Impact of Trikafta on Individuals Living With Cystic Fibrosis

Methodology Notes

Canadian Institute for Health Information
Institut canadien d'information sur la santé

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Identifying information

Project name	Cystic Fibrosis in Canada
Project description	CIHI has received funding from the Health Canada–led National Strategy for Drugs for Rare Diseases to improve the collection and use of real-world evidence to support decision-making. This project is to assess and understand the real-world impact of Trikafta on the care pathway of patients living with cystic fibrosis. This analysis includes 6 parts: 1. Identifying Trikafta claimants 2. Creating the Trikafta cohort for analysis 3. Exploring emergency department care before and after starting Trikafta 4. Exploring acute hospital care before and after starting Trikafta 5. Exploring pharmaceutical use (excluding Trikafta) before and after starting Trikafta 6. Exploring physician visits in hospitals and outpatient/community settings before and after starting Trikafta
Project time frame	November 2023 to November 2024
Resources	Discharge Abstract Database (DAD) metadata National Ambulatory Care Reporting System (NACRS) metadata National Prescription Drug Utilization Information System (NPDUIS) metadata Pharmaceutical Data Tool Cost of a Standard Hospital Stay
General inquiries	drugs@cihi.ca

Project analysis 1: Identifying Trikafta claimants

Objective of analysis	To identify the number of Trikafta claimants per month since its approval (June 2021)
Data sources	National Prescription Drug Utilization Information System (NPDUIS), Canadian Institute for Health Information
Data time frame	Fiscal years 2021–2022 and 2022–2023
Geographic coverage	Newfoundland and Labrador, New Brunswick, Ontario, Manitoba, Saskatchewan, Alberta and British Columbia
Cohort description	Patients with a Trikafta claim submitted between June 1, 2021, and December 31, 2022
Inclusions	1. Claimants with a Trikafta claim (drugs with Anatomical Therapeutic Chemical [ATC] Level 5 code R07AX32) submitted between June 1, 2021, and December 31, 2022 2. Claimants age 10 and older **Note** ATC is a classification system that divides drugs into different groups according to the organ or system on which they act and their chemical, pharmacological and therapeutic properties. This analysis used the 2024 version of the World Health Organization (WHO) ATC classification system.
Exclusions	1. Claims from Prince Edward Island, Nova Scotia, Quebec and the territories 2. Claims submitted from the Non-Insured Health Benefits Drug program (see note) **Note** Claims submitted through the Non-Insured Benefits Drug program are primarily for First Nations, Inuit and Métis. Per CIHI policy, inclusion of Indigenous-identifiable data needs to be approved by appropriate Indigenous authorities.
Linkage	None
Calculation description	Number of unique Trikafta claimants per month between June 1, 2021, and December 31, 2022

Project analysis 2: Creating the Trikafta cohort for analysis

Objective of analysis	To create a cohort of claimants with a first Trikafta claim submitted in fiscal year 2021–2022
Data sources	National Prescription Drug Utilization Information System (NPDUIS), Canadian Institute for Health Information
Data time frame	Fiscal years 2010–2011 to 2021–2022
Geographic coverage	Newfoundland and Labrador, New Brunswick, Ontario, Manitoba, Saskatchewan, Alberta and British Columbia
Cohort description	Patients with a first Trikafta claim submitted in fiscal year 2021–2022
Inclusions	1. Claimants with their first Trikafta claim (drugs with ATC level 5 code R07AX32) submitted in fiscal year 2021–2022 2. Claimants age 10 and older
Exclusions	1. Claims from Prince Edward Island, Nova Scotia, Quebec and the territories 2. Claims from the Non-Insured Health Benefits Drug program (see note) 3. Claimants with a Trikafta claim (drugs with ATC level 5 code R07AX32) submitted before fiscal year 2021–2022 4. Claimants who have been on other cystic fibrosis transmembrane conductance regulator (CFTR) modulators (drugs with ATC level 5 codes R07AX02, R07AX30 or R07AX31) at any time since April 2010, prior to their first Trikafta claim. **Notes** Claims submitted through the Non-Insured Benefits Drug program are primarily for First Nations, Inuit and Métis. Per CIHI policy, inclusion of Indigenous-identifiable data needs to be approved by appropriate Indigenous authorities. ATC is a classification system that divides drugs into different groups according to the organ or system on which they act and their chemical, pharmacological and therapeutic properties. This analysis used the 2024 version of the WHO ATC classification system.
Linkage	Linked NPDUIS data over time using CIHI's standard client linkage methodology
Calculation description	1. Age of claimants i. Number and percentage of the cohort in the following age groups: 10–19, 20–29, 30–39, 40–49, 50–59, 60+ 2. Reported sex or gender of claimants (number and percentage) 3. Province of claimants associated with the submitted claim (number and percentage) 4. Neighbourhood income quintile (number and percentage) i. Claimants were assigned to a neighbourhood income quintile based on the postal codes of place of residence using the Postal Code Conversion File Plus (PCCF+) version 8A. Cases with missing or invalid postal codes were excluded.

