Fulyzaq (crofelemer) and HIV drug-related diarrhea

Fulyzaq is a prescription medicine used to ease the symptoms of non-infectious diarrhea in HIV-positive people who are taking HIV medications. It was approved by the FDA in December 2012. The product is a botanical compound made from the red sap of the Croton lechleri tree of South America.

What were the clinical study results?
The ADVENT study was conducted in 374 HIV-positive people on stable HIV regimens with a history of diarrhea for one or more months. Most were men (85%) and average age was 45. Average time since HIV diagnosis was 12 years. The average time since onset of diarrhea was 4 years, while the average number of bowel movements per day was 2.5. 39% of people had a CD4 count below 404. The vast majority (93%) had controlled viral loads below 1,000. 46% were Caucasian and 32% were African American.

A somewhat complicated study design was used. The first stage included all people taking a placebo for 10 days (screening period). Then, those who had one or more watery bowel movements per day on at least 5 of the previous 7 days were randomized to two groups: taking Fulyzaq or taking placebo for another 31 days. This was then followed by 5 months of a placebo-free period: people who were taking Fulyzaq continued on it while people who had been on placebo the entire time were randomized to various doses of Fulyzaq.

The primary endpoint was the percentage of people who responded to Fulyzaq, with at least 17 watery bowel movements before Fulyzaq down to 2 or fewer watery bowel movements per week during at least 2 of the 4 weeks of the placebo phase (total of 4 or less down from 17 or more over 2 weeks). Using this measurement of change, 17.6% of those on Fulyzaq had fewer watery bowel movements, compared to 8.0% of those on placebo. However, the 17.6% who improved did not include others who also had fewer watery bowel movements but were not as dramatically successful, such as 17 bowel movements before Fulyzaq down to 10 or 8 or even 5 bowel movements after using Fulyzaq. Data were not released on these other less dramatic improvements. In some people, a continued anti-diarrheal effect was seen through 20 weeks.

Who is more likely to benefit from the drug?
The clinical study reported that patients with the following characteristics are more likely to respond to Fulyzaq.

• more than 2 years of diarrhea
• 2 or more bowel movements each day
• earlier use of other anti-diarrheal drug(s)
• use of an anti-diarrheal drug within the last 4 weeks without relief
• “pourable” poop, or bowel movements that could be poured out of a bucket

What type of diarrhea?
The product is used only for diarrhea from taking HIV meds and not for diarrhea due from a bacterial, viral or fungal infection. Therefore, before being prescribed Fulyzaq, your health provider should rule out any infectious conditions of the stomach and intestines.

In the clinical study, diarrhea was defined as either ongoing loose stools despite taking anti-diarrheal meds, or one or more watery bowel movements each day without anti-diarrheal meds.
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How is it taken?
One 125mg Fulyzaq pill is taken by mouth every 12 hours, with or without food. It’s a delayed-release tablet and should be swallowed whole. It should not be crushed or chewed. It is not recommended that Fulyzaq be taken more often for severe diarrhea or in people with high viral loads or low CD4 counts.

How does it work?
Fulyzaq helps ease diarrhea by preventing the secretion of electrolytes and excess water into the gastrointestinal tract. It does not provide immediate relief for diarrhea, and may need to be taken over several weeks or more before its true effect on diarrhea is seen by some individuals. It’s not known what results or side effects may occur if it’s taken with over-the-counter products such as Immodium.

What are the side effects?
Side effects mentioned by 2-6% of the study participants who took the 125mg dose included: upper respiratory infection (5.7%), bronchitis (3.9%), cough (3.5%), excess gas (3.1%), higher bilirubin (3.1%), nausea (2.6%), back pain (2.6%), joint pain (2.6%), urinary tract infection (2.2%), sinus inflammation (2.2%), musculoskeletal pain (2.2%), hemorrhoids (2.2%), giardiasis (2.2%), anxiety (2.2%), higher ALT (2.2%), and stomach distension (2.2%).

Is Fulyzaq safe for all patients?
Fulyzaq appeared as safe in people with lower CD4 counts (<404) as in people with higher counts (>404). Likewise, it appears as safe in people with viral loads below 400 as above 400. However, the effects on CD4 counts and viral load from the long-term use of Fulyzaq are unknown due to the short duration of the ADVENT study.

Fulyzaq should be used during pregnancy only if it’s clearly needed. Although it has not been studied in pregnant women, animal studies show some issues. On a positive note, when Fulyzaq was given to rats at 177 times the human dose, it showed no evidence of affecting fertility or fetal harm. However, in pregnant rabbits, Fulyzaq caused abortions when it was given at 96 times the human dose.

Among racial groups, Fulyzaq was equally effective except for African Americans. The drug was less effective in African Americans than in non-African Americans.

It’s not known whether Fulyzaq is present in breast milk. Nursing babies may have reactions to Fulyzaq. Women who want to nurse and take Fulyzaq should talk to their providers about not breast-feeding or not taking the medicine.

For people aged 65 years and older, not enough were included in the study to know whether they respond differently to Fulyzaq. Fulyzaq has not been studied in children under 18 years of age.

Does Fulyzaq interact with HIV meds?
In a separate drug-drug interaction study, Fulyzaq did not show significant interactions with Viracept (nelfinavir), Retrovir (AZT, zidovudine), or Epivir (3TC, lamivudine). Other HIV drugs were not studied.

Most people in the ADVENT study were on protease inhibitor regimens. The most commonly used HIV meds were Truvada (tenofovir/emtricitabine), Norvir (ritonavir) and Kaletra (lopinavir/ritonavir). No significant interactions were seen.

Resources
- FDA announcement (www.fda.gov/ForConsumers/By-Audience/ForPatientAdvocates/HIVandAIDSActivities/ucm333826.htm)