# Common Payer Questions and Objections to Covering RELiZORB®

RELiZORB launched commercially in mid-2016, before clinical evidence was available and a permanent, separately billable Medicare billing code was assigned by CMS. Much has changed over the past three years. Some payers may have outdated information regarding RELiZORB.

***Common Payer Questions About RELiZORB***

- What is RELiZORB? RELiZORB is the only FDA-approved product indicated to hydrolyze (breakdown) fats in enteral feeding.

- Why is RELiZORB Needed? Some enterally fed patients have difficulty breaking down fats in their enteral formula, resulting in fat malabsorption. These patients (i) have trouble maintaining/gaining weight (increased weight = better lung function and fewer pulmonary exacerbations), (ii) suffer from respiratory issues, chronic infections, impaired bone health, and a chronic deficiency of fatty acids in plasma and tissue, and (iii) experience chronic gastrointestinal symptoms including diarrhea, fatty stools, abdominal pain, nausea, bloating, constipation, flatulence, and vomiting. RELiZORB addresses these issues.

- What Type of Patient Use RELiZORB? RELiZORB primarily serves ultra-orphan patient populations. For example, RELiZORB is used in a population of ~3,500 patients who have cystic fibrosis and are enterally fed.

- What is RELiZORB's Indication? RELiZORB is indicated for use in pediatric patients (ages 5 years and above) and adult patients to hydrolyze fats in enteral formula.

***Common Payer Objections to Covering RELiZORB and Possible Responses***

- Objection: "RELiZORB is experimental/investigational"

    - While RELiZORB may have been viewed as "experimental" or "investigational" when it was launched in 2016 and lacked clinical trial data, there is now substantial published evidence establishing RELiZORB's safety and efficacy.

    - Two clinical trials (covering both pediatric and adult patients) have been completed, both met their primary endpoints, both found use of RELiZORB to be safe and effective, and their results have been published in peer-reviewed journals. The trials showed, among other things, real benefits in absorption of fatty acids and decrease in GI adverse events, exactly what these patients need.

- Objection: "The trials on RELiZORB are too small" or "There are no large-scale trials"

    - Keep in mind that RELiZORB primarily serves ultra-orphan patient populations. For example, the population of enterally fed patients with cystic fibrosis that may benefit from RELiZORB is only ~3,500 patients. Thus, there can never be any "large-scale trials" on RELiZORB.

    - While the trial population appears small (n=33 for Trial 497 and n=36 for the 498/ASSURE trial), these trials covered nearly 2% of enterally fed patients with cystic fibrosis in the US, a significantly larger percentage of the representative population versus the proportion studied even in most drug studies.

    - Also, it's important to remember that the RELiZORB trials were powered to show a statistically significant difference in a small study population, a higher bar, and those differences were shown.

*Important Note: This document is intended to provide Physicians, Registered Dieticians, and other HCPs that treat patients that may benefit from the inclusion of RELiZORB as part of an enteral nutrition regimen with possible responses to questions and objections frequently expressed by insurers/payers in deciding whether to cover RELiZORB. This document is provided for informational purposes only and its use does not guarantee that reimbursement for RELiZORB for a particular patient will be obtained. This document is intended for use with insurers/payers only.*

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- By way of comparison on trial size, similar studies in other orphan disease populations have utilized equivalent subsets of overall populations and achieved FDA clearance and broad coverage by payors, *e.g*, Gattex (teduglutide) in short bowel syndrome and Kalydeco (ivacaftor) in cystic fibrosis. The Kalydeco trial covered ~1% of the total CF population. The Gattex trial covered less than 1% of the total SBS population. Neither of these were "large scale studies."

- Objection: "There is no long-term data on RELiZORB"

  - That may have been the case in 2017, but that is not the case now. A second clinical trial was completed and published in a peer reviewed journal in 2018. That trial, the "498/ASSURE" trial, provides longer term data, and found that RELiZORB was safe and effective, and provided real benefits in fat absorption and reduction of GI adverse events, including no reports of diarrhea at Day 90.

- Objection: "RELiZORB isn't approved for use in pediatric patients"

  - That's outdated information. While in 2016 RELiZORB was originally cleared for use only in adults, the labelling was updated on July 12, 2017 to include pediatric patients; the 497 study served as the basis for the pediatric approval by the FDA.

