoenix healthcare distribution ltd)
34512	erythromycin 250mg gastro-resistant capsules (teva uk ltd)
55397	erythromycin 250mg gastro-resistant capsules (waymade healthcare plc)
34837	erythromycin 250mg gastro-resistant tablet (co-pharma ltd)
63	erythromycin 250mg gastro-resistant tablets
24127	erythromycin 250mg gastro-resistant tablets (a a h pharmaceuticals ltd)
33703	erythromycin 250mg gastro-resistant tablets (abbott laboratories ltd)
29344	erythromycin 250mg gastro-resistant tablets (actavis uk ltd)
52906	erythromycin 250mg gastro-resistant tablets (alliance healthcare (distribution) ltd)
42661	erythromycin 250mg gastro-resistant tablets (almus pharmaceuticals ltd)
52952	erythromycin 250mg gastro-resistant tablets (co-pharma ltd)
42296	erythromycin 250mg gastro-resistant tablets (dr reddy's laboratories (uk) ltd)
34334	erythromycin 250mg gastro-resistant tablets (generics (uk) ltd)
24129	erythromycin 250mg gastro-resistant tablets (ivax pharmaceuticals uk ltd)
53986	erythromycin 250mg gastro-resistant tablets (medreich plc)
55483	erythromycin 250mg gastro-resistant tablets (milpharm ltd)
52428	erythromycin 250mg gastro-resistant tablets (phoenix healthcare distribution ltd)
31530	erythromycin 250mg gastro-resistant tablets (ranbaxy (uk) ltd)
34479	erythromycin 250mg gastro-resistant tablets (sovereign medical ltd)
33685	erythromycin 250mg gastro-resistant tablets (teva uk ltd)
34873	erythromycin 250mg tablet (berk pharmaceuticals ltd)
34189	erythromycin 250mg tablet (c p pharmaceuticals ltd)
553	erythromycin 250mg.5ml oral suspension
47242	erythromycin 250mg/5ml liquid (c p pharmaceuticals ltd)
41584	erythromycin 250mg/5ml liquid (ivax pharmaceuticals uk ltd)
3408	erythromycin 500 mg cap
401	erythromycin 500mg ec gastro-resistant tablets
34869	erythromycin 500mg tablet (c p pharmaceuticals ltd)
41604	erythromycin 500mg tablet (hillcross pharmaceuticals ltd)
26365	erythromycin 500mg tablet (ivax pharmaceuticals uk ltd)
55300	erythromycin 500mg tablet (teva uk ltd)
47676	erythromycin 500mg/5ml liquid (c p pharmaceuticals ltd)
2326	erythromycin 500mg/5ml oral suspension
37796	erythromycin estolate 125mg/5ml suspension
9903	erythromycin estolate 250mg capsules
40073	erythromycin estolate 250mg/5ml suspension
37694	erythromycin estolate 500mg tablets
2429	erythromycin ethyl succinate 125mg/5ml oral suspension
13167	erythromycin ethyl succinate 125mg/5ml oral suspension (a a h pharmaceuticals ltd)
49978	erythromycin ethyl succinate 125mg/5ml oral suspension (focus pharmaceuticals ltd)
50948	erythromycin ethyl succinate 125mg/5ml oral suspension (phoenix healthcare

CPRD Prodcode	Description
	distribution ltd)
47126	erythromycin ethyl succinate 125mg/5ml oral suspension (pinewood healthcare)
34779	erythromycin ethyl succinate 125mg/5ml oral suspension (sandoz ltd)
4672	erythromycin ethyl succinate 125mg/5ml oral suspension sugar free
33697	erythromycin ethyl succinate 125mg/5ml oral suspension sugar free (a a h pharmaceuticals ltd)
42659	erythromycin ethyl succinate 125mg/5ml oral suspension sugar free (abbott laboratories ltd)
55589	erythromycin ethyl succinate 125mg/5ml oral suspension sugar free (alliance healthcare (distribution) ltd)
48101	erythromycin ethyl succinate 125mg/5ml oral suspension sugar free (focus pharmaceuticals ltd)
33695	erythromycin ethyl succinate 125mg/5ml oral suspension sugar free (generics (uk) ltd)
34795	erythromycin ethyl succinate 125mg/5ml oral suspension sugar free (ivax pharmaceuticals uk ltd)
45870	erythromycin ethyl succinate 125mg/5ml oral suspension sugar free (pinewood healthcare)
33705	erythromycin ethyl succinate 125mg/5ml oral suspension sugar free (teva uk ltd)
2376	erythromycin ethyl succinate 250mg/5ml oral suspension
13120	erythromycin ethyl succinate 250mg/5ml oral suspension (a a h pharmaceuticals ltd)
32902	erythromycin ethyl succinate 250mg/5ml oral suspension (kent pharmaceuticals ltd)
46696	erythromycin ethyl succinate 250mg/5ml oral suspension (sandoz ltd)
2225	erythromycin ethyl succinate 250mg/5ml oral suspension sugar free
32898	erythromycin ethyl succinate 250mg/5ml oral suspension sugar free (a a h pharmaceuticals ltd)
46154	erythromycin ethyl succinate 250mg/5ml oral suspension sugar free (abbott laboratories ltd)
52860	erythromycin ethyl succinate 250mg/5ml oral suspension sugar free (alliance healthcare (distribution) ltd)
33694	erythromycin ethyl succinate 250mg/5ml oral suspension sugar free (generics (uk) ltd)
30177	erythromycin ethyl succinate 250mg/5ml oral suspension sugar free (ivax pharmaceuticals uk ltd)
34853	erythromycin ethyl succinate 250mg/5ml oral suspension sugar free (teva uk ltd)
733	erythromycin ethyl succinate 500mg tablets
2226	erythromycin ethyl succinate 500mg/5ml oral suspension
30980	erythromycin ethyl succinate 500mg/5ml oral suspension (kent pharmaceuticals ltd)
14171	erythromycin ethyl succinate 500mg/5ml oral suspension sugar free
31514	erythromycin ethyl succinate 500mg/5ml oral suspension sugar free (abbott laboratories ltd)
25595	erythromycin ethyl succinate 500mg/5ml oral suspension sugar free (ivax pharmaceuticals uk ltd)
27203	erythromycin ethyl succinate 500mg/5ml oral suspension sugar free (teva uk ltd)
25751	erythromycin ethylsuccinate (coated) 250mg/5ml oral suspension sugar free
30234	erythromycin ethylsuccinate 125mg sachets

