

# Cystic Fibrosis Research News

**Title:**

Adverse events to elexacaftor/tezacaftor/ivacaftor in people with cystic fibrosis due to elevated drug exposure?: A case series

**Lay Title:**

Do people with cystic fibrosis experience side effects from Elexacaftor/Tezacaftor/Ivacaftor because of high drug levels?

**Authors:**

Syendon B C Baromeo<sup>a</sup>, Renske van der Meer<sup>b</sup>, Richard C J M van Rossen<sup>c</sup>, Erik B Wilms<sup>c</sup>

**Affiliations:**

<sup>a</sup>Department of Pharmacy, Haga Hospital, Els Borst-Eilersplein 275, 2545 AA The Hague, The Netherlands.

<sup>b</sup>Department of Pulmonology and Adult CF Centre, Haga Hospital, Els Borst-Eilersplein 275, 2545 AA The Hague, The Netherlands.

<sup>c</sup>Central Hospital Pharmacy (Laboratory AHZ), Charlotte Jacobslaan 70, 2545 AB The Hague, The Netherlands.

**What was your research question?**

In this study, we looked at whether those who had side effects had higher levels of ETI in their blood and whether reducing the dose could help minimize these side effects while still being effective.

**Why is this important?**

For a long time, people with cystic fibrosis (pwCF) had a shorter life expectancy due to limited treatment options. In recent years, major advancements have been made, especially with the development of CFTR modulator medications like elexacaftor/tezacaftor/ivacaftor (ETI). This treatment has helped many pwCF by improving lung function, reducing symptoms, and enhancing their quality of life. Although ETI works well for most people, some adults experience side effects that require lowering their dose or discontinuing ETI treatment.

**What did you do?**

We studied 10 pwCF who had side effects and had to take a lower dose of ETI. We measured how much ETI was in their blood and checked how well the treatment was working by



# Cystic Fibrosis Research News

measuring sweat chloride levels during routine hospital visit. We also recorded the type and severity of side effects.

## **What did you find?**

At the full dose, the medication levels in the blood were higher than what was found in previous studies. The most common side effects were related to mental health and the nervous system. The side effects got better by lowering the dose. The sweat chloride levels increased slightly after the dose was lowered, but the treatment still appeared effective on the short term.

## **What does this mean and reasons for caution?**

This study suggests that high levels of ETI in the blood might be linked to side effects. Lowering the dose can reduce side effects while still keeping the treatment effective on the short term.

## **What's next?**

Future studies should focus on identifying optimal dose reduction strategies and evaluating the long-term safety and effectiveness of ETI in larger groups.

## **Original manuscript citation in PubMed**

<https://pubmed.ncbi.nlm.nih.gov/40069050/>