25 June 2026
EMADOC-1700519818-3323611
Human Medicines Division

Assessment report for paediatric studies submitted in accordance with article 46 of regulation (EC) No 1901/2006

Paxlovid

Nirmatrelvir / Ritonavir

Procedure no: EMA/PAM/0000338024

Note

Assessment report as adopted by the CHMP with all information of a commercially confidential nature deleted.

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Status of this report and steps taken for the assessment			
Current step	**Description**	**Planned date**	**Actual Date**
☐	CHMP Rapporteur AR	1 June 2026	19 May 2026
☐	CHMP comments	15 June 2026	15 June 2026
☐	Updated CHMP Rapporteur AR	18 June 2026	18 June 2026
☒	CHMP outcome	25 June 2026	25 June 2026

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1. Introduction

On 17 March 2026, the MAH submitted a completed paediatric study for Paxlovid, in accordance with Article 46 of Regulation (EC) No1901/2006, as amended.

A short critical expert overview has also been provided.

2. Scientific discussion

2.1. Information on the development program

In EU, Paxlovid received first regulatory Conditional Marketing Authorization approval, converted to a full Marketing Authorisation on 24 Feb 2023 for the treatment of COVID-19 in adults who do not require supplemental oxygen and who are at increased risk of progressing to severe COVID-19. On 26 Nov 2025 (EC Decision following variation procedure EMEA/H/C/005973/II/0061/G) indication to paediatric patients 6 years of age and older weighing at least 20 kg was approved.

2.2. Information on the pharmaceutical formulation used in the study

The commercial formulation of Paxlovid is the same as that used in all Phase 2/3 studies. The recommended doses of Paxlovid are:

- For adults and paediatric patients ≥6 years of age weighing ≥40 kg: 300 mg nirmatrelvir (two 150 mg tablets) with 100 mg ritonavir (one 100 mg tablet) with all 3 tablets taken together orally twice daily for 5 days.

- For paediatric patients ≥6 years of age weighing ≥20 to <40 kg: 150 mg nirmatrelvir (one 150 mg tablet) with 100 mg ritonavir (one 100 mg tablet) taken together orally every 12 hours for 5 days

2.3. Clinical aspects

Introduction

The MAH submitted a final report for study C4671040 (Title: A Standing Cohort to Understand the Characteristics of Patients With COVID-19 and Contextualize the COVID-19 Complications and Safety Events of Interest Using US OPTUM EHR Data).

Clinical study

Study C4671040: A standing cohort to understand the characteristics of patients with COVID-19 and contextualize the COVID-19 complication and safety events of interests using US OPTUM EHR data

Description

This is a non-interventional, population-based, observational, retrospective cohort study using structured data with ongoing retrospective and prospective data collection from electronic healthcare data in the US. This study included adults (≥18 years of age) and paediatric patients (<18 years of age) with a COVID-19 diagnosis (ie, positive PCR or antigen results of direct SARS-CoV-2 viral testing or confirmed COVID-19 diagnosis codes). Within the population-based general cohort (COVID-19 Cohort), a sub-cohort was created based on similar eligibility criteria as those used in select Paxlovid

clinical trials (eg, C4671005 [NCT04960202], C4671002 [NCT05011513]) to attempt to emulate the characteristics of select clinical trial program populations (Paxlovid Trial Similar COVID-19 Sub-cohorts). Patients with a Paxlovid prescription were included in a subgroup analysis. All Paxlovid users were included in the study. The study population was followed from the COVID-19 diagnosis or Paxlovid prescription to identify outcomes of interests (health outcomes, COVID-19 complications, and Long COVID).

The study was conducted using Optum's COVID-19 Electronic Health Record Data during the period of 01 Jan 2020 to 30 Jun 2024.

Methods

Study participants

The study population consisted of patients who tested positive or were diagnosed with COVID-19 (ie, positive PCR or antigen results of direct SARS-CoV-2 viral testing or have confirmed COVID-19 diagnosis codes). All Paxlovid users were included in the study.

Within the study population, three source cohorts of general population with COVID-19 will be formed:

- 1a: Overall COVID-19 patients.