CPRD Prodcode	Description
12330	erythromycin ethylsuccinate 1g sachets
13635	erythromycin ethylsuccinate 250mg sachets
15713	erythromycin ethylsuccinate 500mg sachets
1037	erythromycin ethylsuccinate sf 125 mg/5ml sus
3907	erythromycin sf sach 250 mg
438	erythromycin stearate 250mg tablets
2350	erythromycin stearate 500mg tablets
3572	erythroped 250mg powder (abbott laboratories ltd)
16747	erythroped 250mg sachets (abbott laboratories ltd)
105	erythroped 250mg/5ml liquid (abbott laboratories ltd)
532	erythroped 250mg/5ml oral suspension (abbott laboratories ltd)
4596	erythroped a 1g sachets (abbott laboratories ltd)
327	erythroped a 500mg tablet (abbott laboratories ltd)
39632	erythroped a 500mg tablets (amdipharm plc)
54098	erythroped a 500mg tablets (lexon (uk) ltd)
56203	erythroped a 500mg tablets (sigma pharmaceuticals plc)
4372	erythroped forte 500mg sachets (abbott laboratories ltd)
993	erythroped forte 500mg/5ml liquid (abbott laboratories ltd)
4610	erythroped forte 500mg/5ml oral suspension (abbott laboratories ltd)
39642	erythroped forte sf 500mg/5ml oral suspension (amdipharm plc)
3042	erythroped pi 125mg sachets (abbott laboratories ltd)
997	erythroped pi 125mg/5ml liquid (abbott laboratories ltd)
825	erythroped pi 125mg/5ml oral suspension (abbott laboratories ltd)
39623	erythroped pi sf 125mg/5ml oral suspension (amdipharm plc)
39669	erythroped sf 250mg/5ml oral suspension (amdipharm plc)
18930	flemoxin 375mg soluble tablet (paines & byrne ltd)
24396	flemoxin 750mg soluble tablet (paines & byrne ltd)
14386	galenamox 125mg/5ml oral suspension (galen ltd)
14371	galenamox 250mg capsules (galen ltd)
14407	galenamox 250mg/5ml oral suspension (galen ltd)
14396	galenamox 500mg capsules (galen ltd)
18682	ilosone 125mg/5ml liquid (dista products ltd)
17207	ilosone 250mg capsule (dista products ltd)
19330	ilosone 250mg/5ml liquid (dista products ltd)
18643	ilosone 500mg tablet (dista products ltd)
23244	ilotycin 250mg tablet (eli lilly and company ltd)
12541	imperacin 250mg tablet (astrazeneca uk ltd)
7485	keflex 125mg/5ml liquid (eli lilly and company ltd)
27072	keflex 125mg/5ml oral suspension (flynn pharma ltd)
7430	keflex 250mg capsule (eli lilly and company ltd)
11989	keflex 250mg capsules (flynn pharma ltd)
9157	keflex 250mg tablet (eli lilly and company ltd)
830	keflex 250mg tablets (flynn pharma ltd)
10455	keflex 250mg/5ml liquid (eli lilly and company ltd)
28722	keflex 250mg/5ml oral suspension (flynn pharma ltd)

