NON-INTERVENTIONAL STUDY PROTOCOL

Study information

Title	Non-Interventional Postmarketing Safety Study of the COMIRNATY 2025-2026 Formula (LP.8.1) in the United States
Protocol number	C4591077
Protocol version identifier	2.0
Date	05 March 2026
EU Post Authorization Study (PAS) register number	EUPAS1000000932
Active substance	COVID-19 vaccine, mRNA
Medicinal product	COMIRNATY 2025-2026 Formula
Research question and objectives	Research question: What is the incidence of pre-specified adverse events of special interest (AESIs) among individuals who receive the COMIRNATY 2025-2026 Formula in the United States? The study will be conducted in two phases, each with its own specific objectives. <u>Phase 1</u> Phase 1 will be designed to sequentially monitor the occurrence of pre-specified AESIs in near real-time following vaccination. Primary objective: • To estimate the incidence of pre-specified AESIs in a risk window following vaccination with the COMIRNATY 2025-2026 Formula compared to the incidence of these events during a control window (ie, expected rates of these events). <u>Phase 2</u> Phase 2 will be designed to compare the incidence of pre-specified AESIs for up to 1 year among individuals who receive the COMIRNATY 2025-2026 Formula to individuals with no recorded coronavirus disease 2019 (COVID-19) vaccination. Primary objective: • To estimate the incidence of pre-specified AESIs among individuals who receive the COMIRNATY 2025-2026 Formula

	compared to the incidence among individuals with no recorded COVID-19 vaccination. Secondary objective: • To estimate the incidence of pre-specified AESIs among individuals who receive the COMIRNATY 2025-2026 Formula compared to the incidence among individuals with no recorded COVID-19 vaccination within subgroups of individuals with prior severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection; individuals with prior COVID-19 vaccination; individuals with administration of non-COVID-19 vaccines; children 5 through 17 years of age; adults 65 years of age and older; and individuals 5 years through 64 years of age with at least one underlying condition that puts them at high risk for severe outcomes from COVID-19, if sample size permits.
Country of study	United States
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1. LIST OF ABBREVIATIONS

Abbreviation	Definition
ADEM	Acute disseminated encephalomyelitis
AESI	Adverse event of special interest
AMA	American Medical Association
BEST	Biologics Effectiveness and Safety
CBER	Center for Biologics Evaluation and Research
CDC	Centers for Disease Control and Prevention
CI	Confidence interval
CMS	Centers for Medicare and Medicaid Services
COPD	Chronic obstructive pulmonary disease
COVID-19	Coronavirus disease 2019
CPT	Current Procedural Terminology
CVST	Cerebral venous sinus thrombosis
EC	Ethics committee
ED	Emergency department
EMA	European Medicines Agency
FDA	Food and Drug Administration
GPP	Good pharmacoepidemiology practices
HCPCS	Healthcare Common Procedure Coding System
HIV	Human immunodeficiency virus
ICD-10	International Classification of Diseases, 10th Revision
ICD-10-CM	International Classification of Diseases, 10th Revision, Clinical Modification

Abbreviation	Definition
IIS	Immunization Information Systems
IP	Inpatient
IRB	Institutional Review Board
MA-PD	Medicare Advantage and Medicare Part D
mRNA	Messenger RNA
MS	Multiple sclerosis
NDC	National Drug Code
NSTEMI	Non-ST elevation myocardial infarction
OP	Outpatient
ORD	Optum Research Database
PAS	Post authorization study
PASS	Post-authorization safety study
PE	Pulmonary embolism
RSV	Respiratory syncytial virus
SAP	Statistical analysis plan
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
SAS	Statistical Analysis System
SCRI	Self-controlled risk interval
SOP	Standard operating procedure
STEMI	ST elevation myocardial infarction
TM	Transverse myelitis
US	United States

2. RESPONSIBLE PARTIES

Principal Investigator(s) of the Protocol

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3. ABSTRACT

Title: Non-Interventional Postmarketing Safety Study of the COMIRNATY 2025-2026 Formula (LP.8.1) in the United States

Version: 2.0

Date: 05 March 2026

Authors: Optum: Elizabeth Mostofksy, ScD, Senior Epidemiologist, Epidemiology; Florence T. Wang, ScD, Vice President, Epidemiology; Pfizer: Jenny Sun, PhD, Associate Director, Epidemiology, Safety Surveillance Research

Rationale and background: In August 2025, the United States (US) Food and Drug Administration (FDA) approved the COMIRNATY 2025-2026 Formula, a monovalent messenger RNA (mRNA) vaccine targeting the LP.8 strain of severe acute respiratory virus coronavirus 2 (SARS-CoV-2). To date, postmarketing safety data for the variant-adapted vaccines, including the recent COMIRNATY 2024-2025 Formula, have not revealed new safety signals. More information is needed to determine whether the safety profile of the COMIRNATY 2025-2026 Formula remains consistent with the safety profile of the previous formulations of COMIRNATY in the overall population and in subpopulations of interest.

Pfizer/BioNTech propose to conduct a non-interventional study to assess the safety of the COMIRNATY 2025-2026 Formula. This non-interventional study is designated as a post-authorization safety study (PASS) and is being conducted voluntarily by Pfizer.

Research question and objectives:

Research question: What is the incidence of pre-specified adverse events of special interest (AESIs) among individuals who receive the COMIRNATY 2025-2026 Formula in the United States?

The study will be conducted in two phases, each with its own specific objectives.

Phase 1

Phase 1 will be designed to sequentially monitor the occurrence of pre-specified AESIs in near real-time following vaccination.

Primary objective:

- To estimate the incidence of pre-specified AESIs in a risk window following vaccination with the COMIRNATY 2025-2026 Formula compared to the incidence of these events during a control window (ie, expected rates of these events).

Phase 2

Phase 2 will be designed to compare the incidence of pre-specified AESIs for up to 1 year among individuals who receive the COMIRNATY 2025-2026 Formula to individuals with no recorded coronavirus disease 2019 (COVID-19) vaccination.

Primary objective:

- To estimate the incidence of pre-specified AESIs among individuals who receive the COMIRNATY 2025-2026 Formula compared to the incidence among individuals with no recorded COVID-19 vaccination.

Secondary objective:

- To estimate the incidence of pre-specified AESIs among individuals who receive the COMIRNATY 2025-2026 Formula compared to the incidence among individuals with no recorded COVID-19 vaccination within subgroups of individuals with prior SARS-CoV-2 infection; individuals with prior COVID-19 vaccination; individuals with administration of non-COVID-19 vaccines; children 5 through 17 years of age; adults 65 years of age and older; and individuals 5 years through 64 years of age with at least one underlying condition that puts them at high risk for severe outcomes from COVID-19, if sample size permits.

Study design: This is a non-interventional observational study utilizing administrative claims databases in the US. Phase 1 will utilize a self-controlled risk interval (SCRI) design, and Phase 2 will utilize a matched cohort design. These two different study designs are complementary, each with its own strengths. The SCRI design is less impacted by misclassification of COVID-19 vaccine exposure and confounding by time-fixed characteristics, while the cohort study design enables a longer follow-up period.

Population: The study population will be identified from a nationwide healthcare insurance claims database. It will include all eligible individuals who receive the COMIRNATY 2025-2026 Formula from 27 August 2025 (the date of product approval in the US) through 31 March 2026. The end date of 31 March 2026 was chosen based on the assumption that the seasonal time trend in vaccine uptake will be similar to uptake during prior vaccine seasons.

The source population for this study will consist of all individuals with at least one medical or pharmacy claim from 27 August 2025 through 31 March 2026.

In Phase 1, individuals aged ≥ 5 years will be eligible for inclusion if they receive at least 1 dose of the COMIRNATY 2025-2026 Formula from 27 August 2025 through 31 March 2026, have continuous medical and pharmacy insurance coverage in the 365 days prior to their vaccination date, experience a safety outcome of interest during a risk or control period, and do not experience the safety event of interest during the clean period prior to vaccination.

In Phase 2, individuals aged ≥ 5 years will be eligible for inclusion in the exposed cohort if they receive a dose of the COMIRNATY 2025-2026 Formula from 27 August 2025 through 31 March 2026 and have continuous medical and pharmacy insurance coverage in the 365 days prior to their vaccination. Individuals aged ≥ 5 years will be eligible for inclusion in the unexposed cohort if they have a healthcare encounter (outpatient physician visit or receipt of a non-COVID-19 vaccine) from 27 August 2025 through 31 March 2026 and if they have continuous medical and pharmacy insurance coverage in the 365 days prior to their outpatient healthcare encounter. Individuals in the unexposed cohort will be matched to

those in the exposed cohort if their outpatient healthcare encounter is within the same 14-day calendar period as the exposed individual's vaccination date and if they are in the same age group. Individuals in the cohort analysis will be followed for up to 1 year.

Variables:

- *Exposures*: Exposures to the COMIRNATY 2025-2026 Formula and non-COVID vaccines will be defined by the presence of National Drug Codes (NDC) on pharmacy claims or Current Procedural Terminology (CPT) codes[1] on medical claims, while other healthcare encounters will be defined by the presence of CPT codes on medical claims.
- *Outcomes*: The pre-specified AESIs include the following: acute disseminated encephalomyelitis (ADEM), anaphylaxis, Bell's palsy, cerebral venous sinus thrombosis (CVST), convulsions/seizures (non-febrile), encephalitis/myelitis/encephalomyelitis (not ADEM or transverse myelitis [TM]), glomerulonephritis, Guillain-Barré syndrome, herpes zoster, immune-mediated myositis, immune thrombocytopenia, Kawasaki disease, multi inflammatory syndrome (in children and adults), multiple sclerosis (MS), myocardial infarction (MI), myocarditis/pericarditis, pulmonary embolism (PE), hemorrhagic stroke, ischemic stroke, subacute thyroiditis, and TM. All study outcomes will be identified through claims indicators using published validated claims-based algorithms with high performance when available.
- *Covariates*: Baseline covariates will include information related to patient demographics, comorbidities, prior COVID-19 and non-COVID-19 vaccinations, vaccination with non-COVID-19 vaccines on cohort entry date, healthcare utilization, and medication history. Additional baseline covariates will be identified on an empiric basis by examining the most frequently occurring diagnoses, drugs dispensed, and procedures performed among individuals with and without COMIRNATY 2025-2026 Formula exposure. Demographic attributes will be determined on the vaccination/cohort entry date, while other factors will be assessed in the 1 year prior to the vaccination date or cohort entry date.

Data sources: The patients included in this study will be drawn from the Optum Pre-Adjudicated Claims Databases for both the commercially insured population (the Optum Research Database [ORD]) and the Optum Medicare Advantage and Medicare Part D Database (MA-PD) for the interim report (Phase 1) and from the ORD and the MA-PD for the final report (Phases 1 and 2). The Optum Pre-Adjudicated Claims Databases for the ORD and the MA-PD include pre-adjudicated hospital and physician health insurance claims, supplemented with adjudicated pharmacy claims and health plan enrollment information. The individuals included in the pre-adjudicated databases are fully insured by their respective health plans, which provide reimbursement of medical and pharmacy services regardless of site of care. The ORD is a proprietary research database containing eligibility and adjudicated pharmacy and medical claims data from a large US health plan affiliated with Optum, and the MA-PD contains complete medical and pharmacy information for Medicare enrollees with Medicare Part D coverage. In 2023, data were available for

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approximately 11 million individuals with medical and pharmacy coverage in the ORD and for approximately 7.4 million individuals with medical and pharmacy coverage in the MA-PD.

Study size: The sample size achieved will depend on the number of recipients of the COMIRNATY 2025-2026 Formula in the databases. All individuals who meet the study's eligibility criteria during the study period will be included.

Data analysis:

Phase 1: For the SCRI design, the observed incidence rates of the pre-specified AESIs will be estimated in the risk window and the control window. Among individuals who experience an AESI in either the risk window or the control window (but not both), an exact conditional Poisson regression model with the natural logarithm of the person-time as the offset will be used to calculate the relative incidence (rate ratio) and corresponding 95% confidence interval (CI) of events occurring during the risk interval relative to the control period. The results from the SCRI utilizing the Optum Pre-Adjudicated Claims Databases will be presented in the interim report, while results utilizing the ORD and the MA-PD will be presented in the final report.

Phase 2: In the cohort study, propensity score-matched cohorts of COMIRNATY 2025-2026 Formula-vaccinated patients and comparator patients with no recorded COVID-19 vaccination will be created. Following the application of outcome-specific exclusions, the incidence rate of each AESI will be estimated among the COMIRNATY 2025-2026 Formula-exposed group and its matched comparator group. The rate ratio will be estimated using Poisson regression. Secondary analyses will be conducted among subgroups of individuals with prior SARS-CoV-2 infection, individuals with prior COVID-19 vaccination, individuals with administration of non-COVID-19 vaccines, children 5 to 17 years of age, adults 65 years of age and older, and individuals 5 years through 64 years of age with at least one underlying condition that puts them at high risk for severe outcomes of COVID-19, if sample size permits.

Milestones: The planned start of data collection for the interim report is 02 March 2026. The planned completion date for the interim report is 30 June 2026. The planned end of data collection for the study is September 2027, and the planned completion date for the final report is 28 February 2028.

4. AMENDMENTS AND UPDATES

Version Identifier	Date	Amendment Type (substantial or administrative)	Protocol Section(s) Changed	Summary of Amendment(s)	Reason
2.0	05 March 2026	Substantial	8.2.4, 8.3.2.	Extended the clean period to 365 days prior to vaccination for all AESIs	Improved exclusion of pre-existing conditions prior to vaccination and provides consistency across AESIs
2.0	05 March 2026	Substantial	8.3.2.	Expands the circumstances where medical records may be retrieved to include analyses beyond safety signals in the primary SCRI analysis in the interim report	Provides operational flexibility to obtain medical records in the final report or in analyses besides the primary SCRI analysis if a safety signal is detected or if estimates are approaching the safety signal threshold
2.0	05 March 2026	Substantial	8.3.3.4.	Expands the list of baseline covariates to include other non-COVID-19 vaccinations (besides the seasonal influenza and RSV vaccines) and number of vaccinations in the prior year	Improved adjustment for potential confounding by other vaccines given prior to the COMIRNATY 2025-2026 Formula
2.0	05 March 2026	Administrative	Title Page, 2, 3	Modified the investigator list	Change in Optum investigator

Version Identifier	Date	Amendment Type (substantial or administrative)	Protocol Section(s) Changed	Summary of Amendment(s)	Reason
2.0	05 March 2026	Administrative	Title Page	Added EU PAS register number	EU PAS register number is now available

5. MILESTONES

Milestone	Planned Date
Final study protocol	31 January 2026
Registration in the HMA-EMA Catalogues of RWD studies	Prior to the start of data collection
Start of data collection [a]	02 March 2026
Interim report [b]	30 June 2026
End of data collection [c]	16 September 2027
Final study report	28 February 2028

a For studies with secondary data collection, the start of data collection is defined as the planned date for starting data extraction for the purposes of the interim analysis.
b The milestone date was chosen to inform decision making for the next adapted vaccine before Fall 2026. To meet this milestone, the data extraction for the interim reporting will occur in March 2026.
c For studies with secondary data collection, the end of data collection is defined as the planned date on which the analytical dataset will be first completely available; the analytic dataset is the minimum set of data required to perform the statistical analysis for the final reporting.

6. RATIONALE AND BACKGROUND

The development of vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been critical to ending the coronavirus disease 2019 (COVID-19) pandemic. In the United States (US), the first vaccines to become available were the messenger RNA (mRNA) vaccines BNT162B2 (COMIRNATY) (Pfizer Inc/BioNTech, 2024) and mRNA-1273 (Moderna US, Inc., 2023). Authorized for emergency use by the US Food and Drug Administration (FDA) on 11 December 2020 and 18 December 2020, respectively, these first-generation vaccines contained a piece of the original SARS-CoV-2 virus's mRNA, instructing cells in the body to make the virus's distinctive "spike" protein and triggering an immune response (FDA, 2020a, 2020b; Nabizadeh et al., 2023). Beginning in August 2022, in response to the new circulating Omicron variant of SARS-CoV-2, the vaccines were adapted to add an mRNA component from the Omicron lineages BA.4 and BA.5, in addition to mRNA from the original viral strain, and were thereafter referred to as bivalent vaccines (FDA, 2022a, 2022b, 2022c). For the 2023-2024 season, a monovalent (single) mRNA component was used to target the Omicron XBB sublineage (COMIRNATY 2023-2024 Formula) (FDA, 2023). In August 2024, the COMIRNATY 2024-2025 Formula, which consisted of a monovalent mRNA component corresponding to the Omicron variant KP.2, was approved for individuals ≥ 12 years of age and authorized under emergency use in individuals 6 months through 11 years of age in the US (Pfizer Inc/BioNTech, 2024; FDA, 2024). Most recently, the COMIRNATY 2025-2026 Formula, a monovalent vaccine targeting the Omicron variant LP.8.1 (Pfizer Inc/BioNTech, 2025), was approved on 27 August 2025 for use in individuals age 65 years and older or 5 years through 64 years of age with at least one underlying condition that puts them at high risk for severe outcomes from COVID-19 (FDA, 2025).

The US prescribing information for COMIRNATY highlights the following warning and precaution:

- "Analyses of postmarketing data from use of authorized or approved mRNA COVID-19 vaccines, including COMIRNATY, have demonstrated increased risks of myocarditis and pericarditis, with onset of symptoms typically in the first week following vaccination. The observed risk has been highest in males 12 years through 24 years of age" (Pfizer Inc/BioNTech, 2025).

More information is needed on whether the safety profile of the COMIRNATY 2025-2026 Formula remains consistent with the safety profile of the original formula in the overall population and subpopulations of interest.

Pfizer/BioNTech, sponsor of the first COVID-19 vaccine to be authorized in the US, is conducting a non-interventional post-authorization safety study (PASS) to collect information on the safety profile of its most recently authorized strain of the COVID-19 vaccine, the Omicron LP.8.1 monovalent vaccine (COMIRNATY 2025-2026 Formula; Pfizer Inc/BioNTech, 2025). This combined protocol and statistical analysis plan (SAP) describes a non-interventional observational study using claims data from two databases of a large US insurer to evaluate the safety of the COMIRNATY 2025-2026 Formula in the general

population as well as in subpopulations of interest. This non-interventional study is designated as a PASS and is being conducted voluntarily by Pfizer.

7. RESEARCH QUESTION AND OBJECTIVES

Research question: What is the incidence of pre-specified adverse events of special interest (AESIs) among individuals who receive the COMIRNATY 2025-2026 Formula in the United States?

The study will be conducted in two phases, each with its own specific objectives.

7.1. Phase I

Phase 1 will be designed to sequentially monitor the occurrence of pre-specified AESIs in near real-time following vaccination.

7.1.1. Primary Objective

To estimate the incidence of pre-specified AESIs in a risk window following vaccination with the COMIRNATY 2025-2026 Formula compared to the incidence of these events during a control window (ie, expected rates of these events).

7.2. Phase II

Phase 2 will be designed to compare the incidence of pre-specified AESIs for up to 1 year among individuals who receive the COMIRNATY 2025-2026 Formula to individuals with no recorded COVID-19 vaccination.

7.2.1. Primary Objective

To estimate the incidence of pre-specified AESIs among individuals who receive the COMIRNATY 2025-2026 Formula compared to the incidence among individuals with no recorded COVID-19 vaccination.

7.2.2. Secondary Objective

To estimate the incidence of pre-specified AESIs among individuals who receive the COMIRNATY 2025-2026 Formula compared to the incidence among individuals with no recorded COVID-10 vaccination within subgroups of individuals with prior SARS-CoV-2 infection; individuals with prior COVID-19 vaccination; individuals with administration of non-COVID-19 vaccines; children 5 through 17 years of age; adults 65 years of age and older; and individuals 5 years through 64 years of age with at least one underlying condition that puts them at high risk for severe outcomes from COVID-19, if sample size permits.

8. RESEARCH METHODS

8.1. Study Design

This non-interventional study will be conducted in two phases. Phase 1 will include a study of self-controlled risk interval (SCRI) design conducted using pre-adjudicated claims databases for the interim report. For the final report, the SCRI study will be repeated using

the Optum Research Database (ORD) and the Medicare Advantage and Medicare Part D Database (MA-PD), which are adjudicated claims databases. Phase 2 will be a comparative safety cohort design using the ORD and the MA-PD and will also be included in the final report.

Table 1 summarizes the study designs and data sources included in the interim and final reports. These two different study designs are complementary, each with its own strengths. The SCRI design is better suited for assessing acute endpoints and is less impacted by misclassification of COVID-19 vaccine exposure and confounding by time-fixed characteristics, while the cohort study design enables a longer follow-up period.

Table 1. Study design and data sources for interim and final reporting

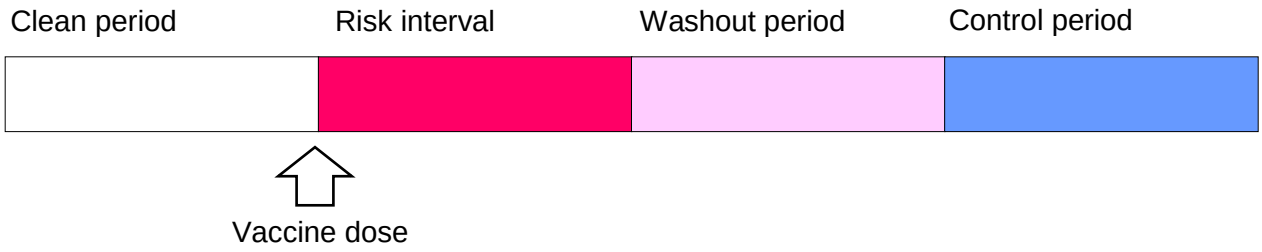
	Interim Report	**Final Report**
Study Design	SCRI, Phase 1 (Section 8.1.1)	SCRI, Phase 1 (Section 8.1.1) Cohort, Phase 2 (Section 8.1.2)
Data Source	Optum Pre-Adjudicated Claims Databases (Section 8.4.1)	ORD (adjudicated) (Section 8.4.2) and MA-PD (adjudicated) (Section 8.4.3)

8.1.1. SCRI

Phase 1 will monitor the incidence rate of pre-specified AESIs in a general population of individuals who receive the COMIRNATY 2025-2026 Formula using an SCRI study design that tracks post-vaccination risk intervals and control (reference) periods for each vaccinated individual. For the interim report, individuals who receive the COMIRNATY 2025-2026 Formula from 27 August 2025 through early March 2026 will be included in the SCRI study. This will be the latest date of data capture that allows for the interim results to inform decision-making for the 2026-2027 season and will likely capture most COMIRNATY vaccinations from the 2025-2026 season. For the final report, individuals who receive the COMIRNATY 2025-2026 Formula from 27 August 2025 through 31 March 2026 will be included. Monitoring will be conducted during a pre-specified risk interval immediately following vaccination, and the observed rate of events during this risk interval will be compared to that of a control period temporally removed from the vaccination event; this approach has also used in vaccine research conducted by the FDA's Biologics Effectiveness and Safety (BEST) Initiative (CBER, 2022). Only individuals who receive the COMIRNATY 2025-2026 Formula, experience a safety outcome of interest during a risk or control period, and do not experience the safety event of interest during the clean period prior to vaccination will be included in the SCRI study (Baker et al., 2015). Figure 1 depicts the periods included in the SCRI design. Within each individual, outcomes occurring during the risk interval will be compared with those occurring during the control period, in order to determine whether these outcomes occur more frequently immediately after vaccination as compared with a reference period. A washout period will be inserted between the risk

interval and the control period to ensure that events relating to the vaccine are not incorrectly attributed to the control period. To ensure that observed outcomes are truly incident, a period free from the outcome of interest (clean period) will be required prior to vaccination.

Figure 1. Self-controlled risk interval design



Follow-up will be censored at the time of receipt of a second dose of the COMIRNATY 2025-2026 Formula (Section 8.2.5.1); only the first eligible dose will contribute to the analysis.

The AESIs, along with relevant clean windows, risk intervals, and washout and control periods, are listed in Section 8.3.2.

8.1.2. Cohort Design

Phase 2 will consist of a propensity score-matched cohort study of individuals with a recorded dose of the COMIRNATY 2025-2026 Formula or with a non-COVID-19 vaccination or other qualifying healthcare encounter, conducted within the ORD and the MA-PD. During the accrual period of 27 August 2025 through 31 March 2026, individuals who receive the COMIRNATY 2025-2026 Formula will be classified as exposed, and those with no recorded COVID-19 vaccination but who have a healthcare encounter (an outpatient visit or a non-COVID-19 vaccination) will be classified as comparators. Propensity score matching will be performed to control for potential confounding, with matching to be conducted within age group and calendar periods. Age group will be defined as: 5–11 years; 12–17 years; 18–64 years; and ≥ 65 years, while calendar periods will be defined by 14-day increments (eg, 27 August 2025 to 9 September 2025, 10 September 2025 to 24 September 2025), if feasible. Alternate age groups (eg, 5–17 years) and/or calendar periods (eg, 1 month) may be utilized. Therefore, within any given calendar period, comparators of the same age group will be matched to a COMIRNATY recipient on propensity score, without replacement, down to a maximum allowable level of precision (Section 8.7.2.1).

