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Today

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INTRODUCING ... align®

Align is a daily probiotic supplement. It is the *only* product that contains the probiotic strain *Bifidobacterium infantis* 35624 (Bifantis®), which has been clinically proven to build and maintain a strong, healthy digestive system. Daily administration of Align helps to create a natural defense against common episodic digestive upsets, including:

- Constipation
- Urgency
- Diarrhea
- Gas
- Abdominal discomfort
- Bloating

WHAT ARE PROBIOTICS?

The World Health Organization (WHO) and the Food and Agriculture Organization (FAO) of the United Nations define probiotics as “live microorganisms which, when administered in adequate amounts, confer a health benefit on the host.” The word “probiotic” literally means “for life” or “favorable to life.”

Most probiotics are strains of microorganisms that normally inhabit the human gastrointestinal tract. The colonization of the gastrointestinal tract by commensal microorganisms begins at birth; by the time a person reaches adulthood, the commensal microbiota include more than 500 species. These colonizing microbes—some of which possess health-promoting effects, some of which are pathogenic—form a dynamic ecosystem that varies substantially from person to person.

Imbalances in the intestinal microbiota are associated with disease and may even be the cause of some diseases. Probiotics are administered in a deliberate attempt to manipulate that balance and skew it toward beneficial microbes. Probiotics usually are administered orally, either in foods (e.g., added to yogurts or dairy drinks) or as dietary supplements (e.g., formulated as capsules or powders).

The majority of probiotics are bacteria belonging to the *Bifidobacterium* or *Lactobacillus* genera. The yeast *Saccharomyces boulardii* (a strain of *Saccharomyces cerevisiae*) also is used as a probiotic.

The term “probiotics” sometimes is misused to refer broadly to any potentially beneficial microorganisms. However, a microorganism does not qualify as a probiotic until it is:

- Isolated and purified.
- Shown in human studies to impart a health benefit.
- Proven safe under conditions of use.

Probiotics also must be identified by genus, species, and strain, using appropriate biochemical and genetic techniques. The strain usually is an alphanumeric

designation (e.g., *B. infantis* 35624, *Lactobacillus rhamnosus* GG). Some probiotics have an additional proprietary or familiar name; for example, *B. infantis* 35624 is known as *Bifantis*®, and *L. rhamnosus* GG is known as LGG.

PROBIOTIC PRODUCT SELECTION CONSIDERATIONS

It is estimated that more than 100 companies in the United States currently market products that claim to contain probiotics. Pharmacists have an important role in helping patients choose the most appropriate product and ensuring that they end up with a quality product.

Before recommending any probiotic product, pharmacists should consider the following information (as well as the tips in **WHAT TO LOOK FOR ON THE LABEL OF A PROBIOTIC PRODUCT** on page 3). *The P's and Q's of Probiotics: A Consumer Guide for Making Smart Choices*, available from the International Scientific Association for Probiotics and Prebiotics at http://www.isapp.net/docs/Consumer_Guidelines_final.pdf, provides a patient-friendly summary of important information about probiotics.

Probiotics Are Not Interchangeable

Probiotics are likely to be of interest to two broad groups of patients:

- *Patients with specific health concerns.* Probiotics are being investigated for possible benefits in a number of gastrointestinal disorders, as well as in conditions such as atopic dermatitis and urogenital infections.
- *Patients who are generally healthy and seek probiotics to support general wellness.* There is some evidence that probiotics can enhance immune function and reduce the risk of illness (e.g., the common cold).

It is important for patients in both groups to understand that the beneficial effects of probiotics are considered to be strain-specific. Even closely related probiotic species can have very different properties; for example, *L. rhamnosus* GR-1 has different effects from *L. rhamnosus* GG. It also is possible for probiotics to have detrimental effects; for example, *L. rhamnosus* GG actually worsened the condition of some patients with Crohn's disease.

Thus, probiotics must not be considered interchangeable. Positive results obtained with one probiotic strain cannot—and should not—be extrapolated to any other strain. There are no “one size fits all” products; pharmacists should recommend only those probiotic strains that have been shown in clinical trials to be effective for the health benefit desired by the patient.