CPRD Prodcode	Description
12276	keflex 500mg capsule (eli lilly and company ltd)
24618	keflex 500mg capsules (flynn pharma ltd)
9603	keflex 500mg tablet (eli lilly and company ltd)
31110	keflex 500mg tablets (flynn pharma ltd)
26233	keftid 125mg/5ml oral suspension (co-pharma ltd)
26207	keftid 250mg capsules (co-pharma ltd)
41853	keftid 250mg/5ml oral suspension (co-pharma ltd)
26236	keftid 500mg capsules (co-pharma ltd)
33304	kerymax 250mg gastro-resistant capsules (kent pharmaceuticals ltd)
26989	kiflone 125mg/5ml oral solution (berk pharmaceuticals ltd)
21835	kiflone 250mg capsule (berk pharmaceuticals ltd)
21979	kiflone 250mg/5ml oral solution (berk pharmaceuticals ltd)
27017	kiflone 500mg capsule (berk pharmaceuticals ltd)
26992	kiflone 500mg tablet (berk pharmaceuticals ltd)
3736	klaricid 125mg/5ml oral suspension (abbott laboratories ltd)
2719	klaricid 250mg tablets (abbott laboratories ltd)
52411	klaricid 250mg tablets (necessity supplies ltd)
9583	klaricid 250mg/5ml oral suspension (abbott laboratories ltd)
6623	klaricid 500 tablets (abbott laboratories ltd)
14816	klaricid adult 250mg granules sachets (abbott laboratories ltd)
38997	klaricid paediatric 125mg/5ml oral suspension (abbott laboratories ltd)
39010	klaricid paediatric 250mg/5ml oral suspension (abbott laboratories ltd)
6121	klaricid xl 500mg tablets (abbott laboratories ltd)
7439	ledermycin 150mg capsule (wyeth pharmaceuticals)
16613	ledermycin 150mg capsules (mercury pharma group ltd)
22076	ledermycin 300mg tablet (wyeth pharmaceuticals)
6295	levofloxacin 250mg tablets
55708	levofloxacin 250mg tablets (actavis uk ltd)
56012	levofloxacin 250mg tablets (dr reddy's laboratories (uk) ltd)
5238	levofloxacin 500mg tablets
53673	levofloxacin 500mg/100ml infusion bags
453	lymecycline 408mg capsules
19001	megaclor 170mg capsule (pharmax ltd)
3413	minocin 100mg tablets (wyeth pharmaceuticals)
164	minocin 50mg tablets (wyeth pharmaceuticals)
1039	minocin mr 100mg capsules (meda pharmaceuticals ltd)
9380	minocycline 100mg capsules
2578	minocycline 100mg modified-release capsules
34077	minocycline 100mg modified-release capsules (a a h pharmaceuticals ltd)
46954	minocycline 100mg tablet (lagap)
1532	minocycline 100mg tablets
34926	minocycline 100mg tablets (a a h pharmaceuticals ltd)
40383	minocycline 100mg tablets (actavis uk ltd)
429	minocycline 50mg capsules
43700	minocycline 50mg tablet (lagap)

CPRD Prodcode	Description
2999	minocycline 50mg tablets
46947	minocycline 50mg tablets (actavis uk ltd)
6306	moxifloxacin 400mg tablets
1013	mysteclin capsule (bristol-myers squibb pharmaceuticals ltd)
17222	mysteclin oral solution (bristol-myers squibb pharmaceuticals ltd)
1828	mysteclin tablet (bristol-myers squibb pharmaceuticals ltd)
15071	nordox 100mg capsule (sankyo pharma uk ltd)
8393	novobiocin/tetracycline 125 mg cap
25752	nystatin with tetracycline hc capsule
9361	oxymycin 250mg tablets (dr reddy's laboratories (uk) ltd)
2458	oxytetracycline 100 mg tab
9034	oxytetracycline 125mg/5ml syrup
8285	oxytetracycline 250 mg syr
132	oxytetracycline 250mg capsules
34888	oxytetracycline 250mg tablet (c p pharmaceuticals ltd)
77	oxytetracycline 250mg tablets
34044	oxytetracycline 250mg tablets (a a h pharmaceuticals ltd)
34040	oxytetracycline 250mg tablets (actavis uk ltd)
34336	oxytetracycline 250mg tablets (ivax pharmaceuticals uk ltd)
40483	oxytetracycline 250mg tablets (sandoz ltd)
34141	oxytetracycline 250mg tablets (teva uk ltd)
3025	oxytetracycline 500 mg tab
17703	oxytetramix 250 tablets (ashbourne pharmaceuticals ltd)
30520	primacine 125mg/5ml liquid (pinewood healthcare)
39118	primacine 250mg/5ml liquid (pinewood healthcare)
27504	primacine 500mg/5ml liquid (pinewood healthcare)
27681	ranclav 125mg/31mg/5ml sf oral suspension (ranbaxy (uk) ltd)
25370	ranclav 375mg tablets (ranbaxy (uk) ltd)
22015	respillin 125mg/5ml oral solution (opd pharm)
22017	respillin 125mg/5ml oral solution (opd pharm)
24203	respillin 250mg capsule (opd pharm)
24200	respillin 500mg capsule (opd pharm)
31428	retcin 250mg tablet (ddsa pharmaceuticals ltd)
21808	rommix 125mg/5ml oral suspension sugar free (ashbourne pharmaceuticals ltd)
11611	rommix 250 ec tablets (ashbourne pharmaceuticals ltd)
25278	rommix 500mg tablet (ashbourne pharmaceuticals ltd)
24097	rondomycin 150mg capsule (pfizer ltd)
18109	sebomin mr 100mg capsules (actavis uk ltd)
37440	sebren mr 100mg capsules (teva uk ltd)
19693	sustamycin 250mg capsule (boehringer mannheim uk ltd)
17693	tavanic 250mg tablets (sanofi)
6206	tavanic 500mg tablets (sanofi)
27254	tenkorex 500mg capsule (opd pharm)
7455	terramycin 250mg capsule (pfizer ltd)