- 1b: Hospitalized patients (ie, hospitalized within 30 days of index date) for COVID-19

- 1c: Non-hospitalized patients (ie, not hospitalized within 30 days of index date) with COVID-19

Within source cohort of 1a, 1b, and 1c, the following trial similar sub cohorts, will be formed:

Patients at high risk of progression to severe illness:

2a: Subgroup of the general population cohort 1a who meet relevant inclusion/exclusion criteria of the Paxlovid clinical trial (C4671005) which include age ≥18 years, confirmed COVID-19 infection diagnosis, high-risk for progression to severe COVID-19 and absence of prior hospitalization for COVID-19 (other than for incident event), liver / renal disease, HIV, recent (≤7 days) hospitalizations or surgeries and prohibited medications (CYP3A4 inducers).

2b: Subgroup of the hospitalized patient cohort 1b who meet relevant inclusion/exclusion criteria of the Paxlovid clinical trial (C4671005), as noted above in 2a.

2c: Subgroup of the non-hospitalized patient cohort 1c who meet relevant inclusion/exclusion criteria of the Paxlovid clinical trial (C4671005), as noted above in 2a.

Patients at standard risk of progression to severe illness:

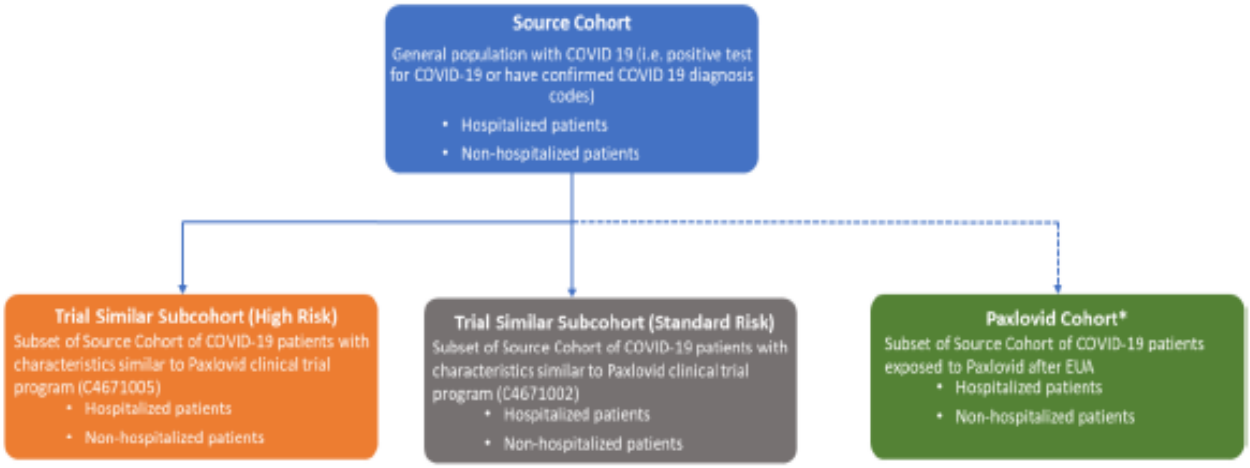
3a: Subgroup of the general population cohort 1a who meet relevant inclusion/exclusion criteria of the Paxlovid clinical trial (C4671002) which include age ≥18 years, confirmed COVID-19 infection diagnosis, Non-hospitalized at diagnosis, low or standard-risk for progression to severe COVID-19 and absence of high-risk medical conditions for severe COVID-19, evidence of immunosuppression.

3b: Subgroup of the hospitalized patient cohort 1b who meet relevant inclusion/exclusion criteria of the Paxlovid clinical trial (C4671002), as noted above in 3a.

3c: Subgroup of the non-hospitalized patient cohort 1b who meet relevant inclusion/exclusion criteria of the Paxlovid clinical trial (C4671002), as noted above in 3a.

A sub-cohort of patients who were exposed to Paxlovid in real-world settings were created.

If a patient had an exposure to Paxlovid without COVID PCR/antigen testing/diagnosis data, this patient can be captured in the Paxlovid cohort.



Note: Any addition of a special population (eg, immunocompromised patients, paediatric population, severe renal cohort etc.) as well as patients with multiple infections of COVID-19 or patients who received COVID-19 vaccines can be a subset of either Source Cohort or high/standard risk cohort. For Paxlovid cohort, if a patient had an exposure to Paxlovid without COVID PCR/ antigen testing/diagnosis data, this patient can be captured in the Paxlovid cohort.