  - The Instructions for Use for RELiZORB (Sec. 2.0) states that "RELiZORB is indicated for use in pediatric patients (ages 5 years and above) and adult patients to hydrolyze fats in enteral formula."

- Objection: "Medicare Doesn't Cover RELiZORB" or "There's no separate billing code"

  - Effective January 1, 2019, RELiZORB has a permanent, separately billable Medicare billing code (**B4105**). The description for B4105 is: "In-Line Cartridge Containing Digestive Enzyme(s) for Enteral Feeding, each." B4105, and its associated coverage and payment indicators ("C" and "39" respectively), make clear that RELiZORB may be billed and paid as a separate, stand-alone product as part of enteral nutrition therapy.

  - RELiZORB used to be assigned at various times to B4035, Q9994, and other codes. That's not the case today, it's just B4105. You can confirm this in the PDAC/DMECs database and on the CMS website.

- Objection: "The Hayes Report says RELiZORB is experimental/ investigational"

  - The company is aware of the Hayes Report and strongly disagrees with it. They also believe that the Hayes Report is false and misleading in a number of material respects. There is ample evidence to evaluate the safety and efficacy of RELiZORB, including two published, peer-reviewed clinical trials that both found RELiZORB safe and effective, as well as significant data from case studies. That information led the FDA to clear RELiZORB for use in both adult and pediatric populations.

  - In fact, the Company feels so strongly that the Hayes report is false and misleading that they recently sued Hayes in federal court to address the situation.

- Objection: "There are alternatives to RELiZORB that we already cover" or
  "Enzyme Pills/PERTs are available so RELiZORB is not needed"

  - HCPs sometimes prescribe oral enzyme pills (PERTs) to hydrolyze fats in enteral feedings. However, PERTs were ***not designed for use in enteral feeding***, there is ***no safety or efficacy data supporting their use in enteral feeding***, use in enteral feeding is ***off-label***, and they have been ***shown to be ineffective in enteral feeding***. In addition, using PERTs with enteral feeding may result in serious problems, including, for example, clogging, over-exposure to enzymes, and risks to care-givers due to crushing of pills and accidental inhalation of crushed PERTs.

- Objection: "RELiZORB is not included in any evidence-based guidelines"
    - RELiZORB is a relatively new product, having been on the market for only about three years.
    - Evidence-based guidelines typically only get updated every 5-6 years, and the process leading to an update is lengthy.
    - So, you wouldn't expect RELiZORB to be in any guidelines yet regardless, because RELiZORB was not yet approved or available for use when the current guidelines were being finalized.
    - That said, over the past couple of years, two clinical trials have since been conducted and completed. The results of both trials have been published in peer reviewed journals and found that RELiZORB is safe and effective.
    - Access to RELiZORB is supported by The Cystic Fibrosis Foundation. Dr. Albert Faro, Sr. Director of Clinical Affairs at the CFF, testified in support of RELiZORB at the 2017 Public Meeting for the Medicare HCPCS coding process. In his testimony, Dr. Faro stated:
        - "*It is in the best interest of those individuals who require overnight tube feeds to have timely access to this product*."
        - "*RELiZORB is the only product approved to address the significant problem of fat malabsorption in enteral feeding*."
        - "*By having the feed go through the cartridge lined with enzymes, RELiZORB directly addresses the significant unmet need for better absorption of nutrients during overnight feeds in people with CF who are pancreatic insufficient*."

      The CFF's willingness to testify to HHS/CMS regarding the need for access to RELiZORB, and the benefits of using RELiZORB, speaks volumes.
- Objection: "RELiZORB use is too rare to cover."
    - RELiZORB has been sold commercially for more than three years, and during that time, more than 725,000 cartridges have been used by nearly 2,000 patients. Despite that widespread usage, there have been no medical device reports (MDRs)/adverse events reported to the FDA and there have been no recalls.
    - RELiZORB is used at many prestigious institutions at the forefront of treating the neediest patients, including Stanford University Medical Center, Brigham and Women's Hospital, the Cleveland Clinic, Boston Children's Hospital, and the Children's Hospital of Philadelphia, and is on formulary at more than 78 hospitals (almost all on an "open formulary" basis).
    - More than 136 other commercial insurances plans cover RELiZORB, and this number is increasing each month, including plans like Affinity Health Plan, Anthem BCBS, Caremark, Express Scripts, and many Medicaid plans.