Disclaimer

The following report(s) provides findings from an FDA-initiated query using Sentinel. While Sentinel queries may be undertaken to assess potential medical product safety risks, they may also be initiated for various other reasons. Some examples include determining a rate or count of an identified health outcome of interest, examining medical product use, exploring the feasibility of future, more detailed analyses within Sentinel, and seeking to better understand Sentinel capabilities.

Data obtained through Sentinel are intended to complement other types of evidence such as preclinical studies, clinical trials, postmarket studies, and adverse event reports, all of which are used by FDA to inform regulatory decisions regarding medical product safety. The information contained in this report is provided as part of FDA's commitment to place knowledge acquired from Sentinel in the public domain as soon as possible. Any public health actions taken by FDA regarding products involved in Sentinel queries will continue to be communicated through existing channels.

FDA wants to emphasize that the fact that FDA has initiated a query involving a medical product and is reporting findings related to that query does not mean that FDA is suggesting health care practitioners should change their prescribing practices for the medical product or that patients taking the medical product should stop using it. Patients who have questions about the use of an identified medical product should contact their health care practitioners.

The following report contains a description of the request, request specifications, and results from the modular program run(s).

If you are using a web page screen reader and are unable to access this document, please contact the Sentinel Operations Center for assistance at info@sentinelsystem.org.

Overview for Request: cder_iqp_wp040

Request ID: cder_iqp_wp040_tnx_v01

Request Description: In this report we aimed to detail the most frequent diagnoses, procedures, medications and labs associated with use of Finerenone, a new molecular entity (NME) approved by the FDA in 2021 using the TriNetX Live™ platform.

Data Source: We ran this query on April 17 and 18, 2024. This query contains data from 60 health care organizations (HCOs), provided through the TriNetX Live™ platform in their USA Network with Minimal Shift from December 18, 2020 to February 29, 2024.
TriNetX aggregates electronic health record (EHR) systems data from its partner HCOs to create queryable datasets. TriNetX datasets primarily comprise clinical patient data such as demographics, diagnoses, procedures, labs, and medications. The USA Network with Minimal Shift contains HCOs that date shift their data by 14 or fewer days (including 0). For more information on the TriNetX Live™ platform and the TriNetX data visit their website here: https://trinetx.com/

Study Design: In this retrospective cohort study, we identified patients with evidence of exposure to Finerenone, a mineralocorticoid receptor (MR) antagonist over the query period of December 18, 2020 to February 29, 2024. We used the Query Builder module in the TriNetX Live™ platform to create the mentioned patient cohort .
We further used the Analytics module, specifically the Analyze Outcomes Analytics module with the Characteristics analysis type to identify the list of common diagnoses, procedures, medications and labs in time period between -183 days and -1 day from the index finerenone date (first finerenone prescription/dispensing in the query period) i.e., from 183 days prior to index date to the day before the index date.
Exposures of Interest: We defined the exposure of interest, finerenone, using an RxNorm medication term in the Query Builder module. In order to be included in the cohort we required evidence of at least one finerenone prescription or dispensing between December 18, 2020 and February 29, 2024. Please see Appendix A for the specific terms used to define finerenone in this request.
Cohort Eligibility Criteria: We created one cohort for finerenone users as detailed in the "Exposures of Interest" section. Patients of all ages were included in the cohort.
Please see Appendix B for the specifications of the cohort parameters as included in the Query Builder.
Baseline Characteristics:
We utilized the Analyze Outcomes Analytics module with the Characteristics analysis type to assess the most frequent diagnoses, procedures, medication classes prescribed/dispensed and labs ordered (with values) in our cohort in the 183 days prior to the day before the index finerenone date.

1. Most frequent diagnoses: We identified the most frequent baseline diagnoses/comorbid conditions defined as 3-digit International Classification of Diseases, 10th revision, Clinical Modification (ICD-10-CM) diagnoses codes using the relevant coding hierarchies in the TriNetX platform. For each 3-digit ICD-10-CM code, we included the most common 4-digit code within the hierarchy (i.e,, 4-digit code ABC.X within 3-digit ABC code). Overall, we included up to 40 diagnoses codes using the outlined approach. The codes with the descriptions along with their prevalence in the cohort (over [-183, -1] days from index) are given in Table 1.