These matched cohorts will be followed for up to 1 year for occurrence of safety outcomes (Section 8.2.5.2). The AESIs are listed in Section 8.3.2.

8.2. Setting

The source population for this study will consist of all individuals with at least one medical or pharmacy claim from 27 August 2025 (the date of product approval) through 31 March 2026. The end date of 31 March 2026 was chosen based on the assumption that the timing of

vaccine uptake will be similar to the timing of uptake in previous vaccine seasons (Sun et al., 2024). During prior COVID-19 seasons, the end of March reflected the time when uptake of the COVID-19 vaccine was no longer increasing (ie, most individuals who received the COVID-19 vaccine had done so prior to March) (CDC, 2025b), and COVID-19 cases declined substantially from their fall/winter peak (CDC, 2025a).

Each study design will have its own inclusion and exclusion criteria, as listed below.

8.2.1. SCRI

8.2.1.1. Inclusion Criteria

Patients must meet all of the following inclusion criteria to be eligible for inclusion in Phase I of the study:

1. Receive at least one dose of the COMIRNATY 2025-2026 Formula from 27 August 2025 (the date of the COMIRNATY 2025-2026 US approval for marketed use) through 31 March 2026.

2. Aged ≥ 5 years when receiving their first recorded dose of the COMIRNATY 2025-2026 Formula.

3. Have continuous medical and pharmacy insurance coverage in the 365 days prior to their vaccination date (as defined in Section 8.2.3).

4. Experience a safety outcome of interest during a risk interval or control period (on or after vaccination, as defined in Section 8.3.2).

5. Do not experience the safety outcome of interest during the clean period (prior to vaccination, as defined in Section 8.3.2).

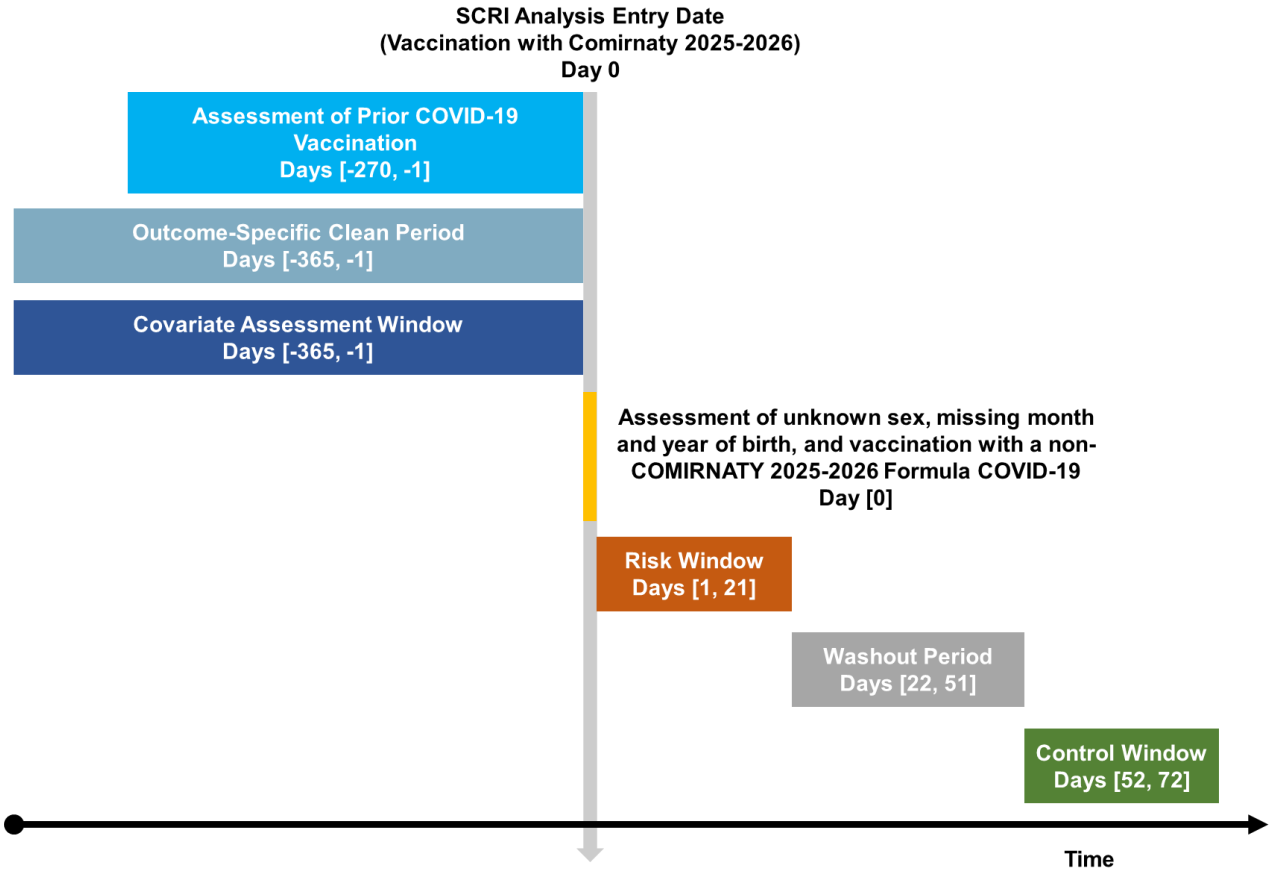
8.2.1.2. Exclusion Criteria

Patients meeting any of the following criteria will not be included in Phase 1 of the study:

1. Are of unknown sex.
2. Have a missing month and year of birth.
3. Have received any COVID-19 vaccine in the 270 days prior to the COMIRNATY 2025-2026 Formula vaccination date (as defined in Section 8.2.3).
4. Have received a COVID-19 vaccine other than the COMIRNATY 2025-2026 Formula on the COMIRNATY 2025-2026 Formula vaccination date (defined in Section 8.2.3).

Figure 2 depicts the SCRI study design using the outcome of myocarditis/pericarditis, using the clean periods and risk intervals as shown in Table 2, as an example.

Figure 2. Self-controlled risk interval design for AESI of myocarditis/pericarditis



8.2.2. Cohort Study

8.2.2.1. Inclusion Criteria

Patients must meet all of the following criteria to be eligible for inclusion in Phase 2 of the study:

1. Aged ≥ 5 years on the day of receiving their first recorded dose of the COMIRNATY 2025-2026 Formula (if a vaccine recipient), or on the day they experience a qualifying healthcare encounter (if a comparator), defined as the cohort entry date (Section 8.2.3).
2. Have continuous medical and pharmacy insurance coverage in the 365 days prior to the cohort entry date.

8.2.2.2. Exclusion Criteria

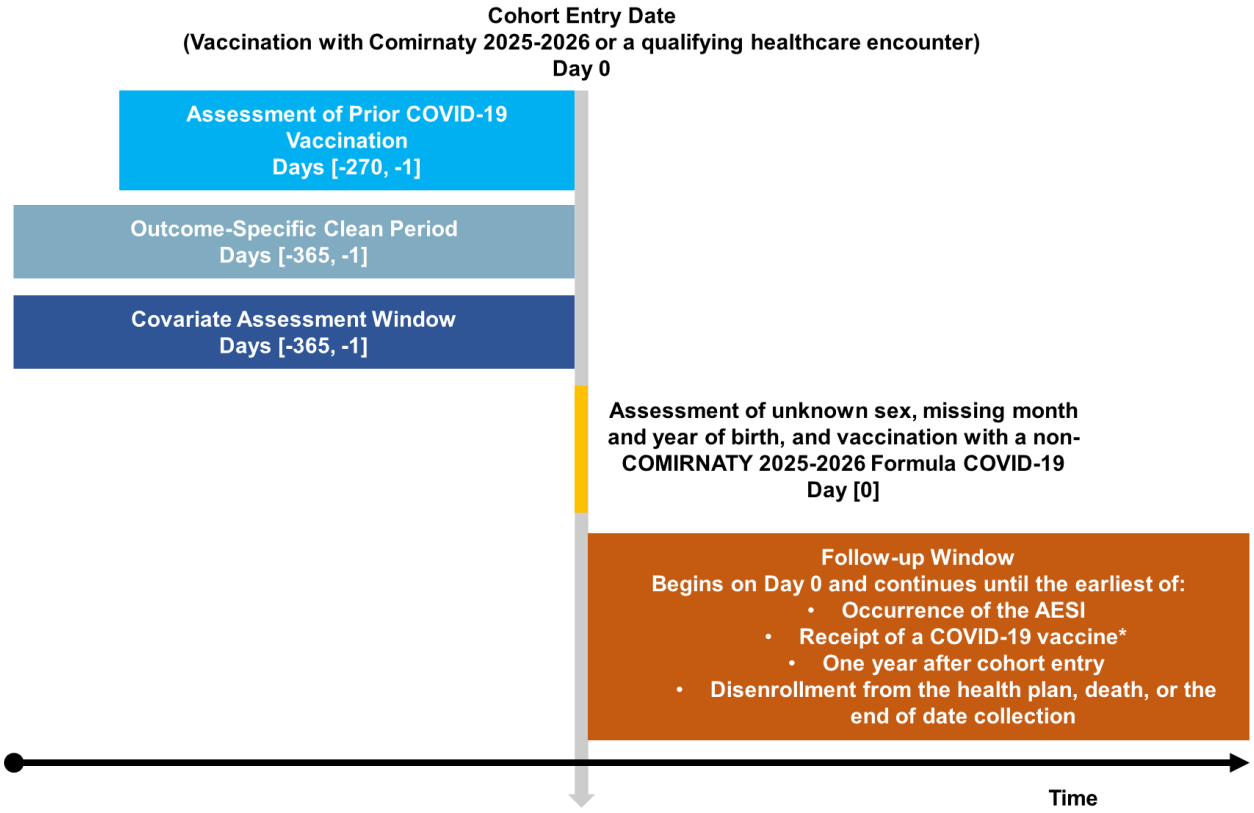
Patients meeting any of the following criteria will not be included in Phase 2 of the study:

1. Are of unknown sex.
2. Have a missing month and year of birth.

3. Have received any COVID-19 vaccine in the 270 days prior to cohort entry date (as defined in Section 8.2.3).
4. Have received both the COMIRNATY 2025-2026 Formula and a COVID-19 vaccine other than the COMIRNATY 2025-2026 Formula on the cohort entry date (defined in Section 8.2.3).

In both phases of the study, when creating the analytic population for each specific safety outcome of interest, individuals will be excluded if they experienced that safety outcome during the portion of the baseline period designated as the clean period (Section 8.2.4). Figure 3 depicts the cohort study design using the outcome of myocarditis/pericarditis, using the clean periods as shown in Table 2, as an example.

Figure 3. Cohort study design for AESI of myocarditis/pericarditis



* Receipt of a COVID-19 vaccine other than the COMIRNATY 2025-2026 Formula will censor follow-up. For COMIRNATY 2025-2026 Formula recipients, receipt of subsequent dose(s) of COMIRNATY 2025-2026 Formula will not censor follows-up. For comparators, receipt of COMIRNATY 2025-2026 Formula will censor follow-up in the comparator cohort; the patient may then be eligible for inclusion in the exposed cohort.

8.2.3. Vaccination Date and Cohort Entry Date

In the Phase 1 SCRI analysis, the date of first vaccination with the COMIRNATY 2025-2026 Formula will be set as the vaccination date.

In the Phase 2 cohort analysis, the cohort entry date will be the date individuals in the COMIRNATY group receive their first recorded dose of the COMIRNATY 2025-2026 Formula. For individuals in the comparator cohort, the cohort entry date will be set as the date of first qualifying healthcare encounter, as defined by an outpatient visit or receipt of a non-COVID-19 vaccine (Section 8.3.1.2).

8.2.4. Baseline Period

The baseline period will consist of all continuously enrolled available time up to 1 year (365 days) prior to the vaccination date (SCRI) or cohort entry date (cohort study). Recognizing that narrower or specific windows of assessment may better capture select patient attributes of interest, specific covariates may be assessed using alternate time period(s). In this study, all individuals are required to have a minimum of 365 days of continuous health plan enrollment prior to the vaccination or cohort entry date (Sections 8.2.1.1 and 8.2.2.1).

In both study designs, the baseline period will be used to exclude individuals with prevalent outcomes prior to vaccination or cohort entry date. This portion of the baseline period will be referred to as the 'clean period.' For a list of outcome-specific clean periods, which are the same for both the SCRI and the cohort study, please see Section 8.3.2.

8.2.5. Follow-Up Period

8.2.5.1. SCRI

In the SCRI analysis, follow-up for the risk interval will begin upon (for the outcomes of anaphylaxis and convulsions/seizures) or one day after (for all other outcomes) receipt of the COMIRNATY 2025-2026 Formula (Table 2) and continue until the earliest of:

- Receipt of a subsequent COVID-19 vaccine;
- The end of the outcome-specific risk interval as defined in Section 8.3.2;
- Disenrollment from the health plan, death, or the end of data collection (31 March 2027).

After the outcome-specific pre-specified washout period following the risk interval, follow-up for the control period will begin and continue until the earliest of:

- Receipt of a subsequent COVID-19 vaccine;
- The end of the control period as defined in Section 8.3.2;
- Disenrollment from the health plan, death, or the end of data collection.

Individuals will be followed for each safety outcome during both the risk and control periods, such that events observed during the risk interval or washout period will not censor follow-up for the control period.

8.2.5.2. Cohort Study

In the cohort study (Phase 2), depending on the safety outcome of interest, follow-up will begin on cohort entry (for the outcomes of anaphylaxis and convulsions/seizures) or the day following cohort entry (for all other outcomes) and extend until the earliest of:

- The occurrence of an outcome of interest (Section 8.3.2);
- For COMIRNATY 2025-2026 Formula recipients, receipt of a COVID-19 vaccine other than the COMIRNATY 2025-2026 Formula; for comparators, receipt of any COVID-19 vaccine;
- One year after cohort entry;
- Disenrollment from the health plan, death, or the end of data collection;

Comparators who later receive a dose of COMIRNATY 2025-2026 Formula will be eligible for inclusion in the COMIRNATY 2025-2026 Formula cohort if they meet the eligibility criteria for cohort entry.

8.3. Variables

8.3.1. Exposures

8.3.1.1. COMIRNATY 2025-2026 Formula

The SCRI analysis and the cohort analysis will include individuals with exposure to the COMIRNATY 2025-2026 Formula. The code list to define exposure is available in Annex 2 (Appendix I).

8.3.1.2. Comparator Cohort

The Phase 2 cohort study will include comparators with no recorded COVID-19 vaccination. To improve comparability with the COMIRNATY 2025-2026 Formula vaccinated cohort, patients included in the comparator cohort will be required to have a code indicative of an outpatient healthcare encounter, including one of the following:

- Presence of a code for a non-COVID-19 vaccine;
- Presence of a code indicative of an outpatient physician visit.

Codes relating to other vaccines or outpatient visits are provided in Annex 2 (Appendix II).

8.3.2. Outcomes

In both the SCRI and cohort studies, the pre-specified AESIs will include the following:

- Acute disseminated encephalomyelitis (ADEM)
- Anaphylaxis
- Bell's palsy
- Cerebral venous sinus thrombosis (CVST)
- Convulsions/seizures (non-febrile)
- Encephalitis/myelitis/encephalomyelitis [not ADEM or transverse myelitis (TM)]
- Glomerulonephritis
- Guillain-Barré syndrome
- Herpes zoster
- Immune-mediated myositis
- Immune thrombocytopenia
- Kawasaki disease
- Multi inflammatory syndrome (in children and adults)
- Multiple sclerosis (MS)*
- Myocardial infarction (MI)
- Myocarditis/pericarditis
- Pulmonary embolism (PE)
- Stroke, hemorrhagic
- Stroke, ischemic
- Subacute thyroiditis
- Transverse myelitis (TM)

*The cohort analysis will include MS, but the AESI will be excluded from the SCRI analysis due to its chronic nature.

Code lists for the safety outcomes of interest are provided in Annex 2 (Appendix III). Corresponding site of care requirements for both the SCRI and cohort analysis are listed in Table 2. When possible, outcomes will be defined using a validated claims-based algorithm with high performance (CBER, 2021).

If a safety signal is detected in the interim report, medical records may be retrieved for a subset of participants to confirm the presence of that study outcome. A safety signal that requires confirmation through medical record review will be defined as a rate ratio of > 3.0

and a corresponding P value of < 0.01 in the primary analysis of the SCRI design (details in Section 8.7.1.). Additionally, medical record review may be conducted for analyses beyond the primary SCRI analysis if a safety signal (defined as a rate ratio of > 3.0 and a corresponding P value of < 0.01) is detected in the interim or final report. Medical records may also be retrieved for AESIs with estimates approaching the pre-specified safety signal threshold.

Table 2. Clean periods and risk intervals for safety outcomes of interest

Outcome	Clean Period*	Vaccine Risk Interval*	Care Setting
ADEM	Days -365 to -1	Days 0 to 21	IP
Anaphylaxis	Days -365 to -1	Days 0 to 1	IP, ED
Bell's palsy	Days -365 to 0	Days 1 to 42	IP, OP
CVST	Days -365 to 0	Days 1 to 28	IP, OP
Convulsions/seizures, non-febrile	Days -365 to -1	Days 0 to 21	IP, OP
Encephalitis/myelitis/encephalomyelitis (not ADEM or TM)	Days -365 to 0	Days 1 to 42	IP
Glomerulonephritis	Days -365 to 0**	Days 1 to 42**	IP, OP
Guillain-Barré syndrome	Days -365 to 0	Days 1 to 42	IP-primary position only
Herpes zoster	Days -365 to 0	Days 1 to 30	IP, OP
Immune-mediated myositis	Days -365 to 0**	Days 1 to 28	IP, OP
Immune thrombocytopenia	Days -365 to 0	Days 1 to 42	IP, OP
Kawasaki disease	Days -365 to 0	Days 1 to 21	IP, OP
Multi inflammatory syndrome	Days -365 to 0	Days 1 to 42	IP, ED
MS (cohort study only)	Days -365 to 0	NA	IP, OP
MI	Days -365 to 0	Days 1 to 28	IP
Myocarditis/pericarditis	Days -365 to 0	Days 1 to 21	IP, OP
PE	Days -365 to 0	Days 1 to 28	IP, OP
Stroke, hemorrhagic	Days -365 to 0	Days 1 to 28	IP
Stroke, ischemic	Days -365 to 0	Days 1 to 28	IP
Subacute thyroiditis	Days -365 to 0	Days 1 to 42**	IP, ED
TM	Days -365 to 0	Days 1 to 42	IP, ED

*Expressed in relation to the day of vaccination or cohort entry (Day 0). When more than one vaccine risk interval had been cited in the prior literature, the present risk interval was chosen from the literature using the following order of priority for all outcomes other than myocarditis/pericarditis: 1) CBER 2021; 2) the most frequently cited risk interval in prior literature; and 3) the shortest risk interval cited in prior literature. The risk interval for myocarditis/pericarditis was chosen based on CBER 2022.
**Could not be determined from the literature, so modeled after other outcome intervals in CBER 2021.
ADEM, acute disseminated encephalomyelitis; IP, inpatient; CVST, cerebral venous sinus thrombosis; ED, emergency department visit; MI, myocardial infarction; MS, multiple sclerosis; NA, not applicable; OP, outpatient facility claims and professional/provider claims; PE, pulmonary embolism; TM, transverse myelitis.

8.3.2.1. Outcome-Specific Risk and Control Periods

The SCRI design (Section 8.2.1) requires that clean periods, risk intervals, washout periods, and control intervals be specified for every study outcome. The lengths of the clean periods and risk intervals are listed in Table 2. The washout period for all outcomes will begin

immediately after the end of the risk interval and continue for 30 days (Akpandak et al., 2022); the control period will follow the washout period and be equivalent in length to the risk interval. Interval lengths were determined based on prior vaccine literature, including COVID-19 vaccine studies conducted as part of the FDA's Center for Biologics Evaluation and Research (CBER) BEST System, as available (Akpandak et al., 2022; Barda et al., 2021; CBER, 2021; Joy et al., 2023; Klein et al., 2021; Liu et al., 2023; Martin et al., 2021; McCarthy et al., 2013; Wack et al., 2021).

8.3.3. Covariates

All individuals included in the SCRI and cohort analyses will be described according to covariates identified in the claims data. Demographic attributes will be determined on the vaccination/cohort entry date, while other factors will be assessed during the 1-year baseline period prior to the cohort entry date. Unless specified as being for descriptive purposes only, the covariates listed will be included in the propensity score models. Code lists for the covariates can be found in Appendix IV.

8.3.3.1. Demographic Attributes

- Sex
- Age (in years); for the purposes of matching the exposed and unexposed cohorts in Phase 2, the following age groups will be used, if feasible: 5–11 years, 12–17 years, 18–64 years, and ≥ 65 years
- Calendar month of the vaccination date or cohort entry date
- Geographic region

8.3.3.2. Comorbidities

- Asthma
- Non-malignant blood disorders, including sickle cell disease
- Chronic lung disease, including chronic obstructive pulmonary disease (COPD)
- Down syndrome
- Heart disease
- History of SARS-CoV-2 infection
- Hypertension
- Immunocompromised status (ie, history of human immunodeficiency virus [HIV]; organ, bone marrow or stem cell transplant; use of immunosuppressant medication)
- Kidney disorders, including chronic kidney disease
- Liver disorders
- Long COVID-19
- Neurological or neurodevelopmental conditions
- Malignant neoplasms
- Obesity
- Type 2 diabetes
- Binary indicator for the presence of at least one underlying condition conferring high risk of severe outcomes from COVID-19 (CDC, 2025c)
    - Asthma

- Cancer
- Cerebrovascular disease
- Chronic kidney disease
- Chronic lung disease, limited to bronchiectasis, chronic obstructive pulmonary disease (COPD), interstitial lung disease, pulmonary embolism, and pulmonary hypertension
- Chronic liver disorders, limited to cirrhosis, non-alcoholic fatty liver disease, alcoholic liver disease, and autoimmune hepatitis
- Cystic fibrosis
- Diabetes mellitus, type 1
- Diabetes mellitus, type 2
- Disabilities, including Down syndrome
- Heart conditions
- Human immunodeficiency virus (HIV)
- Mental health conditions, limited to mood disorders, including depression; and schizophrenia spectrum disorders
- Neurologic conditions, limited to dementia and Parkinson's disease
- Obesity (defined as body mass index [BMI] of ≥ 30 kg/m^2 in adults or ≥ 95^{th} percentile in children)
- Physical inactivity
- Pregnancy and recent pregnancy
- Primary immunodeficiencies
- Smoking, current and former
- Solid organ or blood stem cell transplantation
- Tuberculosis
- Use of corticosteroids or other immunosuppressive medications

8.3.3.3. Healthcare Utilization

- Number of hospitalizations in prior year
- Number of emergency room visits in prior year
- Number of outpatient encounters in prior year
- Number of non-COVID-19 vaccinations in the prior year

8.3.3.4. Medication and Vaccination History

- Systemic immunomodulators
- Oral corticosteroids
- Antivirals
- Antibiotics
- Recorded vaccines administered in prior year
  - Seasonal influenza
  - Respiratory syncytial virus (RSV)
  - Any other non-COVID-19 vaccine (besides seasonal influenza and RSV)
- Non-COVID-19 vaccinations received on day of cohort entry
  - Seasonal influenza
  - RSV

In addition to the covariates listed above, baseline attributes will be identified on an empiric basis by examining the 25 most frequently occurring diagnoses, drugs dispensed, and procedures performed among individuals with and without COMIRNATY 2025-2026 Formula exposure. These empiric covariates will be considered for inclusion in the PS models if they are potential confounders.

8.3.3.5. Descriptive only (not for inclusion in PS model)

- Current COVID-19 vaccination
  - Site of vaccination (eg, outpatient, pharmacy)
  - Source of vaccination information (eg, Current Procedural Terminology [CPT] code, NDC
  - Average number of days between doses of COMIRNATY 2025-2026 Formula, among those with multiple doses
- Prior COVID-19 vaccination
  - COVID-19 vaccine (any brand) during the baseline period
  - Days from the most recent prior COVID-19 vaccine dose (any brand) to first vaccination with 2025-2026 formulations (for all Phase 1 individuals, as well as for Phase 2 individuals receiving COMIRNATY or another 2025-2026 formulation)

8.4. Data Sources

The patients included in this study will be drawn from the Optum Pre-Adjudicated Claims Databases for the interim reporting to expedite the identification of vaccinated patients and AESIs, and from the ORD and the MA-PD for the final reporting. These data sources are described below.