Figure 1. Flowchart outlining the study cohort and sub-cohorts

The population of interest for the current paediatric procedure is the subset of paediatric subjects in the Paxlovid cohort, i.e. paediatric subjects who were exposed to Paxlovid in real-world settings and captured in the US OPTUM EHR data from January 2020 to June 2024.

Treatments

This is a non-interventional observational retrospective study, no treatment was administered. Some subjects may have been treated with Paxlovid as part of their therapeutic management.

Objective(s)

The primary research objectives for the study were as follows:

1. Describe the distribution of demographics, co-morbid conditions, medical history, selected biomarkers, and healthcare utilization at baseline for COVID-19 patients (including subpopulation with Long COVID)

2. Describe the time to clinical events (eg, hospitalization, ICU admission, death)

3. Estimate background incidence of COVID-19 manifestations/complications and safety outcome of interests following COVID-19 infection or Paxlovid exposure

4. Estimate incidence of Long COVID-19 or post-acute sequalae SARS CoV-2 (PASC) and assess health effects of Long COVID.

5. Describe the health equity and demographic and clinical characteristics (eg, comorbid conditions, outcomes, treatment patterns, healthcare utilization) among patients treated with Paxlovid

The secondary research objective for the study was as follows:

1. Estimate the incidence of oxygen supplementation among COVID-19 patients hospitalized with mechanical ventilation/ECMO.

The exploratory research objectives for the study were as follows:

1. Identify predictors of COVID-19 severe outcomes/manifestations and Long COVID with machine learning (ML) methods.

2. Predict risk of developing severe outcomes/manifestation and Long COVID with machine learning (ML) methods at the patient level.

3. Assess the feasibility of Real-world effectiveness of Paxlovid in reducing the COVID 19 related outcomes (eg, hospitalization).

Sample size

Study C4671040 was a non-interventionnal study with no minimum sample size. Primary and secondary objectives were all descriptive. Based on initial feasibility assessment for exploratory objectives, the Optum EHR database had over 100,000 COVID-19 diagnoses and over 1,000 Paxlovid prescriptions, as well as over 2,500 Long COVID diagnoses as defined by PCC criteria.

Statistical Methods

Baseline characteristics were summarized for Source Cohort, Trial Similar Cohorts, and Paxlovid cohort. Means with standard deviations, medians with interquartile were provided for continuous variables. Numbers and percentages were provided for dichotomous variables or categorical variables.

Results

Participant flow

Overall, a total of 1,663,017 patients were included in the Source Cohort analysis, 923,042 patients in the High-Risk Cohort analysis, 590,469 patients in the Standard Risk Cohort analysis, and 16,583 patients for the Paxlovid Cohort analysis.

Results

A focus is placed on paediatric patients. Of note, exact age is unknown because the Optum database only reports birth year.

Objective 1: Describe the distribution of demographics, co-morbid conditions, medical history, selected biomarkers, and healthcare utilization at baseline for COVID-19 patients

Paediatric patient demographics and clinical characteristics between the Paxlovid-treated group and the non-Paxlovid group are summarized below:

Table 1 Paediatric patient demographics and baseline clinical characteristics by Paxlovid use