Project analysis 3: Exploring emergency department (ED) care before and after starting Trikafta

Objective of analysis	To explore use of emergency care before and after patients started taking Trikafta
Data sources	National Prescription Drug Utilization Information System (NPDUIS), Canadian Institute for Health Information National Ambulatory Care Reporting System (NACRS), Canadian Institute for Health Information
Data time frame	Fiscal years 2020–2021 to 2022–2023
Geographic coverage	Ontario and Alberta, provinces for which there is both Trikafta information and emergency department care use information available
Cohort description	Patients who started Trikafta in fiscal year 2021–2022
Inclusions	1. Patients identified in Trikafta cohort (Project analysis 2) 2. *Unscheduled or unplanned* ED visits by patients in the Trikafta cohort
Exclusions	1. Records where recorded sex or gender is neither male nor female 2. Records with invalid (unlinkable) health card numbers
Linkage	Linked NPDUIS with NACRS using CIHI's standard client linkage methodology
Calculation description	Total number of ED visits 1 year before and 1 year after Trikafta start date 1. The number of ED visits with a registration date on the Trikafta start date or within 365 days prior to the Trikafta start date. 2. The number of ED visits with a registration date within 365 days after the Trikafta start date (exclusive of the Trikafta start date itself). Patient profile 1. Age of patients i. Number and percentage of the cohort in the following age groups: 10–19, 20–29, 30–39, 40–49, 50–59, 60+ ii. Total number of patients in cohort visiting the ED before and after the Trikafta start date Resource use 1. Number of ED visits that ended in hospital admission 2. Average and total costs of ED visits 3. Top 5 main problems before and after starting Trikafta i. The main problem for the visit is the ICD-10-CA code that describes the most clinically significant diagnosis, condition, problem or circumstance for the client's visit (see NACRS metadata for details).

Project analysis 4: Exploring acute hospital care before and after starting Trikafta