CPRD Prodcode	Description
17467	terramycin 250mg tablets (pfizer ltd)
9014	tetrabid-organon 250mg capsule (organon laboratories ltd)
8219	tetrachel 250mg capsule (berk pharmaceuticals ltd)
3816	tetrachel 250mg tablet (berk pharmaceuticals ltd)
25017	tetracycline
56044	tetracycline 125mg/5ml oral solution
8284	tetracycline 125mg/5ml syrup
21804	tetracycline 125mg/5ml syrup
41547	tetracycline 250mg capsule (berk pharmaceuticals ltd)
121	tetracycline 250mg capsules
34011	tetracycline 250mg capsules
56181	tetracycline 250mg tablet (celltech pharma europe ltd)
45271	tetracycline 250mg tablet (numark management ltd)
386	tetracycline 250mg tablets
43538	tetracycline 250mg tablets (a a h pharmaceuticals ltd)
41636	tetracycline 250mg tablets (actavis uk ltd)
54214	tetracycline 250mg tablets (alliance healthcare (distribution) ltd)
53117	tetracycline 250mg tablets (almus pharmaceuticals ltd)
48100	tetracycline 250mg tablets (teva uk ltd)
2922	tetracycline 250mg with nystatin 250000units tablets
2636	tetracycline 500 mg cap
3528	tetracycline 500 mg tab
21654	tetracycline ear/eye
21629	tetracycline eye
31425	tetracycline hcl/pancreatic concentrate cap
28736	tetracycline hydrochloride/amphotericin syr
15355	tetracycline with chlortetracycline & demeclocycline tablets
25071	tetracycline with nystatin capsules
4951	tetralysal 300 capsules (galderma (uk) ltd)
20054	tetralysal 408mg capsule (pharmacia ltd)
25280	tiloryth 250mg gastro-resistant capsules (tillomed laboratories ltd)
268	vibramycin 100mg capsules (pfizer ltd)
3152	vibramycin 100mg dispersible tablet (pfizer ltd)
2202	vibramycin 50 capsules (pfizer ltd)
10454	vibramycin 50mg/5ml oral solution (pfizer ltd)
9267	vibramycin acne pack 50mg capsules (pfizer ltd)
56198	vibramycin-d 100mg dispersible tablets (mawdsley-brooks & company ltd)
14904	vibramycin-d 100mg dispersible tablets (pfizer ltd)
52967	vibramycin-d 100mg dispersible tablets (stephar (u.k.) ltd)
53135	vibramycin-d 100mg dispersible tablets (waymade healthcare plc)
26392	vibrox 100mg capsules (kent pharmaceuticals ltd)
21829	zoxycil 250mg capsule (trinity pharmaceuticals ltd)
26262	zoxycil 500mg capsule (trinity pharmaceuticals ltd)

Prescriptions of pre-specified oral corticosteroid (OCS)

CPRD Prodcode	Description
30971	decortisyl 25 mg tab
21833	decortisyl 5mg tablet (roussel laboratories ltd)
27962	deltastab 1mg tablet (waymade healthcare plc)
30390	deltastab 2 mg tab
28859	deltastab 5mg tablet (waymade healthcare plc)
54432	lodotra 1mg modified-release tablets (napp pharmaceuticals ltd)
44803	lodotra 2mg modified-release tablets (napp pharmaceuticals ltd)
44802	lodotra 5mg modified-release tablets (napp pharmaceuticals ltd)
25272	precortisyl 1mg tablet (hoechst marion roussel)
23512	precortisyl 5mg tablet (hoechst marion roussel)
20095	precortisyl forte 25mg tablet (aventis pharma)
1063	prednesol 5mg tablet (sovereign medical ltd)
27889	prednisolone
27959	prednisolone
2799	prednisolone 10 mg tab
7710	prednisolone 15 mg tab
34914	prednisolone 1mg tablet (celltech pharma europe ltd)
34631	prednisolone 1mg tablet (co-pharma ltd)
13522	prednisolone 2 mg tab
28376	prednisolone 2.5mg gastro-resistant tablet (biorex laboratories ltd)
2368	prednisolone 2.5mg tablet
38407	prednisolone 20mg tablet
7584	prednisolone 4 mg tab
34109	prednisolone 5 mg gastro-resistant tablet
3059	prednisolone 50 mg tab
9727	prednisolone 50mg tablets
33691	prednisolone 5mg gastro-resistant tablet (biorex laboratories ltd)
47142	prednisolone 5mg soluble tablet (amdipharm plc)
45302	prednisolone 5mg tablet (biorex laboratories ltd)
33988	prednisolone 5mg tablet (co-pharma ltd)
33990	prednisolone 5mg tablet (ivax pharmaceuticals uk ltd)
95	prednisolone 5mg tablets
20670	prednisolone e/c
24716	prednisolone e/c
2390	prednisolone e/c 1 mg tab
31327	prednisolone steaglate 6.65mg tablet
13615	prednisone 10 mg tab
44380	prednisone 1mg modified-release tablets
3557	prednisone 1mg tablets
2044	prednisone 2.5 mg tab
46711	prednisone 2mg modified-release tablets
7934	prednisone 30 mg tab
16724	prednisone 50 mg tab

