HELP YOURSELF TO GLUTEN-FREE MEDICATION

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Gluten in medication: A problem with inactive ingredients.

- Why add inactive ingredients?
- In the late 19th and early 20th centuries, medication were compounded by hand and packaged as powder in powder papers. With modern manufacturing and robotics, tablets capsules and extended release products are available. However, the process necessitates the addition of many other inactive substances which do not affect the pharmacology of the active drug.
- Amount of active ingredient may be minute, possibly so small that it may not be measurable without being expanded with fillers and diluents.
- Examples:
    - digoxin (Lanoxin) 0.125mg
    - levothyroxine (Synthroid) 0.05mg
- Manufacturing process: Ingredients are added to make powder glide through chutes; become compressible in molds, to bind tablets into solid form, and lubricate against sticking to surfaces.
- Improve the therapeutic effect in the body: special coatings, disintegrants, preservatives, flavors, and dyes help to improve compliance, reduce confusion, and aid the active ingredient to be absorbed at the proper place in the intestinal tract.
- Inactive Ingredients: Inactive ingredients, also know as pharmaceutical excipients, are added to an active drug to perform a specific function during or after the manufacturing process:
    - Fillers / diluents
    - Coatings
    - Glidants
    - Sweeteners
    - Lubricants
    - Flavors
    - Anti-adherents
    - Colors / Dyes
    - Disintegrants
    - Preservatives
    - Binders
    - Sorbants (protect against humidity)
- Problem Grains: Problem grains used in medication manufacturing: wheat, barley, and possibly oats.
- Source of Inactive Ingredients: Inactive ingredients in medication are derived from many sources, both synthetic and natural. Some of the more common natural sources are corn, wheat, barley (malt), rice, tapioca, and potatoes. Inactive ingredients such as starch or starch derivatives that are manufactured from wheat or barley MAY be a hidden source of gluten. Ingredients derived from corn starch, rice starch, tapioca starch, and potato starch are gluten free.

Unfortunately, the original substance from which an ingredient is derived often is not readily identifiable from reading the labeling that accompanies the medication. As an example, a pharmaceutical manufacturer may list“starch” as an inactive ingredient. The United States Pharmacopeia/National Formulary (USP/NF) contains only one monograph for starch. Within the monograph, starch is described as granules separated from mature grains of corn, wheat or from tubers of the potato. In medication, the manufacturer need only state starch as the ingredient no matter what the source of the starch.

- **Product Formulations:** Only those medications that come into direct contact with the intestinal tract (oral formulations such as tablets, capsules, syrups, oral solutions, as well as rectal suppositories) must be checked for possible sources of gluten. Medications which are administered by injection, by transdermal systems (skin patches), or by inhalation (provided the medication is not inadvertently swallowed) will not contact the lining of the intestinal tract. These formulations generally will not cause a problem for the celiac patient.

Good News / Bad News !

- **Good News:** More and more pharmaceutical manufacturers are avoiding gluten sources in their products. In a survey study published in the American Journal of Health-Systems Pharmacy (March, 2001), thirty-four innovator and generic companies indicated that NONE of their product contained ingredients derived from wheat, rye, oats, barley or spelt. (See Table 2 at the end of handout)
- **Bad News:** With more and more of U.S. corn production going into ethanol production for gasoline production, wheat starch may be used more often by some pharmaceutical companies.
- **Good News:** The fact that wheat is well known as one of the top 10 allergens may cause pharmaceutical companies from using it as a form of starch in formulations of medications.
- **Bad News:** A relatively new medication for bladder control, Sanctura (trospium) (not the SR form) lists wheat starch as an inactive ingredient.

Ingredients MORE LIKELY To Be Sources of Gluten

- **Starch:** Starch functions in tablets and capsules as a diluent, a disintegrant, and as a binder. Starch may be derived from corn, potatoes, WHEAT, rice, or tapioca. The starch origin may or may not be identified (i.e.: “starch” or “corn starch,” or “tapioca starch,” etc.) in the medication labeling. Unidentified starch could be wheat starch. All unidentified starch is suspect, as starch USP can be derived from corn, wheat, or potatoes.

Wheat flour contains up to 17% protein (predominantly gluten). Wheat starch is derived from wheat flour and contains < 0.5% protein.

According to the FDA Inactive Ingredient Guide, the amount of “wheat starch” or unspecified “starch” found in pharmaceuticals ranges from less than one to several hundred milligrams.

- **Pregelatinized Starch:** May be derived from wheat starch, corn starch, or tapioca starch. Pregelatinized starches retain many characteristics of the starches from which they are derived, but are modified to be more free flowing and compressible. The good news is that pregelatinized wheat starch at this time has been removed from the Handbook of Pharmaceutical Excipients due to disuse in medication. It is used predominantly in foods.

