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Beyond Celiac Continues the Fight for Safe, Gluten-free Medications

Imagine that your doctor said very few of your drugs contain rat poison, but some do, and it is very hard to identify which ones. You certainly would be reluctant to trust any of them.

That is the situation patients who have celiac disease and gluten sensitivity face every day. It points out the urgency of improving access to safe, gluten-free medications.

Here are some of the key reasons for Beyond Celiac's commitment to better labeling of prescription and over-the counter drugs:

1. **There is a clear need for a simple and reliable way for those who have celiac disease or gluten sensitivity to identify gluten-free medications.**

   Fear of getting sick from gluten in drugs drives decision-making for the 21 million patients who have to determine if a drug needed to manage another health condition actually will make them sicker by triggering gluten-related symptoms.

   In a 2011, as part of the first of its kind FDA-funded study of gluten in medications, Beyond Celiac surveyed nearly 6,000 patients with celiac disease and gluten sensitivity regarding their experiences with gluten in medications. Twenty five percent said they suspected they had had an adverse reaction caused by gluten

   Patients and healthcare providers, including pharmacists, find it extremely hard to figure out whether a medication is gluten-free. This causes many people anxiety, lack of confidence, medication substitutions and non-compliance with taking their medications.

   The study noted that because of anxiety over medications, patients did not adhere to their prescribed medical regimen, with many choosing not to take a drug prescribed

by their doctor to treat another condition. "This was not an isolated case of patients going it alone," study researchers wrote. "Sometimes ending a medical regimen was against medical advice."

Without a reliable source of gluten-free medications, patients have to research and analyze whether every drug they take is gluten-free. They have to interrogate their prescribing physician, who usually does not know the answer, their pharmacist, who has to go to great lengths to find credible information, and often the drug company itself, only to find that the information they need is not forthcoming. And this process has to be repeated each time the prescription is refilled because inactive ingredients change from lot to lot and from manufacturer to manufacturer. While generic drug companies have to use the same active ingredient as brand-name drugs, that does not apply to inactive ingredients. Attempts to develop consumer friendly lists of safe drugs have been attempted, according to the researchers, but they require constant updating and can contain errors.

Meanwhile, a study published this year in the *American Journal of Pharmaceutical Education* found that while community pharmacists, the practitioners most patients rely on for drug information, possess some knowledge of the disease, they would benefit from and desire additional education about this disorder.

2. **Inactive ingredients used in the manufacture of medications include a number that have the potential to contain gluten because they are made from wheat, barley or rye. Ingredients in this category are:**

- Wheat
- Modified starch (source not specified)
- Pregelatinized starch (source not specified)
- Pregelatinized modified starch (source not specified)
- Dextrates (source not specified)
- Dextrin (source not specified but usually corn or potato)
- Dextrimaltose (when barley malt is used)
- Caramel coloring (when barley malt is used)

Prescription drugs labels rarely indicate which of these ingredients they contain. This information is only available on insert in the package that goes to the pharmacy, which consumers typically do not see. That means patients have to contact the pharmacist or drug company to get the information. The package insert often does not indicate the source of an ingredient, for example, whether the modified starch is made from corn and therefore safe, or made from wheat, and harmful.

Pharmacists often have as much trouble getting this information as the patient. Customer Service Representatives at a given pharmaceutical company often do not have details about inactive ingredients

While over-the-counter drugs do not include a list of inactive ingredients, the list often does not specify the source.

In food, highly processed ingredients derived from wheat, such as caramel coloring, dextrin, glucose syrup, and maltodextrin, are generally considered safe for individuals with celiac disease and other gluten-related disorders to consume. The way these ingredients are processed renders the amount of gluten in the final product safe for those with a medical need to be gluten-free.

However, in medications, inactive ingredients in medications are frequently sourced from a global supply chain, often China or India, and suppliers may change without notice. The scientific documentation regarding the gluten content of these ingredients when they are in medication is inconsistent, so they may pose a risk to patients.

3. **Celiac disease and gluten sensitive patients worry about every drug they take because they can't be sure which ones are safe.** This widespread anxiety is consequently out-of-proportion to the relatively small percentage of drugs that contain gluten. Unfortunately, patients don't have any choice.

   Anecdotally, patients have told Beyond Celiac they are afraid to take drugs to treat even an acute medical condition, which requires relatively quick and short-term use of a drug, for example an antibiotic to treat an infection. Certainly, and sadly, this can put patients at more risk from the acute condition than from the presence of gluten. However, long term use of a drug that contains even a tiny bit of gluten poses the greatest risk in relationship to celiac disease or gluten sensitivity. A drug that contains gluten could cause an ongoing immune reaction and system inflammation. Systemic damage caused by gluten affects not only the gastro-intestinal system, but also the brain and nervous system.

4. **Beyond Celiac has been a leader in addressing the problems patients face regarding gluten in medications.**

   Most recently, we weighed in on the FDA's draft guidance regarding labeling for gluten in oral drug products, (Docket Number: FDA-2017-D-6352), calling for a mandatory "contains gluten" labeling for statement for medications.