8.4.1. Optum Pre-Adjudicated Claims Databases

The databases include pre-adjudicated medical claims from both the ORD and the MA-PD (which are described below), supplemented with adjudicated pharmacy claims and health plan enrollment information. As claims for pharmacy services are typically submitted electronically by the pharmacy at the time prescriptions are filled or vaccinations are administered and are updated in the underlying database on a weekly basis, they are not included in the pre-adjudicated feed. The pre-adjudicated medical claims encompass hospital and physician claims that are submitted and processed daily from a large US commercial health plan and affiliated Medicare Advantage plans. The individuals included in the pre-adjudicated medical claims databases are fully insured by their respective health plan, which provides reimbursement of medical and pharmacy services regardless of site of care, and individuals are geographically diverse within the US. The claims adjudication process involves numerous assessments and adjustments and may result in claims being returned to the provider for revision or sent for payment processing. The pre-adjudicated claims are maintained in databases that allow for the capture of up to three years of prior data, with an average lag time of four weeks from the time of service until the claims are available in the database. These pre-adjudicated claims have been used for research previously, and for federally funded public health surveillance (Dore et al., 2012; FDA, 2021a; Moll et al., 2023; Schneider et al., 2023).

The data include demographics, details from pharmacy claims (reflecting dispensings), and all pre-adjudicated medical and facility claims, including information on the types of services or procedures and their accompanying diagnoses. The coding of medical claims conforms to insurance industry standards, including:

- Use of designated claims forms (eg, physicians use the CMS-1500 format and hospitals use the UB-04 format)
- International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) diagnosis codes
- CPT-4® codes
- Centers for Medicare and Medicaid Services (CMS) Healthcare Common Procedure Coding System (HCPCS) codes

Claims for pharmacy services are typically submitted electronically by the pharmacy at the time prescriptions are filled. These data allow for longitudinal tracking of medication refill patterns and changes in medications and include:

- NDC
- Drug name
- Dosage form
- Drug strength
- Fill date
- Days of supply
- Cost information
- De-identified patient and prescriber codes

8.4.2. Optum Research Database

The ORD is a proprietary research database containing eligibility and adjudicated pharmacy and medical claims data from a large US health plan affiliated with Optum. The individuals covered by this health plan are geographically diverse across the US. As early as 1993, medical and pharmacy claims data are available for 65 million individuals with both medical and pharmacy benefit coverage. In 2023, data were available for approximately 11 million individuals with medical and pharmacy coverage. Optum research activities use de-identified data from the research database. In limited instances, patient identifiers may be accessed where applicable law allows the use of patient-identifiable data, and when the study obtains appropriate approvals for accessing data that are not de-identified.

8.4.3. Medicare Advantage and Medicare Part D Data

Beginning in 2006, complete medical and pharmacy information is available for Medicare enrollees with medical and Medicare Part D coverage. The pharmacy claims contain sufficient information to trace patients' pharmacy expenditures through the multiple phases of the Medicare Part D plans. For example, for 2023, data is available for approximately 7.4 million individuals with both medical and pharmacy benefit coverage. Underlying information is geographically diverse across the country and is representative of the U.S.

Medicare Advantage population. Optum research activities use de-identified data from the MA-PD. In limited instances, patient identifiers may be accessed where applicable law allows the use of patient-identifiable data, and when the study obtains appropriate approvals for accessing data that are not de-identified.

8.5. Study Size

The sample size achieved will depend on the number of recipients of the COMIRNATY 2025-2026 Formula in the databases. All individuals who meet the study's eligibility criteria during the study period will be included.

8.6. Data Management

All analyses will be conducted using Statistical Analysis System (SAS) version 9.4 (SAS Institute Inc., Cary, North Carolina) and SAS Enterprise Guide 6.1 or later. The data will be extracted once per report. All reports will utilize the structured data only. The interim report will include summarized results from the Optum Pre-Adjudicated Claims Databases described in Section 8.4.1. The final report will include results summarized from the ORD and the MA-PD as described in Section 8.4.2 and Section 8.4.3, respectively. The characteristics of patients to be included in each data extract (eg, required vaccine codes) and the specific timeframes of each data extract will reflect the study inclusion/exclusion criteria described in Section 8.2, the baseline and follow-up periods in Section 8.2.4 and Section 8.2.5, respectively, and the study variables in Section 8.3. All reports and deliverables will contain aggregated results only and will not identify individual patients, physicians, or facilities.

8.7. Data Analysis

Results for both the SCRI and the cohort study will be presented separately by data source.

8.7.1. SCRI

Descriptive statistics will be used to summarize the baseline characteristics (see Section 8.3.3) of those who receive the COMIRNATY 2025-2026 Formula. Counts of each safety outcome of interest will be reported within pre-specified risk and control windows. The observed incidence rates of the pre-specified AESIs will be estimated in the risk window and the control window. Among the individuals who experience an AESI in either the risk window or the control window (but not both), an exact conditional Poisson regression model with the natural logarithm of the person-time as the offset will be used to calculate the relative incidence (rate ratio) and corresponding 95% confidence interval (CI) of events occurring during the risk interval relative to the control period. With the self-controlled design, whereby each individual serves as their own comparator, this unadjusted analysis accounts for the factors that vary across but not within individuals (ie, time-invariant covariates).

Among individuals receiving seasonal influenza vaccine in the 2025-2026 season (01 August 2025 through 31 March 2026), the following subgroup analysis will be presented: 1) receipt of seasonal influenza vaccination from 30 days prior to the COMIRNATY 2025-2026 Formula vaccination through the day before the COMIRNATY 2025-2026 Formula vaccination, and 2) receipt of seasonal influenza vaccination on the same day as

the COMIRNATY 2025-2026 Formula vaccination. Additionally, subgroup analyses will be conducted among children aged 5 to 17 years and among adults 65 years of age and older for AESIs with at least 5 events in either the risk or control window, separately by data source. Finally, a subgroup analysis will be conducted among individuals 5 years through 64 years of age with at least one underlying condition that puts them at high risk for severe outcomes from COVID-19.

The results from the SCRI utilizing the Optum Pre-Adjudicated Claims Databases will be presented in the interim report, while results from the SCRI utilizing the ORD and the MA-PD will be presented in the final report.

8.7.2. Cohort Study

8.7.2.1. Propensity Score Modeling and Matching

The COMIRNATY 2025-2026 Formula-exposed and unexposed comparator cohorts will be created as described in Section 8.2.2. Each cohort member will be described with respect to baseline covariates as listed in Section 8.3.3. These cohort members will be included in the propensity score modelling and matching.

Propensity score-matched comparators will be matched on age group and calendar time. Regarding age, matching will be performed between patients within age groups (eg, 5–11 years, 12–17 years, 18–64 years, and ≥ 65 years). Regarding calendar time, patients will be matched within 14-day windows (eg, 27 August 2025 to 9 September 2025, 10 September 2025 to 24 September 2025) in which individuals in the exposed cohort will have received vaccination with the COMIRNATY 2025-2026 Formula and individuals in the unexposed cohort will have had a qualifying healthcare encounter but no recorded COVID-19 vaccination. Alternate calendar periods (eg, one month) may be empirically explored. For matched comparators, the cohort entry date will be the date within the matched 14-day calendar period on which they had the qualifying healthcare encounter.

This study will use a single propensity score model that encompasses risk factors for multiple outcomes, an approach demonstrated in other studies conducted to fulfill post-licensure regulatory commitments and requirements to the FDA and other regulatory agencies (Seeger et al., 2023; Ziyadeh et al., 2020). While not all risk factors may be associated with all outcomes to the same degree, adjusting for covariates that are weakly or not at all associated with a given outcome is expected to result in negligible bias if residual confounding is small (Brookhart et al., 2006; Myers et al., 2011). Incorporating a wide array of outcome predictors (Section 8.3.3) into the propensity score is expected to minimize residual confounding, producing groups with similar patterns of both measured and unmeasured factors (Guertin et al., 2016).
The propensity score model will incorporate the pre-specified demographic and comorbidity covariates, healthcare utilization, and calendar period as independent variables (see Section 8.3.3), and an indicator for receipt of the COMIRNATY 2025-2026 Formula as the dependent variable. Two-way interactions of all variables with calendar period, or empirically defined variables that are potential confounders, may also be considered for inclusion in the model.

A greedy digit-based matching algorithm will be used, in which patients exposed to the COMIRNATY 2025-2026 Formula are matched without replacement to comparator patients at a given level of precision defined by the number of digits of the propensity score, within strata defined by age group and calendar period (Parsons, 2001). When no further matches are available at a given level of precision, the number of digits is sequentially reduced until a maximum allowable caliper of 0.1 is reached, thereby ensuring that the matched cohorts are comparable with respect to the underlying measured risk factors. A matching ratio (eg, up to 1:10) may be implemented.

Propensity score matching will produce a single matched cohort (the master cohort) that will be used to conduct all primary, secondary, and subgroup analyses for the study outcomes. Balance between the propensity score-matched cohorts will be evaluated by overlaying graphs of the propensity score distributions in COMIRNATY-exposed and comparator cohorts before and after propensity score matching. Additionally, standardized differences between the propensity score-matched cohorts for each covariate in the model will also be assessed. Variables with an absolute standardized difference less than 0.1 will be considered balanced (Austin, 2009). If a variable has an absolute standardized difference that is greater than 0.1, further propensity score model modifications (eg, addition of interaction terms) or inclusion of the imbalanced covariates in an outcome model will be considered (Normand et al., 2001). If there are confounders identified that would only be appropriate to include for one outcome and not the others, a separate propensity score model for the specific outcome will be considered.

8.7.2.2. Primary Analysis

Once the matched cohorts have been created, outcome-specific exclusion criteria will be applied to the master cohort before the outcome-specific analysis; the matched cohort that remains will be the analytic cohort for that specific outcome. If a COMIRNATY 2025-2026 Formula-exposed individual is excluded due to outcome-specific exclusion criteria, all of their matched comparators will also be excluded from the outcome-specific analysis. Conversely, if all matched comparators of a COMIRNATY 2025-2026 Formula recipient are excluded due to outcome-specific exclusion criteria, the COMIRNATY 2025-2026 Formula recipient will also be excluded from the outcome-specific analysis.

Incidence rate of each safety outcome will be estimated among the remaining COMIRNATY 2025-2026 Formula-exposed group and its matched comparator group. The rate ratio will be estimated using unconditional Poisson regression utilizing robust variance estimators to account for individuals contributing to both cohorts. If standardized differences show covariate imbalances in the matched cohorts, imbalanced covariates may be included in the unconditional Poisson models.

8.7.2.3. Secondary Analysis

The main analysis will compare the occurrence of AESIs in the COMIRNATY 2025-2026 Formula-exposed group to that of the matched comparator group. Secondary analyses will compare the incidence of AESIs in the COMIRNATY 2025-2026 Formula-exposed group with various subsets of the matched comparator group, including:

1. Comparators who received a non-COVID-19 vaccine on cohort entry;

2. Comparators who did not receive a vaccine on cohort entry but had an outpatient physician encounter.

8.7.2.4. Subgroup Analysis

If sample size permits, the main analysis will be restricted to the following subgroups:

- Individuals with prior SARS-CoV-2 infection
- Individuals with prior COVID-19 vaccination
- Individuals with administration of a non-COVID-19 vaccine (eg, seasonal influenza, RSV) on cohort entry date; specific analyses will be performed among individuals receiving seasonal influenza vaccine, and separately among those receiving RSV vaccine
- Children aged 5 to 17 years
- Individuals aged ≥ 65 years
- Individuals 5 years through 64 years of age with at least one underlying condition that puts them at high risk for severe outcomes from COVID-19

All results from Phase 2 analyses will be presented in the Final Report.

8.8. Quality Control

For the final reporting, this study will use the ORD and Optum MA-PD Database derived from claims submitted for payment. Although the health insurance claims data represent financial transactions and are not research records, the financial transactions related to the services provided create financial incentives to record them correctly and fully, so the billable medical services represented in the database are likely to be complete. The validity of this claims research database for epidemiologic research (as compared with data abstracted from medical records) has been widely published (Dore et al., 2011; Eng et al., 2012; Laughlin, 2011).

The study will be carried out according to Optum Epidemiology's internal standard operating procedures (SOPs) that are consistent with the Guidelines for Good Pharmacoepidemiology Practices (GPP) published by the European Medicines Agency (EMA) and International Society for Pharmacoepidemiology (European Medicines Agency, 2017; Public Policy Committee, International Society of Pharmacoepidemiology, 2016) as well as the FDA's Best Practices for Conducting and Reporting Pharmacoepidemiologic Safety Studies Using Electronic Healthcare Data (FDA, 2013).

Programming for this project will be conducted by a primary analyst and reviewed by a second analyst (validation analyst). Validation of all statistical programs and results consists of a combination of visual checks (ie, examination of the programming log, visual printouts before and after data management steps, etc.) and computational checks (ie, repeating calculations for comparison purposes) performed by the validation analyst. In addition, an epidemiologist and a senior scientist will perform a substantive review of all study deliverables. All validation and quality control procedures are conducted in accordance with Optum SOPs, which prescribe that processes and deliverables are documented, reviewed, and validated in sufficient detail to allow for subsequent re-examination or replication.

8.9. Limitations of the Research Methods

The proposed project is based on analysis of automated medical and prescription claims, including pre-adjudicated (interim reporting) and fully adjudicated claims (final reporting).

For the interim report, the SCRI analysis will be based on automated and prospectively collected pre-adjudicated medical and adjudicated prescription claims. A strength of pre-adjudicated medical claims is the shorter lag time between the receipt of care and the appearance of the claim within the databases, while the accompanying limitation is that these pre-adjudicated claims may be subject to revision during the adjudication process.

While adjudicated claims data are extremely valuable for the efficient and effective examination of healthcare outcomes, treatment patterns, healthcare resource utilization, and costs, all claims databases have certain inherent limitations because the claims are collected for the purpose of payment, not research. The presence of a diagnosis code on a medical claim is not confirmation of disease, as the diagnosis code may be incorrectly coded or included as rule-out criteria rather than actual disease.

Another limitation of claims data relates to potential misclassification of exposure and covariates. For instance, vaccines that are administered as part of a government program or an office-based or school-based vaccination clinic may not be captured in the study database if insurance information was not provided during the vaccine encounter. This potential exposure misclassification is minimized in the self-controlled design in Phase 1; misclassification of exposure in Phase 2 would be expected to bias the results towards the null (CDC, 2023b). Furthermore, the presence of a claim for a filled prescription does not indicate that the medication was consumed or that it was taken as prescribed. Medications paid for out-of-pocket, as well as those not dispensed through a pharmacy, will not be observed in the claims data. Similarly, we may not have complete history of comorbidity or treatment for individuals who choose to switch health plan insurer or who choose not to seek medical care for their condition. For example, milder SARS-CoV-2 infections that do not lead to a healthcare encounter may not be captured.

The study power may be limited by the revised indications for the COMIRNATY 2025-2026 Formula as compared to prior formulations, as well as by the relatively short follow-up period, particularly during Phase 1, as observing the full follow-up period may be not possible for several outcomes. Full follow-up for all individuals through the end of the control period will be assessed in the fully adjudicated dataset used in the final report.

Lastly, in all observational studies, treatment is not randomly assigned, and there is potential for residual confounding by factors not captured or poorly measured in claims databases. However, a strength of the current study is its incorporation of a self-controlled design, which eliminates the concern of confounding by time-fixed characteristics that vary across individuals. Similarly, in Phase 2, propensity score matching of the COMIRNATY and comparator cohorts, along with requiring a healthcare encounter as a measure of health-seeking behavior in the comparator cohort, is expected to minimize residual confounding in the cohort analysis. Finally, capture of current COVID-19 vaccines is likely better within the commercially insured and Medicare population as compared to prior years, when there were

more opportunities for individuals to receive a COVID-19 for free without utilizing their insurance (CDC, 2023b).

8.10. Other Aspects

Not applicable.

9. PROTECTION OF HUMAN PARTICIPANTS

9.1. Patient Information

This study involves data that exist in deidentified/anonymized structured format and contain no patient personal information.

9.2. Patient Consent

As this study involves deidentified/anonymized structured data, which according to applicable legal requirements do not contain data subject to privacy laws, obtaining informed consent from patients by Pfizer is not required.

9.3. Institutional Review Board (IRB)/Ethics Committee (EC)

Optum will prepare and submit the appropriate documents to a central IRB for Optum's conduct of the project. Optum will communicate directly with the IRB to address any questions and/or provide any additional information in connection with the review. Pfizer shall provide any necessary assistance or documents required for the submission to the IRB. Approval from an IRB for this project is not guaranteed. This project will be undertaken only after the study combined protocol/SAP has been approved by the IRB or granted an Exemption Determination Letter from the IRB. The IRB will monitor the study for the life of the project and may require formal re-review and approval on an annual basis. Changes to the project may also require re-review and approval by the IRB.

There must be prospective approval of the study protocol, protocol amendments, and other relevant documents (eg, informed consent forms if applicable) from the relevant IRBs/ECs. All correspondence with the IRB/EC must be retained. Copies of IRB/EC approvals must be forwarded to Pfizer.

9.4. Ethical Conduct of the Study

The study will be conducted in accordance with legal and regulatory requirements, as well as with scientific purpose, value, and rigor and follow generally accepted research practices described in the following guidance documents:

- Guidelines for GPP. Public Policy Committee, International Society of Pharmacoepidemiology. Pharmacoepidemiology and Drug Safety 2015; 25:2-10;
- FDA Guidance for Industry and FDA Staff: Best Practices for Conducting and Reporting Pharmacoepidemiologic Safety Studies Using Electronic Healthcare Data, May 2013.

10. MANAGEMENT AND REPORTING OF ADVERSE EVENTS/ADVERSE REACTIONS

This study involves data that exist as structured data by the time of study start. In these data sources, it is not possible to link (ie, identify a potential association between) a particular product and medical event for any individual. Thus, the minimum criteria for reporting an adverse event (AE) (ie, identifiable patient, identifiable reporter, a suspect product, and event) cannot be met.

11. PLANS FOR DISSEMINATING AND COMMUNICATING STUDY RESULTS

In the event of any prohibition or restriction imposed (eg, clinical hold) by an applicable competent authority in any area of the world, or if Optum becomes aware of any new information which might influence the evaluation of the benefits and risks of a Pfizer product, Pfizer should be informed immediately.

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13. LIST OF TABLES

14. LIST OF FIGURES

15. ANNEX 1. LIST OF STANDALONE DOCUMENTS

None.

16. ANNEX 2. CODE LISTS

The following lists contain codes that will be utilized in the study. These lists may be updated as new codes become available.

16.1. Appendix I – COMIRNATY 2025-2026 Formula

The following CPT[2] and NDC codes are sourced from the Immunization Information Systems (IIS) at the Center for Disease Control and Prevention (CDC, 2023a). Other codes will be included as they become available.

16.1.1. CPT Codes

91319	Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (coronavirus disease [COVID-19]) vaccine, mRNA-LNP, spike protein, 10 mcg/0.3 mL dosage, tris-sucrose formulation, for intramuscular use
91320	Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (coronavirus disease [COVID-19]) vaccine, mRNA-LNP, spike protein, 30 mcg/0.3 mL dosage, tris-sucrose formulation, for intramuscular use

16.1.2. NDC Codes

00069-2528-01	Ages 12 years and older; SYRINGE, PRE-FILLED, GLASS, 30 mcg/0.3 mL – DO NOT FREEZE
00069-2501-01	Ages 5 through 11 years; VIAL, SINGLE-DOSE, 10 mcg/0.3 mL DO NOT DILUTE

16.2. Appendix II – Comparator Codes

16.2.1. COVID-19 Vaccine 2025-2026 Formulations Other than the COMIRNATY 2025-2026 Formula – To be used to exclude potential comparators

16.2.1.1. Moderna mNEXSPIKE

16.2.1.1.1. CPT Codes

91322	Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (coronavirus disease [COVID-19]) vaccine, mRNA-LNP, 50 mcg/0.5 mL dosage, for intramuscular use
91323	Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (coronavirus disease [COVID-19]) vaccine, mRNA-LNP, 10 mcg/0.2 mL dosage, for intramuscular use

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91321 Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (coronavirus disease [COVID-19]) vaccine, mRNA-LNP, 25 mcg/0.25 mL dosage, for intramuscular use

16.2.1.1.2. NDC Codes

80777-0112-01 Ages 12 years and older; SYRINGE, PRE-FILLED, 50 mcg/0.5 mL

80777-0400-17 Ages 12 years and older; SYRINGE, PRE-FILLED, 10 mcg/0.2 mL

80777-0113-09 Ages 6 months through 11 years; SYRINGE, PRE-FILLED, 25 mcg/0.25 mL

16.2.1.2. Novavax COVID-19 Vaccine, Adjuvanted

16.2.1.2.1. CPT codes[3]

91304 Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (coronavirus disease [COVID-19]) vaccine, recombinant spike protein nanoparticle, saponin-based adjuvant, preservative free, 5 mcg/0.5 mL dosage, for intramuscular use

16.2.1.2.2. NDC Codes

80631-0207-01 Ages 12 years and older; SYRINGE, PRE-FILLED, 5 mcg/0.5 mL DO NOT FREEZE

16.2.2. Non-COVID-19 Vaccines

CPT and NDC codes are sourced from the Immunization Information Systems (IIS) at the Center for Disease Control and Prevention (CDC, 2023a). Other codes will be included as they become available.

16.2.2.1. CPT Codes

90630, 90653-90664, 90666-90668, 90672-90674, 90682-90689, 90694, 90724, 90756	Influenza virus vaccine
90380-90381, 90678-90679, 96380-96381	Respiratory syncytial virus vaccine
90470	H1N1 immunization
90476-90477	Adenovirus vaccine
90581	Anthrax vaccine

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90585, 90728	Tuberculosis BGC vaccine
90611, 90622	Smallpox/monkeypox vaccine
90619-90621, 90644, 90733-90734	Meningococcal vaccine
90625, 90725	Cholera vaccine
90626-90627, 90738[4]	Tick-borne/Japanese encephalitis virus vaccine
90632-90636, 90730	Hepatitis A vaccine
90636, 90739-90740, 90743-90748, 90759, 90731	Hepatitis B vaccine
90645-90648, 90737	Hemophilus influenza type B vaccine
90649-90651	Human Papillomavirus vaccine
90665	Lyme disease vaccine
90669-90671, 90732	Pneumococcal vaccine
90675-90676, 90726	Rabies vaccine
90680-90681	Rotavirus vaccine
90690-90693	Typhoid vaccine
90696-90702, 90714-90715, 90720-90723	Diphtheria vaccine
90696-90703, 90714-90715, 90723	Tetanus vaccine
90696-90698, 90700, 90715, 90723	Pertussis vaccine
90704, 90707, 90709-90710	Mumps vaccine
90705, 90707-90708, 90710	Measles vaccine
90706, 90707-90710	Rubella vaccine
90696-90698, 90712-90713	Poliovirus vaccine

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90710, 90716	Varicella virus vaccine
90717	Yellow fever vaccine
90727	Plague vaccine
90736, 90750	Zoster (shingles) vaccine
90758	Ebolavirus vaccine
90584, 90587	Dengue vaccine

16.2.2.2. NDC Codes

The below list includes generic vaccine names classified by therapeutic use. Codes for generic vaccines are based on the Hierarchical Ingredient Code List (HICL) system proprietary to First Databank. All associated NDC codes will be utilized. Other vaccines will be included as they become available.

Adenovirus vaccine, live

Anthrax vaccine

Anthrax vaccine, adsorbed

BCG vaccine

BCG vaccine, live

Chikungunya vaccine

Cholera vaccine

Dengue vaccine

Diphtheria, pertussis, tetanus, and haemophilis influenzae type B vaccine

Hepatitis A virus vaccine

Hepatitis A virus and hepatitis B virus vaccine

Hepatitis B and haemophilus influenzae type B vaccine

Hepatitis B, diphtheria, and poliomyelitis virus vaccine

Hepatitis B, haemophilus influenzae type B, and meningococcal vaccine

Hepatitis B virus vaccine

HPV vaccine

Influenza A (H1N1) vaccine

Influenza A (H1N1) vaccine, live

Influenza virus vaccine

Influenza virus vaccine, trivalent

Influenza virus vaccine, trivalent, live

Japanese encephalitis vaccine

Measles and rubella vaccine

Measles, mumps, and rubella vaccine

Measles vaccine, live, attenuated

Mumps vaccine, live

Plague vaccine

Poliomyelitis vaccine, killed

Poliomyelitis vaccine, live

Rabies vaccine

Rabies vaccine, human diploid

Respiratory syncytial virus

Rotavirus vaccine, live

Rubella and mumps vaccine

Rubella vaccine

Smallpox, monkeypox, live

Smallpox vaccine, live

Staphylococcus vaccine

Typhoid vaccine

Varicella virus vaccine, live

Yellow fever vaccine

Zoster vaccine, live

16.2.3. Outpatient Physician Evaluation and Management CPT Codes[5]

99201-99205

99211-99215

99241-99245

99354-99355

99381-99387

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99391-99397

16.3. Appendix III – Adverse Events of Special Interest

All codes are ICD-10 diagnosis codes; all outcomes will be defined based on the presence of a single code unless otherwise specified. In order to qualify as an outcome, the outcome-specific codes must be identified during emergency department visits, inpatient hospitalizations, or outpatient visits, as detailed in Table 2. Outpatient visits are defined through the presence of physician evaluation and management codes (Section 16.2.3). Exploratory analysis may be conducted to further refine this definition to include only outpatient visits for preventive care.