CPRD Prodcode	Description
44723	prednisone 5mg modified-release tablets
43544	prednisone 5mg tablet (knoll ltd)
2949	prednisone 5mg tablets
3345	sintisone tablet (pharmacia ltd)

Exacerbation symptoms

CPRD Medcode	Description	Symptom
735	[d]breathlessness	breathless
3092	[d]dyspnoea	breathless
2563	[d]respiratory distress	breathless
9297	[d]respiratory insufficiency	breathless
741	[d]shortness of breath	breathless
31143	breathless - at rest	breathless
7683	breathless - lying flat	breathless
7932	breathless - mild exertion	breathless
6326	breathless - moderate exertion	breathless
24889	breathless - strenuous exertion	breathless
1429	breathlessness	breathless
21801	breathlessness nos	breathless
5175	breathlessness symptom	breathless
2931	difficulty breathing	breathless
5896	dyspnoea - symptom	breathless
53771	dyspnoea on exertion	breathless
18116	nocturnal dyspnoea	breathless
7000	o/e - dyspnoea	breathless
7534	o/e - respiratory distress	breathless
6434	paroxysmal nocturnal dyspnoea	breathless
2737	respiratory distress syndrome	breathless
22094	short of breath dressing/undressing	breathless
2575	short of breath on exertion	breathless
4822	shortness of breath	breathless
5349	shortness of breath symptom	breathless
40813	Unable to complete a sentence in one breath	breathless
1160	[d]cough	cough
8239	[d]cough with haemorrhage	cough
1025	bronchial cough	cough
1273	c/o - cough	cough
292	chesty cough	cough
92	cough	cough
60903	cough aggravates symptom	cough
100515	cough swab	cough
7707	cough symptom nos	cough
18907	cough with fever	cough
3645	coughing up phlegm	cough
22318	difficulty in coughing up sputum	cough
4931	dry cough	cough
29318	evening cough	cough
4070	morning cough	cough
3068	night cough present	cough
4836	nocturnal cough / wheeze	cough
7706	productive cough -clear sputum	cough

CPRD Medcode	Description	Symptom
7773	productive cough -green sputum	cough
1234	productive cough nos	cough
7708	productive cough-yellow sputum	cough
1251	[d]abnormal sputum	sputum
36515	[d]abnormal sputum - tenacious	sputum
23582	[d]abnormal sputum nos	sputum
8760	[d]positive culture findings in sputum	sputum
20086	[d]sputum abnormal - amount	sputum
15430	[d]sputum abnormal - colour	sputum
44214	[d]sputum abnormal - odour	sputum
11072	acute purulent bronchitis	sputum
1025	bronchial cough	sputum
100931	brown sputum	sputum
292	chesty cough	sputum
100647	copious sputum	sputum
3645	Coughing up phlegm	sputum
22318	difficulty in coughing up sputum	sputum
36880	green sputum	sputum
103209	grey sputum	sputum
100524	moderate sputum	sputum
7706	productive cough -clear sputum	sputum
7773	productive cough -green sputum	sputum
1234	productive cough nos	sputum
7708	productive cough-yellow sputum	sputum
101782	profuse sputum	sputum
9807	sputum - symptom	sputum
14273	sputum appearance	sputum
14804	sputum appears infected	sputum
18964	sputum clearance	sputum
14271	sputum culture	sputum
43270	sputum evidence of infection	sputum
16026	sputum examination: abnormal	sputum
14272	sputum microscopy	sputum
23252	sputum microscopy nos	sputum
8287	sputum sample obtained	sputum
3727	sputum sent for c/s	sputum
30904	sputum sent for examination	sputum
54177	sputum: excessive - mucoid	sputum
24181	sputum: mucopurulent	sputum
49694	sputum: organism on gram stain	sputum
49144	sputum: pus cells present	sputum
100484	volume of sputum	sputum
100629	white sputum	sputum
30754	yellow sputum	sputum