Overview for Request: cder_iqp_wp040

2. Most frequent procedures: We identified the most frequent procedures, using International Classification of Diseases, 10th Revision - Procedure Coding System (ICD-10-PCS), Healthcare Common Procedure Coding System (HCPCS), Current Procedural Terminology and Systematized Nomenclature of Medicine (SNOMED) codes in the TriNetX platform. We used coding hierarchies, where applicable - the code chapter of the relevant system, followed by codes within, and included up to 40 procedure codes using the outlined approach. In certain situations, we focussed on a level of the coding hierarchy that describe a procedure or set of similar procedures, rather than the detailed specific procedure code itself. See the note below for details. The codes with the descriptions along with their prevalence in the cohort are given in Table 2.

Note : TriNetX uses a hierarchical tree system within CPT codes using CPT subsets, which are developed for EHR systems and specific physician specialties for ease of data capture or data retrieval. These CPT subsets are 7-digit codes or parent terms, which encompasses child terms beneath, which could be other 7-digit subset or 5-digit CPT codes. *Additional details can be found at https://cpt-international.ama-assn.org/implementation-framework* . This is distinct from insurance claims databases (most of the Data Partners in the Sentinel Distributed Database), where only 5-digit CPT codes are used for billing purposes.

In the list of most frequent procedure codes, we included 7-digit CPT subset codes (parent terms) in addition to the 5-digit specific CPT codes, where relevant. Specifically, in situations where the procedure category or parent term was relevant to the medication and was frequent enough to be included in the list but the child terms were not.

3. Most frequent medication classes prescribed/dispensed: We identified the most frequent medication classes prescribed or dispensed using the Veterans Affairs (VA) Drug Classification System, which uses 5-character alphanumeric code to classify all medication products available in the United States. We listed the major classification system, followed by subcategories, and included up to 30 classes along with their prevalence in the cohort (Table 3).
Note : A specific generic ingredient can be listed in multiple classes, based on their route of administration or therapeutic category in the VA classification system.

4. Most common labs: We identified the most frequent lab terms (including vitals) using TriNetX aggregate lab terms (TNX:LAB) that group clinically relevant Logical Observation Identifiers Names and Codes (LOINC) together for each test. We listed the lab terms within the relevant lab categories curated by TriNetX (e.g., metabolic tests, lipid panel, etc.) with their description in Table 4. We also included the proportion of the cohort that had the test performed in the period of [-183, -1] days from index, and certain summary measures of the lab values closest to the index date (the mean and standard deviation, minimum and maximum value).

Limitations: Algorithms used to define exposures, characteristics, and mapping of source data to the data model are imperfect and susceptible to misclassification. Additionally, EHR data in the US lacks longitudinality. The information before or after patients' healthcare encounters could be missing, especially if patient care was administered across different HCOs that may or might not participate in the TriNetX USA network. We are unable to determine if absence of evidence of a condition implies a true absence of a condition or if the condition was not observed in the data. Furthermore, not all HCOs provide brand name or route information for RxNorm terms or laboratory data. Therefore, data should be interpreted with these limitations in mind.

The VA Classification System classifies medication products, rather than the generic ingredient. Hence, the same generic ingredient (e.g., sodium chloride, aspirin, etc.) can be classified in different drug classes, based on what route of administration or therapeutic category it belongs to. TriNetX uses two classification systems on their platform: the VA Classification System (classified available US products) and the Anatomical Chemical and Therapuetic (ATC) Classification Systems (used gloabally), neither of which classifies drugs into mutually exclusive classes.

Overview for Request: cder_iqp_wp040
The units for lab tests in TriNetX are harmonized across labs when bringing new data onto the network. However, TriNetX does not remove outlier values so as to not bias the data. Hence, certain unexpected or implausible lab values may be observed in the database. Additionally, lab values of 0 units could be observed in the database, but its interpretation could be different based on organization-specific practices for rounding, errors or indicating inconclusive results. All counts provided through the TriNetX Live™ platform are rounded up to the nearest 10 to protect patient privacy. This rounding affects error, especially as sample sizes decrease. Error due to rounding can range from <0.09% when sample sizes are >10,000 to nearly 20% as sample sizes drop. Thus, all estimates should be interpreted as ranges, and small sample sizes should be interpreted with caution. Additionally, percentages are calculated based on these rounded numerators and denominators. Thus, due to rounding, the sum of each value in a category may not total to 100%. A subset of HCOs that contribute to the TriNetX USA Minimal Shift network may implement date shifting between 1 and 14 days in either direction at the level of the patient record prior to data ingestion at TriNetX as a method to preserve patient privacy. When interpreting the results of an analysis, the impact of date shifting should be considered; readers should exercise caution when extrapolating information related to time. **Notes:** We ran this query on April 17 and 18, 2024. A re-run of this query for the same query period in the future may not yield the same results owing to the dynamic nature of the TriNetX Live™ network. Please contact the Sentinel Operations Center (info@sentinelsystem.org) for questions and to provide comments/suggestions for future enhancements to this document. For more information on Sentinel's querying in the TriNetX platform, please refer to the Sentinel Website (https://www.sentinelinitiative.org/methods-data-tools/methods/trinetx-rapid-querying).