*Outcome codes marked with an asterisk are based on COVID-19 vaccine studies conducted as part of the FDA's CBER BEST system (CBER, 2021; CBER, 2022).

- Acute disseminated encephalomyelitis (ADEM)*
  - G04.00 – Acute disseminated encephalitis and encephalomyelitis, unspecified
- Anaphylaxis*
  - T80.52XA – Anaphylactic reaction due to vaccination, initial encounter
  - T78.2XXA – Anaphylactic shock, unspecified, initial encounter
- Bell's palsy*
  - G51.0 – Bell's palsy
  - G51.8 – Other disorders of facial nerve
  - G51.9 – Disorder of facial nerve, unspecified
- Cerebral venous sinus thrombosis (CVST)
  - I67.6 – Nonpyogenic thrombosis of intracranial venous system
  - I63.6 – Cerebral infarction due to cerebral venous thrombosis, nonpyogenic
- Convulsions/seizures (non-febrile)
  - G40.001 – Localization-related (focal) (partial) idiopathic epilepsy and epileptic syndromes with seizures of localized onset, not intractable, with status epilepticus
  - G40.009 – Localization-related (focal) (partial) idiopathic epilepsy and epileptic syndromes with seizures of localized onset, not intractable, without status epilepticus
  - G40.011 – Localization-related (focal) (partial) idiopathic epilepsy and epileptic syndromes with seizures of localized onset, intractable, with status epilepticus

- G40.019 – Localization-related (focal) (partial) idiopathic epilepsy and epileptic syndromes with seizures of localized onset, intractable, without status epilepticus
- G40.101 – Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with simple partial seizures, not intractable, with status epilepticus
- G40.109 – Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with simple partial seizures, not intractable, without status epilepticus
- G40.111 – Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with simple partial seizures, intractable, with status epilepticus
- G40.119 – Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with simple partial seizures, intractable, without status epilepticus
- G40.201 – Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with complex partial seizures, not intractable, with status epilepticus
- G40.209 – Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with complex partial seizures, not intractable, without status epilepticus
- G40.211 – Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with complex partial seizures, intractable, with status epilepticus
- G40.219 – Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with complex partial seizures, intractable, without status epilepticus
- G40.301 – Generalized idiopathic epilepsy and epileptic syndromes, not intractable, with status epilepticus
- G40.309 – Generalized idiopathic epilepsy and epileptic syndromes, not intractable, without status epilepticus
- G40.311 – Generalized idiopathic epilepsy and epileptic syndromes, intractable, with status epilepticus
- G40.319 – Generalized idiopathic epilepsy and epileptic syndromes, intractable, without status epilepticus
- G40.401 – Other generalized epilepsy and epileptic syndromes, not intractable, with status epilepticus
- G40.409 – Other generalized epilepsy and epileptic syndromes, not intractable, without status epilepticus

- G40.411 – Other generalized epilepsy and epileptic syndromes, intractable, with status epilepticus
- G40.419 – Other generalized epilepsy and epileptic syndromes, intractable, without status epilepticus
- G40.501 – Epileptic seizures related to external causes, not intractable, with status epilepticus
- G40.509 – Epileptic seizures related to external causes, not intractable, without status epilepticus
- G40.801 – Other epilepsy, not intractable, with status epilepticus
- G40.802 – Other epilepsy, not intractable, without status epilepticus
- G40.803 – Other epilepsy, intractable, with status epilepticus
- G40.804 – Other epilepsy, intractable, without status epilepticus
- G40.811 – Lennox-Gastaut syndrome, not intractable, with status epilepticus
- G40.812 – Lennox-Gastaut syndrome, not intractable, without status epilepticus
- G40.813 – Lennox-Gastaut syndrome, intractable, with status epilepticus
- G40.814 – Lennox-Gastaut syndrome, intractable, without status epilepticus
- G40.821 – Epileptic spasms, not intractable, with status epilepticus
- G40.822 – Epileptic spasms, not intractable, without status epilepticus
- G40.823 – Epileptic spasms, intractable, with status epilepticus
- G40.824 – Epileptic spasms, intractable, without status epilepticus
- G40.89 – Other seizures
- G40.901 – Epilepsy, unspecified, not intractable, with status epilepticus
- G40.909 – Epilepsy, unspecified, not intractable, without status epilepticus
- G40.911 – Epilepsy, unspecified, intractable, with status epilepticus
- G40.919 – Epilepsy, unspecified, intractable, without status epilepticus
- G40.A01 – Absence epileptic syndrome, not intractable, with status epilepticus
- G40.A09 – Absence epileptic syndrome, not intractable, without status epilepticus
- G40.A11 – Absence epileptic syndrome, intractable, with status epilepticus
- G40.A19 – Absence epileptic syndrome, intractable, without status epilepticus
- G40.B01 – Juvenile myoclonic epilepsy, not intractable, with status epilepticus

- G40.B09 – Juvenile myoclonic epilepsy, not intractable, without status epilepticus
- G40.B11 – Juvenile myoclonic epilepsy, intractable, with status epilepticus
- G40.B19 – Juvenile myoclonic epilepsy, intractable, without status epilepticus
- R56.1 – Post traumatic seizures
- R56.9 – Unspecified convulsions

- Encephalitis/myelitis/encephalomyelitis (not ADEM or TM)*
  - G04.02 – Postimmunization acute disseminated encephalitis, myelitis, and encephalomyelitis
  - G04.00 – Acute disseminated encephalitis and encephalomyelitis, unspecified
  - G04.81 – Other encephalitis and encephalomyelitis
  - G04.90 – Encephalitis and encephalomyelitis
  - G05.3 – Encephalitis and encephalomyelitis in diseases classified elsewhere
- Glomerulonephritis
  - N06.A Isolated proteinuria with C3 glomerulonephritis
  - N06.7 Isolated proteinuria with diffuse crescentic glomerulonephritis
  - N06.5 Isolated proteinuria with diffuse mesangiocapillary glomerulonephritis
  - N06.4 Isolated proteinuria with diffuse endocapillary proliferative glomerulonephritis
  - N04.A Nephrotic syndrome with C3 glomerulonephritis
  - N04.2 Nephrotic syndrome with diffuse membranous glomerulonephritis
  - N04.7 Nephrotic syndrome with diffuse crescentic glomerulonephritis
  - N04.5 Nephrotic syndrome with diffuse mesangiocapillary glomerulonephritis
  - N04.3 Nephrotic syndrome with diffuse mesangial proliferative glomerulonephritis
  - N04.4 Nephrotic syndrome with diffuse endocapillary proliferative glomerulonephritis
  - N05.A Unspecified nephritic syndrome with C3 glomerulonephritis
  - N05.7 Unspecified nephritic syndrome with diffuse crescentic glomerulonephritis
  - N05.2 Unspecified nephritic syndrome with diffuse membranous glomerulonephritis
  - N05.5 Unspecified nephritic syndrome with diffuse mesangiocapillary glomerulonephritis

- N03.A Chronic nephritic syndrome with C3 glomerulonephritis
- N03.7 Chronic nephritic syndrome with diffuse crescentic glomerulonephritis
- N03.2 Chronic nephritic syndrome with diffuse membranous glomerulonephritis
- N03.5 Chronic nephritic syndrome with diffuse mesangiocapillary glomerulonephritis
- N00.A Acute nephritic syndrome with C3 glomerulonephritis
- N00.2 Acute nephritic syndrome with diffuse membranous glomerulonephritis
- N00.5 Acute nephritic syndrome with diffuse mesangiocapillary glomerulonephritis
- N00.7 Acute nephritic syndrome with diffuse crescentic glomerulonephritis
- N07.A Hereditary nephropathy, not elsewhere classified with C3 glomerulonephritis
- N02.7 Recurrent and persistent hematuria with diffuse crescentic glomerulonephritis
- N02.A Recurrent and persistent hematuria with C3 glomerulonephritis

- Guillain-Barré syndrome*
  - G61.0 – Guillain-Barré syndrome
- Herpes zoster
  - B02.* Zoster [herpes zoster]
- Immune-mediated myositis
  - G72.49 – Other inflammatory and immune myopathies, not elsewhere classified
- Immune thrombocytopenia*
  - D69.3 – Immune thrombocytopenic purpura
- Kawasaki disease*
  - M30.3 – Mucocutaneous lymph node syndrome [Kawasaki]
- Multi inflammatory syndrome (in children and adults)*
  - U07.1 – COVID-19 **and one of the following:**
  - M35.8 – Other specified systemic involvement of connective tissue
  - M35.81 – Multisystem inflammatory syndrome
  - M35.89 – Other specified systemic involvement of connective tissue
- Multiple sclerosis
  - G35 – Multiple sclerosis

- Myocardial infarction*
  - I21.01 – ST elevation (STEMI) myocardial infarction involving left main coronary artery
  - I21.02 – ST elevation (STEMI) myocardial infarction involving left anterior descending coronary artery
  - I21.09 – ST elevation (STEMI) myocardial infarction involving other coronary artery of anterior wall
  - I21.11 – ST elevation (STEMI) myocardial infarction involving right coronary artery
  - I21.19 – ST elevation (STEMI) myocardial infarction involving other coronary artery of inferior wall
  - I21.21 – ST elevation (STEMI) myocardial infarction involving left circumflex coronary artery
  - I21.29 – ST elevation (STEMI) myocardial infarction involving other sites
  - I21.3 – ST elevation (STEMI) myocardial infarction of unspecified site
  - I21.4 – Non-ST elevation (NSTEMI) myocardial infarction
  - I21.9 – Acute myocardial infarction, unspecified
  - I21.A1 – Myocardial infarction type 2
  - I21.A9 – Other myocardial infarction type
  - I22.0 – Subsequent ST elevation (STEMI) myocardial infarction of anterior wall
  - I22.1 – Subsequent ST elevation (STEMI) myocardial infarction of inferior wall
  - I22.2 – Subsequent non-ST elevation (NSTEMI) myocardial infarction
  - I22.8 – Subsequent ST elevation (STEMI) myocardial infarction of other sites
  - I22.9 – Subsequent ST elevation (STEMI) myocardial infarction of unspecified site
- Myocarditis/pericarditis*
  - B33.22 – Viral myocarditis
  - B33.23 – Viral pericarditis
  - I30.0 – Acute nonspecific idiopathic pericarditis
  - I30.1 – Infective pericarditis
  - I30.8 – Other forms of acute pericarditis
  - I30.9 – Acute pericarditis, unspecified
  - I32 – Pericarditis in diseases classified elsewhere

- I41 – Myocarditis in diseases classified elsewhere
- I40.0 – Infective myocarditis
- I40.1 – Isolated myocarditis
- I40.8 – Other acute myocarditis
- I40.9 – Acute myocarditis, unspecified
- I51.4 – Myocarditis, unspecified

- Pulmonary embolism*
  - I26.02 – Saddle embolus of pulmonary artery with acute cor pulmonale
  - I26.09 – Other pulmonary embolism with acute cor pulmonale
  - I26.92 – Saddle embolus of pulmonary artery without acute cor pulmonale
  - I26.93 – Single subsegmental pulmonary embolism without acute cor pulmonale
  - I26.94 – Multiple subsegmental pulmonary emboli without acute cor pulmonale
  - I26.99 – Other pulmonary embolism without acute cor pulmonale
- Stroke, hemorrhagic*
  - I61.0 – Nontraumatic intracerebral hemorrhage in hemisphere, subcortical
  - I61.1 – Nontraumatic intracerebral hemorrhage in hemisphere, cortical
  - I61.2 – Nontraumatic intracerebral hemorrhage in hemisphere, unspecified
  - I61.3 – Nontraumatic intracerebral hemorrhage in brain stem
  - I61.4 – Nontraumatic intracerebral hemorrhage in cerebellum
  - I61.5 – Nontraumatic intracerebral hemorrhage, intraventricular
  - I61.6 – Nontraumatic intracerebral hemorrhage, multiple localized
  - I61.8 – Other nontraumatic intracerebral hemorrhage
  - I61.9 – Nontraumatic intracerebral hemorrhage, unspecified
  - I62.00 – Nontraumatic subdural hemorrhage, unspecified
  - I62.01 – Nontraumatic acute subdural hemorrhage
  - I62.02 – Nontraumatic subacute subdural hemorrhage
  - I62.9 – Nontraumatic intracranial hemorrhage, unspecified
- Stroke, ischemic*
  - I63.00 – Cerebral infarction due to thrombosis of unspecified precerebral artery
  - I63.011 – Cerebral infarction due to thrombosis of right vertebral artery

- I63.012 – Cerebral infarction due to thrombosis of left vertebral artery
- I63.013 – Cerebral infarction due to thrombosis of bilateral vertebral arteries
- I63.019 – Cerebral infarction due to thrombosis of unspecified vertebral artery
- I63.02 – Cerebral infarction due to thrombosis of basilar artery
- I63.031 – Cerebral infarction due to thrombosis of right carotid artery
- I63.032 – Cerebral infarction due to thrombosis of left carotid artery
- I63.033 – Cerebral infarction due to thrombosis of bilateral carotid arteries
- I63.039 – Cerebral infarction due to thrombosis of unspecified carotid artery
- I63.09 – Cerebral infarction due to thrombosis of other precerebral artery
- I63.10 – Cerebral infarction due to embolism of unspecified precerebral artery
- I63.111 – Cerebral infarction due to embolism of right vertebral artery
- I63.112 – Cerebral infarction due to embolism of left vertebral artery
- I63.113 – Cerebral infarction due to embolism of bilateral vertebral arteries
- I63.119 – Cerebral infarction due to embolism of unspecified vertebral artery
- I63.12 – Cerebral infarction due to embolism of basilar artery
- I63.131 – Cerebral infarction due to embolism of right carotid artery
- I63.132 – Cerebral infarction due to embolism of left carotid artery
- I63.133 – Cerebral infarction due to embolism of bilateral carotid arteries
- I63.139 – Cerebral infarction due to embolism of unspecified carotid artery
- I63.19 – Cerebral infarction due to embolism of other precerebral artery
- I63.20 – Cerebral infarction due to unspecified occlusion or stenosis of unspecified precerebral arteries
- I63.211 – Cerebral infarction due to unspecified occlusion or stenosis of right vertebral arteries
- I63.212 – Cerebral infarction due to unspecified occlusion or stenosis of left vertebral arteries
- I63.213 – Cerebral infarction due to unspecified occlusion or stenosis of bilateral vertebral arteries
- I63.219 – Cerebral infarction due to unspecified occlusion or stenosis of unspecified vertebral arteries
- I63.22 – Cerebral infarction due to unspecified occlusion or stenosis of basilar arteries
- I63.231 – Cerebral infarction due to unspecified occlusion or stenosis of right carotid arteries

- I63.232 – Cerebral infarction due to unspecified occlusion or stenosis of left carotid arteries
- I63.233 – Cerebral infarction due to unspecified occlusion or stenosis of bilateral carotid arteries
- I63.239 – Cerebral infarction due to unspecified occlusion or stenosis of unspecified carotid arteries
- I63.29 – Cerebral infarction due to unspecified occlusion or stenosis of other precerebral arteries
- I63.30 – Cerebral infarction due to thrombosis of unspecified cerebral artery
- I63.311 – Cerebral infarction due to thrombosis of right middle cerebral artery
- I63.312 – Cerebral infarction due to thrombosis of left middle cerebral artery
- I63.313 – Cerebral infarction due to thrombosis of bilateral middle cerebral arteries
- I63.319 – Cerebral infarction due to thrombosis of unspecified middle cerebral artery
- I63.321 – Cerebral infarction due to thrombosis of right anterior cerebral artery
- I63.322 – Cerebral infarction due to thrombosis of left anterior cerebral artery
- I63.323 – Cerebral infarction due to thrombosis of bilateral anterior cerebral arteries
- I63.329 – Cerebral infarction due to thrombosis of unspecified anterior cerebral artery
- I63.331 – Cerebral infarction due to thrombosis of right posterior cerebral artery
- I63.332 – Cerebral infarction due to thrombosis of left posterior cerebral artery
- I63.333 – Cerebral infarction due to thrombosis of bilateral posterior cerebral arteries
- I63.339 – Cerebral infarction due to thrombosis of unspecified posterior cerebral artery
- I63.341 – Cerebral infarction due to thrombosis of right cerebellar artery
- I63.342 – Cerebral infarction due to thrombosis of left cerebellar artery
- I63.343 – Cerebral infarction due to thrombosis of bilateral cerebellar artery
- I63.349 – Cerebral infarction due to thrombosis of unspecified cerebellar artery
- I63.39 – Cerebral infarction due to thrombosis of other cerebral artery

- I63.40 – Cerebral infarction due to embolism of unspecified cerebral artery
- I63.411 – Cerebral infarction due to embolism of right middle cerebral artery
- I63.412 – Cerebral infarction due to embolism of left middle cerebral artery
- I63.413 – Cerebral infarction due to embolism of bilateral middle cerebral artery
- I63.419 – Cerebral infarction due to embolism of unspecified middle cerebral arteries
- I63.421 – Cerebral infarction due to embolism of right anterior cerebral artery
- I63.422 – Cerebral infarction due to embolism of left anterior cerebral artery
- I63.423 – Cerebral infarction due to embolism of bilateral anterior cerebral arteries
- I63.429 – Cerebral infarction due to embolism of unspecified anterior cerebral artery
- I63.431 – Cerebral infarction due to embolism of right posterior cerebral artery
- I63.432 – Cerebral infarction due to embolism of left posterior cerebral artery
- I63.433 – Cerebral infarction due to embolism of bilateral anterior cerebral arteries
- I63.439 – Cerebral infarction due to embolism of unspecified posterior cerebral artery
- I63.441 – Cerebral infarction due to embolism of right cerebellar artery
- I63.442 – Cerebral infarction due to embolism of left cerebellar artery
- I63.443 – Cerebral infarction due to embolism of bilateral cerebellar arteries
- I63.449 – Cerebral infarction due to embolism of unspecified cerebellar artery
- I63.49 – Cerebral infarction due to embolism of other cerebellar artery
- I63.50 – Cerebral infarction due to embolism of unspecified cerebral artery
- I63.511 – Cerebral infarction due to embolism of right middle cerebral artery
- I63.512 – Cerebral infarction due to embolism of left middle cerebral artery
- I63.513 – Cerebral infarction due to embolism of bilateral middle cerebral arteries
- I63.519 – Cerebral infarction due to embolism of unspecified middle cerebral artery
- I63.521 – Cerebral infarction due to embolism of right anterior cerebral artery
- I63.522 – Cerebral infarction due to embolism of left anterior cerebral artery

- I63.523 – Cerebral infarction due to embolism of bilateral anterior cerebral artery
- I63.529 – Cerebral infarction due to embolism of unspecified anterior cerebral artery
- I63.531 – Cerebral infarction due to embolism of right posterior cerebral artery
- I63.532 – Cerebral infarction due to embolism of left posterior cerebral artery
- I63.533 – Cerebral infarction due to embolism of bilateral posterior cerebral arteries
- I63.539 – Cerebral infarction due to embolism of unspecified posterior cerebral artery
- I63.541 – Cerebral infarction due to embolism of right cerebellar artery
- I63.542 – Cerebral infarction due to embolism of left cerebellar artery
- I63.543 – Cerebral infarction due to embolism of bilateral cerebellar arteries
- I63.549 – Cerebral infarction due to embolism of unspecified cerebellar artery
- I63.59 – Cerebral infarction due to embolism of other cerebellar artery
- I63.6 – Cerebral infarction dye to cerebral venous thrombosis, nonpyogenic
- I63.81 – Other cerebral infarction due to occlusion or stenosis of small artery
- I63.89 – Other cerebral infarction
- I63.9 – Cerebral infarction, unspecified

- Subacute thyroiditis
  - E06.1 – Subacute thyroiditis
- Transverse myelitis*
  - G37.3 – Acute transverse myelitis in demyelinating disease of central nervous system

16.4. Appendix IV – Covariate Codes

16.4.1. Comorbidities

16.4.1.1. Asthma

16.4.1.1.1. ICD-10-CM Codes

J45.20	Mild intermittent asthma, uncomplicated
J45.21	Mild intermittent asthma with (acute) exacerbation
J45.22	Mild intermittent asthma with status asthmaticus
J45.30	Mild persistent asthma, uncomplicated
J45.31	Mild persistent asthma with (acute) exacerbation
J45.32	Mild persistent asthma with status asthmaticus
J45.40	Moderate persistent asthma, uncomplicated
J45.41	Moderate persistent asthma with (acute) exacerbation
J45.42	Moderate persistent asthma with status asthmaticus
J45.50	Severe persistent asthma, uncomplicated
J45.51	Severe persistent asthma with (acute) exacerbation
J45.52	Severe persistent asthma with status asthmaticus
J45.901	Unspecified asthma with (acute) exacerbation
J45.902	Unspecified asthma with status asthmaticus
J45.909	Unspecified asthma, uncomplicated
J45.991	Cough variant asthma
J45.998	Other asthma
J82.83	Eosinophilic asthma

16.4.1.2. Non-Malignant Blood Disorders, Including Sickle Cell Disease

16.4.1.2.1. ICD-10-CM Codes

D55.0	Anemia due to G6PD deficiency
D55.1	Anemia due to other disorders of glutathione metabolism

D55.21	Anemia due to pyruvate kinase deficiency
D55.29	Anemia due to other disorders of glycolytic enzymes
D55.3	Anemia due to disorders of nucleotide metabolism
D55.8	Other anemias due to enzyme disorders
D55.9	Anemia due to enzyme disorder, unspecified
D56.0	Alpha thalassemia
D56.1	Beta thalassemia
D56.2	Delta-beta thalassemia
D56.3	Thalassemia minor
D56.4	Hereditary persistence of fetal hemoglobin [HPFH]
D56.5	Hemoglobin E-beta thalassemia
D56.8	Other thalassemias
D56.9	Thalassemia, unspecified
D57.00	Hb-SS disease w/ crisis, unspecified
D57.01	Hb-SS disease w/ acute chest syndrome
D57.02	Hb-SS disease w/ splenic sequestration
D57.03	Hb-SS disease with cerebral vascular involvement
D57.04	Hb-SS disease with dactylitis
D57.09	Hb-SS disease with crisis with other specified complication
D57.1	Sickle cell disease w/o crisis
D57.20	Sickle cell/Hb-C disease w/o crisis
D57.21	Sickle cell/Hb-C disease w/ crisis
D57.211	Sickle cell/Hb-C disease w/ acute chest syndrome
D57.212	Sickle cell/Hb-C disease w/ splenic sequestration

D57.213	Sickle-cell/Hb-C disease with cerebral vascular involvement
D57.214	Sickle-cell/Hb-C disease with dactylitis
D57.218	Sickle-cell/Hb-C disease with crisis with other specified complication
D57.219	Sickle cell/Hb-C disease w/ crisis, unspecified
D57.3	Sickle cell trait
D57.40	Sickle cell thalassemia w/o crisis
D57.41	Sickle-cell thalassemia w/ crisis
D57.411	Sickle cell thalassemia w/ acute chest syndrome
D57.412	Sickle cell thalassemia w/ splenic sequestration
D57.413	Sickle-cell thalassemia, unspecified, with cerebral vascular involvement
D57.414	Sickle-cell thalassemia, unspecified, with dactylitis
D57.418	Sickle-cell thalassemia, unspecified, with crisis with other specified complication
D57.419	Sickle cell thalassemia w/ crisis, unspecified
D57.42	Sickle-cell thalassemia beta zero without crisis
D57.431	Sickle-cell thalassemia beta zero with acute chest syndrome
D57.432	Sickle-cell thalassemia beta zero with splenic sequestration
D57.433	Sickle-cell thalassemia beta zero with cerebral vascular involvement
D57.434	Sickle-cell thalassemia beta zero with dactylitis
D57.438	Sickle-cell thalassemia beta zero with crisis with other specified complication
D57.439	Sickle-cell thalassemia beta zero with crisis, unspecified
D57.44	Sickle-cell thalassemia beta plus without crisis
D57.451	Sickle-cell thalassemia beta plus with acute chest syndrome