	Nirmatrelvir/ Ritonavir	Non-nirmatrelvir/ Ritonavir	Standardized Difference
	N=89	N=11,674	
Age, years, mean ± SD	15 (1.5)	14 (1.7)	0.401
Age bracket 12-17 (inclusive), n (%)	89 (100.0)	11,674 (100.0)	.
Male sex, n (%)	47 (52.8)	5,688 (48.7)	0.082
Race, n (%)			
Caucasian	63 (70.8)	7,711 (66.1)	0.102
African American	18 (20.2)	1,476 (12.6)	0.206
Asian	3 (3.4)	328 (2.8)	0.032
Other/Unknown	5 (5.6)	2,159 (18.5)	0.403
Ethnicity, n (%)			
Hispanic	12 (13.5)	1,962 (16.8)	0.093
Not Hispanic	61 (68.5)	7,888 (67.6)	0.021
Unknown	16 (18.0)	1,824 (15.6)	0.063
Cohort entry month/year, n (%)			
Dec 2021	.	1,643 (14.1)	.
Jan 2022	10 (11.2)	7,391 (63.3)	1.278
Feb 2022	4 (4.5)	845 (7.2)	0.117
Mar 2022	1 (1.1)	261 (2.2)	0.087
Apr 2022	10 (11.2)	338 (2.9)	0.33
May 2022	49 (55.1)	884 (7.6)	1.192
Jun 2022	15 (16.9)	312 (2.7)	0.492
Insurance type, n (%)			
Commercial	63 (70.8)	7,379 (63.2)	0.162
Medicare	.	63 (0.5)	.
Medicaid	15 (16.9)	2,907 (24.9)	0.199
Other Payor Type	4 (4.5)	421 (3.6)	0.045
Uninsured	.	37 (0.3)	.
Unknown	7 (7.9)	867 (7.4)	0.016
Geographic region, n (%)			
Northeast	30 (33.7)	4,910 (42.1)	0.173
Midwest	26 (29.2)	4,167 (35.7)	0.139
West	7 (7.9)	324 (2.8)	0.228
South	25 (28.1)	1,820 (15.6)	0.306
Other/Unknown	1 (1.1)	453 (3.9)	0.177
Comorbidities, n (%)			
Asthma	30 (33.7)	2,471 (21.2)	0.284
COPD	2 (2.2)	82 (0.7)	0.128
Coronary Heart Disease	.	2 (0.0)	.
Hypertension	2 (2.2)	140 (1.2)	0.081
Chronic Kidney Disease	3 (3.4)	87 (0.7)	0.186
Smoker	23 (25.8)	4,688 (40.2)	0.308
BMI>=30 or obesity	30 (33.7)	4,023 (34.5)	0.016
Diabetes Mellitus	4 (4.5)	169 (1.4)	0.18
Cancer	2 (2.2)	52 (0.4)	0.157
Comorbidity index, Mean ± SD	1 (1.1)	0 (0.6)	0.403
Receipt of ≥1 COVID-19 vaccination, n (%)	48 (53.9)	4,132 (35.4)	0.38
Number of previous SARS-CoV-2 infections, n (%)			
0	81 (91.0)	10,744 (92.0)	0.037
1	8 (9.0)	881 (7.5)	0.052
2+	0 (0.0)	49 (0.4)	1.202

The Paxlovid-treated group was slightly older than the non-Paxlovid group (mean 15 years vs 14 years). There were higher proportions of African American individuals in the Paxlovid-treated group compared to the non-Paxlovid group (20.2% vs 12.6%), as well as Caucasian individuals (70.8% vs 66.1%). The Paxlovid-treated group had a higher proportion of individuals with asthma (33.7% vs 21.2%), whereas the non-Paxlovid group had a higher proportion of Smokers (40.2% vs 25.8%), which includes the use of vape and nicotine products. Both groups had similar counts of prior COVID 19 infections, whereas the Paxlovid-treated group had a higher proportion of COVID-19 vaccination (53.9% vs 35.4%).

Healthcare utilization in the 12 months prior to index date is summarized below:

Table 2 Paediatric healthcare utilization within 12 months before the index date

	Nirmatrelvir/ Ritonavir	Non-nirmatrelvir/ Ritonavir	Standardized Difference
	N=89	N=11,674	
Number of hospitalizations			
0	79 (88.8)	11,331 (97.1)	0.328
1	8 (9.0)	268 (2.3)	0.293
2+	2 (2.2)	75 (0.6)	0.135
Mean±SD	0 (0.5)	0 (0.3)	0.276
Length of stay, days Mean±SD	7 (7.7)	6 (8.4)	0.08
Emergency room visits			
0	69 (77.5)	8,459 (72.5)	0.117
1	12 (13.5)	1,837 (15.7)	0.064
2+	8 (9.0)	1,378 (11.8)	0.092
Mean±SD	0 (0.9)	0 (1.2)	0.117
Physician office visits			
0	1 (1.1)	861 (7.4)	0.314
1	9 (10.1)	1,380 (11.8)	0.055
2+	79 (88.8)	9,433 (80.8)	0.223
Mean±SD	9 (9.7)	5 (7.0)	0.376
Telemedicine visits			
0	35 (39.3)	5,071 (43.4)	0.084
1	10 (11.2)	1,865 (16.0)	0.139
2+	44 (49.4)	4,738 (40.6)	0.179
Mean±SD	5 (9.6)	2 (6.3)	0.28
Urgent care visits			
0	85 (95.5)	10,292 (88.2)	0.271
1	2 (2.2)	817 (7.0)	0.228
2+	2 (2.2)	565 (4.8)	0.141
Mean±SD	0 (0.4)	0 (0.8)	0.223