Reviewer: Regina Mears, BPharm, MA
President
Life Management, LLC
Staff Pharmacist
Target Pharmacy
Orlando, Florida

Disclosure: This publication was prepared by Cynthia Knapp Dlugosz, BPharm, of CKD Associates, LLC, on behalf of the American Pharmacists Association.

This program was developed by the American Pharmacists Association and supported by Procter & Gamble. The publication went through a full medical and legal review by Procter & Gamble.

Probiotics Must Be Administered in Adequate Amounts

Probiotics must be administered in adequate amounts to be effective. Doses of probiotics are expressed most commonly in terms of colony-forming units (CFU)—the number of viable microbes that are capable of dividing and forming colonies. Doses typically consist of very large numbers of microbes, in the range of 10^8 to 10^{12} CFU per day.

What constitutes an adequate amount of a probiotic depends on the specific strain, dosage form, and health effect. “More” (i.e., a higher CFU count) is not necessarily better. As a rule, patients should follow the dosing regimen used in the clinical trials that demonstrated the efficacy of the specific probiotic product for the desired health benefit. The doses shown to be effective in clinical trials reflect any possible influences of the delivery vehicle and excipients; they also take into account any losses of viable microorganism that might occur during transit through the gastrointestinal tract.

Most efficacy studies have shown that probiotics must be consumed every day to remain effective. Probiotics do not establish permanent colonies in the gastrointestinal tract, so they are eliminated quickly when dosing stops.

Questions your patients may have about ALIGN®

Q. *If Align helps with episodic digestive upsets, why do I have to take it every day?*

A. Taking Align once a day, every day, builds and maintains the level of good bacteria (*Bifantis*) needed for a strong, healthy digestive system. When these good bacteria are at desirable levels, they work as a buffer against triggers of episodic digestive upsets such as stress, eating out, and travel. If you stop taking Align, the levels of good bacteria begin to decline.

Q. *How soon will Align begin working?*

A. Many people notice an improvement in digestive balance within the first 2 or 3 weeks of taking Align. In some people, 7 to 8 weeks of daily use may be needed to realize the full benefits of Align. The “Daily Digestive Tracker” provided in each package allows you to track your progress and explains what you can expect during each of the first 4 weeks you use Align.

Q. *What should I do if I forget to take my daily Align capsule?*

A. If you miss a day, just start again the next day. There’s no need to take two Align capsules in one day to make up for the capsule you missed.

Q. *When is the best time of day to take Align?*

A. You can take Align at any time of the day. Align may be taken with or without food, and it can be taken at the same time as vitamins or medications. To help make Align part of your daily routine, pick a time that will be easy to remember—such as when you take your usual vitamins or medications or with your first cup of coffee.

Probiotics Must Be Alive When Administered

By definition, probiotics must be live microorganisms. Probiotic products are regulated as foods or dietary supplements; as such, they are not subject to the strict quality control standards required for prescription and nonprescription drugs. There have been several published

What to Look for on the Label of a Probiotic Product

Pharmacists and patients should look for probiotic products that provide the following information:

- › Genus, species, and strain designation of the probiotic(s).
- › Minimum viable numbers of each probiotic strain at the end of shelf life.
- › “Best used by” date and a batch or lot code.
- › Health claim(s)—an accurate description of what to expect from product use, as allowable by law.^a
- › Dose or serving size that delivers the effective amount of the probiotic(s) related to the health claim.
- › Safety in the conditions of recommended use.
- › Recommended storage conditions.
- › Corporate contact details such as a Web site or toll-free telephone number.

A growing number of manufacturers are using yogurt and other fermented dairy products as a vehicle for specific probiotic strains. Patients should be advised to treat these yogurts as they would any other probiotic product: they should check for the information listed above and verify the existence of published evidence that supports a measured health benefit.

^aIn the United States, probiotic products are regulated as foods or dietary supplements. The Food and Drug Administration currently does not permit probiotic products to make any claims that relate the product to a reduction in the risk of disease or treatment of a specific disease.

reports of probiotic products failing to meet label claims with regard to the numbers and types of viable microbes.

