Tazarotene (Fabior Foam)


Indication: Fabior Foam (tazarotene) 0.1% is indicated for the topical treatment of acne vulgaris in patients 12 years of age or older.

Drug Class: Fabior Foam 0.1% contains the compound tazarotene, a member of the acetylenic class of retinoids. Tazarotene is known chemically as ethyl 6-{[(4, 4-dimethylthiochroman-6-yl) ethynyl]nicotinate.

Uniqueness of Drug: In the 0.1% strength, this product is the only retinoid available in a topical foam.

Warnings and Precautions:

Fetal risk. Systemic exposure to tazarotenic acid depends on the extent of the body surface area treated. In patients who are treated topically over a sufficient body surface area, exposure could be on the same order of magnitude as in orally treated animals. Tazarotene is teratogenic, but the level of exposure that is required for teratogenicity in humans is not known.

There were five reported pregnancies in patients who participated in clinical trials of topical tazarotene foam. One of the patients was found to have used the foam for 25 days, two had used a vehicle foam, and the other two had not received either tazarotene foam or vehicle foam. Patients were withdrawn from the trials when the pregnancies were reported. One pregnant woman who was inadvertently exposed to topical tazarotene during the trial delivered a full-term healthy infant.

Females of childbearing age. Patients should be warned of the potential risk and should use adequate birth control measures during tazarotene therapy. Treatment should begin during a normal menstrual period. Patients should be advised of the need to use an effective method of contraception to avoid pregnancy.

Local irritation. Fabior Foam should be used with caution in patients with a history of local reactions or local hypersensitivity. Retinoids should not be used on abraded or eczematous skin, because they can cause severe irritation. Contact of the foam with the mouth, eyes, and mucous membranes should be avoided. In case of accidental contact, the area should be rinsed well with water.

Some individuals may experience skin redness, peeling, burning, or excessive pruritus with the use of Fabior Foam. If these effects occur, either the foam should be discontinued until the integrity of the skin is restored, or the dosage should be reduced to an interval the patient can tolerate. However, the efficacy of the product, when it is applied less frequently, has not been established.

Weather extremes, such as wind and cold, may be irritating to patients who use this product.

Irritation with concomitant topical agents. Concomitant topical acne medications should be used with caution because a cumulative irritant effect may occur. If irritation or dermatitis occurs, the foam may be applied less frequently and/or treatment may be temporarily interrupted. Therapy may be resumed after the irritation subsides. Treatment should be discontinued if irritation persists.

Photosensitivity and risk of sunburn. Because of a heightened susceptibility to burning, patients should avoid exposure to sunlight and sunlamps. Patients should be advised to use sunscreens and protective clothing during therapy with the foam. If patients have sunburn, they should not use Fabior Foam until they have fully recovered. Patients who may have considerable sun exposure as a result of their occupation and patients with inherent sensitivity to sunlight should exercise caution when using the product, and they should observe all precautions. Because of the potential for photosensitivity resulting in a greater risk for sunburn, Fabior Foam should be used with caution in patients with a personal or a family history of skin cancer. Caution is also advised for patients who are taking drugs known to increase photosensitivity (e.g., thiazides, tetracyclines, fluoroquinolones, phenothiazines, and sulfonamides).

Flammability. The propellant in Fabior Foam is flammable. Patients should be instructed to avoid fire, flame, and smoking during and immediately following an application.

Dosage and Administration: Fabior Foam 0.1% is designed for topical use only; it is not intended for oral, ophthalmic, or intravaginal use. Patients should apply the foam once daily during and immediately following an application.

The foam should not come into contact with the eyes, lips, or mucous membranes. Patients should wash their hands after the application, and they may use moisturizer as needed. If redness, peeling, or discomfort occurs, the treatment may be applied less often or it may be temporarily interrupted. Treatment may be resumed after irritation subsides, but it should be discontinued if irritation persists.

Commentary: Acne is the most common skin problem in the U.S., affecting about 40 to 50 million Americans, most frequently adolescents and young adults. Hormones and other substances can act on the skin’s sebaceous glands and hair follicles, leading to clogged pores and outbreaks such as pimples. Researchers believe that acne can result from hormonal changes, heredity and genetics, some medications, and greasy cosmetics.