D57.452	Sickle-cell thalassemia beta plus with splenic sequestration
D57.454	Sickle-cell thalassemia beta plus with dactylitis
D57.458	Sickle-cell thalassemia beta plus with crisis with other specified complication
D57.459	Sickle-cell thalassemia beta plus with crisis, unspecified
D57.80	Other sickle cell disorders w/o crisis
D57.811	Other sickle cell disorders w/ acute chest syndrome
D57.812	Other sickle cell disorders w/ splenic sequestration
D57.813	Other sickle-cell disorders with cerebral vascular involvement
D57.814	Other sickle-cell disorders with dactylitis
D57.818	Other sickle-cell disorders with crisis with other specified complication
D57.819	Other sickle cell disorders w/ crisis, unspecified
D58.0	Hereditary spherocytosis
D58.1	Hereditary elliptocytosis
D58.2	Other hemoglobinopathies
D58.8	Other specified hereditary hemolytic anemias
D58.9	Hereditary hemolytic anemia, unspecified
D59.0	Drug-induced autoimmune hemolytic anemia
D59.10	Autoimmune hemolytic anemia, unspecified
D59.11	Warm autoimmune hemolytic anemia
D59.12	Cold autoimmune hemolytic anemia
D59.13	Mixed type autoimmune hemolytic anemia
D59.19	Other autoimmune hemolytic anemia
D59.2	Drug-induced nonautoimmune hemolytic anemia

D59.30	Hemolytic-uremic syndrome, unspecified
D59.31	Infection-associated hemolytic-uremic syndrome
D59.32	Hereditary hemolytic-uremic syndrome
D59.39	Other hemolytic-uremic syndrome
D59.4	Other nonautoimmune hemolytic anemias
D59.5	Paroxysmal nocturnal hemoglobinuria [Marchiafava-Micheli]
D59.6	Hemoglobinuria due to hemolysis from other external causes
D59.8	Other acquired hemolytic anemias
D59.9	Acquired hemolytic anemia, unspecified
D60.0	Chronic acquired pure red cell aplasia
D60.1	Transient acquired pure red cell aplasia
D60.8	Other acquired pure red cell aplasias
D60.9	Acquired pure red cell aplasia, unspecified
D61.01	Constitutional (pure) red blood cell aplasia
D61.02	Shwachman-Diamond syndrome
D61.09	Other constitutional aplastic anemia
D61.1	Drug-induced aplastic anemia
D61.2	Aplastic anemia due to other external agents
D61.3	Idiopathic aplastic anemia
D61.810	Antineoplastic chemotherapy induced pancytopenia
D61.811	Other drug-induced pancytopenia
D61.818	Other pancytopenia
D61.82	Myelophthisis
D61.89	Other specified aplastic anemias and other bone marrow failure syndromes

D61.9	Aplastic anemia, unspecified
D62	Acute posthemorrhagic anemia
D63.0	Anemia in neoplastic disease
D63.1	Anemia in chronic kidney disease
D63.8	Anemia in other chronic diseases classified elsewhere
D64.0	Hereditary sideroblastic anemia
D64.1	Secondary sideroblastic anemia due to disease
D64.2	Secondary sideroblastic anemia due to drugs and toxins
D64.3	Other sideroblastic anemias
D64.4	Congenital dyserythropoietic anemia
D64.81	Anemia due to antineoplastic chemotherapy
D64.89	Other specified anemias
D64.9	Anemia, unspecified
D65	Disseminated intravascular coagulation
D66	Hereditary factor VIII deficiency
D67	Hereditary factor IX deficiency
D68.00	Von Willebrand disease, unspecified
D68.1	Hereditary factor XI deficiency
D68.01	Von Willebrand disease, type 1
D68.020	Von Willebrand disease, type 2A
D68.021	Von Willebrand disease, type 2B
D68.022	Von Willebrand disease, type 2M
D68.023	Von Willebrand disease, type 2N
D68.029	Von Willebrand disease, type 2, unspecified

D68.03	Von Willebrand disease, type 3
D68.04	Acquired von Willebrand disease
D68.09	Other von Willebrand disease
D68.1	Hereditary factor XI deficiency
D68.2	Hereditary deficiency of other clotting factors
D68.311	Acquired hemophilia
D68.312	Antiphospholipid antibody with hemorrhagic disorder
D68.318	Other hemorrhagic disorder due to intrinsic circulating anticoagulants, antibodies, or inhibitors
D68.32	Hemorrhagic disorder due to extrinsic circulating anticoagulants
D68.4	Acquired coagulation factor deficiency
D68.51	Activated protein C resistance
D68.52	Prothrombin gene mutation
D68.59	Other primary thrombophilia
D68.61	Antiphospholipid syndrome
D68.62	Lupus anticoagulant syndrome
D68.69	Other thrombophilia
D68.8	Other specified coagulation defects
D68.9	Coagulation defect, unspecified
D69.0	Allergic purpura
D69.1	Qualitative platelet defects
D69.2	Other nonthrombocytopenic purpura
D69.3	Immune thrombocytopenic purpura
D69.41	Evans syndrome

D69.42	Congenital and hereditary thrombocytopenia purpura
D69.49	Other primary thrombocytopenia
D69.51	Post-transfusion purpura
D69.59	Other secondary thrombocytopenia
D69.6	Thrombocytopenia, unspecified
D69.8	Other specified hemorrhagic conditions
D69.9	Hemorrhagic condition, unspecified
D70.0	Congenital agranulocytosis
D70.1	Agranulocytosis secondary to cancer chemotherapy
D70.2	Other drug-induced agranulocytosis
D70.3	Neutropenia due to infection
D70.4	Cyclic neutropenia
D70.8	Other neutropenia
D70.9	Neutropenia, unspecified,
D71	Functional disorders of polymorphonuclear neutrophils
D72.0	Genetic anomalies of leukocytes
D72.10	Eosinophilia, unspecified
D72.110	Idiopathic hypereosinophilic syndrome [IHES]
D72.111	Lymphocytic Variant Hypereosinophilic Syndrome [LHES]
D72.118	Other hypereosinophilic syndrome
D72.119	Hypereosinophilic syndrome [HES], unspecified
D72.12	Drug rash with eosinophilia and systemic symptoms syndrome
D72.18	Eosinophilia in diseases classified elsewhere
D72.19	Other eosinophilia

D72.810	Lymphocytopenia
D72.818	Other decreased white blood cell count
D72.819	Decreased white blood cell count, unspecified
D72.820	Lymphocytosis (symptomatic)
D72.821	Monocytosis (symptomatic)
D72.822	Plasmacytosis
D72.823	Leukemoid reaction
D72.824	Basophilia
D72.825	Bandemia
D72.828	Other elevated white blood cell count
D72.829	Elevated white blood cell count, unspecified
D72.89	Other specified disorders of white blood cells
D72.9	Disorder of white blood cells, unspecified

16.4.1.3. Chronic Lung Disease, Including COPD

16.4.1.3.1. ICD-10-CM Codes

P27.0	Wilson-Mikity syndrome
P27.1	Bronchopulmonary dysplasia originating in the perinatal period
P27.8	Other chronic respiratory diseases originating in the perinatal period
P27.9	Unspecified chronic respiratory disease originating in the perinatal period
E84.0	Cystic fibrosis with pulmonary manifestations
E84.11	Meconium ileus in cystic fibrosis
E84.19	Cystic fibrosis with other intestinal manifestations
E84.8	Cystic fibrosis with other manifestations
E84.9	Cystic fibrosis, unspecified

I27.0	Primary pulmonary hypertension
I27.1	Kyphoscoliotic heart disease
I27.20	Pulmonary hypertension, unspecified
I27.21	Secondary pulmonary arterial hypertension
I27.22	Pulmonary hypertension due to left heart disease
I27.23	Pulmonary hypertension due to lung diseases and hypoxia
I27.24	Chronic thromboembolic pulmonary hypertension
I27.29	Other secondary pulmonary hypertension
I27.81	Cor pulmonale (chronic)
I27.82	Chronic pulmonary embolism
I27.83	Eisenmenger's syndrome
I27.89	Other specified pulmonary heart diseases
I27.9	Pulmonary heart disease, unspecified
I28.0	Arteriovenous fistula of pulmonary vessels
I28.1	Aneurysm of pulmonary artery
I28.8	Other diseases of pulmonary vessels
I28.9	Disease of pulmonary vessels, unspecified
J41	Simple and mucopurulent chronic bronchitis
J41.0	Simple chronic bronchitis
J41.1	Mucopurulent chronic bronchitis
J41.8	Mixed simple and mucopurulent chronic bronchitis
J42	Unspecified chronic bronchitis
J43.0	Unilateral pulmonary emphysema [MacLeod’s syndrome]
J43.1	Panlobular emphysema

J43.2	Centrilobular emphysema
J43.8	Other emphysema
J43.9	Emphysema, unspecified
J44.0	Chronic obstructive pulmonary disease with (acute) lower respiratory infection
J44.1	Chronic obstructive pulmonary disease with (acute) exacerbation
J44.81	Bronchiolitis obliterans and bronchiolitis obliterans syndrome
J44.89	Other specified chronic obstructive pulmonary disease
J44.9	Chronic obstructive pulmonary disease, unspecified
J60	Coal worker’s pneumoconiosis
J61	Pneumoconiosis due to asbestos and other mineral fibers
J62.0	Pneumoconiosis due to talc dust
J62.8	Pneumoconiosis due to other dust containing silica
J63.0	Aluminosis (of lung)
J63.1	Bauxite fibrosis (of lung)
J63.2	Berylliosis
J63.3	Graphite fibrosis (of lung)
J63.4	Siderosis
J63.5	Stannosis
J63.6	Pneumoconiosis due to other specified inorganic dusts
J64	Unspecified pneumoconiosis
J65	Pneumoconiosis associated with tuberculosis
J66.0	Byssinosis
J66.1	Flax-dressers' disease
J66.2	Cannabinosis

J66.8	Airway disease due to other specific organic dusts
J67	Hypersensitivity pneumonitis due to organic dust
J67.0	Farmer’s lung
J67.1	Bagassosis
J67.2	Bird fancier's lung
J67.3	Suberosis
J67.4	Maltworker's lung
J67.5	Mushroom-worker's lung
J67.6	Maple-bark-stripper's lung
J67.7	Air conditioner and humidifier lung
J67.8	Hypersensitivity pneumonitis due to other organic dusts
J67.9	Hypersensitivity pneumonitis due to unspecified organic dust
J68.4	Chronic respiratory conditions due to chemicals, gases, fumes and vapors
J68.8	Other respiratory conditions due to chemicals, gases, fumes and vapors
J68.9	Unspecified respiratory condition due to chemicals, gases, fumes and vapors
J70.1	Chronic and other pulmonary manifestations due to radiation
J70.3	Chronic drug-induced interstitial lung disorders
J70.5	Respiratory conditions due to smoke inhalation
J81.1	Chronic pulmonary edema
J82.81	Chronic eosinophilic pneumonia
J84.01	Alveolar proteinosis
J84.02	Pulmonary alveolar microlithiasis
J84.03	Idiopathic pulmonary hemosiderosis

J84.09	Other alveolar and parieto-alveolar conditions
J84.10	Pulmonary fibrosis, unspecified
J84.111	Idiopathic interstitial pneumonia, not otherwise specified
J84.112	Idiopathic pulmonary fibrosis
J84.113	Idiopathic non-specific interstitial pneumonitis
J84.115	Respiratory bronchiolitis interstitial lung disease
J84.116	Cryptogenic organizing pneumonia
J84.117	Desquamative interstitial pneumonia
J84.170	Interstitial lung disease with progressive fibrotic phenotype in diseases classified elsewhere
J84.178	Other interstitial pulmonary diseases with fibrosis in diseases classified elsewhere
J84.2	Lymphoid interstitial pneumonia
J84.81	Lymphangioleiomyomatosis
J84.82	Adult pulmonary Langerhans cell histiocytosis
J84.83	Surfactant mutations of the lung
J84.841	Neuroendocrine cell hyperplasia of infancy
J84.842	Pulmonary interstitial glycogenosis
J84.843	Alveolar capillary dysplasia with vein misalignment
J84.848	Other interstitial lung diseases of childhood
J84.89	Other specified interstitial pulmonary diseases
J84.9	Interstitial pulmonary disease, unspecified
Z77.090	Contact with and (suspected) exposure to asbestos
J85.0	Gangrene and necrosis of lung
J93.81	Chronic pneumothorax

16.4.1.4. Down Syndrome

16.4.1.4.1. ICD-10-CM Codes

Q90.0	Trisomy 21, nonmosaicism (meiotic nondisjunction)
Q90.1	Trisomy 21, mosaicism (mitotic nondisjunction)
Q90.2	Trisomy 21, translocation
Q90.9	Down syndrome, unspecified

16.4.1.5. Heart Disease

16.4.1.5.1. ICD-10-CM Codes

I01.0	Acute rheumatic pericarditis
I01.1	Acute rheumatic endocarditis
I01.2	Acute rheumatic myocarditis
I01.8	Other acute rheumatic heart disease
I01.9	Acute rheumatic heart disease, unspecified
I02.0	Rheumatic chorea with heart involvement
I05.0	Rheumatic mitral stenosis
I05.1	Rheumatic mitral insufficiency
I05.2	Rheumatic mitral stenosis with insufficiency
I05.8	Other rheumatic mitral valve diseases
I05.9	Rheumatic mitral valve disease, unspecified
I06.0	Rheumatic aortic stenosis
I06.1	Rheumatic aortic insufficiency
I06.2	Rheumatic aortic stenosis with insufficiency
I07.0	Rheumatic tricuspid stenosis
I07.1	Rheumatic tricuspid insufficiency
I07.2	Rheumatic tricuspid stenosis and insufficiency

I07.8	Other rheumatic tricuspid valve diseases
I07.9	Rheumatic tricuspid valve disease, unspecified
I06.8	Other rheumatic aortic valve diseases
I06.9	Rheumatic aortic valve disease, unspecified
I08.0	Rheumatic disorders of both mitral and aortic valves
I08.1	Rheumatic disorders of both mitral and tricuspid valves
I08.2	Rheumatic disorders of both aortic and tricuspid valves
I08.3	Combined rheumatic disorders of mitral, aortic and tricuspid valves
I08.8	Other rheumatic multiple valve diseases
I08.9	Rheumatic multiple valve disease, unspecified
I09.0	Rheumatic myocarditis
I09.1	Rheumatic diseases of endocardium, valve unspecified
I09.2	Chronic rheumatic pericarditis
I09.81	Rheumatic heart failure
I09.89	Other specified rheumatic heart diseases
I09.9	Rheumatic heart disease, unspecified
I11.0	Hypertensive heart disease with heart failure
I11.9	Hypertensive heart disease without heart failure
I13.0	Hypertensive heart and chronic kidney disease with heart failure and stage 1 through stage 4 chronic kidney disease, or unspecified chronic kidney disease
I13.10	Hypertensive heart and chronic kidney disease without heart failure, with stage 1 through stage 4 chronic kidney disease, or unspecified chronic kidney disease
I13.11	Hypertensive heart and chronic kidney disease without heart failure, with stage 5 chronic kidney disease, or end stage renal disease

I13.2	Hypertensive heart and chronic kidney disease with heart failure and with stage 5 chronic kidney disease, or end stage renal disease
I20.0	Unstable angina
I20.1	Angina pectoris with documented spasm
I20.8	Other forms of angina pectoris
I21.01	ST elevation (STEMI) myocardial infarction involving left main coronary artery
I21.02	ST elevation (STEMI) myocardial infarction involving left anterior descending coronary artery
I21.09	ST elevation (STEMI) myocardial infarction involving other coronary artery of anterior wall
I21.11	ST elevation (STEMI) myocardial infarction involving right coronary artery
I21.19	ST elevation (STEMI) myocardial infarction involving other coronary artery of inferior wall
I21.21	ST elevation (STEMI) myocardial infarction involving left circumflex coronary artery
I21.29	ST elevation (STEMI) myocardial infarction involving other sites
I21.3	ST elevation (STEMI) myocardial infarction of unspecified site
I21.4	Non-ST elevation (NSTEMI) myocardial infarction
I21.9	Acute myocardial infarction, unspecified
I21.A1	Myocardial infarction type 2
I21.A9	Other myocardial infarction type
I22.0	Subsequent ST elevation (STEMI) myocardial infarction of anterior wall
I22.1	Subsequent ST elevation (STEMI) myocardial infarction of inferior wall
I22.2	Subsequent non-ST elevation (NSTEMI) myocardial infarction
I22.8	Subsequent ST elevation (STEMI) myocardial infarction of other sites

I22.9	Subsequent ST elevation (STEMI) myocardial infarction of unspecified site
I23.0	Hemopericardium as current complication following acute myocardial infarction
I23.1	Atrial septal defect as current complication following acute myocardial infarction
I23.2	Ventricular septal defect as current complication following acute myocardial infarction
I23.3	Rupture of cardiac wall without hemopericardium as current complication following acute myocardial infarction
I23.4	Rupture of chordae tendineae as current complication following acute myocardial infarction
I23.5	Rupture of papillary muscle as current complication following acute myocardial infarction
I23.6	Thrombosis of atrium, auricular appendage, and ventricle as current complications following acute myocardial infarction
I23.7	Postinfarction angina
I23.8	Other current complications following acute myocardial infarction
I24.0	Acute coronary thrombosis not resulting in myocardial infarction
I24.1	Dressler's syndrome
I24.8	Other forms of acute ischemic heart disease
I24.9	Acute ischemic heart disease, unspecified
I25.10	Atherosclerotic heart disease of native coronary artery without angina pectoris
I25.110	Atherosclerotic heart disease of native coronary artery with unstable angina pectoris
I25.111	Atherosclerotic heart disease of native coronary artery with angina pectoris with documented spasm
I25.118	Atherosclerotic heart disease of native coronary artery with other forms of angina pectoris

I25.119	Atherosclerotic heart disease of native coronary artery with unspecified angina pectoris
I25.3	Aneurysm of heart
I25.41	Coronary artery aneurysm
I25.42	Coronary artery dissection
I25.5	Ischemic cardiomyopathy
I25.6	Silent myocardial ischemia
I25.700	Atherosclerosis of coronary artery bypass graft(s), unspecified, with unstable angina pectoris
I25.701	Atherosclerosis of coronary artery bypass graft(s), unspecified, with angina pectoris with documented spasm
I25.708	Atherosclerosis of coronary artery bypass graft(s), unspecified, with other forms of angina pectoris
I25.709	Atherosclerosis of coronary artery bypass graft(s), unspecified, with unspecified angina pectoris
I25.710	Atherosclerosis of autologous vein coronary artery bypass graft(s) with unstable angina pectoris
I25.711	Atherosclerosis of autologous vein coronary artery bypass graft(s) with angina pectoris with documented spasm
I25.718	Atherosclerosis of autologous vein coronary artery bypass graft(s) with other forms of angina pectoris
I25.719	Atherosclerosis of autologous vein coronary artery bypass graft(s) with unspecified angina pectoris
I25.720	Atherosclerosis of autologous artery coronary artery bypass graft(s) with unstable angina pectoris
I25.721	Atherosclerosis of autologous artery coronary artery bypass graft(s) with angina pectoris with documented spasm
I25.728	Atherosclerosis of autologous artery coronary artery bypass graft(s) with other forms of angina pectoris
I25.729	Atherosclerosis of autologous artery coronary artery bypass graft(s) with unspecified angina pectoris

I25.730	Atherosclerosis of nonautologous biological coronary artery bypass graft(s) with unstable angina pectoris
I25.731	Atherosclerosis of nonautologous biological coronary artery bypass graft(s) with angina pectoris with documented spasm
I25.738	Atherosclerosis of nonautologous biological coronary artery bypass graft(s) with other forms of angina pectoris
I25.739	Atherosclerosis of nonautologous biological coronary artery bypass graft(s) with unspecified angina pectoris
I25.750	Atherosclerosis of native coronary artery of transplanted heart with unstable angina
I25.751	Atherosclerosis of native coronary artery of transplanted heart with angina pectoris with documented spasm
I25.758	Atherosclerosis of native coronary artery of transplanted heart with other forms of angina pectoris
I25.759	Atherosclerosis of native coronary artery of transplanted heart with unspecified angina pectoris
I25.760	Atherosclerosis of bypass graft of coronary artery of transplanted heart with unstable angina
I25.761	Atherosclerosis of bypass graft of coronary artery of transplanted heart with angina pectoris with documented spasm
I25.768	Atherosclerosis of bypass graft of coronary artery of transplanted heart with other forms of angina pectoris
I25.769	Atherosclerosis of bypass graft of coronary artery of transplanted heart with unspecified angina pectoris
I25.790	Atherosclerosis of other coronary artery bypass graft(s) with unstable angina pectoris
I25.791	Atherosclerosis of other coronary artery bypass graft(s) with angina pectoris with documented spasm
I25.798	Atherosclerosis of other coronary artery bypass graft(s) with other forms of angina pectoris
I25.799	Atherosclerosis of other coronary artery bypass graft(s) with unspecified angina pectoris

I25.810	Atherosclerosis of coronary artery bypass graft(s) without angina pectoris
I25.811	Atherosclerosis of native coronary artery of transplanted heart without angina pectoris
I25.812	Atherosclerosis of bypass graft of coronary artery of transplanted heart without angina pectoris
I25.82	Chronic total occlusion of coronary artery
I25.83	Coronary atherosclerosis due to lipid rich plaque
I25.84	Coronary atherosclerosis due to calcified coronary lesion
I25.89	Other forms of chronic ischemic heart disease
I25.9	Chronic ischemic heart disease, unspecified
I26.01	Septic pulmonary embolism with acute cor pulmonale
I26.02	Saddle embolus of pulmonary artery with acute cor pulmonale
I26.09	Other pulmonary embolism with acute cor pulmonale
I27.1	Kyphoscoliotic heart disease
I27.22	Pulmonary hypertension due to left heart disease
I27.81	Cor pulmonale (chronic)
I27.83	Eisenmenger's syndrome
I27.9	Pulmonary heart disease, unspecified
I30.0	Acute nonspecific idiopathic pericarditis
I30.1	Infective pericarditis
I30.8	Other forms of acute pericarditis
I30.9	Acute pericarditis, unspecified
I31.0	Chronic adhesive pericarditis
I31.1	Chronic constrictive pericarditis
I31.2	Hemopericardium, not elsewhere classified

I31.3	Pericardial effusion (noninflammatory)
I31.4	Cardiac tamponade
I31.8	Other specified diseases of pericardium
I31.9	Disease of pericardium, unspecified
I33.0	Acute and subacute infective endocarditis
I33.9	Acute and subacute endocarditis, unspecified
I34.0	Nonrheumatic mitral (valve) insufficiency
I34.1	Nonrheumatic mitral (valve) prolapse
I34.2	Nonrheumatic mitral (valve) stenosis
I34.8	Other nonrheumatic mitral valve disorders
I34.9	Nonrheumatic mitral valve disorder, unspecified
I35.0	Nonrheumatic aortic (valve) stenosis
I35.1	Nonrheumatic aortic (valve) insufficiency
I35.2	Nonrheumatic aortic (valve) stenosis with insufficiency
I35.8	Other nonrheumatic aortic valve disorders
I35.9	Nonrheumatic aortic valve disorder, unspecified
I36.0	Nonrheumatic tricuspid (valve) stenosis
I36.1	Nonrheumatic tricuspid (valve) insufficiency
I36.2	Nonrheumatic tricuspid (valve) stenosis with insufficiency
I36.8	Other nonrheumatic tricuspid valve disorders
I36.9	Nonrheumatic tricuspid valve disorder, unspecified
I37.0	Nonrheumatic pulmonary valve stenosis
I37.1	Nonrheumatic pulmonary valve insufficiency
I37.2	Nonrheumatic pulmonary valve stenosis with insufficiency

I37.8	Other nonrheumatic pulmonary valve disorders
I37.9	Nonrheumatic pulmonary valve disorder, unspecified
I38	Endocarditis, valve unspecified
I39	Endocarditis and heart valve disorders in diseases classified elsewhere
I40.0	Infective myocarditis
I40.1	Isolated myocarditis
I40.8	Other acute myocarditis
I40.9	Acute myocarditis, unspecified
I41	Myocarditis in diseases classified elsewhere
I42.0	Dilated cardiomyopathy
I42.1	Obstructive hypertrophic cardiomyopathy
I42.2	Other hypertrophic cardiomyopathy
I42.3	Endomyocardial (eosinophilic) disease
I42.4	Endocardial fibroelastosis
I42.5	Other restrictive cardiomyopathy
I42.6	Alcoholic cardiomyopathy
I42.7	Cardiomyopathy due to drug and external agent
I42.8	Other cardiomyopathies
I42.9	Cardiomyopathy, unspecified
I43	Cardiomyopathy in diseases classified elsewhere
I44.0	Atrioventricular block, first degree
I44.1	Atrioventricular block, second degree
I44.2	Atrioventricular block, complete
I44.3	Other and unspecified atrioventricular block