Pharmacists and patients should look for products from established, reputable manufacturers. They also should choose products that are labeled to contain minimum viable numbers of each probiotic strain “through the end of shelf life,” not just “at the time of manufacture.”

Refrigerated probiotic products are not necessarily superior to products that can be stored at room temperature. Sophisticated modern technologies make it possible to grow large numbers of microorganisms, concentrate them, freeze-dry them, and package them as capsules, powders, tablets, or other shelf-stable dosage forms. The microorganisms remain alive but dormant until they are exposed to moisture in the gastrointestinal tract, where they begin to grow again. (Note that exposure to moisture from *any* source will bring the dormant microorganisms back to life, so products must be protected from moisture and environmental humidity during storage.)

Questions your patients may have about ALIGN®

Q. *What forms does Align come in, and how many bacteria does it contain?*

A. Align is available as capsules that deliver *B. infantis* 35624 in a consistent and quality-controlled manner. Each capsule contains 1×10^9 live bacteria (i.e., 1 billion bacteria) when manufactured and provides an effective level of probiotic bacteria until at least the “best by” date printed on the package.

Q. *How do I store Align? Can I put Align in my pill organizer?*

A. The good bacteria in Align are sensitive to air and moisture. To maximize the effectiveness of Align, store the capsules

continued on page 4

at room temperature in their original container (vial or blister). For best results, do *not* put Align into other containers such as pill organizers.

Q. Why doesn't Align need to be refrigerated?

A. Probiotic bacteria need to be alive to be effective. Many manufacturers recommend refrigeration because their probiotic formulations are not stable at room temperature. Align has been formulated and tested in controlled clinical trials to confirm that the good bacteria (Bifantis) remain alive and Align remains effective without refrigeration for a 24-month shelf life.

Q. Can I open the capsule and sprinkle the contents into my food or drinks?

A. The Align capsule was designed to be swallowed whole, and it is best to take it this way if you are able. If you are unable to swallow the capsule, it is okay to open the capsule and sprinkle the contents into a cold drink or food. Use the product immediately after mixing the contents. Do not sprinkle the contents into hot food or beverages.

ARE PROBIOTICS SAFE?

Probiotic products that contain microorganisms identical to those found in the human gastrointestinal system generally are regarded as safe. Bifidobacteria and lactobacilli in particular have an extensive record of safety in the generally healthy population. Some patients may experience gas, bloating, or mild diarrhea when they begin using probiotics, but those symptoms usually resolve with continued administration.

Some products marketed as probiotics contain mixtures of unspecified or uncharacterized microorganisms, mislabeled microorganisms (e.g., "*Lactobacillus sporogenes*" most likely is the spore-forming bacterium *Bacillus coagulans*, rather than a true lactobacilli), or microorganisms that are not found in the human gastrointestinal tract. The safety of these types of products may not be known and cannot be predicted reliably.

Although probiotics theoretically could cause invasive

systemic infections in any user, documented infections have occurred primarily in immunocompromised adults. It is prudent for patients who may be at elevated risk for infection to consult with a health care provider before using probiotics. This includes patients who:

- Are immunocompromised or taking immunosuppressive drugs.
- Are recovering from surgery.
- Are receiving chemotherapy or radiation therapy.
- Have compromised gut integrity.

Pregnant women should consult with a health care provider before using probiotics containing the yeast *S. boulardii*.

Questions your patients may have about ALIGN®

Q. What are the side effects of Align?

A. In clinical studies, there was no difference in side effects between Align and placebo. Some people experience a temporary increase in gas and bloating, but this goes away as your body adjusts to healthy digestive balance.

Q. Is there anybody who should not use Align?

A. Align contains trace amounts of milk protein and soy protein, therefore people who have allergies to either of these proteins should not use Align.

Q. Can I take Align if I am pregnant/nursing/trying to become pregnant?

A. The good bacteria (Bifantis) in Align can be taken during pregnancy, while breastfeeding, or while attempting to become pregnant. However, you should consider seeing a health care professional to determine if Align is right for you during this time.