Sentinel

Table of Contents

Glossary of Terms for Analyses Using TriNetX Live™ Platform*

Characteristic - A medical fact (e.g., diagnosis, procedure, lab result) that occurred on or before the cohort-defining index event

Explore Cohort - A description module on the TriNetX platform that presents a clinical profile of patients in a given cohort. Patient counts are rounded up to the nearest 10 before percentages are calculated, so the sum each of the values in one category may not total to 100%.

Date Shifting - A data obfuscation technique that some HCOs use to preserve patient privacy. Date shifting entails assigning each patient a random number of days (eg, -365 to +365 days) and consistently adjusting each of their dates by that number of days, thus maintaining temporal relationships between records within a single patient.

Fact - (Medical Fact) A unit of utilization that represents a medical observation on a patient (e.g., diagnosis, procedure, clinical observation).

Filter - A method of limiting terms included in queries to a specific subset of data. Filters include age at time of event, data source (electronic health record or natural language processing); brand name, route, and strength for medication terms; occurrence (first or most recent) for lab terms; and priority for diagnosis and procedure terms.

Group - A series of codes and terms defined with Boolean logic that are used to create a query cohort. For each group, users have the ability to specified time periods of interest, and the number of instances that the group must occur for cohort entry.

- **Subgroup -** Within a group, additional subgroups can be specified to define temporal relationships between the terms in the subgroup (e.g., terms in subgroup B must occur within 5 days after terms in subgroup A). Users can require that these temporal constraints be applied to the 1) first, 2) last, or 3) any instance of each subgroup.

Health Care Organization (HCO) - Organizations that contribute electronic healthcare record data to the TriNetX data networks. HCOs include academic institutions and community health provider systems and a single HCO may contain one or more individual sites or facilities.

Index - The first date when a patient meets all of the cohort-defining criteria. In Analytics modules, the index can be defined as the date when a patient meets all of the cohort criteria, or only one specific group's criteria.

Module - A subsection of the TriNetX platform that performs a distinct functionality. Cohorts are created using the Query Builder module. Descriptive modules include Healthcare Organizations, Explore Cohorts, Rate of Arrival, Summary Statistics, and Analyze Criteria. Advanced analytic modules include Analyze Outcomes, Compare Outcomes, Compare Cohorts, Treatment Pathways, and Incidence and Prevalence.

Network - An aggregation of HCOs contributing data to the platform. Multiple networks are available for querying on the platform; the different networks represent subsets of HCOs organized by date-shifting practices or availability of downloadable datasets.

Outcome - A medical fact (e.g., diagnosis, procedure, lab result) that occurred on or after the cohort-defining index event.

Query - In the TriNetX platform, a query is a distinct cohort with a unique set of terms and logic. Query cohorts are created using the Query Builder platform module.

Risk - In Advanced Analytics modules, risk refers to the percentage of patients in each cohort with the specified outcome of interest.

Priority - An indication whether the code was the condition that the provider spent the most time evaluating or treating during a visit. Possible values include primary, secondary, or unknown.

Term - The codes used to specify patient cohort criteria in a query. Code options include diagnoses, procedures, medications, labs, demographics, genomics, and visits. Terms can be linked together using and/or Boolean logic. TriNetX also creates terms that group together multiple medical codes into single clinical concepts.

- **Cannot Have Term -** A category of terms within a query group that patients must not have evidence of to be included in the cohort.
- **Must Have Term -** A category of terms within a query group that patients must have evidence of to be included in the cohort.

Time Constraint - used to define time periods of interest for each group within a query. Time constraints can be defined relative to the date the query was run (e.g., any time before today), or defined based on specific dates (e.g., January 1, 2015 to September 30, 2020).

Treatment Pathway - In Advanced Analytics modules, the Treatment Pathways module returns the order in which patients received treatment and the prevalence of treatments, including combination of medications, following an index event.

Glossary of Terms for Analyses Using TriNetX Live™ Platform*

TriNetX Codes - For commonly used laboratory terms, TriNetX aggregates Logical Observation Identifiers Names and Codes (LOINC) laboratory codes at a clinically significant level to new queryable TNX:LAB terms.