   Our commitment to finding solutions to the problem of gluten in medications goes back more than a decade.

   Highlights include publication of a Beyond Celiac co-authored article, 'Medications: A Hidden Source of Gluten,' in the August 2009 edition of *Practical Gastroenterology*.

   A month later, Beyond Celiac coordinated and led a workshop about Prescription Drug Risks and Benefits with the purpose of aligning the gluten-free labeling efforts being conducted in parallel by the FDA's Center for Food Safety and Applied

Nutrition (food labeling) and the FDA's Center for Drug Evaluation and Research (OTC medications).

In response to the FDA's request for public input about prescription drug risks and benefits, Beyond Celiac provided comment, advocating for the labeling of gluten in medications on November 11, 2009.

In 2010, CEO Alice Bast poke at the American Pharmacists Association (APhA) Annual Meeting in Washington, DC in March and later that year at the Safe Use Initiative Public Workshop, Beyond Celiac presented a statement about gluten in medications, which made an appeal to the FDA with regard to labeling the source of inactive ingredients that may contain gluten.

In 2011, we received the FDA grant entitled Gluten in Medication: Qualifying the extent of exposure to people with celiac disease and identifying a hidden and preventable cause of an adverse drug event. This preliminary research highlighted the need for an additional, large scale, comprehensive study identifying safe thresholds of gluten in medication, its impact on people with celiac disease, and the pervasiveness of gluten in binders and excipients.

In 2012, we supported the proposed Gluten in Medication Act of 2012 introduced by Representatives Tim Ryan (OH) and Nita Lowey (NY) and submitted a response in the comment period for the FDA Docket Number FDA-2011-N-0842 advocating for labeling of gluten in medications. We supported the gluten in medication act when it was again introduced in 2013 and 2015.

The research team collaborating on the FDA-funded gluten in medications study completed the testing of the identified medications in spring 2014. Beyond Celiac delivered its final report to the FDA in fall 2014.

In December 2015, *Pharmacy Today*, a publication of the American Pharmacists Association (APhA), published an article in the One to One column entitled "Gluten in medications: A dangerous prescription for patients with celiac disease." The article noted that Beyond Celiac, formerly known as the National Foundation for Celiac Awareness (NFCA), "has long called for gluten to be listed on medication labels or completely removed from medications."

We continue to see addressing gluten in medications as a critical unmet need for celiac disease and gluten sensitive patients and work tirelessly to change that.

5. **Government regulation of gluten in drugs and labeling of gluten in drugs has not provided a solution to this problem.**

In the most recent development regarding labeling, the FDA proposed voluntary labeling of gluten in drugs. While this move could reduce some of the uncertainty for celiac disease and gluten sensitive patients, if does not go far enough. Beyond Celiac, along with individual patients and other stakeholders, is urging the FDA to require mandatory "contains gluten" labeling. So far, the FDA has taken no action

Legislation regarding labeling of gluten in mediation, supported by Beyond Celiac, has been introduced several times but never passed. The most recent version in 2015 would have amended the Federal Food, Drug, and Cosmetic Act to prohibit the sale of any drug intended for human use that contains an ingredient other than a polyol that constitutes or is derived from a grain or starch-containing ingredient and whose label does not include a parenthetical statement identifying the source of that ingredient.

Meanwhile, patients need a reliable way to find safe medications. The situation mirrors the introduction of gluten-free certification of food by independent groups during the many years it took for the FDA to pass meaningful gluten-free food labeling rules. That certification has proven so valuable to gluten-free consumers that it continues even though the FDA finally acted on labeling of gluten-free packaged products.

6. **Testing for gluten in medication has specific challenges.**

When Beyond Celiac was awarded a $50,000 grant from the FDA to study the impact of gluten in mediations, we put together a research team to determine if gluten is present in medications. The team analyzed results from 39 drugs reported as causing a gluten reaction by patients who responded to the related survey.

Researchers used two assays to quantify the gluten in content in the tested medications, one of which specifically looked for gluten in hydrolyzed ingredients. This competitive assay had a level of quantification of 10 parts per million (ppm) or more, while a sandwich assay also used tested for 5 ppm or more. None of the medications tested positive at the 5-ppm level, but three were positive using the hydrolyzed test.

When some proteins are hydrolyzed (i.e. broken down) they may not have enough of the gluten molecule to be recognized by the antibody in the sandwich testing kit. The competitive assay can detect the protein where the sandwich assay cannot.

Researchers noted that commercially available assays are designed to test for gluten in food – not drugs. Because the size of some medications' dosage is considerably smaller than food samples, they experienced some problems measuring gluten content. The testing kits used have not been validated to test for gluten in medicine, which means studies to ascertain the accuracy of the assays when testing medication have not been done.

Researchers concluded the study provides the foundation for additional investigation to identify and develop improved testing methods for gluten in medicine.