Q. I have lactose intolerance. Can I use Align?

A. Align does not contain lactose and should not cause problems for people who are lactose intolerant.

Q. Can my child take Align?

A. Align can be taken by children. If you are unsure if Align is right for your child, consult your child's physician or health care professional.

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Many patients suffer from a range of digestive upsets, and finding a therapeutic option for the entire spectrum is challenging

Only

align[®]

contains **BIFANTIS[®]** – clinically proven to help manage a full range of episodic digestive upsets



- Bifantis (*Bifidobacterium infantis* 35624) is a unique probiotic strain clinically proven to build and maintain a strong, healthy digestive system*^{1,2}
- Align helps build and maintain a natural defense against a full range of episodic digestive upsets* such as:
 - Constipation • Diarrhea • Urgency • Gas • Abdominal discomfort • Bloating

Align is available at pharmacies and major retailers nationwide

- No prescription is necessary
- Align is also available at AlignGI.com or by calling 1-800-208-0112

Recommend Align for your patients with episodic digestive upsets

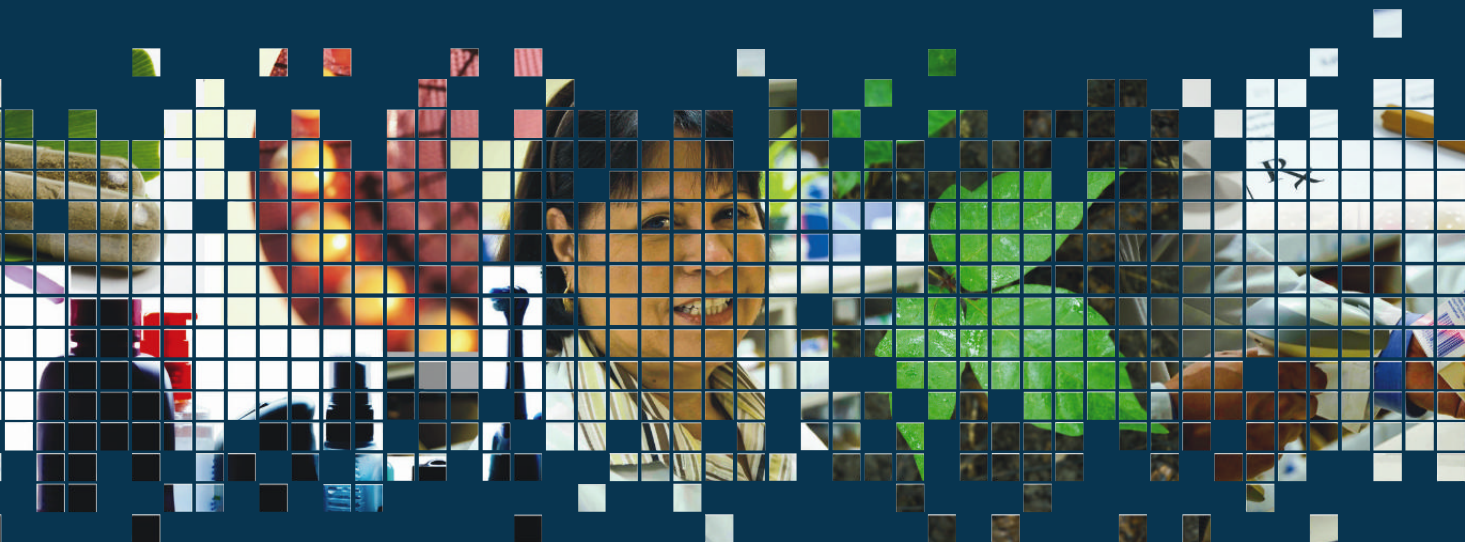
* These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

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NEW

The Practitioner's Pocket Guide to Nonprescription Drugs

Edited by Cynthia Knapp Dlugosz

This pocket guide is intended as a quick reference for practitioners—pharmacists and other clinicians alike—as they determine the best treatment for each patient's condition. All the material in the book is pulled from the 16th edition of *the Handbook of Nonprescription Drugs*. It covers the common conditions that patients self-treat, including headache, colds, cough, acne, and dermatitis. Each chapter will center on the treatment algorithm found in the Handbook and feature concise tabular material and bullet points for quick access to key information.