Visit - A type of term used to specify the type of medical encounter or facility where the encounter was recorded. Visit terms are derived by TriNetX from the source data. Visits are recorded separately from the codes or labs that occurred during the encounter; care settings are not attached to individual codes. Values for visit terms include: ambulatory, emergency, field, home health, inpatient encounter, inpatient acute, inpatient non-acute, laboratory, observation, pharmacy, pre-admission, short stay, virtual, and unknown.

*all terms may not be used in this report

Table 1. Most Frequent Diagnoses* Among Patients with Finerenone Exposures in the TriNetX USA Network (Minimal Date Shift) from December 18, 2020 through February 29, 2024

	Finerenone Users	
	N	%
Total Number of Patients	4010	100.0
Endorine, nutritional and metabolic diseases (E00-E89)	2840	70.8
Type 2 diabetes mellitus (E11)	2430	60.6
Type 2 diabetes mellitus with kidney complications (E11.2)	1400	34.9
Disorders of lipoprotein metabolism and other lipidemias (E78)	1990	49.6
Hyperlipidemia, unspecified (E78.5)	1340	33.4
Overweight and obesity (E66)	760	19.0
Obesity due to excess calories (E66.0)	380	9.5
Obesity, unspecified (E66.9)	380	9.5
Vitamin D deficiency (E55)	500	12.5
Vitamin D deficiency, unspecified (E55.9)	500	12.5
Other disorders of fluid, electrolyte and acid-base balance (E87)	460	11.5
Hyperkalemia (E87.5)	170	4.2
Diseases of the circulatory system (I00-I99)	2670	66.6
Essential (primary) hypertension (I10)	2180	54.4
Hypertensive chronic kidney disease (I12)	750	18.7
Hypertensive chronic kidney disease with stage 1 through stage 4 chronic kidney disease, or unspecified chronic kidney disease (I12.9)	730	18.2
Chronic ischemic heart disease (I25)	750	18.7
Atherosclerotic heart disease of native coronary artery (I25.1)	700	17.5
Heart failure (I50)	540	13.5
Heart failure, unspecified (I50.9)	240	6.0
Atrial fibrillation and flutter (I48)	380	9.5
Unspecified atrial fibrillation and atrial flutter (I48.9)	220	5.5
Factors influencing health status and contact with health services (Z00-Z99)	2340	58.4
Long term (current) drug therapy (Z79)	1350	33.7
Long term (current) use of insulin (Z79.4)	870	21.7
Body mass index [BMI] (Z68)	710	17.7
Body mass index [BMI] 30-39, adult (Z68.3)	380	9.5
Encounter for screening for malignant neoplasms (Z12)	550	13.7
Encounter for screening for malignant neoplasm of breast (Z12.3)	240	6.0
Personal history of other diseases and conditions (Z87)	480	12.0
Personal history of other specified conditions (Z87.8)	360	9.0
Encounter for immunization (Z23)	400	10.0
Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified (R00-R99)	2230	55.6
Proteinuria (R80)	850	21.2
Proteinuria, unspecified (R80.9)	710	17.7
Abnormalities of breathing (R06)	460	11.5
Dyspnea (R06.0)	420	10.5
Diseases of the genitourinary system (N00-N99)	2200	54.9
Chronic kidney disease (CKD) (N18)	1850	46.1
Chronic kidney disease, stage 3 (moderate) (N18.3)	1340	33.4
Diseases of the musculoskeletal system and connective tissue (M00-M99)	1370	34.2
Other joint disorders, not elsewhere classified (M25)	440	11.0
Pain in joint (M25.5)	400	10.0
Diseases of the nervous system (G00-G99)	1010	25.2
Sleep disorders (G47)	540	13.5
Sleep apnea (G47.3)	460	11.5
Diseases of the digestive system (K00-K95)	890	22.2
Gastro-esophageal reflux disease (K21)	440	11.0

Table 1. Most Frequent Diagnoses* Among Patients with Finerenone Exposures in the TriNetX USA Network (Minimal Date Shift) from December 18, 2020 through February 29, 2024

	Finerenone Users	
	N	%
Gastro-esophageal reflux disease without esophagitis (K21.9)	430	10.7

* Diagnoses were assessed using the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) diagnoses codes over the period of -183 to -1 days before index finerenone date.