I44.30	Unspecified atrioventricular block
I44.39	Other atrioventricular block
I44.4	Left anterior fascicular block
I44.5	Left posterior fascicular block
I44.60	Unspecified fascicular block
I44.69	Other fascicular block
I44.7	Left bundle-branch block, unspecified
I45.0	Right fascicular block
I45.10	Unspecified right bundle-branch block
I45.19	Other right bundle-branch block
I45.2	Bifascicular block
I45.3	Trifascicular block
I45.4	Nonspecific intraventricular block
I45.5	Other specified heart block
I45.6	Pre-excitation syndrome
I45.81	Long QT syndrome
I45.89	Other specified conduction disorders
I45.9	Conduction disorder, unspecified
I46.2	Cardiac arrest due to underlying cardiac condition
I46.8	Cardiac arrest due to other underlying condition
I46.9	Cardiac arrest, cause unspecified
I47.0	Re-entry ventricular arrhythmia
I47.1	Supraventricular tachycardia
I47.2	Ventricular tachycardia

I47.9	Paroxysmal tachycardia, unspecified
I48.0	Paroxysmal atrial fibrillation
I48.11	Longstanding persistent atrial fibrillation
I48.19	Other persistent atrial fibrillation
I48.20	Chronic atrial fibrillation, unspecified
I48.21	Permanent atrial fibrillation
I48.3	Typical atrial flutter
I48.4	Atypical atrial flutter
I48.91	Unspecified atrial fibrillation
I48.92	Unspecified atrial flutter
I49.01	Ventricular fibrillation
I49.02	Ventricular flutter
I49.1	Atrial premature depolarization
I49.2	Junctional premature depolarization
I49.3	Ventricular premature depolarization
I49.40	Unspecified premature depolarization
I49.49	Other premature depolarization
I49.5	Sick sinus syndrome
I49.8	Other specified cardiac arrhythmias
I49.9	Cardiac arrhythmia, unspecified
I50.1	Left ventricular failure, unspecified
I50.21	Acute systolic (congestive) heart failure
I50.22	Chronic systolic (congestive) heart failure
I50.23	Acute on chronic systolic (congestive) heart failure

I50.30	Unspecified diastolic (congestive) heart failure
I50.31	Acute diastolic (congestive) heart failure
I50.32	Chronic diastolic (congestive) heart failure
I50.33	Acute on chronic diastolic (congestive) heart failure
I50.40	Unspecified combined systolic (congestive) and diastolic (congestive) heart failure
I50.41	Acute combined systolic (congestive) and diastolic (congestive) heart failure
I50.42	Chronic combined systolic (congestive) and diastolic (congestive) heart failure
I50.43	Acute on chronic combined systolic (congestive) and diastolic (congestive) heart failure
I50.810	Right heart failure, unspecified
I50.811	Acute right heart failure
I50.812	Chronic right heart failure
I50.813	Acute on chronic right heart failure
I50.814	Right heart failure due to left heart failure
I50.82	Biventricular heart failure
I50.83	High output heart failure
I50.84	End stage heart failure
I50.89	Other heart failure
I50.9	Heart failure, unspecified
I51.0	Cardiac septal defect, acquired
I51.1	Rupture of chordae tendineae, not elsewhere classified
I51.2	Rupture of papillary muscle, not elsewhere classified
I51.3	Intracardiac thrombosis, not elsewhere classified

I51.4	Myocarditis, unspecified
I51.5	Myocardial degeneration
I51.7	Cardiomegaly
I51.81	Takotsubo syndrome
I51.89	Other ill-defined heart diseases
I51.9	Heart disease, unspecified
I52	Other heart disorders in diseases classified elsewhere

16.4.1.6. History of SARS-CoV-2 Infection

16.4.1.6.1. ICD-10-CM Codes

U07.1	COVID-19, virus identified
B97.29	Other coronavirus as the cause of diseases classified elsewhere
J12.82	Pneumonia due to coronavirus disease 2019
Z86.16	Personal history of COVID-19

16.4.1.7. Hypertension

16.4.1.7.1. ICD-10-CM Codes

I10	Essential (primary) hypertension
I15	Secondary hypertension
I1A	Other hypertension

16.4.1.8. Immunocompromised Status

16.4.1.8.1. ICD-10-CM Codes

D80.0	Hereditary hypogammaglobulinemia
D80.1	Nonfamilial hypogammaglobulinemia
D80.2	Selective deficiency of immunoglobulin A [IgA]
D80.3	Selective deficiency of immunoglobulin G [IgG] subclasses
D80.4	Selective deficiency of immunoglobulin M [IgM]
D80.5	Immunodeficiency with increased immunoglobulin M [IgM]

D80.6	Antibody deficiency with near-normal immunoglobulins or with hyperimmunoglobulinemia
D80.7	Transient hypogammaglobulinemia of infancy
D80.8	Other immunodeficiencies with predominantly antibody defects
D80.9	Immunodeficiency with predominantly antibody defects, unspecified
D81.0	Severe combined immunodeficiency [SCID] with reticular dysgenesis
D81.1	Severe combined immunodeficiency [SCID] with low T- and B-cell numbers
D81.2	Severe combined immunodeficiency [SCID] with low or normal B-cell numbers
D81.30	Adenosine deaminase deficiency, unspecified
D81.31	Severe combined immunodeficiency due to adenosine deaminase deficiency
D81.32	Adenosine deaminase 2 deficiency
D81.39	Other adenosine deaminase deficiency
D81.4	Nezelof's syndrome
D81.5	Purine nucleoside phosphorylase [PNP] deficiency
D81.6	Major histocompatibility complex class I deficiency
D81.7	Major histocompatibility complex class II deficiency
D81.8	Other combined immunodeficiencies
D81.81	Biotin-dependent carboxylase deficiency
D81.810	Biotinidase deficiency
D81.818	Other biotin-dependent carboxylase deficiency
D81.819	Biotin-dependent carboxylase deficiency, unspecified
D81.89	Other combined immunodeficiencies
D81.9	Combined immunodeficiency, unspecified

D82.0	Wiskott-Aldrich syndrome
D82.1	Di George's syndrome
D82.2	Immunodeficiency with short-limbed stature
D82.3	Immunodeficiency following hereditary defective response to Epstein-Barr virus
D82.4	Hyperimmunoglobulin E [IgE] syndrome
D82.8	Immunodeficiency associated with other specified major defects
D82.9	Immunodeficiency associated with major defect, unspecified
D83	Common variable immunodeficiency
D83.0	Common variable immunodeficiency with predominant abnormalities of B-cell numbers and function
D83.1	Common variable immunodeficiency with predominant immunoregulatory T-cell disorders
D83.2	Common variable immunodeficiency with autoantibodies to B- or T-cells
D83.8	Other common variable immunodeficiencies
D83.9	Common variable immunodeficiency, unspecified
D84.0	Lymphocyte function antigen-1 [LFA-1] defect
D84.1	Defects in the complement system
D84.8	Other specified immunodeficiencies
D84.9	Immunodeficiency, unspecified
B20	Human immunodeficiency virus [HIV] disease
Z21	Asymptomatic human immunodeficiency virus [HIV] infection status
O98.7	Human immunodeficiency virus [HIV] disease complicating pregnancy, childbirth and the puerperium
B97.35	Human immunodeficiency virus, type 2 [HIV 2] as the cause of diseases classified elsewhere

Z94.0	Kidney transplant status
Z94.1	Heart transplant status
Z94.2	Lung transplant status
Z94.3	Heart and lungs transplant status
Z94.4	Liver transplant status
Z94.5	Skin transplant status
Z94.6	Bone transplant status
Z94.7	Corneal transplant status
Z94.81	Bone marrow transplant status
Z94.82	Intestine transplant status
Z94.83	Pancreas transplant status
Z94.84	Stem cells transplant status
Z94.89	Other transplanted organ and tissue status
Z94.9	Transplanted organ and tissue status, unspecified

16.4.1.8.2. CPT Codes[6]

33935	Heart-lung transplant with recipient cardiectomy-pneumonectomy
33945	Heart transplant, with or without recipient cardiectomy
80158	Cyclosporine
80197	Tacrolimus
80195	Sirolimus
80180	Mycophenolate (mycophenolic acid)

16.4.1.8.3. HCPCS Codes

J0485	Injection, belatacept, 1 mg

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J7500	Azathioprine, oral, 50 mg
J7501	Azathioprine, parenteral, 100 mg
J7502	Cyclosporine, oral, 100 mg
J7503	Tacrolimus, extended release, (Envarsus XR), oral, 0.25 mg
J7504	Lymphocyte immune globulin, antithymocyte globulin, equine, parenteral, 250 mg
J7505	Muromonab-CD3, parenteral, 5 mg
J7507	Tacrolimus, immediate release, oral, 1 mg
J7508	Tacrolimus, extended release, (Astagraf XL), oral, 0.1 mg
J7509	Methylprednisolone oral, per 4 mg
J7510	Prednisolone oral, per 5 mg
J7511	Lymphocyte immune globulin, antithymocyte globulin, rabbit, parenteral, 25 mg
J7512	Prednisone, immediate release or delayed release, oral, 1 mg
J7513	Daclizumab, parenteral, 25 mg
J7515	Cyclosporine, oral, 25 mg
J7516	Cyclosporin, parenteral, 250 mg
J7517	Mycophenolate mofetil, oral, 250 mg
J7518	Mycophenolic acid, oral, 180 mg
J7519	Injection, mycophenolate mofetil, 10 mg
J7520	Sirolimus, oral, 1 mg
J7525	Tacrolimus, parenteral, 5 mg
J7527	Everolimus, oral, 0.25 mg
J7599	Immunosuppressive drug, not otherwise classified
J8530	Cyclophosphamide; oral, 25 mg

J8610 Methotrexate; oral, 2.5 mg

16.4.1.8.4. NDC Codes

NDC codes corresponding to the above immunosuppressant medications will be utilized where applicable.

16.4.1.9. Kidney Disorders, Including Chronic Kidney Disease

16.4.1.9.1. ICD-10-CM Codes

N00.0 Acute nephritic syndrome with minor glomerular abnormality

N00.1 Acute nephritic syndrome with focal and segmental glomerular lesions

N00.2 Acute nephritic syndrome with diffuse membranous glomerulonephritis

N00.3 Acute nephritic syndrome with diffuse mesangial proliferative glomerulonephritis

N00.4 Acute nephritic syndrome with diffuse endocapillary proliferative glomerulonephritis

N00.5 Acute nephritic syndrome with diffuse mesangiocapillary glomerulonephritis

N00.6 Acute nephritic syndrome with dense deposit disease

N00.7 Acute nephritic syndrome with diffuse crescentic glomerulonephritis

N00.8 Acute nephritic syndrome with other morphologic changes

N00.9 Acute nephritic syndrome with unspecified morphologic changes

N01.0 Rapidly progressive nephritic syndrome with minor glomerular abnormality

N01.1 Rapidly progressive nephritic syndrome with focal and segmental glomerular lesions

N01.2 Rapidly progressive nephritic syndrome with diffuse membranous glomerulonephritis

N01.3 Rapidly progressive nephritic syndrome with diffuse mesangial proliferative glomerulonephritis

N01.4 Rapidly progressive nephritic syndrome with diffuse endocapillary proliferative glomerulonephritis

N01.5	Rapidly progressive nephritic syndrome with diffuse mesangiocapillary glomerulonephritis
N01.6	Rapidly progressive nephritic syndrome with dense deposit disease
N01.7	Rapidly progressive nephritic syndrome with diffuse crescentic glomerulonephritis
N01.8	Rapidly progressive nephritic syndrome with other morphologic changes
N01.9	Rapidly progressive nephritic syndrome with unspecified morphologic changes
N02.0	Recurrent and persistent hematuria with minor glomerular abnormality
N02.1	Recurrent and persistent hematuria with focal and segmental glomerular lesions
N02.2	Recurrent and persistent hematuria with diffuse membranous glomerulonephritis
N02.3	Recurrent and persistent hematuria with diffuse mesangial proliferative glomerulonephritis
N02.4	Recurrent and persistent hematuria with diffuse endocapillary proliferative glomerulonephritis
N02.5	Recurrent and persistent hematuria with diffuse mesangiocapillary glomerulonephritis
N02.6	Recurrent and persistent hematuria with dense deposit disease
N02.7	Recurrent and persistent hematuria with diffuse crescentic glomerulonephritis
N02.8	Recurrent and persistent hematuria with other morphologic changes
N02.9	Recurrent and persistent hematuria with unspecified morphologic changes
N03.0	Chronic nephritic syndrome with minor glomerular abnormality
N03.1	Chronic nephritic syndrome with focal and segmental glomerular lesions
N03.2	Chronic nephritic syndrome with diffuse membranous glomerulonephritis

N03.3	Chronic nephritic syndrome with diffuse mesangial proliferative glomerulonephritis
N03.4	Chronic nephritic syndrome with diffuse endocapillary proliferative glomerulonephritis
N03.5	Chronic nephritic syndrome with diffuse mesangiocapillary glomerulonephritis
N03.6	Chronic nephritic syndrome with dense deposit disease
N03.7	Chronic nephritic syndrome with diffuse crescentic glomerulonephritis
N03.8	Chronic nephritic syndrome with other morphologic changes
N03.9	Chronic nephritic syndrome with unspecified morphologic changes
N04.0	Nephrotic syndrome with minor glomerular abnormality
N04.1	Nephrotic syndrome with focal and segmental glomerular lesions
N04.2	Nephrotic syndrome with diffuse membranous glomerulonephritis
N04.3	Nephrotic syndrome with diffuse mesangial proliferative glomerulonephritis
N04.4	Nephrotic syndrome with diffuse endocapillary proliferative glomerulonephritis
N04.5	Nephrotic syndrome with diffuse mesangiocapillary glomerulonephritis
N04.6	Nephrotic syndrome with dense deposit disease
N04.7	Nephrotic syndrome with diffuse crescentic glomerulonephritis
N04.8	Nephrotic syndrome with other morphologic changes
N04.9	Nephrotic syndrome with unspecified morphologic changes
N05.0	Unspecified nephritic syndrome with minor glomerular abnormality
N05.1	Unspecified nephritic syndrome with focal and segmental glomerular lesions
N05.2	Unspecified nephritic syndrome with diffuse membranous glomerulonephritis

N05.3	Unspecified nephritic syndrome with diffuse mesangial proliferative glomerulonephritis
N05.4	Unspecified nephritic syndrome with diffuse endocapillary proliferative glomerulonephritis
N05.5	Unspecified nephritic syndrome with diffuse mesangiocapillary glomerulonephritis
N05.6	Unspecified nephritic syndrome with dense deposit disease
N05.7	Unspecified nephritic syndrome with diffuse crescentic glomerulonephritis
N05.8	Unspecified nephritic syndrome with other morphologic changes
N05.9	Unspecified nephritic syndrome with unspecified morphologic changes
N06.0	Isolated proteinuria with minor glomerular abnormality
N06.1	Isolated proteinuria with focal and segmental glomerular lesions
N06.2	Isolated proteinuria with diffuse membranous glomerulonephritis
N06.3	Isolated proteinuria with diffuse mesangial proliferative glomerulonephritis
N06.4	Isolated proteinuria with diffuse endocapillary proliferative glomerulonephritis
N06.5	Isolated proteinuria with diffuse mesangiocapillary glomerulonephritis
N06.6	Isolated proteinuria with dense deposit disease
N06.7	Isolated proteinuria with diffuse crescentic glomerulonephritis
N06.8	Isolated proteinuria with other morphologic lesion
N06.9	Isolated proteinuria with unspecified morphologic lesion
N07.0	Hereditary nephropathy, not elsewhere classified with minor glomerular abnormality
N07.1	Hereditary nephropathy, not elsewhere classified with focal and segmental glomerular lesions

N07.2	Hereditary nephropathy, not elsewhere classified with diffuse membranous glomerulonephritis
N07.3	Hereditary nephropathy, not elsewhere classified with diffuse mesangial proliferative glomerulonephritis
N07.4	Hereditary nephropathy, not elsewhere classified with diffuse endocapillary proliferative glomerulonephritis
N07.5	Hereditary nephropathy, not elsewhere classified with diffuse mesangiocapillary glomerulonephritis
N07.6	Hereditary nephropathy, not elsewhere classified with dense deposit disease
N07.7	Hereditary nephropathy, not elsewhere classified with diffuse crescentic glomerulonephritis
N07.8	Hereditary nephropathy, not elsewhere classified with other morphologic lesions
N07.9	Hereditary nephropathy, not elsewhere classified with unspecified morphologic lesions
N08	Glomerular disorders in diseases classified elsewhere
N10	Acute pyelonephritis
N11.0	Nonobstructive reflux-associated chronic pyelonephritis
N11.1	Chronic obstructive pyelonephritis
N11.8	Other chronic tubulo-interstitial nephritis
N11.9	Chronic tubulo-interstitial nephritis, unspecified
N12	Tubulo-interstitial nephritis, not specified as acute or chronic
N13.0	Hydronephrosis with ureteropelvic junction obstruction
N13.1	Hydronephrosis with ureteral stricture, not elsewhere classified
N13.2	Hydronephrosis with renal and ureteral calculous obstruction
N13.30	Unspecified hydronephrosis
N13.39	Other hydronephrosis

N13.4	Hydroureter
N13.5	Crossing vessel and stricture of ureter without hydronephrosis
N13.6	Pyonephrosis
N13.70	Vesicoureteral-reflux, unspecified
N13.71	Vesicoureteral-reflux without reflux nephropathy
N13.721	Vesicoureteral-reflux with reflux nephropathy without hydroureter, unilateral
N13.722	Vesicoureteral-reflux with reflux nephropathy without hydroureter, bilateral
N13.729	Vesicoureteral-reflux with reflux nephropathy without hydroureter, unspecified
N13.731	Vesicoureteral-reflux with reflux nephropathy with hydroureter, unilateral
N13.732	Vesicoureteral-reflux with reflux nephropathy with hydroureter, bilateral
N13.739	Vesicoureteral-reflux with reflux nephropathy with hydroureter, unspecified
N13.8	Other obstructive and reflux uropathy
N13.9	Obstructive and reflux uropathy, unspecified
N14.0	Analgesic nephropathy
N14.1	Nephropathy induced by other drugs, medicaments and biological substances
N14.2	Nephropathy induced by unspecified drug, medicament or biological substance
N14.3	Nephropathy induced by heavy metals
N14.4	Toxic nephropathy, not elsewhere classified
N15.0	Balkan nephropathy
N15.1	Renal and perinephric abscess

N15.8	Other specified renal tubulo-interstitial diseases
N15.9	Renal tubulo-interstitial disease, unspecified
N16	Renal tubulo-interstitial disorders in diseases classified elsewhere
N17.0	Acute kidney failure with tubular necrosis
N17.1	Acute kidney failure with acute cortical necrosis
N17.2	Acute kidney failure with medullary necrosis
N17.8	Other acute kidney failure
N17.9	Acute kidney failure, unspecified
N18.1	Chronic kidney disease, stage 1
N18.2	Chronic kidney disease, stage 2 (mild)
N18.3	Chronic kidney disease, stage 3 (moderate)
N18.4	Chronic kidney disease, stage 4 (severe)
N18.5	Chronic kidney disease, stage 5
N18.6	End stage renal disease
N18.9	Chronic kidney disease, unspecified
N19	Unspecified kidney failure
N20.0	Calculus of kidney
N20.1	Calculus of ureter
N20.2	Calculus of kidney with calculus of ureter
N20.9	Urinary calculus, unspecified
N23	Unspecified renal colic
N25.0	Renal osteodystrophy
N25.1	Nephrogenic diabetes insipidus
N25.81	Secondary hyperparathyroidism of renal origin

N25.89	Other disorders resulting from impaired renal tubular function
N25.9	Disorder resulting from impaired renal tubular function, unspecified
N26	Unspecified contracted kidney
N26.1	Atrophy of kidney (terminal)
N26.2	Page kidney
N26.9	Renal sclerosis, unspecified
N27.0	Small kidney, unilateral
N27.1	Small kidney, bilateral
N27.9	Small kidney, unspecified
N28.0	Ischemia and infarction of kidney
N28.1	Cyst of kidney, acquired
N28.81	Hypertrophy of kidney
N28.82	Megaloureter
N28.83	Nephroptosis
N28.84	Pyelitis cystica
N28.85	Pyeloureteritis cystica
N28.86	Ureteritis cystica
N28.89	Other specified disorders of kidney and ureter
N28.9	Disorder of kidney and ureter, unspecified
N29	Other disorders of kidney and ureter in diseases classified elsewhere

16.4.1.10. Liver Disorders

16.4.1.10.1. ICD-10-CM Codes

K70.10	Alcoholic hepatitis without ascites
K70.11	Alcoholic hepatitis with ascites
K70.2	Alcoholic fibrosis and sclerosis of liver
K70.30	Alcoholic cirrhosis of liver without ascites
K70.31	Alcoholic cirrhosis of liver with ascites
K70.40	Alcoholic hepatic failure without coma
K70.41	Alcoholic hepatic failure with coma
K70.9	Alcoholic liver disease, unspecified
K71.0	Toxic liver disease with cholestasis
K71.10	Toxic liver disease with hepatic necrosis, without coma
K71.11	Toxic liver disease with hepatic necrosis, with coma
K71.2	Toxic liver disease with acute hepatitis
K71.3	Toxic liver disease with chronic persistent hepatitis
K71.4	Toxic liver disease with chronic lobular hepatitis
K71.50	Toxic liver disease with chronic active hepatitis without ascites
K71.51	Toxic liver disease with chronic active hepatitis with ascites
K71.6	Toxic liver disease with hepatitis, not elsewhere classified
K71.7	Toxic liver disease with fibrosis and cirrhosis of liver
K71.8	Toxic liver disease with other disorders of liver
K71.9	Toxic liver disease, unspecified K72 Hepatic failure, not elsewhere classified Includes: fulminant hepatitis NEC, with hepatic failure
K72.00	Acute and subacute hepatic failure without coma
K72.01	Acute and subacute hepatic failure with coma

K72.10	Chronic hepatic failure without coma
K72.11	Chronic hepatic failure with coma
K72.90	Hepatic failure, unspecified without coma
K72.91	Hepatic failure, unspecified with coma
K73.0	Chronic persistent hepatitis, not elsewhere classified
K73.1	Chronic lobular hepatitis, not elsewhere classified
K73.2	Chronic active hepatitis, not elsewhere classified
K73.8	Other chronic hepatitis, not elsewhere classified
K73.9	Chronic hepatitis, unspecified
K74.0	Hepatic fibrosis
K74.1	Hepatic sclerosis
K74.2	Hepatic fibrosis with hepatic sclerosis
K74.3	Primary biliary cirrhosis
K74.4	Secondary biliary cirrhosis
K74.5	Biliary cirrhosis, unspecified
K74.60	Unspecified cirrhosis of liver
K74.69	Other cirrhosis of liver
K75.0	Abscess of liver
K75.1	Phlebitis of portal vein
K75.2	Nonspecific reactive hepatitis
K75.3	Granulomatous hepatitis, not elsewhere classified
K75.4	Autoimmune hepatitis
K75.81	Nonalcoholic steatohepatitis (NASH)
K75.89	Other specified inflammatory liver diseases

K75.9	Inflammatory liver disease, unspecified
K76.0	Fatty (change of) liver, not elsewhere classified
K76.1	Chronic passive congestion of liver
K76.2	Central hemorrhagic necrosis of liver
K76.3	Infarction of liver
K76.4	Peliosis hepatis
K76.5	Hepatic veno-occlusive disease
K76.6	Portal hypertension
K76.7	Hepatorenal syndrome
K76.81	Hepatopulmonary syndrome
K76.89	Other specified diseases of liver
K76.9	Liver disease, unspecified
K77	Liver disorders in diseases classified elsewhere

16.4.1.11. Long COVID

16.4.1.11.1. ICD-10-CM Codes

U09.9	Post COVID-19 condition, unspecified

16.4.1.12. Neurological or Neurodevelopmental Conditions

16.4.1.12.1. ICD-10-CM Codes

F70	Mild intellectual disabilities
F71	Moderate intellectual disabilities
F72	Severe intellectual disabilities
F73	Profound intellectual disabilities
F78	Other intellectual disabilities
F79	Unspecified intellectual disabilities
F80.0	Phonological disorder

F80.1	Expressive language disorder
F80.2	Mixed receptive-expressive language disorder
F80.4	Speech and language development delay due to hearing loss
F80.81	Childhood onset fluency disorder
F80.82	Social pragmatic communication disorder
F80.89	Other developmental disorders of speech and language
F80.9	Developmental disorder of speech and language, unspecified
F81.0	Specific reading disorder
F81.2	Mathematics disorder
F81.81	Disorder of written expression
F81.89	Other developmental disorders of scholastic skills
F81.9	Developmental disorder of scholastic skills, unspecified
F82	Specific developmental disorder of motor function
F84.0	Autistic disorder
F84.2	Rett's syndrome
F84.3	Other childhood disintegrative disorder
F84.5	Asperger's syndrome
F84.8	Other pervasive developmental disorders
F84.9	Pervasive developmental disorder, unspecified
F89	Unspecified disorder of psychological development