Conditions:

- Headache
- Fever
- Musculoskeletal injuries and disorders
- Common cold
- Seasonal allergic rhinitis
- Perennial allergic rhinitis
- Cough
- Heartburn
- Constipation
- Acute diarrhea in children 1 month to 5 years
- Acute diarrhea in patients older than 5 years
- Ophthalmic disorders (eye surface disorders)
- Eyelid disorders
- Tooth hypersensitivity
- Recurrent aphthous stomatitis
- Herpes simplex labialis
- Dermatitis
- Scaly dermatoses
- Contact dermatitis
- Diaper dermatitis
- Pediculosis
- Acne
- Minor burns and sunburn
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IRRITABLE BOWEL SYNDROME AND PROBIOTICS

Irritable bowel syndrome (IBS) is a chronic disorder characterized by recurring symptoms of abdominal pain or discomfort and associated with disturbed defecation. It affects as many as one in five American adults and is among the most common syndromes seen by gastroenterologists and primary care providers. IBS occurs more frequently in women than in men; it is diagnosed before the age of 35 years in about half of patients.

Table. Rome III Diagnostic Criteria for Irritable Bowel Syndrome

Recurrent abdominal pain or discomfort (an uncomfortable sensation not described as pain) at least 3 days per month in the past 3 months, associated with two or more of the following:

- Improvement with defecation.
- Onset associated with a change in frequency of stool.
- Onset associated with a change in form (appearance) of stool.

The criteria must be fulfilled for the last 3 months with symptom onset at least 6 months before diagnosis.

Source: Reprinted from Longstreth et al. (see REFERENCES) with permission from Elsevier.

IBS is referred to as a “functional disorder,” meaning that it has no known or detectable organic causes. The diagnosis is made on the basis of symptom-based criteria known as the “Rome criteria” (TABLE). IBS may be further categorized into one of three subtypes, according to the predominant bowel symptom:

- IBS with constipation (more common in women).
- IBS with diarrhea (more common in men).
- IBS with alternating symptoms of constipation and diarrhea.

Each group accounts for approximately one third of all patients.

IBS causes substantial discomfort and emotional distress. In addition to constipation, diarrhea, and abdominal pain, IBS symptoms may include cramping, bloating, fecal urgency, flatulence, a sense of incomplete evacuation, and straining. The symptoms can be unpredictable and disabling; some patients are unable to work, attend social events, or even travel short distances. Patients report a diminished quality of life similar to that reported by patients with diabetes or chronic renal failure. As many as 70% of patients with IBS do not seek or do not receive medical care for their symptoms (see IS IT IRRITABLE BOWEL SYNDROME?).

Currently, there is no cure for IBS, so treatment is aimed at controlling symptoms. Unfortunately, even symptomatic treatment is hindered by a dearth of truly effective therapies. The serotonergic medications tegaserod (Zelnorm®) and alosetron (Lotronex®)—both of which had been shown to improve patients’ overall quality of life and moderate many of the motor and sensory abnormalities associated with IBS—were withdrawn from the U.S. market following reports of serious adverse effects. (Alosetron currently is available through a restricted prescribing program only for the treatment of women with severe IBS with diarrhea; tegaserod is available for use in emergency situations only.) Lubiprostone (Amitiza®), a locally acting chloride channel activator, was approved in April 2008 for the treatment of IBS with constipation in women aged 18 years and older. It is not approved for use in men or for the treatment of other IBS subtypes.

There is strong and growing interest in probiotics as a promising therapeutic strategy for IBS. Researchers have reported significant alterations in the intestinal microbiota of patients with IBS, including a relative decrease in the number of bifidobacteria. Probiotics have the potential to influence many of the mechanisms that may underlie the symptoms of IBS, including immune function, intestinal motility, and the intraluminal milieu. A growing number of studies show probiotics to be a safe, convenient option for improving a wide variety of IBS symptoms.