Lower respiratory tract infections (LRTIs)

CPRD Medcode	Read Code	Description
99214	Hyu1100	[x]acute bronchiolitis due to other specified organisms
73100	Hyu1000	[x]acute bronchitis due to other specified organisms
98257	Hyu0400	[x]flu+oth respiratory manifestations,'flu virus identified
97605	Hyu0600	[x]influenza+oth respiratory manifestatns,virus not identifd
97279	Hyu0700	[x]influenza+other manifestations, virus not identified
97936	Hyu0500	[x]influenza+other manifestations,influenza virus identified
66397	Hyu1.00	[x]other acute lower respiratory infections
24800	H060x00	acute bacterial bronchitis unspecified
1019	H061.00	acute bronchiolitis
66228	H061600	acute bronchiolitis due to other specified organisms
18451	H061500	acute bronchiolitis due to respiratory syncytial virus
17917	H061z00	acute bronchiolitis nos
17185	H061200	acute bronchiolitis with bronchospasm
312	H060.00	acute bronchitis
29669	H06..00	acute bronchitis and bronchiolitis
54830	H460000	acute bronchitis due to chemical fumes
93153	H060B00	acute bronchitis due to coxsackievirus
65916	H060F00	acute bronchitis due to echovirus
29273	H060C00	acute bronchitis due to parainfluenza virus
48593	H060D00	acute bronchitis due to respiratory syncytial virus
64890	H060E00	acute bronchitis due to rhinovirus
20198	H060z00	acute bronchitis nos
41137	H06z.00	acute bronchitis or bronchiolitis nos
54533	H061000	acute capillary bronchiolitis
21145	H060400	acute croupous bronchitis
69192	H061300	acute exudative bronchiolitis
50396	H060000	acute fibrinous bronchitis
21492	H060800	acute haemophilus influenzae bronchitis
6124	H062.00	acute lower respiratory tract infection
37447	H06z112	acute lower respiratory tract infection
101775	H060100	acute membranous bronchitis
49794	H060900	acute neisseria catarrhalis bronchitis
41589	H061100	acute obliterating bronchiolitis
9043	H060600	acute pneumococcal bronchitis
71370	H060200	acute pseudomembranous bronchitis
11072	H060300	acute purulent bronchitis
43362	H060700	acute streptococcal bronchitis
11101	H060500	acute tracheobronchitis
1382	H060w00	acute viral bronchitis unspecified
5978	H060.11	acute wheezy bronchitis
18207	H33zz13	allergic bronchitis nec
100650	AB63600	aspergillus bronchitis
94930	H29..00	avian influenza
63697	43jQ.00	avian influenza virus nucleic acid detection
26125	H312300	bronchiolitis obliterans

CPRD Medcode	Read Code	Description
3480	H30z.00	bronchitis nos
148	H30..00	bronchitis unspecified
2476	H07..00	chest cold
68	H06z011	chest infection
17359	H30..11	chest infection - unspecified bronchitis
2581	H06z000	chest infection nos
24316	H24..11	chest infection with infectious disease ec
15626	H310000	chronic catarrhal bronchitis
21061	H3y0.00	chronic obstruct pulmonary dis with acute lower resp infectn
14798	H312100	emphysematous bronchitis
2157	H27z.11	flu like illness
96286	4JUF.00	human parainfluenza virus detected
556	H27..00	influenza
98102	H2A..11	influenza a (h1n1) swine flu
98143	4J3L.00	influenza a virus h1n1 subtype detected
97062	4JU4.00	influenza a virus, other or untyped strain detected
96017	4JU5.00	influenza b virus detected
98129	H2A..00	influenza due to influenza a virus subtype h1n1
96019	4JU0.00	influenza h1 virus detected
102918	4JU1.00	influenza h2 virus detected
96018	4JU2.00	influenza h3 virus detected
98156	4JU3.00	influenza h5 virus detected
5947	H27z.12	influenza like illness
16388	H27z.00	influenza nos
46157	H27y000	influenza with encephalopathy
14791	H27y100	influenza with gastrointestinal tract involvement
15774	H271000	influenza with laryngitis
47472	H27y.00	influenza with other manifestations
31363	H27yz00	influenza with other manifestations nos
43625	H271.00	influenza with other respiratory manifestation
29617	H271100	influenza with pharyngitis
23488	H271z00	influenza with respiratory manifestations nos
8980	16L..00	influenza-like symptoms
1934	H301.00	laryngotracheobronchitis
3358	H06z100	lower resp tract infection
24248	H313.00	mixed simple and mucopurulent chronic bronchitis
11150	H311.00	mucopurulent chronic bronchitis
61513	H311z00	mucopurulent chronic bronchitis nos
6181	H061400	obliterating fibrous bronchiolitis
63216	H464100	obliterative bronchiolitis due to chemical fumes
94130	43jx.00	parainfluenza type 1 nucleic acid detection
94858	43jy.00	parainfluenza type 2 nucleic acid detection
91123	43jz.00	parainfluenza type 3 nucleic acid detection
98103	1W0..00	possible influenza a virus h1n1 subtype
40159	H311000	purulent chronic bronchitis
4899	H06z200	recurrent chest infection