Objective of analysis	To explore use of acute hospital care before and after patients started taking Trikafta
Data sources	National Prescription Drug Utilization Information System (NPDUIS), Canadian Institute for Health Information Discharge Abstract Database (DAD), Canadian Institute for Health Information
Data time frame	Fiscal years 2020–2021 to 2022–2023
Geographic coverage	Newfoundland and Labrador, Nova Scotia, New Brunswick, Ontario, Manitoba, Saskatchewan, Alberta and British Columbia
Cohort description	Patients who started Trikafta in fiscal year 2021–2022
Inclusions	1. Patients identified in Trikafta cohort (Project analysis 2) 2. Patients who have at least 1 acute care hospitalization 1 year before or after starting to take Trikafta (see note) **Note** A hospitalization is defined as an episode of care. An episode of care refers to all contiguous inpatient hospitalizations and day procedure visits.
Exclusions	1. Records where recorded sex or gender is neither male nor female 2. Records submitted by Quebec hospitals 3. Records with invalid (unlinkable) health card numbers
Linkage	Linked NPDUIS with DAD using CIHI's standard client linkage methodology
Calculation description	Total number of hospitalizations 1 year before and 1 year after the Trikafta start date 1. The number of hospitalizations where (a) discharge date was on the Trikafta start date or within 365 days prior to the Trikafta start date; (b) Trikafta start date was between admission date and discharge date. 2. The number of hospitalizations where admission date was within 365 days after the Trikafta start date (exclusive of the Trikafta start date itself). Patient profile 1. Total number of patients hospitalized 1 year before and after the Trikafta start date 2. Age of patients i. Number and percentage of the cohort in the following age groups: 10–19, 20–29, 30–39, 40–49, 50–59, 60+ Hospital resource use 1. Number of hospitalizations grouped by length of hospital stay (1–2 days, 3–7 days, 8–14 days, 15–30 days, 31+ days) 2. Average length of stay i. For more information, please see Average Length of a Hospital Stay (Days). 3. Average and total costs of hospitalizations 4. Top 3 most responsible diagnoses (MRDx) i. The MRDx is defined as the 1 diagnosis or condition that is most responsible for the patient's stay in a facility. If there is more than one such diagnosis, the 1 diagnosis most responsible for the greatest portion of the length of stay or greatest use of resources is selected (see DAD metadata for details).

Project analysis 5: Exploring pharmaceutical use (excluding Trikafta) before and after starting Trikafta

Objective of analysis	To explore non-Trikafta drug claims before and after patients started taking Trikafta
Data sources	National Prescription Drug Utilization Information System (NPDUIS), Canadian Institute for Health Information
Data time frame	Fiscal years 2020–2021 to 2022–2023
Geographic coverage	Manitoba, Saskatchewan and British Columbia
Cohort description	Patients who started Trikafta in fiscal year 2021–2022
Inclusions	Patients identified in Trikafta cohort (Project analysis 2)
Exclusions	1. Pseudo-drug identification number flag is Y i. A pseudo-drug identification number (PDIN) is assigned by a drug program in cases where a drug has not been assigned a drug identification number (DIN) by Health Canada. 2. Trikafta claims (ATC level 5 code R07AX32)
Linkage	Linkage using CIHI's standard client linkage methodology
Calculation description	Claims data 1 year before and 1 year after Trikafta start date 1. Calculate the difference in days between the Trikafta start date and the drug claim date. 2. For pre-Trikafta claims, the difference in days should be between -365 and 0 days. 3. For post-Trikafta claims, the difference in days should be between 1 and 365 days. Number of claimants and supply days for chronic use of pharmaceuticals (other than Trikafta) by the Trikafta cohort 1. Identify the number of claimants with 2 or more claims with at least 180 cumulative supply days by ATC level 2 and ATC level 4 group. 2. Report the top 5 ATC level 2 groups for chronic use of pharmaceuticals based on number of claimants and supply days pre– and post–Trikafta start date. 3. For each ATC level 2 group, report the top 3 ATC level 4 groups for chronic use of pharmaceuticals based on number of claimants and supply days pre– and post–Trikafta start date. Number of claimants and supply days for commonly used oral antibiotics for acute infections by the Trikafta cohort 1. Identify cohort member drug claims submitted for commonly used oral antibiotics for acute infections identified by clinicians (see Appendix, Table 3). 2. Report the number of claimants and total supply days for each chemical (ATC level 5) pre– and post–Trikafta start date in descending order (based on number of claimants). **Notes** The definition of chronic use of pharmaceuticals is based on CIHI's report *Drug Use Among Seniors in Canada, 2016*. ATC is a classification system that divides drugs into different groups according to the organ or system on which they act and their chemical, pharmacological and therapeutic properties. This analysis used the 2024 version of the WHO ATC classification system.