The FDA’s approval of Fabior Foam (tazarotene) 0.1% was based on two randomized, double-blind phase 3 studies conducted in the U.S. and Canada.
**Pharmaceutical Approval Update**

**Sources:** www.stiefel.com; www.rxlist.com/fabior-drug/indICATIONs-Dosage.htm

**Estradiol Valerate and Estradiol Valerate/Dienogest Tablets (Natazia)**

**Manufacturer:** Bayer Health Care, Wayne, N.J.

**Indication:** First approved as a four-phasic oral contraceptive in May 2010, Natazia is now also indicated for the treatment of heavy menstrual bleeding in women without other conditions such as endometrial polyps or uterine fibroids.

**Uniqueness of Drug:** This is the only contraceptive with an indication for the treatment of heavy menstrual bleeding.

**Drug Class:** Natazia contains two female hormones: an estrogen (estradiol valerate) and a progestin (dienogest).

**Boxed Warning:** Women who smoke and who are older than 35 years of age should not use Natazia. Smoking increases the risk of serious adverse effects from oral contraceptives. These effects can be life-threatening and may include blood clots, strokes, or heart attacks. This risk increases with age and with the number of cigarettes smoked.

**Warnings and Precautions:** Natazia increases the risk of serious conditions, including blood clots, strokes, and heart attacks. The risk of blood clots is highest during the first year of use and when they restart the same oral contraceptive or a different one after an interruption of 4 weeks or more. Patients should inform their health care professional immediately if they have persistent leg pain; sudden shortness of breath; sudden partial or complete blindness; severe angina; sudden, severe headaches; weakness or numbness in an arm or leg; trouble speaking; or jaundice.

**Dosage and Administration:** Natazia is taken once daily. The regimen consists of 28 tablets of varying doses of estradiol valerate and estradiol valerate in combination with dienogest, as follows: 22 days of estradiol valerate/dienogest tablets, 4 days of estradiol valerate tablets, and 2 days of hormone-free tablets.

**Commentary:** In addition to Bayer’s levonorgestrel-releasing intrauterine system, Mirena, Natazia represents a non-invasive treatment approach for heavy menstrual bleeding. Natazia is the first combined oral contraceptive that contains an estradiol valerate in combination with dienogest. Estradiol valerate is converted to estradiol, the same estrogen produced in a woman’s body.

The approval of the new indication was based on two identically designed, multicenter, double-blind, randomized, placebo controlled trials. The studies included a total of 421 women 18 years of age or older, with heavy, prolonged, or frequent bleeding without organic disease. Patients with blood loss of 80 mL or more in at least two bleeding episodes during a 90-day run-in phase who received Natazia achieved a statistically significant reduction in menstrual blood loss compared with patients in the placebo group.

**Sources:** www.fda.gov; www.berlex.bayerhealthcare.com; www.drugs.com; www.news-medical.net

**Taliglucerase alfa for Injection (Elelyso)**

**Manufacturer:** Protalix BioTherapeutics/Pfizer

**Indication:** Taliglucerase alfa (Elelyso), an orphan drug, is indicated as a long-term enzyme replacement therapy for adults with type-1 (non-neuropathic) Gaucher’s disease.

**Drug Class:** Elelyso is a hydrolytic lysosomal glucocerebrosidase-specific enzyme for intravenous (IV) infusion. It is a recombinant active form of the lysosomal enzyme, beta-glucocerebrosidase, which is expressed in genetically modified carrot plant root cells cultured in a disposable bioreactor system (ProCellEx). Beta-glucocerebrosidase (beta-glucosyl-N-acetylglucosaminylceramide hydrolyase, Enzyme Commission No. 3.2.1.45) is a lysosomal glycoprotein enzyme that catalyzes the hydrolysis of the glycolipid glucocerebroside to glucose and ceramide.

