Xocova – Incidence of Dysgeusia

This medical response contains information in addition to that provided in the XOCOVA® (ensitrelvir) tablets, for oral use Full Prescribing Information approved by the U.S. Food and Drug Administration (FDA). Shionogi does not recommend the use of XOCOVA in any manner other than as described in the Full Prescribing Information. **Please read the attached XOCOVA Full Prescribing Information.**

1. CLINICAL TRIALS and RWE

- There were no reports of drug-related dysgeusia with ensitrelvir observed in the published Shionogi clinical trials thus far, which includes: the SCORPIO-PEP Phase 3 study (NCT05897541), the SCORPIO-HR Phase 3 study (NCT05305547), the Phase 2/3 study (jRCT2031210350), and the Phase 1 studies (jRCT2031210202, jRCT2031210595, NCT05363215, NCT05409911, and NCT06775730).[1-15]
- In the PLATCOV Phase 2 study (NCT05041907) comparing the efficacy and safety of ensitrelvir and nirmatrelvir-ritonavir, a total of 55/589 (9%) dysgeusia cases were observed (**Table 1**).[16,17]
  - 2/197 (1%) cases of dysgeusia in the ensitrelvir group
  - 52/201 (26%) cases of dysgeusia in the ritonavir-boosted nirmatrelvir group
  - 1/191 (1%) cases of dysgeusia in the group with no treatment
- As of March 2026, a search of RWE studies published for ensitrelvir showed 1 report of drug-related dysgeusia as an AE (**Table 1**).[18-37]

Table 1. Dysgeusia Cases Seen in Clinical Trials and Post-Marketing Surveillance

Study Name	Trial Status	Study Design	Description	Dysgeusia Cases
Antiviral efficacy of oral ensitrelvir versus oral ritonavir-boosted nirmatrelvir in COVID-19 (PLATCOV): an open-label Phase 2, randomised, controlled, adaptive trial[16,17]	Ongoing	Open-label, Phase 2, Multicenter, Randomised, Active Comparator Controlled	Assessing viral clearance of ensitrelvir in low-risk adults with early symptomatic COVID-19 against nirmatrelvir-ritonavir	• 2/197 (1%) patients reported experiencing dysgeusia while using ensitrelvir on Days 1 and 2 after randomization. For both patients, dysgeusia was no longer reported on Day 4 of treatment. • 52/201 (26%) patients receiving ritonavir-boosted nirmatrelvir reported dysgeusia within the first 3 days after randomization; most cases resolved on Day 5 after randomization. • 1/191 (1%) patient not receiving any treatment reported dysgeusia on Day 5 after randomization
Ensitrelvir for the treatment of COVID-19: Final analysis of a post-marketing surveillance from Japan[35,36]	Completed	Registry of patients from November 2022 to December 2023	Patients were continuously enrolled at each facility until the target enrollment was reached and were followed for 28 days from the start of ensitrelvir administration to monitor and classify ADRs	1/3,760 (0.03%) case of dysgeusia was reported and the patient who experienced dysgeusia recovered by Day 28

2. RELEVANT PRESCRIBING INFORMATION

INDICATIONS AND USAGE

XOCOVA is indicated for post-exposure prophylaxis of coronavirus disease 2019 (COVID-19) in adults and adolescents 12 years of age and older following contact with an individual who has COVID-19.[38]

CONTRAINDICATIONS

XOCOVA is contraindicated in patients with a history of clinically significant hypersensitivity reactions to ensitrelvir or any other components of the product.[38]

XOCOVA is contraindicated in patients taking drugs that are:[38]

- Primarily metabolized by CYP3A for which elevated concentrations may be associated with serious and/or life-threatening reactions and
- Strong CYP3A inducers because they may significantly reduce ensitrelvir plasma concentrations, leading to the potential loss of virologic response.[38]

Please read the attached XOCOVA **Full Prescribing Information**. The use of XOCOVA in any manner other than as described in the Full Prescribing Information approved by the U.S. Food and Drug Administration (FDA) is not recommended.

3. LITERATURE SEARCH, ABBREVIATIONS, & REFERENCES

Literature Search

As of March 2026, a computerized search of the published medical literature using internal and external databases (ie, Medline® and Embase®) failed to identify any additional relevant references regarding information on ensitrelvir and incidence of dysgeusia. Please keep in mind that medical literature databases, while considered a major source of biomedical information, are selective in their sources, and the information derived from them should not be considered all-inclusive.

Abbreviations

3CL	3-chymotrypsin-like	RWE	real-world evidence
ADR	Adverse drug reaction	PLATCOV	Platform trial of COVID-19 treatments
AE	adverse event	SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
COVID-19	Coronavirus disease 2019	SCORPIO-HR	Stopping COVID-19 progression with early protease inhibitor-high risk
MHLW	Ministry of Health Labour, and Welfare	SCORPIO-PEP	SCORPIO-PEP, Stopping COVID-19 progression with early protease inhibitor-post-exposure prophylaxis
PK	pharmacokinetic	US	United States

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ENCLOSURE

XOCOVA® (ensitrelvir) tablets, for oral use [Prescribing Information]. Shionogi Inc