The proportion of individuals that had at least one hospitalization was higher in the Paxlovid-treated group compared to the non-Paxlovid group. There were similar proportions of Emergency Room visits between the groups but the mean numbers of Physician Office visits and Telemedicine visits were higher in the Paxlovid-treated group.

Objective 2: Describe the time to clinical events (eg, hospitalization, ICU admission, death)

The mean time to pneumonia is similar across all cohorts (Source Cohort, High Risk Cohort and Standard Risk Cohort), with the Source and High-Risk cohorts showing a mean time of about 4 days, while the Standard Risk cohort shows a slightly longer mean time of 4.43 days. Hospitalization occurs

most quickly in the Standard Risk cohort, with a mean time of 2.53 days, compared to around 3.94 days in the Source cohort and 3.98 days in the High-Risk cohort.

Due to the small number of events among the 89 Paxlovid-treated patients, results are not able to be contextualized compared to other cohort/s.

Table 3 Time to COVID-19 Complications/interventions since First Paxlovid Prescription, Age 12-17

Study Endpoints	Events	Mean Time (Days)	SD	Median Time (Days)	IQR
Overall					
Paxlovid Cohort					
Pneumonia	1	2	.	2	0
Kidney failure	0	.	.	.	.
Thrombotic event	0	.	.	.	.
Heart failure	0	.	.	.	.
Sepsis/septic shock	0	.	.	.	.
Mechanical ventilation/ECMO	0	.	.	.	.
Hospitalization	0	.	.	.	.
All-cause mortality	0	.	.	.	.
In hospital death	0	.	.	.	.
Multi-organ dysfunction/failure	0	.	.	.	.
Vasopressor use	0	.	.	.	.
Renal impairment	1	28	.	28	0
Hepatic impairment	2	19.5	4.95	19.5	7
Dysgeusia	0	.	.	.	.
Diarrhea	0	.	.	.	.
Hypersensitivity reaction/allergic reaction	1	133	.	133	0

Objective 3: Estimate background incidence of COVID-19 manifestations/complications and safety outcome of interests following COVID-19 infection or Paxlovid exposure

Data on the incidence of COVID-19 complications and interventions within 30 days of infection, and of health outcomes (potential safety related endpoints), among paediatric patients were provided, comparing the Source Cohort, High Risk Cohort and Standard Risk Cohort, with distinctions between overall, hospitalized and non-hospitalized patients.

COVID-19 complications/interventions within 30 days of COVID 19 infection

Hospitalized patients in all cohorts show significantly higher incidence rates for complications such as pneumonia, kidney failure, and ARDS compared to non-hospitalized patients. For example, pneumonia rates are notably higher in hospitalized patients (eg, Source Cohort: 1,751.39 per 1000 person-years) compared to non-hospitalized patients (eg, Source Cohort: 56.93 per 1000 person-years). Mortality rates are low across all cohorts, with higher rates in hospitalized patients (eg, Source Cohort: 70.46 per 1000 person-years) compared to non-hospitalized cohorts (eg, Source Cohort: 0.78 per 1000 person-years), reflecting the overall low mortality among paediatric patients. It is not possible to ascertain precise incidence estimates of COVID-19 complications and interventions among paediatric Paxlovid-treated patients given the low frequency of events in the small cohort.