**Uniqueness of Drug:** Elelyso is produced by recombinant DNA technology using plant (carrot) cell culture. Purified taliglucerase alfa is a monomeric glycoprotein that contains four N-linked glycosylation sites. Taliglucerase alfa differs from native human glucocerebrosidase by two amino acids at the N terminal and by up to 7 amino acids at the C terminal. Taliglucerase alfa is a glycosylated protein with oligosaccharide chains at the glycosylation sites having terminal mannose sugars. These mannose-terminated oligosaccharide chains of taliglucerase alfa are specifically recognized by endocytic carbohydrate receptors on macrophages, which accumulate lipids in Gaucher’s disease.

**Warnings and Precautions:**

**Anaphylaxis.** Severe allergic reactions have been observed with Elelyso. If anaphylaxis occurs, the physician may decide to discontinue treatment immediately. Patients who have experienced anaphylaxis with Elelyso or with another enzyme replacement therapy should proceed with caution before starting treatment again.

**Infusion reactions.** Infusion and allergic reactions are defined as occurring within 24 hours of the infusion. Commonly observed infusion reactions have included headache, chest pain or discomfort, weakness, fatigue, hives, abnormal redness of the skin, elevated blood pressure, back or joint pain, and flushing. Most of these reactions were mild, and treatment was not required. Management is based on the type and severity of the reaction. The physician may decide to temporarily stop the infusion, slow the infusion rate, or use medications such as an antihistamine or a fever reducer. Pretreatment with antihistamines, corticosteroids, or both, may prevent these reactions.

**Other adverse reactions.** Commonly observed adverse effects have included influenza; pain in the extremities; back pain; and upper respiratory, throat, and urinary tract infections. As with all therapeutic proteins, including enzyme replacement therapies, there is the potential for antibody development. However, it is not clear whether this has an effect on the patient’s clinical response or adverse reactions. Patients with an immune response to other enzyme replacement treatments who are switching to Elelyso should continue to be monitored for antibodies. Comparison of the frequency of antibody development in other enzyme replacement treatments may be misleading.

**Dosage and Administration:** The recommended dose is 60 units/kg of body weight, administered once every 2 weeks as a 60- to 120-minute IV infusion. Patients who are being treated with imiglucerase (Cerezyme, Genzyme) for type-1 Gaucher’s disease can be switched to Elelyso. It is recommended that patients who previously received a stable dose of imiglucerase use the same dose when they use Elelyso. Dosage

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adjustments can be made based on achievement and maintenance of each patient’s therapeutic goals. Clinical studies have evaluated dose ranges from 11 to 73 units/kg every other week.

Elelyso should be reconstituted with Sterile Water for Injection and diluted with 0.9% Sodium Chloride Injection, USP, to a final volume of 100 to 200 mL, delivered by IV infusion. The initial infusion rate should be 1.3 mL/minute. After the patient’s tolerability to the infusion rate is established, the rate may be increased to 2.3 mL/minute. The total volume of the infusion solution should be delivered over a period of no less than 1 hour.

Each vial of Elelyso provides 200 units of taliglucerase alfa and is intended for single use only. No more than one vial should be used at one time. Aseptic technique is essential during reconstitution and dilution. Low-protein-binding containers are required to prepare Elelyso. The solution should be administered with a low-protein-binding infusion set equipped with an in-line 0.2-micrometer filter.

**Commentary:** Gaucher’s disease is a rare, autosomal recessive genetic disorder that can cause liver and neurological problems. It affects 1 in 50,000 to 1 in 100,000 people in the general population. Persons of Eastern and Central European (Ashkenazi) Jewish heritage are at highest risk for the disease. In order for a child to have the disease, both the mother and the father must pass one abnormal copy of the gene to the child. The lack of the glucocerebrosidase enzyme causes harmful fatty chemicals to build up in the liver, spleen, bones, nervous system, and bone marrow, thereby preventing the cells and organs from functioning properly.

Two competing agents—imiglucerase and velaglucerase (Vpriv, Shire)—are also available for the treatment of Gaucher’s disease. Made from carrot cells, Elelyso is the first FDA-approved drug manufactured from a genetically engineered plant.

**Source:** www.elelyso.com

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**Pharmaceutical Approval Update**