16.4.1.13. Malignant Neoplasms

16.4.1.13.1. ICD-10-CM Codes

C00-C14	Malignant neoplasms of lip, oral cavity and pharynx
C15-C26	Malignant neoplasms of digestive organs
C30-C39	Malignant neoplasms of respiratory and intrathoracic organs

C40-C41	Malignant neoplasms of bone and articular cartilage
C43-C44	Melanoma and other malignant neoplasms of skin
C45-C49	Malignant neoplasms of mesothelial and soft tissue
C50	Malignant neoplasms of breast
C51-C58	Malignant neoplasms of female genital organs
C60-C63	Malignant neoplasms of male genital organs
C64-C68	Malignant neoplasms of urinary tract
C69-C72	Malignant neoplasms of eye, brain and other parts of central nervous system
C73-C75	Malignant neoplasms of thyroid and other endocrine glands
C7A	Malignant neuroendocrine tumors
C7B	Secondary neuroendocrine tumors
C76-C80	Malignant neoplasms of ill-defined, other secondary and unspecified sites
C81-C96	Malignant neoplasms of lymphoid, hematopoietic and related tissue

16.4.1.14. Obesity

16.4.1.14.1. ICD-10-CM Codes

E66.0	Obesity due to excess calories
E66.01	Morbid (severe) obesity due to excess calories
E66.09	Other obesity due to excess calories
E66.1	Drug-induced obesity
E66.2	Morbid (severe) obesity with alveolar hypoventilation
E66.8	Other obesity
E66.9	Obesity, unspecified
Z68.3*	Body mass index (BMI) 30-39, adult
Z68.4*	Body mass index (BMI, 40 or greater, adult

16.4.1.15. Type 2 Diabetes

16.4.1.15.1. ICD-10-CM Codes

E11.00	Type 2 diabetes mellitus with hyperosmolarity without nonketotic hyperglycemic-hyperosmolar coma (NKHHC)
E11.01	Type 2 diabetes mellitus with hyperosmolarity with coma
E11.10	Type 2 diabetes mellitus with ketoacidosis without coma
E11.11	Type 2 diabetes mellitus with ketoacidosis with coma
E11.21	Type 2 diabetes mellitus with diabetic nephropathy
E11.22	Type 2 diabetes mellitus with diabetic chronic kidney disease
E11.29	Type 2 diabetes mellitus with other diabetic kidney complication
E11.311	Type 2 diabetes mellitus with unspecified diabetic retinopathy with macular edema
E11.319	Type 2 diabetes mellitus with unspecified diabetic retinopathy without macular edema
E11.321	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema
E11.329	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema
E11.331	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema
E11.339	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema
E11.341	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema
E11.349	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema
E11.351	Type 2 diabetes mellitus with proliferative diabetic retinopathy with macular edema
E11.352	Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula

E11.353 Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula

E11.354 Type 2 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment

E11.355 Type 2 diabetes mellitus with stable proliferative diabetic retinopathy

E11.359 Type 2 diabetes mellitus with proliferative diabetic retinopathy without macular edema

E11.36 Type 2 diabetes mellitus with diabetic cataract

E11.37 Type 2 diabetes mellitus with diabetic macular edema, resolved following treatment

E11.39 Type 2 diabetes mellitus with other diabetic ophthalmic complication

E11.40 Type 2 diabetes mellitus with diabetic neuropathy, unspecified

E11.41 Type 2 diabetes mellitus with diabetic mononeuropathy

E11.42 Type 2 diabetes mellitus with diabetic polyneuropathy

E11.43 Type 2 diabetes mellitus with diabetic autonomic (poly)neuropathy

E11.44 Type 2 diabetes mellitus with diabetic amyotrophy

E11.49 Type 2 diabetes mellitus with other diabetic neurological complication

E11.51 Type 2 diabetes mellitus with diabetic peripheral angiopathy without gangrene

E11.52 Type 2 diabetes mellitus with diabetic peripheral angiopathy with gangrene

E11.59 Type 2 diabetes mellitus with other circulatory complications

E11.610 Type 2 diabetes mellitus with diabetic neuropathic arthropathy

E11.618 Type 2 diabetes mellitus with other diabetic arthropathy

E11.620 Type 2 diabetes mellitus with diabetic dermatitis

E11.621 Type 2 diabetes mellitus with foot ulcer

E11.628 Type 2 diabetes mellitus with other skin complications

E11.630 Type 2 diabetes mellitus with periodontal disease

E11.638 Type 2 diabetes mellitus with other oral complications

E11.641 Type 2 diabetes mellitus with hypoglycemia with coma

E11.649 Type 2 diabetes mellitus with hypoglycemia without coma

E11.65 Type 2 diabetes mellitus with hyperglycemia

E11.69 Type 2 diabetes mellitus with other specified complication

E11.8 Type 2 diabetes mellitus with unspecified complications

E11.9 Type 2 diabetes mellitus without complications

16.4.2. Medication History

16.4.2.1. Systemic Immunomodulators

The below list includes generic drug names classified by therapeutic use. All associated NDCs will be utilized. Additional therapies may be added as they are approved.

16.4.2.1.1. Immunomodulators

16.4.2.1.1.1. Colony-Stimulating Factors

ancestim
balugrastim
efbemalenograstim alfa
empegfilgrastim
filgrastim
lenograstim
lipegfilgrastim
molgramostim
pegfilgrastim
pegteograstim
sargramostim

16.4.2.1.1.2. Interferons

albinterferon alfa-2b
cepeginterferon alfa-2b
interferon alfa natural
interferon alfa-2a
interferon alfa-2b
interferon alfacon-1

interferon alfa-n1
interferon beta natural
interferon beta-1a
interferon beta-1b
interferon gamma
peginterferon alfa-2a
peginterferon alfa-2a, combinations
peginterferon alfa-2b
peginterferon alfa-2b, combinations
peginterferon alfacon-2
peginterferon beta-1a
ropeginterferon alfa-2b

16.4.2.1.1.3. Interleukins

aldesleukin
oprelvekin

16.4.2.1.1.4. Other Immunostimulants

BCG vaccine
cridanimod
dasiprotimut-T
elapegademase
glatiramer acetate
histamine dihydrochloride
immunocyanin
lentinan
melanoma vaccine
mifamurtide
pegademase
pidotimod
plerixafor
polyinosinic:polycytidylic acid (poly I:C)
poly ICLC
roquinimex
sipuleucel-T
tasonermin
thymopentin

16.4.2.1.2. Immunosuppressants

16.4.2.1.2.1. Selective Immunosuppressants

abatacept
abetimus
alefacept
alemtuzumab
anifrolumab
antilymphocyte immunoglobulin (horse)
antithymocyte immunoglobulin (rabbit)
apremilast
avacopan
baricitinib
begelomab
belatacept
belimumab
belumosudil
cladribine
deucravacitinib
eculizumab
efalizumab
efgartigimod alfa
emapalumab
everolimus
filgotinib
fingolimod
gusperimus
imlifidase
inebilizumab
itacitinib
leflunomide
muromonab-CD3
mycophenolic acid
natalizumab
ocrelizumab
ofatumumab
ozanimod
peficitinib
pegcetacoplan
ponesimod
ravulizumab

siponimod
sirolimus
sutimlimab
teprotumumab
teriflunomide
tofacitinib
ublituximab
upadacitinib
vedolizumab

16.4.2.1.2.2. Tumor Necrosis Factor Alpha (TNF-α) Inhibitors

adalimumab
afelimomab
certolizumab pegol
etanercept
golimumab
infliximab
opinercept

16.4.2.1.2.3. Interleukin Inhibitors

anakinra
basiliximab
bimekizumab
briakinumab
brodalumab
canakinumab
daclizumab
guselkumab
ixekizumab
netakimab
olokizumab
rilonacept
risankizumab
sarilumab
satralizumab
secukinumab
siltuximab
sirukumab
spesolimab
tildrakizumab
tocilizumab
ustekinumab

16.4.2.1.2.4. Calcineurin Inhibitors

cyclosporine
tacrolimus
voclosporin

16.4.2.1.2.5. Other Immunosuppressants

azathioprine
darvadstrocel
dimethyl fumarate
diroximel fumarate
lenalidomide
methotrexate
pirfenidone
pomalidomide
thalidomide

16.4.2.1.3. Chemotherapeutic Agents

16.4.2.1.3.1. Alkylating Agents

chlorambucil
cisplatin
cyclophosphamide

16.4.2.1.3.2. Antimetabolite Agents

5-fluorouracil
6-mercaptopurine
cytarabine
methotrexate

16.4.2.1.3.3. Antitumor Antibiotics

bleomycin
doxorubicin
mitomycin C

16.4.2.1.3.4. Mitotic Inhibitors

paclitaxel
plant alkaloids (vinblastine, vincristine)

16.4.2.1.3.5. Topoisomerase Inhibitors

etoposide
irinotecan
opotecan

16.4.2.1.4. Myelosuppresive Agents

hydroxyurea

16.4.2.1.5. ICD-10-CM, CPT and HCPCS Codes

In addition to NDC codes for the above, the following ICD-10, CPT and HCPCS codes will be used:

ICD-10-CM:

T45.1***	Poisoning by, adverse effect of and underdosing of antineoplastic and immunosuppressive drugs
Z79.6	Long term (current) use of immunomodulators and immunosuppressants
Z79.60	Long term (current) use of unspecified immunomodulators and immunosuppressants
Z79.61	Long term (current) use of immunomodulator (apremilast, immunomodulatory imide drug, lenalidomide, pomalidomide)
Z79.62	Long term (current) use of immunosuppressant
Z79.620	Long term (current) use of immunosuppressive biologic (adalimumab, etanercept, infliximab, monoclonal antibodies)
Z79.621	Long term (current) use of calcineurin inhibitor (cyclosporine, tacrolimus)
Z79.622	Long term (current) use of Janus kinase inhibitor (tofacitinib)
Z79.623	Long term (current) use of mammalian target of rapamycin (mTOR) inhibitor (sirolimus)
Z79.624	Long term (current) use of inhibitors of nucleotide synthesis (azathioprine, omycophenolate, purine synthesis (IMDH) inhibitors)
Z79.63	Long term (current) use of chemotherapeutic agent
Z79.630	Long term (current) use of alkylating agent (chlorambucil, cisplatin, cyclophosphamide)
Z79.631	Long term (current) use of antimetabolite agent (5-fluorouracil, 6-mercaptopurine, cytarabine, methotrexate)

Z79.632	Long term (current) use of antitumor antibiotic (bleomycin, doxorubicin, mitomycin C)
Z79.633	Long term (current) use of mitotic inhibitor (paclitaxel, plant alkaloids, vinblastine, vincristine)
Z79.634	Long term (current) use of topoisomerase inhibitor (etoposide, irinotecan, topotecan)
Z79.64	Long term (current) use of myelosuppressive agent (hydroxyurea)
Z79.69	Long term (current) use of other immunomodulators and immunosuppressants

ICD-10-PCS:

3E03302	Introduction of High-dose Interleukin-2 into Peripheral Vein, Percutaneous Approach
3E03303	Introduction of Low-dose Interleukin-2 into Peripheral Vein, Percutaneous Approach
3E04002	Introduction of High-dose Interleukin-2 into Central Vein, Open Approach
3E04003	Introduction of Low-dose Interleukin-2 into Central Vein, Open Approach
3E04302	Introduction of High-dose Interleukin-2 into Central Vein, Percutaneous Approach
3E04303	Introduction of Low-dose Interleukin-2 into Central Vein, Percutaneous Approach
3E05002	Introduction of High-dose Interleukin-2 into Peripheral Artery, Open Approach
3E05302	Introduction of High-dose Interleukin-2 into Peripheral Artery, Percutaneous Approach
3E050WK	Introduction of Immunostimulator into Peripheral Artery, Open
3E050WL	Introduction of Immunosuppressive into Peripheral Artery, Open
3E053WL	Introduction of Immunosuppressive into Peripheral Artery, Percutaneous

3E053WL	Introduction of Immunosuppressive into Peripheral Artery, Percutaneous
3E060WK	Introduction of Immunostimulator into Central Artery, Open
3E060WL	Introduction of Immunosuppressive into Central Artery, Open
3E063WK	Introduction of Immunostimulator into Central Artery, Percutaneous
3E063WL	Introduction of Immunosuppressive into Central Artery, Percutaneous
XW01397	Introduction of Satralizumab-mwge into Subcutaneous Tissue, Percutaneous Approach, New Technology Group 7
XW033C6	Introduction of Eculizumab into Peripheral Vein, Percutaneous Approach, New Technology Group 6
XW033H5	Introduction of Tocilizumab into Peripheral Vein, Percutaneous Approach, New Technology Group 5
XW033L6	Introduction of CD24Fc Immunomodulator into Peripheral Vein, Percutaneous Approach, New Technology Group 6
XW033L7	Introduction of Lifileucel Immunotherapy into Peripheral Vein, Percutaneous Approach, New Technology Group 7
XW033M7	Introduction of Brexucabtagene Autoleucel Immunotherapy into Peripheral Vein, Percutaneous Approach, New Technology Group 7
XW03308	Introduction of Spesolimab Monoclonal Antibody into Peripheral Vein, Percutaneous Approach, New Technology Group 8
XW03398	Introduction of Inebilizumab-cdon into Peripheral Vein, Percutaneous Approach, New Technology Group 8
XW04308	Introduction of Spesolimab Monoclonal Antibody into Central Vein, Percutaneous Approach, New Technology Group 8
XW04398	Introduction of Inebilizumab-cdon into Central Vein, Percutaneous Approach, New Technology Group 8
XW043G5	Introduction of Sarilumab into Central Vein, Percutaneous Approach, New Technology Group 5

XW043H5	Introduction of Tocilizumab into Central Vein, Percutaneous Approach, New Technology Group 5
XW043L6	Introduction of CD24Fc Immunomodulator into Central Vein, Percutaneous Approach, New Technology Group 6
XW0DXM6	Introduction of Baricitinib into Mouth and Pharynx, External Approach, New Technology Group 6
XW0G7M6	Introduction of Baricitinib into Upper GI, Via Natural or Artificial Opening, New Technology Group 6
XW0H7M6	Introduction of Baricitinib into Lower GI, Via Natural or Artificial Opening, New Technology Group 6

CPT[7]

80145	Adalimumab
80158	Cyclosporine
80169[8]	Everolimus
80180	Mycophenolate (mycophenolic acid)
80193	Leflunomide
80195	Sirolimus
80197	Tacrolimus
80180	Mycophenolate (mycophenolic acid)
80204	Methotrexate
80230	Infliximab
80280	Vedolizumab
90585	Bacillus Calmette-Guerin vaccine (BCG) for tuberculosis, live, for percutaneous use

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90586	Bacillus Calmette-Guerin vaccine (BCG) for bladder cancer, live, for intravesical use

HCPCS

J0129	Injection, abatacept, 10 mg (code may be used for Medicare when drug administered under the direct supervision of a physician, not for use when drug is self-administered)
J0135	Injection, adalimumab, 20 mg
S0176	Hydroxyurea, oral, 500 mg
J0215	Injection, alefacept, 0.5 mg
J0202	Injection, alemtuzumab, 1 mg
J0480	Injection, basiliximab, 20 mg
J0485	Injection, belatacept, 1 mg
J0490	Injection, belimumab, 10 mg
J0491	Injection, anifrolumab-fnia, 1 mg
J0638	Injection, canakinumab, 1 mg
J0717	Injection, certolizumab pegol, 1 mg (code may be used for Medicare when drug administered under the direct supervision of a physician, not for use when drug is self-administered)
J1300	Injection, eculizumab, 10 mg
J1302	Injection, sutimlimab-jome, 10 mg
J1303	Injection, ravulizumab-cwvz, 10 mg
J1438	Injection, etanercept, 25 mg (code may be used for Medicare when drug administered under the direct supervision of a physician, not for use when drug is self-administered)
J1442	Injection, filgrastim (G-CSF), excludes biosimilars, 1 mcg
J1447	Injection, tbo-filgrastim, 1 mcg
J1449	Injection, eflapegrastim-xnst, 0.1 mg
J1595	Injection, glatiramer acetate, 20 mg

J1602	Injection, golimumab, 1 mg, for intravenous use
J1628	Injection, guselkumab, 1 mg
J1745	Injection, infliximab, excludes biosimilar, 10 mg
J1747	Injection, spesolimab-sbzo, 1 mg
J1823	Injection, inebilizumab-cdon, 1 mg
J1826	Injection, interferon beta-1a, 30 mcg
J1830	Injection interferon beta-1b, 0.25 mg (code may be used for Medicare when drug administered under the direct supervision of a physician, not for use when drug is self-administered)
J2323	Injection, natalizumab, 1 mg
J2327	Injection, risankizumab-rzaa, intravenous, 1 mg
J2329	Injection, ublituximab-xiiy, 1mg
J2350	Injection, ocrelizumab, 1 mg
J2355	Injection, oprelvekin, 5 mg
J2504	Injection, pegademase bovine, 25 IU
J2506	Injection, pegfilgrastim, excludes biosimilar, 0.5 mg
J2562	Injection, plerixafor, 1 mg
J2781	Injection, pegcetacoplan, intravitreal, 1 mg
J2793	Injection, rilonacept, 1 mg
J2820	Injection, sargramostim (GM-CSF), 50 mcg
J2860	Injection, siltuximab, 10 mg
J3241	Injection, teprotumumab-trbw, 10 mg
J3245	Injection, tildrakizumab, 1 mg J3380 Injection, vedolizumab, 1 mg
J3262	Injection, tocilizumab, 1 mg
J3357	Ustekinumab, for subcutaneous injection, 1 mg

J3358	Ustekinumab, for intravenous injection, 1 mg
J7500-J7599:	Immunosuppressive drugs
J8560	Etoposide, oral, 50 mg
J8610	Methotrexate, oral, 2.5 mg
J9000	Injection, doxorubicin HCl, 10 mg
J9015	Injection, aldesleukin, per single use vial
J9030	BCG live intravesical instillation, 1 mg
J9037	Injection, belantamab mafodotin-blmf, 0.5 mg
J9040	Injection, bleomycin sulfate, 15 units
J9060	Injection, cisplatin, powder or solution, 10 mg
J9065	Injection, cladribine, per 1 mg J9047 Injection, carfilzomib, 1 mg
J9070	Cyclophosphamide, 100 mg
J9071	Injection, cyclophosphamide, (AuroMedics), 5 mg
J9098	Injection, cytarabine liposome, 10 mg
J9100	Injection, cytarabine, 100 mg
J9145	Injection, daratumumab, 10 mg
J9144	Injection, daratumumab, 10 mg and hyaluronidase-fihj
J9153	Injection, liposomal, 1 mg daunorubicin and 2.27 mg cytarabine
J9176	Injection, elotuzumab, 1 mg
J9181	Injection, etoposide, 10 mg
J9190	Injection, fluorouracil, 500 mg
J9205	Injection, irinotecan liposome, 1 mg
J9206	Injection, irinotecan, 20 mg

J9210	Injection, emapalumab-lzsg, 1 mg
J9212	Injection, interferon alfacon-1, recombinant, 1 mcg
J9213	Injection, interferon, alfa-2a, recombinant, 3 million units
J9214	Injection, interferon, alfa-2b, recombinant, 1 million units
J9215	Injection, interferon, alfa-N3, (human leukocyte derived), 250,000 IU
J9216	Injection, interferon, gamma 1-b, 3 million units
J9247	Injection, melphalan flufenamide, 1 mg
J9250	Methotrexate sodium, 5 mg
J9259	Injection, paclitaxel protein-bound particles (American Regent) not therapeutically equivalent to J9264, 1 mg
J9260	Methotrexate sodium, 50 mg
J9264	Injection, paclitaxel protein-bound particles, 1 mg
J9267	Injection, paclitaxel, 1 mg
J9302	Injection, ofatumumab, 10 mg
J9331	Injection, sirolimus protein-bound particles, 1 mg
J9332	Injection, efgartigimod alfa-fcab, 2 mg
J9360	Injection, vinblastine sulfate, 1 mg
J9370	Vincristine sulfate, 1 mg
J9371	Injection, vincristine sulfate liposome, 1 mg
J9380	Injection, teclistamab-cqyv, 0.5 mg
M0249	Intravenous infusion, tocilizumab, for hospitalized adults and pediatric patients (2 years of age and older) with COVID-19 who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation
M0250	Intravenous infusion, tocilizumab, for hospitalized adults and pediatric patients (2 years of age and older) with COVID-19

	who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation
Q0249	Injection, tocilizumab, for hospitalized adults and pediatric patients (2 years of age and older) with COVID-19 who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal
Q0510	Pharmacy supply fee for initial immunosuppressive drug(s), first month following transplant
Q2043	Sipuleucel-T, minimum of 50 million autologous CD54+ cells activated with PAP-GM-CSF, including leukapheresis and all other preparatory procedures, per infusion
Q2049	Injection, doxorubicin HCl, liposomal, imported Lipodox, 10 mg
Q2050	Injection, doxorubicin HCl, liposomal, not otherwise specified, 10 mg
Q2056	Ciltacabtagene autoleucel, up to 100 million autologous B-cell maturation antigen (BCMA) directed CAR-positive T cells, including leukapheresis and dose preparation procedures, per therapeutic dose
Q2055	Idecabtagene vicleucel, up to 460 million autologous B-cell maturation antigen (BCMA) directed CAR-positive T cells, including leukapheresis and dose preparation procedures, per therapeutic dose
Q3027	Injection, interferon beta-1a, 1 mcg for intramuscular use
Q3028	Injection, interferon beta-1a, 1 mcg for subcutaneous use
Q5101	Injection, filgrastim-sndz, biosimilar, (Zarxio), 1 mcg
Q5103	Injection, infliximab-dyyb, biosimilar, (Inflectra), 10 mg
Q5104	Injection, infliximab-abda, biosimilar, (Renflexis), 10 mg
Q5108	Injection, pegfilgrastim-jmdb (Fulphila), biosimilar, 0.5 mg
Q5109	Injection, infliximab-qbtx, biosimilar, (Ixifi), 10 mg Q5121 Injection, infliximab-axxq, biosimilar, (AVSOLA), 10 mg
Q5110	Injection, filgrastim-aafi, biosimilar, (Nivestym), 1 mcg

Q5111	Injection, pegfilgrastim-cbqv (Udenyca), biosimilar, 0.5 mg
Q5120	Injection, pegfilgrastim-bmez (ZIEXTENZO), biosimilar, 0.5 mg
Q5122	Injection, pegfilgrastim-apgf (Nyvepria), biosimilar, 0.5 mg
Q5125	Injection, filgrastim-ayow, biosimilar, (Releuko), 1 mcg
Q5127	Injection, pegfilgrastim-fpgk (Stimufend), biosimilar, 0.5 mg
Q5130	Injection, pegfilgrastim-pbbk (Fylnetra), biosimilar, 0.5 mg
Q5131	Injection, adalimumab-aacf (Idacio), biosimilar, 20 mg
S0145	Injection, PEGylated interferon alfa-2A, 180 mcg per ml
S0148	Injection, PEGylated interferon alfa-2B, 10 mcg
S0172	Chlorambucil, oral, 2 mg

16.4.2.2. Oral Corticosteroids

16.4.2.2.1. HICL Codes

The below list includes generic drug names classified by therapeutic use, which will be restricted to oral routes of administration. Codes for generic drugs are based on the Hierarchical Ingredient Code List (HICL) system proprietary to First Databank. All associated NDC codes will be utilized. Additional therapies may be added as they are approved.