Table 4 Incidence of COVID-19 Complications/Interventions within 30 Days of index date among Paxlovid Cohort with age<18 by Hospitalization Status

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate per 1000 person years	95% CI	
Overall						
Paxlovid Cohort						
Pneumonia	115	1	6.48	154.44	21.76	1,096.38
Kidney failure	115	0	6.55	0.00	0.00	3,688.88
Thrombotic event	113	0	6.43	0.00	0.00	3,688.88
ARDS	115	0	6.56	0.00	0.00	3,688.88
Heart failure	116	0	6.63	0.00	0.00	3,688.88
Sepsis/septic shock	116	0	6.63	0.00	0.00	3,688.88
ICU/Mechanical ventilation/ECMO	116	0	6.63	0.00	0.00	3,688.88
Hospitalization	109	0	6.06	0.00	0.00	3,688.88
All-cause mortality	116	0	9.53	0.00	0.00	3,688.88
In hospital death	116	0	6.63	0.00	0.00	3,688.88
Multi-organ dysfunction/failure	113	2	6.27	318.86	79.75	1,274.93
Vasopressor use	109	2	6.06	330.24	82.59	1,320.46
Hospitalized						
Paxlovid Cohort						
Pneumonia	0	.	.	0.00	0.00	3,688.88
Kidney failure	0	.	.	0.00	0.00	3,688.88
Thrombotic event	0	.	.	0.00	0.00	3,688.88
ARDS	0	.	.	0.00	0.00	3,688.88
Heart failure	0	.	.	0.00	0.00	3,688.88
Sepsis/septic shock	0	.	.	0.00	0.00	3,688.88
ICU/Mechanical ventilation/ECMO	0	.	.	0.00	0.00	3,688.88
Hospitalization	0	.	.	0.00	0.00	3,688.88
All-cause mortality	0	.	.	0.00	0.00	3,688.88
In hospital death	0	.	.	0.00	0.00	3,688.88
Multi-organ dysfunction/failure	0	.	.	0.00	0.00	3,688.88
Vasopressor use	0	.	.	0.00	0.00	3,688.88
Non-Hospitalized						
Paxlovid Cohort						
Pneumonia	115	1	6.48	154.44	21.76	1,096.38
Kidney failure	115	0	6.55	0.00	0.00	3,688.88
Thrombotic event	113	0	6.43	0.00	0.00	3,688.88
ARDS	115	0	6.56	0.00	0.00	3,688.88
Heart failure	116	0	6.63	0.00	0.00	3,688.88
Sepsis/septic shock	116	0	6.63	0.00	0.00	3,688.88
ICU/Mechanical ventilation/ECMO	116	0	6.63	0.00	0.00	3,688.88
Hospitalization	109	0	6.06	0.00	0.00	3,688.88
All-cause mortality	116	0	9.53	0.00	0.00	3,688.88
In hospital death	116	0	6.63	0.00	0.00	3,688.88
Multi-organ dysfunction/failure	113	2	6.27	318.86	79.75	1,274.93
Vasopressor use	109	2	6.06	330.24	82.59	1,320.46

Incidence of potential safety endpoints

Hospitalized patients consistently show higher incidence rates for all health outcomes compared to non-hospitalized patients, emphasizing the impact of hospitalization on the frequency of complications. It is not possible to ascertain precise incidence estimates of the select health outcomes included among paediatric Paxlovid patients given the low frequency of events.

Table 5 Incidence of Potential Safety Endpoints among the Paxlovid Cohort with age<18 by Hospitalization Status

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate per 1000 person years	95% CI	
Overall						
Renal impairment	113	0	16.21	0.00	0.00	3,688.88
Hepatic impairment	116	0	17.10	0.00	0.00	3,688.88
Dysgeusia	116	0	17.10	0.00	0.00	3,688.88
Diarrhea	115	1	16.65	60.07	8.46	426.47
Hypersensitivity reaction/allergic reaction	93	5	10.91	458.28	190.75	1,101.03
Hospitalized						
Renal impairment	0	.	.	0.00	0.00	3,688.88
Hepatic impairment	0	.	.	0.00	0.00	3,688.88
Dysgeusia	0	.	.	0.00	0.00	3,688.88
Diarrhea	0	.	.	0.00	0.00	3,688.88
Hypersensitivity reaction/allergic reaction	0	.	.	0.00	0.00	3,688.88
Non-Hospitalized						
Renal impairment	113	0	16.21	0.00	0.00	3,688.88
Hepatic impairment	116	0	17.10	0.00	0.00	3,688.88
Dysgeusia	116	0	17.10	0.00	0.00	3,688.88
Diarrhea	115	1	16.65	60.07	8.46	426.47
Hypersensitivity reaction/allergic reaction	93	5	10.91	458.28	190.75	1,101.03