CPRD Medcode	Read Code	Description
7092	H30..12	recurrent wheezy bronchitis
55391	H060v00	subacute bronchitis unspecified
98125	1J72.00	suspected influenza a virus subtype h1n1 infection
98115	1J72.11	suspected swine influenza
3163	H300.00	tracheobronchitis nos
152	H302.00	wheezy bronchitis

Acute Exacerbation of COPD (AECOPD) – primary care

CPRD Medcode	Read Code	Description
1446	H312200	acute exacerbation of chronic obstructive airways disease
7884	H3y1.00	chron obstruct pulmonary dis wth acute exacerbation, unspec

Acute Exacerbation of COPD (AECOPD) – secondary care

ICD10 Code	Description	Classify
J44.1	Chronic obstructive pulmonary disease with acute exacerbation, unspecified	Definite
J44.0	Chronic obstructive pulmonary disease with acute lower respiratory infection	Definite
J43.2	Centrilobular emphysema	Possible
J44.9	Chronic obstructive pulmonary disease, unspecified	Possible
J43	Emphysema	Possible
J43.9	Emphysema, unspecified	Possible
J43.0	MacLeod's syndrome	Possible
J41.8	Mixed simple and mucopurulent chronic bronchitis	Possible
J41.1	Mucopurulent chronic bronchitis	Possible
J44	Other chronic obstructive pulmonary disease	Possible
J43.8	Other emphysema	Possible
J44.8	Other specified chronic obstructive pulmonary disease	Possible
J43.1	Panlobular emphysema	Possible
J41	Simple and mucopurulent chronic bronchitis	Possible
J41.0	Simple chronic bronchitis	Possible
J22	Unspecified acute lower respiratory infection	Possible
J42	Unspecified chronic bronchitis	Possible

Rescue packs for COPD exacerbations

CPRD Medcode	Read Code	Description
25997	8BP0.00	Deferred antibiotic therapy
100459	8B32.00	Advance supply of steroid medication
101042	8BMW.00	Issue of chronic obstructive pulmonary disease rescue pack

Patient COPD reviews

CPRD Medcode	Read Code	Description
10043	66YJ.00	Asthma annual review
11287	66YM.00	Chronic obstructive pulmonary disease annual review
9520	66YB.00	Chronic obstructive pulmonary disease monitoring
28743	66Yf.00	Number of COPD exacerbations in past year

3. CODE LIST TO DEFINE HOSPITALISED PNEUMONIA (PO3 AND SO2)

Episodes of Pneumonia during the study were identified by a record for a diagnosis of pneumonia while hospitalised using the set of ICD-10 diagnosis codes that follows.

Pneumonia (as outcome) coding definition

ICD10 Code	Description	Classification
J15.9	Bacterial pneumonia, unspecified	Bacterial
J15	Bacterial pneumonianot elsewhere classified	Bacterial
J16.0	Chlamydial pneumonia	Bacterial
A48.1	Legionnaires' disease	Bacterial
J15.8	Other bacterial pneumonia	Bacterial
J15.5	Pneumonia due to Escherichia coli	Bacterial
J14	Pneumonia due to Haemophilus influenzae	Bacterial
J14.0	Pneumonia due to Haemophilus influenzae	Bacterial
J14X	Pneumonia due to Haemophilus influenzae	Bacterial
J15.0	Pneumonia due to Klebsiella pneumoniae	Bacterial
J15.7	Pneumonia due to Mycoplasma pneumoniae	Bacterial
J15.1	Pneumonia due to Pseudomonas	Bacterial
J13	Pneumonia due to Streptococcus pneumoniae	Bacterial
J13.0	Pneumonia due to Streptococcus pneumoniae	Bacterial
J13X	Pneumonia due to Streptococcus pneumoniae	Bacterial
J15.6	Pneumonia due to other aerobic Gram-negative bacteria	Bacterial
J15.4	Pneumonia due to other streptococci	Bacterial
J15.2	Pneumonia due to staphylococcus	Bacterial
J15.3	Pneumonia due to streptococcus, group B	Bacterial
J17.0	Pneumonia in bacterial diseases classified elsewhere	Bacterial
A20.2	Pneumonic plague	Bacterial
A42.0	Pulmonary actinomycosis	Bacterial
A22.1	Pulmonary anthrax	Bacterial
A43.0	Pulmonary nocardiosis	Bacterial
A21.2	Pulmonary tularaemia	Bacterial
B40.0	Acute pulmonary blastomycosis	Fungal
B38.0	Acute pulmonary coccidioidomycosis	Fungal
B39.0	Acute pulmonary histoplasmosis capsulation	Fungal
B38.1	Chronic pulmonary coccidioidomycosis	Fungal
B20.6	HIV disease resulting in Pneumocystis carinii pneumonia	Fungal
B44.0	Invasive pulmonary aspergillosis	Fungal
B44.1	Other pulmonary aspergillosis	Fungal
B59.X	Pneumocystosis	Fungal
J17.2	Pneumonia in mycoses	Fungal
B40.2	Pulmonary blastomycosis, unspecified	Fungal
B37.1	Pulmonary candidiasis	Fungal
B38.2	Pulmonary coccidioidomycosis, unspecified	Fungal