Table 2. Most Frequent Procedures* Among Patients with Finerenone Exposures in the TriNetX USA Network (Minimal Date Shift) from December 18, 2020 through February 29, 2024

	Finerenone Users	
	N	%
Total Number of Patients	4010	100
Most Frequent Procedure ICD-10-PCS/CPT/HCPCS/SNOMED* Codes		
Evaluation and Management (CPT 1013625)	2310	57.6
Established Patient -- Office or Other Outpatient Services (CPT 1013638)	1980	49.4
New Patient -- Office or Other Outpatient Services (CPT 1013627)	690	17.2
New Patient -- Emergency Department Services (CPT 1013712)	520	13.0
Medicine Services and Procedures (CPT 1012569)	1620	40.4
Electrocardiogram, routine ECG with at least 12 leads (CPT 1013012)	720	18.0
Echocardiography Procedures (CPT 1013050)	390	9.7
Therapeutic, Prophylactic, and Diagnostic Injections and Infusions (Excludes Chemotherapy and Other Highly Complex Drug or Highly Complex Biologic Agent Administration) (CPT 1019108)	370	9.2
Vaccines, Toxoids (CPT 1012602)	300	7.5
Non-Invasive Vascular Diagnostic Studies (CPT 1013175)	260	6.5
Immunization Administration for Vaccines/Toxoids (CPT 1012589)	230	5.7
Ophthalmology Services and Procedures (CPT 1012793)	210	5.2
Physical Medicine and Rehabilitation Evaluations (CPT 1013483)	210	5.2
Pathology and Laboratory Procedures (CPT 1011136)	1590	39.7
Blood count (CPT 1011761)	1040	25.9
Hemoglobin; glycosylated (A1C) (CPT 83036)	920	22.9
Comprehensive metabolic panel[a] (CPT 80053)	830	20.7
Creatinine (CPT 1011373)	690	17.2
Urinalysis, by dip stick or tablet reagent for bilirubin, glucose, hemoglobin, ketones, leukocytes, nitrite, pH, protein, specific gravity, urobilinogen, any number of these constituents (CPT 1011224)	670	16.7
Basic metabolic panel (Calcium, total)[b] (CPT 80048)	590	14.7
Lipid panel[c] (CPT 80061)	550	13.7
Albumin (CPT 1011249)	520	13.0
Magnesium (CPT 83735)	430	10.7
Vitamin D (CPT 1020198)	410	10.2
Protein, total, except by refractometry (CPT 1011652)	380	9.5
Thyroid stimulating hormone (TSH) (CPT 84443)	380	9.5
Parathormone (parathyroid hormone) (CPT 83970)	340	8.5
Phosphorus inorganic (phosphate) (CPT 1014270)	310	7.7
Prothrombin time (CPT 1014271)	310	7.7
Renal function panel[d] (CPT 80069)	290	7.2
Glucose, blood by glucose monitoring device(s) cleared by the FDA specifically for home use (CPT 82962)	280	7.0
Infectious Agent Antigen Detection (deprecated 2022) (CPT 1018176)	270	6.7
Iron (CPT 83540)	250	6.2
Ferritin (CPT 82728)	240	6.0
Troponin, quantitative (CPT 84484)	240	6.0
Natriuretic peptide (CPT 83880)	230	5.7
Surgery (CPT 1003143)	1570	39.2
Collection of venous blood by venipuncture (CPT 36415)	1190	29.7
Radiology Procedures (CPT 1010251)	1350	33.7
Diagnostic Radiology (Diagnostic Imaging) Procedures of the Chest (CPT 1010334)	570	14.2
Diagnostic Ultrasound Procedures of the Abdomen and Retroperitoneum (CPT 1010774)	330	8.2

Table 2. Most Frequent Procedures* Among Patients with Finerenone Exposures in the TriNetX USA Network (Minimal Date Shift) from December 18, 2020 through February 29, 2024

	Finerenone Users	
	N	%
Diagnostic Radiology (Diagnostic Imaging) Procedures of the Abdomen (CPT 1010520)	280	7.0
G: Temporary Procedures & Professional Services (HCPCS G section)	910	22.7
Hospital outpatient clinic visit for assessment and management of a patient (HCPCS G0463)	330	8.2
J: Drugs Administered Other Than Oral Method, Chemotherapy Drugs (HCPCS J section)	550	13.7
Injection, midazolam hydrochloride, per 1 mg (J2250)	170	4.2
Injection, fentanyl citrate, 0.1 mg (J3010)	170	4.2
C: Temporary Hospital Outpatient Prospective Payment System (HCPCS C section)	270	6.7
Guide wire (C1769)	80	2.0

* The procedures were assessed over the period of -183 to -1 days before index finerenone date using the following coding systems:
ICD-10-PCS: International Classification of Diseases, Tenth Revision, Procedure Coding System; CPT - Current Procedural Terminology, HCPCS: Healthcare Common Procedure Coding System; SNOMED: Systemized Nomenclature of Medicine – Clinical Terms
The 7-digit CPT codes in the list of procedure codes refer to the CPT subsets, which are developed for EHR systems and specific physician specialties for ease of data capture or data retrieval (hierarchical tree). The CPT subsets are parent terms, which encompass child terms beneath, which could be other 7-digit subset or 5-digit CPT codes.