Objective 4: Estimate incidence of Long COVID-19 or post-acute sequalae SARS CoV-2 (PASC) and assess health effects of Long COVID

Among the Source Cohort, while there was a high frequency of events for any medical condition, there were relatively few with post-COVID syndrome and thus a fairly low incidence rate in the paediatric population. Furthermore, in the paediatric Paxlovid cohort, the incidence rate of any symptom was less than one third of that in the Source Cohort and only one event of Post-COVID syndrome, which made it difficult to ascertain a precise incidence rate. Due to the small sample size and low frequency of events, it is difficult to determine precise incidence estimates for Long COVID among Paediatric patients using Paxlovid.

Table 6 Incidence of Long COVID among Paxlovid Users (Age<18)

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Overall						
Any below medical condition						
Any below medical condition	68	16	5.83	2,746.24	1,682.44	4,482.69
Post-COVID syndrome						
Post-COVID syndrome	116	1	16.97	58.93	8.30	418.35
General symptoms						
Fatigue	113	4	14.80	270.21	101.41	719.94
Intermittent fever	111	4	14.59	274.21	102.92	730.61
Post-exertional malaise	116	1	17.02	58.75	8.28	417.07
Multisystem inflammatory syndrome (MIS)	116	0	17.10	0.00	0.00	3,688.88
Respiratory symptoms						
Dyspnea or Shortness of breath	114	4	15.53	257.49	96.64	686.06
Cough	116	0	17.10	0.00	0.00	3,688.88
Nasal congestion	112	1	16.60	60.23	8.49	427.60
Lung function abnormalities	116	0	17.10	0.00	0.00	3,688.88
Hypoxemia	116	0	17.10	0.00	0.00	3,688.88
Cardiovascular and cerebrovascular symptoms						
Chest pain	113	9	14.23	632.53	329.11	1,215.67
Palpitations or Fast-beating or pounding heart	116	1	17.07	58.59	8.25	415.94
Myocarditis	116	0	17.10	0.00	0.00	3,688.88
Pericarditis	116	0	17.10	0.00	0.00	3,688.88
Myocardial infarction	116	0	17.10	0.00	0.00	3,688.88
Angina	116	0	17.10	0.00	0.00	3,688.88
Atrial fibrillation	116	0	17.10	0.00	0.00	3,688.88
Atrial flutter	116	0	17.10	0.00	0.00	3,688.88
Sinus tachycardia	115	1	16.76	59.68	8.41	423.68
Sinus bradycardia	116	0	17.10	0.00	0.00	3,688.88
Heart Failure	116	0	17.10	0.00	0.00	3,688.88
Stroke	116	0	17.10	0.00	0.00	3,688.88
TIA	116	0	17.10	0.00	0.00	3,688.88
Neurological symptoms						
Headache	116	0	17.10	0.00	0.00	3,688.88
Insomnia	115	0	17.02	0.00	0.00	3,688.88
Cognitive impairment	116	1	16.86	59.30	8.35	421.00
Confusion	116	0	17.10	0.00	0.00	3,688.88
Anosmia or Loss of smell	116	0	17.10	0.00	0.00	3,688.88
Ageusia or Loss of taste	116	0	17.10	0.00	0.00	3,688.88
Depression	111	3	15.85	189.22	61.03	586.68