  Pregelatinized starch contains < 0.5% protein and may range from less than one milligram to several hundred milligrams in pharmaceutical products. Fosamax-D (Merck & Co.) lists modified food starch as an inactive ingredient. According to the company drug information specialist, this can be corn starch or Pregelatinized corn starch. Both are gluten free and the medication Fosamax-D is gluten free.
- **Dextrimaltose:** A specialized ingredient which is a mixture of dextrin and maltose produced by the enzymatic action of barley malt on corn flour. The presence of barley malt in the manufacturing process makes this ingredient highly suspect as a source of gluten. The Good News about dextrimaltose is that it is very expensive to use; therefore it will not be used often!!
- **Flour, Gluten, Dusting Powder:** Flour, gluten and dusting powder of unspecified sources may be listed occasionally as inactive ingredients of tablets and other prescription formulations. The grain source of these ingredients must be identified by the manufacturer before the product can be considered safe for use by the celiac patient.
- **Malt, Malt Syrup:** Although not currently among the items listed on the FDA Inactive Ingredient Guide, these ingredients are derived from barley and may be used in the production of other inactive ingredients (i.e. dextrimaltose).

Ingredients LESS LIKELY To Be a Source of Gluten

- **Dextrin:** Manufactured by the incomplete hydrolysis of starch, dextrin is specified by the British Pharmacopeia as being derived from corn or potato starch. The United States Pharmacopeia, however, does not specify the source of starch that may be used. Although wheat starch can be used in the manufacture of dextrin, most dextrins manufactured in the U.S.A. are corn based products and therefore is gluten free. Dextrates, and cyclodextrins are related compounds. Dextrin contains < 0.5% protein.

- **Maltodextrin:** In the U.S. maltodextrin found in medication is almost always derived from corn starch and therefore gluten free. However, wheat and oat maltodextrin are known to exist but are not known to be employed in pharmaceutical preparations. Wheat maltodextrin is used more commonly in Europe. However, in 2007 the European Food Safety Authority permanently exempted from allergen labeling wheat-based maltodextrin, wheat-based glucose syrup, and wheat-based dextrose. This is due in part to the industry voluntarily agreeing to the following: Code of Good Practice on purification of wheat starch hydrolysates in which the industry commits t0 respect a maximum 20 ppm gluten/dry substance in the above mentioned ingredients as a quality parameter. (See Tricia Thompson at www.glutenfreedietitian.com.)
- **Sodium Starch Glycolate:** (also called carboxymethyl starch): This starch derivative is used as a disintegrant in tablet formulations. It is most commonly derived from potato starch since this type of sodium starch glycolate exhibits the most efficient water uptake and swelling capacity and the fastest disintegration time. The major products used in the U.S.A. are Primogel (Holland) and Explotab (France). Both products are derived from potato starch and are gluten free. Although sodium starch glycolate can be made from wheat, rice, corn, or tapioca starch, it is rarely made from any starch but potato. In a comparison study of the efficacy of sodium starch glycolate from five different starches, the wheat based product showed the least efficacy as a disintegrants.
- **Caramel Color:** The FDA Code of Federal Regulations specifies that caramel color may be manufactured using malt syrup or starch hydrolysates. However, almost all caramel color produced in the U.S.A. is a gluten-free product. Caramel color imported from outside of the U.S. should be checked for its gluten status. A safe practice is to use“dye-free” pharmaceuticals.

Lactose in Medication

- Lactose is a sugar (“milk sugar”) which must be partially digested in the intestinal tract by the enzyme lactase before it can be absorbed as a nutrient. Lactose is an extremely common excipient used as a filler and diluent in tablet and capsule formulations. A single tablet or capsule may contain > 500mg of lactose. If the medication is taken several times a day, an individual may ingest a significant amount of lactose.
- Lactose intolerance occurs when there is a deficiency of lactase in the intestinal tract as might be found in an untreated celiac. Undigested lactose draws water into the intestinal tract thus acting as a laxative, causing bloating and diarrhea. These symptoms may be construed to be symptoms provoked by the ingestion of gluten in the medication even though the medication is gluten free.

Unabsorbable Sugars / Sugar Alcohols

- Sorbitol, maltitol, and xylitol used as sweeteners in medication are gluten free.
- Since these excipients are poorly absorbed from the intestinal tract, they can cause symptoms of celiac disease such as bloating, cramps and diarrhea.

Alcohol (Distilled Ethanol) in Medication

- Alcohol may be produced from wheat starch. However, the distillation process separates gluten from the pure ethanol. Provided that no other ingredients are added after the distillation process, ethanol is gluten free.
- Alcohol, on the other hand, is a solvent and a gastrointestinal irritant which may be harmful to the healing gastrointestinal tract. A safe practice is to request alcohol free medication.