[a]This panel must include the following labs (CPT codes): Albumin (82040) Bilirubin, total (82247) Calcium, total (82310) Carbon dioxide (bicarbonate) (82374) Chloride (82435) Creatinine (82565) Glucose (82947) Phosphatase, alkaline (84075) Potassium (84132) Protein, total (84155) Sodium (84295) Transferase, alanine amino (ALT) (SGPT) (84460) Transferase, aspartate amino (AST) (SGOT) (84450) Urea nitrogen (BUN) (84520)

[b]This panel must include the following labs (CPT codes): Calcium, total (82310) Carbon dioxide (bicarbonate) (82374) Chloride (82435) Creatinine (82565) Glucose (82947) Potassium (84132) Sodium (84295) Urea nitrogen (BUN) (84520)

[c]This panel must include the following labs (CPT codes): Cholesterol, serum, total (82465) Lipoprotein, direct measurement, high density cholesterol (HDL cholesterol) (83718) Triglycerides (84478)

[d]This panel must include the following labs (CPT codes): Albumin (82040) Calcium, total (82310) Carbon dioxide (bicarbonate) (82374) Chloride (82435) Creatinine (82565) Glucose (82947) Phosphorus inorganic (phosphate) (84100) Potassium (84132) Sodium (84295) Urea nitrogen (BUN) (84520)

Table 3. Most Frequent Prescribed Medication Classes* Among Patients with Finerenone Exposures in the TriNetX USA Network (Minimal Date Shift) from December 18, 2020 through February 29, 2024

	Finerenone Users	
	N	%
Total Number of Patients	4010	100
Cardiovascular Medications (CV000)	2630	65.6
Antilipemic agents (CV350)	1450	36.2
Diuretics (CV700)	1100	27.4
Loop diuretics (CV702)	620	15.5
Thiazides/related diuretics (CV701)	540	13.5
Beta blockers/related (CV100)	1080	26.9
Angiotensin ii inhibitor (CV805)	980	24.4
Calcium channel blockers (CV200)	920	22.9
Hormones/synthetics/modifiers (HS000)	2480	61.8
Blood glucose regulation agents (HS500)	2190	54.6
Oral hypoglycemic agents,oral (HS502)	1500	37.4
Insulin (HS501)	1040	25.9
Hypoglycemic agents,other (HS509)	720	18.0
Adrenal corticosteroids (HS050)	860	21.4
Glucocorticoids (HS051)	860	21.4
Central nervous system medications (CN000)	1740	43.4
Analgesics (CN100)	1220	30.4
Non-opioid analgesics (CN103)	1000	24.9
Opioid analgesics (CN101)	790	19.7
Anesthetics (CN200)	710	17.7
Local anesthetics, injection (CN204)	670	16.7
Dermatological agents (DE000)	1500	37.4
Dermatologicals,topical other (DE900)[a]	930	23.2
Gastrointestinal medications (GA000)	1360	33.9
Antacids (GA100)	730	18.2
Sodium bicarbonate containing antacids (GA110)	680	17.0
Ophthalmic agents (OP000)	1360	33.9
Ophthalmics,other (OP900)[a]	1030	25.7
Nasal and throat agents,topical (NT000)	1260	31.4
Nasal and throat,topical,other (NT900)[a]	920	22.9
Respiratory tract medications (RE000)	1240	30.9
Respiratory agents,other (RE900)[a]	840	20.9
Antiasthma/bronchodilators (RE100)	720	18.0
Therapeutic nutrients/minerals/electrolytes (TN000)	1160	28.9
Electrolytes/minerals (TN400)	1120	27.9
Sodium (TN440)[a]	810	20.2
Intravenous (IV) solutions (TN100)	880	21.9
IV solutions without electrolytes (TN101)	870	21.7
IV solutions with electrolytes (TN102)[a]	820	20.4

* The medication drug classes coded based on Veterans Affairs (VA) drug classification system were assessed over the period of -183 to -1 days before index finerenone date. The VA classification system classifies all medication products available in the United States. Please note that a specific generic ingredient can be listed in multiple classes, based on their route of administration.