ICD10 Code	Description	Classification
B45.0	Pulmonary cryptococcosis	Fungal
B39.2	Pulmonary histoplasmosis capsulati, unspecified	Fungal
B46.0	Pulmonary mucormycosis	Fungal
B41.0	Pulmonary paracoccidioidomycosis	Fungal
B42.0	Pulmonary sporotrichosis	Fungal
B58.3	Pulmonary toxoplasmosis	Fungal
J85	Abscess of lung and mediastinum	Lung abscess
J85.1	Abscess of lung with pneumonia	Lung abscess
J85.2	Abscess of lung without pneumonia	Lung abscess
A06.5	Amoebic lung abscess	Lung abscess
J85.0	Gangrene and necrosis of lung	Lung abscess
A19.0	Acute miliary tuberculosis of a single specified site	Mycobacterial
A19.1	Acute miliary tuberculosis of multiple sites	Mycobacterial
A19.2	Acute miliary tuberculosis, unspecified	Mycobacterial
A19	Miliary tuberculosis	Mycobacterial
A19.9	Miliary tuberculosis, unspecified	Mycobacterial
A16.8	Oth respiratory TB without mention of bact or hist confirm	Mycobacterial
A19.8	Other miliary tuberculosis	Mycobacterial
A15.8	Other respiratory TB confirm bact and histologically	Mycobacterial
A16.7	Prim respiratory TB without mention of bact or hist confirm	Mycobacterial
A15.7	Primary respiratory TB confirm bact and histologically	Mycobacterial
A31.0	Pulmonary mycobacterial infection	Mycobacterial
A16.9	Resp TB unspec without mention of bact or hist confirm	Mycobacterial
A15	Respiratory TB bacteriologically and histologically confirmed	Mycobacterial
A16	Respiratory TB not confirmed bacteriologically or histologically	Mycobacterial
A15.9	Respiratory TB unspec confirm bact and histologically	Mycobacterial
A15.4	TB intrathoracic lymph nodes confirm bact histologically	Mycobacterial
A15.0	TB lung confirm sputum microscopy with or without culture	Mycobacterial
A16.2	TB lung without mention of bact or histological confirm	Mycobacterial
A16.5	TB pleurisy without mention of bact or histological confirm	Mycobacterial
A16.1	Tuberculosis lung bact and histological examin not done	Mycobacterial
A15.5	Tuberculosis of larynx, trachea & bronchus conf bact/hist'y	Mycobacterial
A16.0	Tuberculosis of lung, bacteriologically & histolog'y neg	Mycobacterial
A15.1	Tuberculosis of lung, confirmed by culture only	Mycobacterial
A15.3	Tuberculosis of lung, confirmed by unspecified means	Mycobacterial
A15.2	Tuberculosis of lung, confirmed histologically	Mycobacterial
A15.6	Tuberculous pleurisy, conf bacteriologically/his'y	Mycobacterial
B67.1	Other B67.1 Echinococcus granulosus infection of lung	Other
J17.3	Other J17.3 Pneumonia in parasitic diseases	Other
J12.0	Adenoviral pneumonia	Viral
J10.0	Influenza with pneumonia, influenza virus identified	Viral
J11.0	Influenza with pneumonia, virus not identified	Viral
B05.2	Measles complicated by pneumonia	Viral
J12.8	Other viral pneumonia	Viral
J12.2	Parainfluenza virus pneumonia	Viral

ICD10 Code	Description	Classification
J17.1	Pneumonia in viral diseases classified elsewhere	Viral
J12.1	Respiratory syncytial virus pneumonia	Viral
B01.2	Varicella pneumonia	Viral
J12	Viral pneumonia, not elsewhere classified	Viral
J12.9	Viral pneumonia, unspecified	Viral
J18.0	Bronchopneumonia, unspecified	unspecified
J18.1	Lobar pneumonia, unspecified	unspecified
J18.8	Other pneumonia, organism unspecified	unspecified
J16	Pneumonia due to other infectious organisms NEC	unspecified
J16.8	Pneumonia due to other specified infectious organisms	unspecified
J17	Pneumonia in diseases classified elsewhere	unspecified
J17.8	Pneumonia in other diseases classified elsewhere	unspecified
J18.9	Pneumonia, unspecified	unspecified
J18	Pneumoniaorganism unspecified	unspecified