Beclomethasone Dipropionate
Flunisolide
Cortisone Acetate
Hydrocortisone Acetate
Hydrocortisone Cypionate
Hydrocortisone Sod Phosphate
Hydrocortisone Sod Succinate
Hydrocortisone
Prednisolone Acetate
Prednisolone Sod Phosphate
Prednisolone Tebutate
Prednisolone
Methylprednisolone Acetate
Methylprednisolone Sod Succ
Methylprednisolone
Prednisone
Betamet Acet/Betamet Na Ph

Betamethasone Sodium Phosphate
Betamethasone
Dexamethasone Acetate
Dexamethasone Phosphate
Dexamethasone Sod Phosphate
Dexamethasone
Triamcinolone Acetonide
Triamcinolone Diacetate
Triamcinolone Hexacetonide
Triamcinolone
Desoxycorticosterone Acetate
Mometasone Furoate
Betamethasone Acetate
Budesonide
Flunisolide/Menthol
Fluticasone Propionate
Cortisone Acetate
Prednisolone Acetate
Prednisolone
Prednisone
Betamethasone
Betamethasone Sodium Phosphate
Dexamethasone Acetate
Dexamethasone Sod Phosphate
Dexamethasone
Triamcinolone Acetonide
Triamcinolone Diacetate
Triamcinolone
Dexamethasone Isonicotinate
Flunisolide
Methylprednisolone Acetate
Methylprednisolone
Prednisolone Sod Phosphate
Deflazacort
Betamethasone Acetate
Dexameth Ph/Lidocaine Hcl
Triamcinolone/Lidocaine
Beclomethasone Dipropionate
Budesonide
Fluticasone/Salmeterol
Budesonide/Formoterol Fumarate

Budesonide/Formoterol Fumarate
Ciclesonide
Methylprednisolone Sod Succ
Dexamethasone, Micronized
Dexamethasone, Micronized
Budesonide, Micronized
Budesonide, Micronized
Dexamethasone Sod Phosphate/Pf
Fluticasone Propionate
Aldosterone
Methylprednisolone Sod Succ/Pf
Hydrocortisone Sod Succ/Pf
Mometasone/Formoterol
Prednisolon Sod Phos/Peak Flow
Triamcinolone Hexacet, Micro
Methylprednisolone, Micronized
Prednisone Micronized
Dexamethasone Acetate, Micro
Dexamethasone In 0.9 % Nacl
Prednisolone, Micronized
Prednisolone Acetate, Micro
Methylprednisolone Ac, Micro
Methylprednisolone/Bupivacaine
Triamcinolone Diacetate, Micro
Betamethasone Acetate, Micro
Fluticasone Propionate, Micro
Triamcinolone/Lidocaine/Priloc
Betamethason/Norfluran/Pentflu
Me-Prednis/Norfluran/Hfc 245fa
Triamcin/Norflurane/Hfc 245fa
Dexameth/Pf/Norflur/Hfc 245fa
Fluticasone/Umeclidin/Vilanter
Betamethasone Sod Phosph-Water
Methylprednisol Ac/Bupivac/Wat
Methylprednisolone Acet-Water
Triamcinolone Acet/0.9%Nacl/Pf
Betamethasone Ace,Sod Phos/Wtr
Triamcinolone/Bupivacaine/Nacl
Dexamethasone Ac, Sod Ph/Water
Betametha Ac,Sod Phos/Water/Pf
Dexamethasone Ace/Nacl,Iso-Osm

Methylpred Acet/Nacl,Iso-Os/Pf
Triamcinolone Aceton/0.9% Nacl
Triamcinolone Dia/0.9% Nacl/Pf
Triamcinolone Diacet/0.9% Nacl
Budenoside/Glycopyr/Formoterol

16.4.2.2.2. HCPCS Codes

HCPCS

J7509	Methylprednisolone, oral, per 4 mg
J7510	Prednisolone, oral, per 5 mg
J8540	Dexamethasone, oral, 0.25 mg

16.4.2.3. Antivirals

The below list includes generic drug names. All associated NDC codes will be utilized. Additional therapies may be added as they are approved.

16.4.2.3.1. Topical

acyclovir
docosanol
penciclovir

16.4.2.3.2. Eye

fomivirsen
ganciclovir
idoxuridine
trifluridine
vidarabine

16.4.2.3.3. General Antivirals

acyclovir
baloxavir marboxil
brincidofovir
cidofovir
famciclovir
foscarnet

ganciclovir
letermovir
maribavir
oseltamivir
peramivir
ribavirin
rimantadine
tecovirimat
valacyclovir
zanamivir

16.4.2.3.4. HIV-Specific

abacavir
amprenavir
atazanavir
cabotegravir
cobicistat (in combination with others)
darunavir
delavirdine
didanosine
dolutegravir
doravirine
efavirenz
elvitegravir
emtricitabine
enfuvirtide
etravirine
fosamprenavir
fostemsavir
indinavir
lamivudine
lopinavir
maraviroc
nelfinavir
nevirapine
raltegravir
rilpivirine

ritonavir
saquinavir
stavudine
tenofovir
tipranavir
zalcitabine
zidovudine

16.4.2.3.5. ICD-10-PCS, CPT, and HCPCS Codes

In addition to NDC codes for the above, the following ICD-10-PCS, CPT, and HCPCS codes will be used:

ICD-10-PCS

XW0DX38	Introduction of Maribavir Anti-infective into Mouth and Pharynx, External Approach, New Technology Group 8
XW0G738	Introduction of Maribavir Anti-infective into Upper GI, Via Natural or Artificial Opening, New Technology Group 8
XW0H738	Introduction of Maribavir Anti-infective into Lower GI, Via Natural or ArtificialOpening, New Technology Group 8

CPT[9]

4150F	Patient receiving antiviral treatment for Hepatitis C (HEP-C)
4153F	Combination peginterferon and ribavirin therapy prescribed (HEP-C)

HCPCS

J0133	Injection, acyclovir, 5 mg
J0739	Injection, cabotegravir, 1 mg
J0740	Injection, cidofovir, 375 mg
J0741	Injection, cabotegravir and rilpivirine, 2 mg/3 mg
J1324	Injection, enfuvirtide, 1 mg

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J1452	Injection, fomivirsen sodium, intraocular, 1.65 mg
J1455	Injection, foscarnet sodium, per 1,000 mg
J1570	Injection, ganciclovir sodium, 500 mg
J1574	Injection, ganciclovir sodium (Exela) not therapeutically equivalent to J1570, 500 mg
J2547	Injection, peramivir, 1 mg
J3485	Injection, zidovudine, 10 mg
J7310	Ganciclovir, 4.5 mg, long-acting implant
S0104	Zidovudine, oral, 100 mg
S0137	Didanosine (ddI), 25 mg
S0140	Saquinavir, 200 mg

16.4.2.4. Antibiotics

The below list includes generic drug names, organized by therapeutic class codes and hierarchical ingredient codes developed by First Databank. Therapeutic class codes (THERSPEC) and the Hierarchical Ingredient Code List (HICL) are proprietary to First Databank. All associated NDC codes will be utilized. Additional therapies may be added as they are approved.

16.4.2.4.1. Vaginal

clindamycin
metronidazole

16.4.2.4.2. Topical

bacitracin
chloramphenicol
clindamycin
doxycycline
erythromycin
gentamicin
meclocycline
minocycline
mupirocin

neomycin
ozenoxacin
tetracycline

16.4.2.4.3. Eye and Ear

azithromycin
bacitracin
besifloxacin
cefuroxime
chloramphenicol
ciprofloxacin
erythromycin
gatifloxacin
gentamicin
levofloxacin
moxifloxacin
natamycin
neomycin
norfloxacin
ofloxacin
oxytetracycline
polymyxin
tetracycline
tobramycin
vancomycin

16.4.2.4.4. Nose

mupirocin

16.4.2.4.5. Antitubercular

bedaquiline
capreomycin
cycloserine
ethambutol
isoniazid
pretomanid
pyrazinamide

rifampin
rifapentine

16.4.2.4.6. Broad Spectrum

16.4.2.4.6.1. Penicillin Antibiotics

amoxicillin
ampicillin
bacampicillin
carbenicillin
cloxacillin
dicloxacillin
mezlocillin
nafcillin
oxacillin
penicillin
piperacillin
ticarcillin

16.4.2.4.6.2. Tetracycline Antibiotics

demeclocycline
doxycycline
eravacycline
minocycline
omadacycline
oxytetracycline
sarecycline
tetracycline

16.4.2.4.6.3. Macrolide Antibiotics

azithromycin
clarithromycin
dirithromycin
erythromycin
fidaxomicin
troleandomycin

16.4.2.4.6.4. Chloramphenicol Antibiotics and Derivatives

chloramphenicol

16.4.2.4.6.5. Aminoglycoside Antibiotics

amikacin
gentamicin
kanamycin
neomycin
netilmicin
plazomicin
streptomycin
tobramycin

16.4.2.4.6.6. Aminocyclitol Antibiotics

spectinomycin

16.4.2.4.6.7. Vancomycin Antibiotics and Derivatives

vancomycin

16.4.2.4.6.8. Lincosamide Antibiotics

clindamycin
lincomycin

16.4.2.4.6.9. Antibiotics, Miscellaneous, Other

bacitracin
novobiocin

16.4.2.4.6.10. Streptogramin Antibiotics

dalfopristin
quinupristin

16.4.2.4.6.11. Polymyxin Antibiotics and Derivatives

colistin
polymyxin

16.4.2.4.6.12. Oxazolidinone Antibiotics

linezolid

tedizolid

16.4.2.4.6.13. Quinolone Antibiotics

alatrofloxacin
cinoxacin
ciprofloxacin
delafloxacin
enoxacin
gatifloxacin
gemifloxacin
grepafloxacin
levofloxacin
lomefloxacin
moxifloxacin
nalidixic acid
norfloxacin
ofloxacin
sparfloxacin
trovafloxacin

16.4.2.4.6.14. Carbapenem Antibiotics (Thenamycins)

doripenem
ertapenem
imipenem
meropenem

16.4.2.4.6.15. Cephalosporin Antibiotics

cefaclor
cefadroxil
cefamandole
cefazolin
cefdinir
cefditoren
cefepime
cefiderocol
cefixime
cefonicid

cefoperazone
cefotaxime
cefotetan
cefoxitin
cefpodoxime
cefprozil
ceftazidime
ceftibuten
ceftizoxime
ceftolozane
ceftriaxone
cefuroxime
cephalexin
cephalothin
cephapirin
cephradine
loracarbef

16.4.2.4.6.16. Antifungal Antibiotics

amphotericin b
anidulafungin
caspofungin
griseofulvin
ibrexafungerp
micafungin
nystatin
rezafungin

16.4.2.4.6.17. Ketolide Antibiotics

telithromycin

16.4.2.4.6.18. Rifamycins and Related Derivative Antibiotics

rifamycin
rifaximin

16.4.2.4.6.19. Lipoglycopeptide Antibiotics

dalbavancin
oritavancin

telavancin

16.4.2.4.7. ICD-10-CM, CPT[10], and HCPCS Codes

In addition to NDC codes for the above, the following CPT and HCPCS codes will be used:

ICD-10-CM

T36.***	Poisoning by, adverse effect of and underdosing of systemic antibiotics

ICD-10-PCS

XW033R9	Introduction of Rezafungin into Peripheral Vein, Percutaneous Approach, New Technology Group 9
XW043R9	Introduction of Rezafungin into Central Vein, Percutaneous Approach, New Technology Group 9

CPT

4045F	Appropriate empiric antibiotic prescribed (CAP), (EM)
4046F	Documentation that prophylactic antibiotics were given within 4 hours prior to surgical incision or given intraoperatively (PERI 2)
4047F	Documentation of order for prophylactic parenteral antibiotics to be given within 1 hour (if fluoroquinolone or vancomycin, 2 hours) prior to surgical incision (or start of procedure when no incision is required) (PERI 2)
4048F	Documentation that administration of prophylactic parenteral antibiotic was initiated within 1 hour (if fluoroquinolone or vancomycin, 2 hours) prior to surgical incision (or start of procedure when no incision is required) as ordered (PERI 2)
4120F	Antibiotic prescribed or dispensed (URI, PHAR), (A-BRONCH)
80150	Amikacin
80170	Gentamicin

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80200	Tobramycin
80202	Vancomycin

HCPCS

C9462	Injection, delafloxacin, 1 mg
G8710	Patient prescribed antibiotic
G8711	Prescribed antibiotic on or within 3 days after the episode date
G9498	Antibiotic regimen prescribed
G9505	Antibiotic regimen prescribed within 10 days after onset of symptoms for documented medical reason
G8916	Patient with preoperative order for IV antibiotic surgical site infection (SSI) prophylaxis, antibiotic initiated on time
G9286	Antibiotic regimen prescribed within 10 days after onset of symptoms
G9315	Amoxicillin, with or without clavulanate, prescribed as a first line antibiotic at the time of diagnosis
G9712	Documentation of medical reason(s) for prescribing or dispensing antibiotic (eg, intestinal infection, pertussis, bacterial infection, lyme disease, otitis media, acute sinusitis, acute pharyngitis, acute tonsillitis, chronic sinusitis
J0120	Injection, tetracycline, up to 250 mg
J0121	Injection, omadacycline, 1 mg
J0122	Injection, eravacycline, 1 mg
J0200	Injection, alatrofloxacin mesylate, 100 mg
J0278	Injection, amikacin sulfate, 100 mg
J0285	Injection, amphotericin B, 50 mg
J0287	Injection, amphotericin B lipid complex, 10 mg
J0288	Injection, amphotericin B cholesteryl sulfate complex, 10 mg
J0289	Injection, amphotericin B liposome, 10 mg

J0290	Injection, ampicillin sodium, 500 mg
J0291	Injection, plazomicin, 5 mg
J0295	Injection, ampicillin sodium/sulbactam sodium, per 1.5 g
J0348	Injection, anidulafungin, 1 mg
J0349	Injection, rezafungin, 1 mg
J0456	Injection, azithromycin, 500 mg
J0558	Injection, penicillin G benzathine and penicillin G procaine, 100,000 units
J0561	Injection, penicillin G benzathine, 100,000 units
J0637	Injection, caspofungin acetate, 5 mg
J0689	Injection, cefazolin sodium (Baxter), not therapeutically equivalent to J0690, 500 mg
J0690	Injection, cefazolin sodium, 500 mg
J0692	Injection, cefepime HCl, 500 mg
J0694	Injection, cefoxitin sodium, 1 g
J0695	Injection, ceftolozane 50 mg and tazobactam 25 mg
J0696	Injection, ceftriaxone sodium, per 250 mg
J0697	Injection, sterile cefuroxime sodium, per 750 mg
J0698	Injection, cefotaxime sodium, per g
J0699	Injection, cefiderocol, 10 mg
J0701	Injection, cefepime HCl (Baxter), not therapeutically equivalent to Maxipime, 500 mg
J0703	Injection, cefepime HCl (B. Braun), not therapeutically equivalent to Maxipime, 500 mg
J0710	Injection, cephapirin sodium, up to 1 g
J0713	Injection, ceftazidime, per 500 mg

J0714	Injection, ceftazidime and avibactam, 0.5 g/0.125 g
J0715	Injection, ceftizoxime sodium, per 500 mg
J0720	Injection, chloramphenicol sodium succinate, up to 1 g
J0736	Injection, clindamycin phosphate, 300 mg
J0737	Injection, clindamycin phosphate (Baxter), not therapeutically equivalent to J0736, 300 mg
J0742	Injection, imipenem 4 mg, cilastatin 4 mg and relebactam 2 mg
J0743	Injection, cilastatin sodium; imipenem, per 250 mg
J0744	Injection, ciprofloxacin for intravenous infusion, 200 mg
J0875	Injection, dalbavancin, 5 mg
J0878	Injection, daptomycin, 1 mg
J1267	Injection, doripenem, 10 mg
J1335	Injection, ertapenem sodium, 500 mg
J1364	Injection, erythromycin lactobionate, per 500 mg
J1580	Injection, garamycin, gentamicin, up to 80 mg
J1836	Injection, metronidazole, 10 mg
J1840	Injection, kanamycin sulfate, up to 500 mg
J1850	Injection, kanamycin sulfate, up to 75 mg
J1890	Injection, cephalothin sodium, up to 1 g
J1956	Injection, levofloxacin, 250 mg
J2010	Injection, lincomycin HCl, up to 300 mg
J2020	Injection, linezolid, 200 mg
J2021	Injection, linezolid (Hospira) not therapeutically equivalent to J2020, 200 mg
J2184	Injection, meropenem (B. Braun) not therapeutically equivalent to J2185, 100 mg

J2185	Injection, meropenem, 100 mg
J2186	Injection, meropenem, vaborbactam, 10 mg/10 mg, (20 mg)
J2247	Injection, micafungin sodium (Par Pharm) not therapeutically equivalent to J2248, 1 mg
J2248	Injection, micafungin sodium, 1 mg
J2265	Injection, minocycline HCl, 1 mg
J2280	Injection, moxifloxacin, 100 mg
J2281	Injection, moxifloxacin (Fresenius Kabi) not therapeutically equivalent to J2280, 100 mg
J2406	Injection, oritavancin (Kimyrsa), 10 mg
J2407	Injection, oritavancin (Orbactiv), 10 mg
J2460	Injection, oxytetracycline HCl, up to 50 mg
J2510	Injection, penicillin G procaine, aqueous, up to 600,000 units
J2540	Injection, penicillin G potassium, up to 600,000 units
J2543	Injection, piperacillin sodium/tazobactam sodium, 1 g/0.125 g (1.125 g)
J2700	Injection, oxacillin sodium, up to 250 mg
J2770	Injection, quinupristin/dalfopristin, 500 mg (150/350)
J3000	Injection, streptomycin, up to 1 g
J3090	Injection, tedizolid phosphate, 1 mg
J3095	Injection, telavancin, 10 mg
J3260	Injection, tobramycin sulfate, up to 80 mg
J3320	Injection, spectinomycin dihydrochloride, up to 2 g
J3370	Injection, vancomycin HCl, 500 mg
J3371	Injection, vancomycin HCl (Mylan) not therapeutically equivalent to J3370, 500 mg

J3372	Injection, vancomycin HCl (Xellia) not therapeutically equivalent to J3370, 500 mg
J7342	Instillation, ciprofloxacin otic suspension, 6 mg
J7682	Tobramycin, inhalation solution, FDA-approved final product, noncompounded, unit dose form, administered through DME, per 300 mg
J7685	Tobramycin, inhalation solution, compounded product, administered through DME, unit dose form, per 300 mg
Q0144	Azithromycin dihydrate, oral, capsules/powder, 1 g
S0021	Injection, cefoperazone sodium, 1 g
S0032	Injection, nafcillin sodium, 2 g
S0034	Injection, ofloxacin, 400 mg
S0040	Injection, ticarcillin disodium and clavulanate potassium, 3.1 g
S0074	Injection, cefotetan disodium, 500 mg
S0081	Injection, piperacillin sodium, 500 mg

16.4.3. Underlying Conditions Conferring High Risk of Severe Outcomes from COVID-19

16.4.3.1. Asthma

See codes in Section 16.4.1.1.

16.4.3.2. Cancer

See codes in Section 16.4.1.13.

16.4.3.3. Cerebrovascular Disease

I60-I69	Cerebrovascular diseases

16.4.3.4. Chronic Kidney Disease

D63.1	Anemia in chronic kidney disease
E08.22	Diabetes mellitus due to underlying condition with diabetic chronic kidney disease
E09.22	Drug or chemical induced diabetes mellitus with diabetic chronic kidney disease

E10.22	Type 1 diabetes mellitus with diabetic chronic kidney disease
E11.22	Type 2 diabetes mellitus with diabetic chronic kidney disease
E13.22	Other specified diabetes mellitus with diabetic chronic kidney disease
I12	Hypertensive chronic kidney disease
I13	Hypertensive heart and chronic kidney disease
N18	Chronic kidney disease (CKD)

16.4.3.5. Chronic Lung Disease, Limited to Bronchiectasis, COPD, Interstitial Lung Disease, Pulmonary Embolism, and Pulmonary Hypertension

J47	Bronchiectasis
J44	Chronic obstructive pulmonary disease
J84	Other interstitial lung disease
I26	Pulmonary embolism
I27.0	Primary pulmonary hypertension
I27.2	Other secondary pulmonary hypertension
I27.82	Chronic pulmonary embolism

16.4.3.6. Chronic Liver Disorders, Limited to Cirrhosis, Non-Alcoholic Fatty Liver Disease, Alcoholic Liver Disease, and Autoimmune Hepatitis

K70	Alcoholic liver disease
K74.3	Primary biliary cirrhosis
K74.4	Secondary biliary cirrhosis
K74.5	Biliary cirrhosis, unspecified
K74.6	Other and unspecified cirrhosis of liver
K75.4	Autoimmune hepatitis
K76.0	Fatty (change of) liver, not elsewhere classified

16.4.3.7. Cystic Fibrosis

E84	Cystic fibrosis

16.4.3.8. Diabetes Mellitus, Type I

E10	Type 1 diabetes mellitus

16.4.3.9. Diabetes Mellitus, Type II

See codes in Section 16.4.1.15.

16.4.3.10. Disabilities, Including Down Syndrome

See codes in Section 16.4.1.4, Section 16.4.3.14.

E75.22	Gaucher disease
E88.41	MELAS syndrome
E88.42	MERRF syndrome
E88.49	NARP syndrome
F06.7	Mild neurocognitive disorder due to known physiological condition
F08	Activities of daily living treatment
F70-F73	Intellectual disabilities
F78-F79	Other and unspecified intellectual disabilities
F80	Specific developmental disorders of speech and language
F81	Specific developmental disorders of scholastic skills
F84.0	Autistic disorder
F84.2	Rett’s syndrome
F84.3	Other childhood disintegrative disorder
F84.5	Asperger’s syndrome
F84.8	Other pervasive developmental disorders
F84.9	Pervasive developmental disorder, unspecified
F89	Unspecified disorder of psychological development

F90	Attention-deficit hyperactivity disorders
F95.2	Tourette's disorder
G20-G26	Extrapyramidal and movement disorders
G23.8	Other specified degenerative diseases of basal ganglia
G31.82	Leigh's disease
G31.84	Mild cognitive impairment of uncertain or unknown etiology
G71.11	Myotonic muscular dystrophy
G23.1	Progressive supranuclear opthalmoplegia [Steele-Richardson-Olszewski]
G35.0	Multiple sclerosis
G36.0	Amyotrophic lateral sclerosis [ALS]
G61.0	Guillain-Barre syndrome
G70.0	Myasthenia gravis
G70.9	Myoneural disorder, unspecified
G71	Muscular dystrophy
G71.3	Mitochondrial myopathy, not elsewhere classified
G71.9	Neuromuscular disease, unspecified
G80	Cerebral palsy
H47.22	Hereditary optic atrophy
H53-H54	Visual disturbances and blindness
H90	Conductive and sensorineural hearing loss
H91	Other and unspecified hearing loss
H93.01	Transient ischemic deafness
M14.67	Charcot's joint, ankle, and foot

Q00-Q99	Congenital malformations, deformations and chromosomal abnormalities
R41	Other symptoms and signs involving cognitive functions and awareness
S06	Intracranial injury
S34	Injury of lumbar and sacral spinal cord and nerves at abdomen, lower back and pelvis level
Z73.6	Limitations of activity due to disability
Z74	Problems related to care provider dependency
Z87.820	Personal history of traumatic brain injury
Z99.3	Dependence on wheelchair

16.4.3.11. Heart Conditions

See codes in Section 16.4.1.5.

16.4.3.12. HIV

B20	Human immunodeficiency virus [HIV] disease
Z21	Asymptomatic human immunodeficiency virus [HIV] disease status

16.4.3.13. Mental Health Conditions, Limited to Mood Disorders, Including Depression; and Schizophrenia Spectrum Disorders

F20-F29	Schizophrenia, schizotypal, delusional, and other non-mood psychotic disorders
F30-F39	Mood [affective] disorders

16.4.3.14. Neurologic Conditions, Limited to Dementia and Parkinson's Disease

F01	Vascular dementia
F02	Dementia in other diseases classified elsewhere
F03	Unspecified dementia
G20	Parkinson's disease
G30	Alzheimer's disease

G31	Frontotemporal dementia

16.4.3.15. Obesity

See codes in Section 16.4.1.14.

16.4.3.16. Physical Inactivity

Z72.3	Lack of physical exercise

16.4.3.17. Pregnancy and Recent Pregnancy

16.4.3.17.1. ICD-10-CM Codes

O chapter	Pregnancy, childbirth, and the puerperium
Z3A	Weeks of gestation
Z36	Encounter for antenatal screening of mother

16.4.3.17.2. CPT[11] Codes

59000-59325	Amniocentesis, chorionic villous sampling and other fetal monitoring/diagnostic procedures, pregnancy and delivery-related procedures
59400-59618	Routine obstetric care including antepartum care, vaginal delivery

16.4.3.18. Primary Immunodeficiencies

D80-D89	Primary immune deficiencies

16.4.3.19. Smoking, Current and Former

F17	Nicotine dependence
O99.33	Tobacco use disorder complicating pregnancy, childbirth, and the puerperium
Z53.01	Procedure not carried out due to patient smoking
Z71.6	Tobacco abuse counseling
Z87.891	Personal history of nicotine dependence

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16.4.3.20. Solid Organ or Blood Stem Cell Transplantation

Z94	Transplanted organ and tissue status

16.4.3.21. Tuberculosis

A15-A19	Tuberculosis

16.4.3.22. Use of Corticosteroids or Other Immunosuppressive Medications

See codes in Section 16.4.2.2 (not restricted to oral routes of administration) and Section 16.4.2.1.2.

17. ANNEX 3. ADDITIONAL INFORMATION

Not applicable.

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