[a]The most frequent medication in this class was Sodium Chloride (RxNorm 9863) in 810 (20%) patients

Table 4. Most Frequent Lab Terms* Among Patients with Finerenone Exposures in the TriNetX USA Network (Minimal Date Shift) from December 18, 2020 through February 29, 2024

	Finerenone Users				
	N	%	Mean ± SD	Min	Max
Total Number of Patients	4010	100	N/A	N/A	N/A
Most Frequent Lab Terms (and Vitals)*					
Lab Category: Metabolic Panel**					
Glucose [mg/dL] in Serum, Plasma or Blood (TNX: 9025)	2630	65.6	152 ± 69.3	6.8	1000
Sodium [mmol/L] in Serum, Plasma or Blood (TNX: 9029)	2620	65.3	139 ± 3.07	121	153
Potassium [mmol/L] in Serum, Plasma or Blood (TNX: 9028)	2620	65.3	4.34 ± 0.472	1.9	6.2
Chloride [mmol/L] in Serum, Plasma or Blood (TNX: 9023)	2610	65.1	103 ± 3.86	83	119
Calcium [mg/dL] in Serum, Plasma or Blood (TNX: 9022)	2610	65.1	9.39 ± 0.594	1.22	12.7
Bicarbonate [mmol/L] in Serum, Plasma or Blood (TNX: 9021)	2590	64.6	25.1 ± 3.33	10	43
Creatinine [mg/dL] in Serum, Plasma or Blood (TNX: 9024)	2580	64.3	1.64 ± 3.9	0	141
Urea nitrogen [mg/dL] in Serum, Plasma or Blood (TNX: 9030)	2560	63.8	27.3 ± 12.9	6	139
Phosphate [mg/dL] in Serum, Plasma or Blood (TNX: 9027)	1170	29.2	3.68 ± 0.721	1.5	9.5
Magnesium [mg/dL] in Serum, Plasma or Blood (TNX: 9026)	710	17.7	1.97 ± 0.287	1	3.02
Lab Category: Liver Function Tests**					
Albumin [g/dL] in Serum, Plasma or Blood (TNX: 9045)	2290	57.1	3.99 ± 0.551	1.4	6.1
Alanine aminotransferase [U/L] in Serum, Plasma or Blood (TNX: 9044	2040	50.9	24.2 ± 23.7	4	570
Aspartate aminotransferase [U/L] in Serum or Plasma (TNX: 9047)	2040	50.9	24.5 ± 21.8	5	662
Alkaline phosphatase [U/L] in Serum, Plasma or Blood (TNX: 9046)	1990	49.6	88.4 ± 56.4	16	1801
Bilirubin.total [mg/dL] in Serum, Plasma or Blood (TNX: 9050)	1970	49.1	0.564 ± 0.543	0	18.3
Bilirubin.direct [mg/dL] in Serum, Plasma or Blood (TNX: 9048)	210	5.2	0.26 ± 0.599	0	7.4
Bilirubin.indirect [mg/dL] in Serum, Plasma or Blood (TNX: 9049)	70	1.7	0.6 ± 0.424	0.1	2.2
Protein [g/dL] in Serum, Plasma or Blood (TNX: 9053)	1900	47.4	7.04 ± 0.679	4.1	10.5
Lactate dehydrogenase [U/L] in Serum or Plasma (TNX: 9052)	90	2.2	230 ± 182	0.7	1383
Gamma glutamyl transferase [U/L] in Serum or Plasma (TNX: 9051)	30	0.7	119 ± 281	8	1158
Lab Category: Lipid Panel**					
Triglyceride [mg/dL] in Serum, Plasma or Blood (TNX: 9004)	1600	39.9	172 ± 118	29	1353
Cholesterol in HDL [mg/dL] in Serum or Plasma (TNX: 9001)	1590	39.7	45.7 ± 15	8	181
Cholesterol in LDL [mg/dL] in Serum or Plasma (TNX: 9002)	1580	39.4	78.5 ± 35.2	5	275
Cholesterol [mg/dL] in Serum or Plasma (TNX: 9000)	1540	38.4	155 ± 44.7	13	452
Lab Category: Cardiology**					
Natriuretic peptide B [pg/mL] in Serum, Plasma or Blood (TNX: 9003)	230	5.7	434 ± 769	5	6002
Natriuretic peptide.B prohormone N-Terminal [pg/mL] in Serum, Plasma or Blood (TNX: 9072)	170	4.2	2930 ± 5871	36	48581
Troponin I.cardiac [ng/mL] in Serum, Plasma or Blood (TNX: 9005)	60	1.5	2.82 ± 17.7	0	120
Lab Category: Vitals**					
Body height [inches] (TNX: 9077)	2530	63.1	66.5 ± 4.1	56.1	78
Body weight [pounds] (TNX: 9081)	2390	59.6	201 ± 52.7	86.4	419
BMI [kg/m^2] (TNX: 9083)	1030	25.7	32.6 ± 6.28	18.3	50
BMI Percentile (TNX: 9084)	10	0.2	34.5 ± 6.33	24.6	42.2
Blood Pressure, Systolic [mm Hg] (TNX: 9085)	2430	60.6	136 ± 20.9	75	230
Blood Pressure, Diastolic [mm Hg] (TNX: 9086)	2440	60.8	75.5 ± 12.7	30	190
Heart rate [beats per minute] (TNX: 9074)	2130	53.1	77.6 ± 14	2	187
Body temperature [°F] (TNX: 9076)	1520	37.9	92.1 ± 17.6	35.7	103
Respiratory rate [breaths per minute] (TNX: 9073)	1160	28.9	17.4 ± 2.74	10	76
Oxygen saturation [%] (TNX: 9075)	530	13.2	84.6 ± 25.8	0	100