Project analysis 6: Explore physician visits in hospitals and outpatient/community settings before and after starting Trikafta

Objective of analysis	To explore physician visits in hospitals and outpatient/community settings before and after patients started taking Trikafta
Data sources	National Prescription Drug Utilization Information System (NPDUIS), Canadian Institute for Health Information National Physician Database (NPDB), Canadian Institute for Health Information Discharge Abstract Database (DAD), Canadian Institute for Health Information
Data time frame	Fiscal years 2020–2021 to 2022–2023
Geographic coverage	Newfoundland and Labrador, Ontario, Manitoba, Saskatchewan, Alberta and British Columbia
Cohort description	Patients who started Trikafta in fiscal year 2021–2022
Inclusions	1. Patients identified in the Trikafta cohort (Project analysis 2) 2. Physician services provided to these patients 1 year before and 1 year after Trikafta start date
Exclusions	None
Linkage	Linked NPDUIS, DAD and NPDB using CIHI's standard client linkage methodology
Calculation description	Visit data 1 year before and 1 year after Trikafta start date 1. Calculate the difference in days between the Trikafta start date and the physician visit date. 2. For pre-Trikafta claims, the difference in days should be between -365 and 0 days. 3. For post-Trikafta claims, the difference in days should be between 1 and 365 days. **Visit-level analysis** Each visit is represented by a unique combination of the date of service, health card issuing province and encrypted health card number. If a patient saw several physicians in 1 day, it was considered a single visit to avoid over-counting in clinic and hospital, where a patient may see multiple physicians during their visit (~3% of visits). **In-hospital physician visits** Each visit was defined as physician billing claims with the date of service on the same date when the patient had a documented inpatient stay with a corresponding record in the Discharge Abstract Database. **Outpatient and community physician visits** Each visit was defined as physician billing claims with the date of service not on the same date as when the patient had a documented inpatient stay.

Quality statement

Exceptions and limitations	Cell suppression methodology for all requested data tables In accordance with CIHI's privacy policy, when the cell value is fewer than 5 but greater than 0, this number and its associated metrics (e.g., total cost) are suppressed to ensure confidentiality. When the difference in the numbers between corresponding entries (rows) in different tables is less than 5, the number and other associated values are also suppressed to avoid residual disclosure. **Note** There may be exceptions to this rule if warranted. **NPDUIS** Due to the design of public drug programs in Canada (i.e., seniors and low-income families/individuals are the only populations covered in all jurisdictions), we have limited data on claims made by non-seniors. As a result, NPDUIS is not a population-based system (except for Manitoba, Saskatchewan and British Columbia). There may also be differences in population characteristics (such as age and health status) between seniors with and without public coverage. In provinces where a lower proportion of seniors have claims accepted by the public plan (e.g., Newfoundland and Labrador, Nova Scotia, New Brunswick), drug utilization patterns among those with public coverage are more likely to be affected by these differences and, therefore, may be less reflective of utilization patterns among all seniors in the province. Claims for drugs dispensed in hospitals, as well as for those funded through cancer agencies, are not submitted to NPDUIS. NPDUIS does not include information regarding • Prescriptions that were written but never dispensed; • Prescriptions that were dispensed but for which the associated drug costs were not submitted to, or not accepted by, the public drug programs; or • Diagnoses or conditions for which prescriptions were written.

Appendix: Notes for analysis using prescription drug data

Relevant drug products were identified by their DINs assigned by Health Canada and by the following World Health Organization (WHO) ATC codes in NPDUIS:

Table 1 ATC codes for CF drug products

Chemical	ATC code
Ivacaftor, tezacaftor and elexacaftor (Trikafta)	R07AX32
Other CFTR modulators	
Ivacaftor	R07AX02
Ivacaftor and lumacaftor	R07AX30
Ivacaftor and tezacaftor	R07AX31

Table 2 NPDUIS data elements and definitions

Data element	Claims information
Number of Claimants	The number of people who submitted a claim to a public drug program for payment or for processing for documentation under a DIS
Supply Days	The number of supply days dispensed as indicated by the dispensing pharmacy.

Table 3 Commonly used oral antibiotics for acute infections identified by clinicians

Chemical	ATC code
Sulfamethoxazole and trimethoprim	J01EE01
Ciprofloxacin	J01MA02
Doxycycline	J01AA02
Cefalexin	J01DB01
Amoxicillin and beta-lactamase inhibitor	J01CR02

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