Table 1. Commonly Used Pharmaceutical Excipients Known To Be Gluten Free (Not an exhaustive list)**.**

- Acacia
- Alginic acid
- Alpha tocopherol
- Ascorbic acid
- Benzyl Alcohol
- Calcium carbonate
- Carboxymethylcellulose
- Microcrystalline Cellulose
- Citric Acid
- corn starch
- Croscarmellose sodium
- Dextrose
- Docusate sodium
- Fructose
- Glucose
- Hydroxypropyl cellulose
- Lactose
- Magnesium carbonate
- Magnesium Stearate
- Maltitol
- Maltose
- Mannitol
- Polydextrose
- Povidone
- Propylene glycol
- Silicon dioxide
- Simethicone
- Sodium benzoate
- Sodium Lauryl Sulfate
- Sorbitol
- Stearic Acid
- Sucrose
- Hydrogenated vegetable oil
- Vanillin
- Xanthan gum
- Zinc stearate

What To Do With This Information

- Identification of Inactive Ingredients: A “package insert” is included with prescription medication product. The well known book, Physicians Desk Reference (PDR), is a compilation of prescription drug package inserts. The section on inactive ingredients is generally found in the very beginning of the information found in the package insert. Inactive ingredients are listed in alphabetical order. The listing however does not indicate the amount of the ingredient which is contained in the product.

- Become Your Own Advocate: Once you are familiar with the pharmaceutical ingredients which may be sources of gluten, you can check your prescription medications yourself.

To do this, you can:

- Ask your pharmacist for a copy of the package insert.
- Search for the drug on the internet. Most pharmaceutical companies have a web site.
- Find the drug in the PDR and the PDR for generic drugs (which you can purchase at many book stores).
- The PDR also lists pharmaceutical manufacturers, addresses and phone numbers. When in doubt call the manufacturer.
- Unspecified Ingredient: Occasionally, a manufacturer will list “unspecified ingredients” with the other specified inactive ingredients. This may be a trade secret or proprietary information. A call to the manufacturer about the unspecified ingredient is necessary to determine whether the ingredient is gluten free and safe for consumption by a celiac patient. The manufacturer will not necessarily reveal the identity of the ingredient, but should be able to reveal its gluten status.
- A Change in Manufacturer: Be cautious about a change in the appearance of a medication you have previously taken. Many generic companies do not manufacture the medications that they sell under their own label. Occasionally, production problems, etc., may necessitate a switch to a different manufacturer. In most cases, the product will appear different. In any case, whenever you refill a prescription generic medication, always ask the pharmacist if the medication has the same manufacturer (not labeler or distributor) as the medication of your previous prescriptions.
- In Emergencies: Some conditions such as an acute infection require immediate treatment. You may not have time to research the gluten status of a particular antibiotic. Talk to your physician ahead of time about different antibiotics to treat common infections (i.e. urinary tract infections, skin infections, strep throat, sinus infection, etc.). Research these drugs ahead of time to know which are suitable for the individual with celiac disease. In an emergency situation, an intravenous drug may be indicated until a suitable oral agent can be found. However, this will be more costly and may not be covered by insurance.

Pharmaceutical Companies Indicating That No Ingredients From Wheat, Rye, Oats, Barley, or Spelt Are Used in Their Products. (Crowe and Falini, 2001)

- Athena Neurosciences (South San Francisco, CA)
- Blaine Company (Burlington, KY)
- C.B. Fleet Company (Lynchburg, VA)
- Colgate Oral Pharmaceuticals (Canton, MA)
- Dista Products (Indianapolis, IN)
- Eli Lilly and Company (Indianapolis, IN)

- Forest Laboratories (St. Louis, MO)
- G.D. Searle and Company (Chicago, IL)
- Geneva Pharmaceuticals (Broomfield, CO)
- Greenstone Ltd. (Portage, MI)
- Hoechst Marion Roussel (Kansas City, MO)
- Immunex Corporation (Seattle, WA)
- Jacobus Pharmaceutical Company (Princeton, NJ)
- Janssen Pharmaceuticals (Titusville, NJ)
- M.G.I. Pharma (Minnetonka, MN)
- Mission Pharmacal Company (San Antonio, TX)
- Morton Grove Pharmaceuticals (Morton Grove, IL)
- Nephron Pharmaceuticals (Orlando, FL)
- Novartis Pharmaceuticals (East Hanover, NJ)
- Novopharm USA (Schaumburg, IL)
- Pharmaceutical Associates (Conestee, SC)
- Pharmacia and Upjohn (Kalamazoo, MI)
- Proctor and Gamble Pharmaceuticals (Mason, OH)
- Rhone-Poulenc Rorer Pharmaceuticals
- Roche Pharmaceuticals (Nutley, NJ)
- Scandipharm (Birmingham, AL)
- Schein Pharmaceuticals (Florham Park, NJ)
- Sidmak Laboratories (East Hanover, NJ)
- SmithKline Beecham Pharmaceuticals (Philadelphia, PA)
- Tap Pharmaceuticals (Deerfield, IL)
- United Research Laboratories (Philadelphia, PA)
- Vitaline Corporation (Ashland, OR)

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