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Anxiety Disorders	101	4	14.46	276.55	103.79	736.84
Post-traumatic Stress Disorder	116	1	16.98	58.90	8.30	418.15
Substance Use Disorders	116	0	17.10	0.00	0.00	3,688.88
Suicidal behavior and suicide ideation	114	0	16.76	0.00	0.00	3,688.88
Dizziness on standing (lightheadedness)	114	1	16.85	59.36	8.36	421.41
Pins-and-needles feelings	116	0	17.10	0.00	0.00	3,688.88
Dysautonomia	115	0	16.94	0.00	0.00	3,688.88
Digestive symptoms						
Abdominal pain	109	3	15.25	196.69	63.44	609.85
Diarrhea	115	1	16.65	60.07	8.46	426.47
Nausea	115	2	16.84	118.76	29.70	474.86
Constipation	110	2	16.10	124.23	31.07	496.75
Musculoskeletal and Skin						
Arthralgia or joint pain	111	0	16.19	0.00	0.00	3,688.88
Myalgia or muscle pain	116	1	17.01	58.79	8.28	417.34
Body aches	115	0	17.00	0.00	0.00	3,688.88
Rash	116	1	17.09	58.51	8.24	415.34
Alopecia	116	0	17.10	0.00	0.00	3,688.88
Hair loss	116	0	17.10	0.00	0.00	3,688.88
Endocrine symptoms						
Diabetes mellitus (Type I & II)	111	2	15.63	127.96	32.00	511.62
Diabetic ketoacidosis	116	0	17.10	0.00	0.00	3,688.88
Thyroiditis	115	0	16.92	0.00	0.00	3,688.88
Hypothyroidism	115	1	16.31	61.31	8.64	435.28
Hyperthyroidism	116	0	17.10	0.00	0.00	3,688.88
Menstrual/period issues	109	3	15.07	199.01	64.19	617.05
Hematologic symptoms						
DVT	115	0	17.06	0.00	0.00	3,688.88
Pulmonary embolism	116	0	17.10	0.00	0.00	3,688.88
Renal symptoms						
Acute kidney injury	116	0	17.10	0.00	0.00	3,688.88
Chronic kidney disease	113	0	16.21	0.00	0.00	3,688.88
Dialysis	116	0	17.10	0.00	0.00	3,688.88

Objective 5: Describe the health equity and demographic and clinical characteristics (eg, co-morbid conditions, outcomes, treatment patterns, healthcare utilization) among patients treated with Paxlovid

Paediatric Paxlovid users were more likely to be White compared to other racial and ethnic groups and from the South compared to other geographic areas. Only 59 of 997 patients were Black and 60 of 997

were Asian; a total of 263 of 997 patients were missing race or ethnicity data. Gender distribution is nearly equal. All patients were commercially insured.

Asthma is the most common comorbidity among Paxlovid users, with an overall prevalence of 18.76%. White patients have the highest prevalence (21.44%), whereas Asian patients have the lowest (8.33%). Across all groups, a small proportion (<10% across all racial and ethnics groups) of paediatric Paxlovid users previously had COVID-19 infections

Secondary Objective 1: Estimate the incidence of oxygen supplementation among COVID-19 patients hospitalized with mechanical ventilation/ECMO

The incidence of MV/ECMO in paediatric COVID-19 patients was highest in the High Risk TSC Cohort and Source Cohort, compared to the Standard Risk TSC Cohort. The Paxlovid Cohort did not report any events requiring MV/ECMO.

Table 7 Incidence of Oxygen Supplementation Among Paediatric COVID-19 Patients, 1/1/2020-07/20/2022

Overall						
Study Endpoints	**Patients at Risk**	**Events**	**Person-time**	**Incidence Rate per 1000 person years**	**95% CI**	
Source Cohort						
ICU/Mechanical ventilation/ECMO	173,648	690	13,140.31	52.51	48.735	56.578
High Risk Trial Similar Cohort						
ICU/Mechanical ventilation/ECMO	67,187	264	5,175.62	51.01	45.212	57.548
Standard Risk Trial Similar Cohort						
ICU/Mechanical ventilation/ECMO	110,350	316	8,264.06	38.24	34.246	42.695
Paxlovid Cohort						
ICU/Mechanical ventilation/ECMO	116	0	6.63	0	0	3,688.88

Discussion on clinical aspects

This study evaluated the real-world Paxlovid effectiveness in paediatric patients age 12 to <18 years with COVID-19 infection who are at high risk of severe disease, in reducing COVID-19 complications during Omicron predominance. There were no noteworthy safety issues in paediatric participants prescribed Paxlovid (N=89) in Study C4671040. It was not possible to ascertain the incidence of COVID-19 complications among paediatric patients prescribed PAXLOVID due to the very limited sample size and the low frequency of events.

3. Rapporteur's overall conclusion and recommendation

Overall, this observational retrospective real-world cohort study has included 89 paediatric patients treated with Paxlovid. Data from these subjects did not provide any new efficacy or safety information as regards the use of Paxlovid in paediatric subjects.

☒ **Fulfilled:**

No regulatory action required.