Is It Irritable Bowel Syndrome?

Pharmacists can ask the following questions to help detect patients with IBS:

- Do you have recurrent abdominal pain or discomfort?
- Do you often feel bloated?
- Are you frequently constipated?
- Do you have frequent diarrhea?

Any patient with one or more of these symptoms should be encouraged to consult with a health care provider.

Source: Adapted with permission from the American College of Gastroenterology.

BIFIDOBACTERIUM INFANTIS 35624 (BIFANTIS®)

Species of *Bifidobacterium* account for up to 95% of the bacteria in the gastrointestinal tract of breastfed infants. The high proportion of bifidobacteria may be responsible for, or at least contribute to, the health benefits associated with breastfeeding. Although the percentage of bifidobacteria declines with age, they still account for up to 25% of the bacteria in the adult gastrointestinal tract.

B. infantis 35624 is a probiotic strain that was isolated from the resected intestinal epithelium of a healthy adult who underwent urinary tract reconstructive surgery. (Until that time, probiotic candidates had been isolated primarily from feces, rather than from the environment in which they eventually would be required to function.) It has a well-documented genome sequence with no known regions of pathogenicity. Two well-designed clinical trials have confirmed the ability of *B. infantis* 35624 to relieve many of the most troublesome symptoms of IBS.

In the first trial, O'Mahony and colleagues administered *B. infantis* 35624 or *Lactobacillus salivarius* UCC4331 in a malted milk drink—or the malted milk drink alone as a placebo—to 75 adults with IBS. Both bacteria were administered at a dose of 1×10^{10} live cells. The study subjects were asked to consume the drink each morning for 8 weeks and record informa-

tion about their symptoms and stool characteristics each day. Blood samples were obtained at the beginning and end of the study for measurement of cytokine levels.

During the treatment period, patients who received *B. infantis* 35624 had significantly lower scores most weeks for the three cardinal symptoms of IBS—pain/discomfort, bloating/distention, and bowel movement difficulty—than did patients who received placebo. Patients who received *L. salivarius* UCC4331 had significantly lower scores for abdominal pain only, during only 2 weeks of the treatment period. A direct comparison between the groups receiving *B. infantis* 35624 and *L. salivarius* UCC4331 showed significantly lower scores for bowel movement difficulty among patients receiving *B. infantis* 35624. All groups reported similar numbers of bowel movements and similar bowel movement consistency, indicating that the benefits of *B. infantis* 35624 treatment could not be attributed to either a laxative effect or an antidiarrheal effect.

At baseline, study subjects exhibited abnormally low levels of interleukin (IL)-10 and high levels of IL-12, compared with those of a group of age-matched and sex-matched healthy volunteers. These changes were consistent with a pro-inflammatory state. Cytokine levels were normalized (i.e., returned to levels similar

to those observed in healthy volunteers) only in patients who received *B. infantis* 35624, suggesting an immunomodulating role for this probiotic.

In the second trial, Whorwell and colleagues investigated the efficacy of an encapsulated formulation of *B. infantis* 35624 in women with IBS. A total of 362 women were randomized to receive one of three daily doses of *B. infantis* 35624 (1×10^6 , 1×10^8 , or 1×10^{10} CFU/mL) or placebo for 4 weeks. The women reported their symptoms daily using an interactive voice recording system.

Only one of the study doses— 1×10^8 —was associated with a significant improvement in abdominal pain/discomfort (the primary study variable) compared with placebo. This dose also was associated with significant improvements in the secondary study variables of bloating/distention, sense of incomplete evacuation, passage of gas, straining, and bowel habit satisfaction. The improvement in the score for bowel habit satisfaction was significant among patients with the constipation-predominant IBS subtype as well as patients with the diarrhea-predominant subtype. Positive responses to a global assessment of relief from both abdominal pain/discomfort and IBS symptoms at the end of therapy were more than 20% greater for *B. infantis* 35624 than for placebo.

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