Table 4. Most Frequent Lab Terms* Among Patients with Finerenone Exposures in the TriNetX USA Network (Minimal Date Shift) from December 18, 2020 through February 29, 2024

	Finerenone Users				
	N	%	Mean ± SD	Min	Max
Lab Category: Vitals**					
Body surface area [m^2] (TNX: 9087)	120	3.0	2.08 ± 0.266	1.44	2.76
Lab Category: Endocrinology**					
Hemoglobin A1c/Hemoglobin.total in Blood [%] (TNX: 9037)	1940	48.4	7.41 ± 1.55	4.3	15.8
Lab Category: Complete Blood Count**					
Hemoglobin [g/dL] in Blood (TNX: 9014)	2210	55.1	12.8 ± 2.14	5.7	20.1
Platelets [10^3/microliter] in Blood (TNX: 9020)	2190	54.6	240 ± 75.5	43	621
Erythrocytes [10^6/microliter] in Blood (TNX: 9012)	2130	53.1	4.32 ± 0.93	0	7.63
Leukocytes [10^3/microliter] in Blood (TNX: 9015)	1970	49.1	17.1 ± 201	1	4880
Lab Category: Findings**					
Corrected QT Interval (QTc) [milliseconds] (TNX: 2001)	230	5.7	450 ± 35.4	337	590
Left Ventricular Ejection Fraction (LVEF) (%) (TNX: 2003)	100	2.5	58.2 ± 13.4	2	85
NYHA Classification (TNX: 2004)	10	0.2	2.75 ± 0.957	2	4
Lab Category: Other Chemistry**					
C reactive protein [mg/L] in Serum, Plasma or Blood (TNX: 9063)	180	4.5	28.1 ± 56.5	0	300
Erythrocyte sedimentation rate [mm/hr] (TNX: 9066)	180	4.5	39.4 ± 28	0	121

* The lab terms presented were assessed over the period of -183 to -1 days before index finerenone date using TriNetX aggregate lab terms (TNX:LAB) that group clinically relevant Logical Observation Identifiers Names and Codes (LOINC) together for each test.

** The lab tests within categories were curated by TriNetX internal team to harmonize related codes
N/A: Not applicable

Appendix A. List of RxNorm Medication Terms Used to Define Exposure in this Request

Code	Description	Code Type
2562811	Finerenone	RxNorm

Appendix B. Specifications Defining Query Builder Modules in this Request

Network:
USA Minimal Shift network

Cohort 1: Finerenone	
Group 1:	**Time Restrictions**
Subgroup 1A	
Must Have:	
Finerenone	December 18, 2020 - February 29, 2024

Appendix C. Specifications Defining Analytic Modules in this Request

#	Module	Analysis Type	Cohort(s)	Window	Index Event(s)	Characteristics or Outcomes
1	Analyze Outcomes	Characteristics	Finerenone	[-183, -1]	Finerenone	Most frequent diagnoses
2	Analyze Outcomes	Characteristics	Finerenone	[-183, -1]	Finerenone	Most frequent procedures
3	Analyze Outcomes	Characteristics	Finerenone	[-183, -1]	Finerenone	Most frequent medications
4	Analyze Outcomes	Characteristics	Finerenone	[-183, -1]	Finerenone	Most frequent labs