The armamentarium of available therapies and treatments in dermatology saw significant growth in the past year. From aesthetics to clinical dermatology, many new products were approved and launched in 2014, adding to the current index of available therapies and treatments.

**RECENT APPROVALS**

In late November, the FDA approved Valeant Pharmaceuticals International, Inc.’s Onexton Gel (clindamycin phosphate and benzoyl peroxide) 1.2%/3.75% for the once-daily treatment of comedonal and inflammatory acne in patients 12 and older. Onexton Gel is the first and only FDA-approved fixed combination 1.2% clindamycin phosphate and 3.75% benzoyl peroxide medication for the once-daily treatment of comedonal and inflammatory acne. Onexton Gel has a favorable cutaneous tolerability profile and contains no surfactants, alcohol or preservatives.

Last month, the FDA also awarded breakthrough therapy designation to the investigational drug dupilumab for the treatment of adults with moderate-to-severe atopic dermatitis (AD) who had an insufficient response to and/or who are not suitable for topical prescription therapy. Co-developers Sanofi and Regeneron noted that the FDA’s designation was supported by positive data from Phase I and Phase II studies.

The FDA granted 510(K) clearance to Syneron Candela’s PicoWay picosecond device for tattoo removal. PicoWay is a dual wavelength device, with 1064nm and 532nm wavelengths, which utilizes the proprietary PicoWay Technology to generate picosecond pulses for the removal of tattoos. The FDA clearance is for all tattoo colors: red, yellow and orange for the 532nm wavelength; black, brown, green, blue and purple for the 1064nm wavelength. In a clinical study, the majority of subjects (86 percent) achieved at least 50 percent tattoo clearance after only three treatments based on blinded, independent review. Device treatment also presented a favorable safety profile with no device-related serious adverse events, and low levels of pain or discomfort throughout the study.

Cynosure, Inc. received FDA 510(k) clearance to market its PicoSure Picosecond Laser Workstation for the treatment of wrinkles with the company’s new disposable energy delivery system, the FOCUS lens array. In 2012, PicoSure received FDA clearance for the removal of tattoos and benign pigmented lesions.

The FDA accepted the Investigational New Drug (IND) Application to conduct clinical studies for Evosyal, a botulinum toxin Type A neurotoxin that was acquired by Alphaphen last year as part of the acquisition of Evolus Inc. Alphaphen says it expects the initial clinical trial to be fully enrolled by the end of this year.

Ulthera, Inc.’s Ulthera System won FDA approval for the non-invasive treatment of the chest to improve lines and wrinkles of the décolleté. The Ultherapy Décolletage Treatment uses the system’s signature imaging and micro-focused ultrasound therapy capabilities. The treatment, which takes about 30 minutes to administer, stimulates the natural formation of collagen and elastin in the skin’s foundation to gradually smooth chest wrinkles. Results are visible after about three months. As with the FDA-cleared Ultherapy procedure for lifting the neck, eyebrow, and under the chin, results are achieved with one treatment and with no downtime or post-treatment care requirements.

KYTHERA Biopharmaceuticals, Inc.’s New Drug Application (NDA) for ATX-101 (deoxycholic acid) was accepted for filing by the FDA earlier this year. The accep-
The FDA awarded marketing clearance for Valeant Pharmaceuticals International, Inc.’s Restylane Silk Injectable Gel with 0.3% Lidocaine for submucosal implantation for lip augmentation and dermal implantation for correction of perioral rhytids in patients over the age of 21. Restylane Silk is a crystal clear injectable gel composed of hyaluronic acid, a natural substance that already exists in the body. Restylane Silk is non-animal based and free from animal protein. Allergy pretesting is not necessary.

A clinical study to evaluate the safety and effectiveness of injections of Restylane Silk to enhance lip fullness and to improve the wrinkles around the lips included 221 mostly female subjects and evaluated subjects with light and dark skin. Subjects with very dark skin were not studied. Ninety-eight percent of subjects reported improvement in their lip fullness 14 days after injection and 76 percent still had lip improvement six months after their injection. The majority of adverse events were mild in intensity and the most common symptoms were lip swelling, contusion, and lip pain. The incidence of adverse event decreased significantly after the second treatment.

Syneron Medical Ltd. received FDA 510(k) clearance to market the UltraShape System for non-invasive reduction of abdominal circumference via fat cell destruction. The UltraShape System uses pulsed focused ultrasound energy that precisely targets subcutaneous fat, while keeping the surrounding tissue, vasculature, nerves, and muscles intact. UltraShape uses a pure mechanical effect to destroy fat cells without inducing thermal damage. In the randomized, controlled clinical study of UltraShape, which was performed at three clinical sites in the US and one site outside of the US, a total of 150 subjects were treated and followed for up to four months. In this multi-site study, patients demonstrated an average reduction of 2.5cm in the treatment phase and 0.5cm reduction in the control phase. In addition, Syneron Medical Ltd.’s U-Sculpt transducer for the UltraShape received FDA clearance in November. The FDA also cleared the V3.1 platform for a 25 percent increase in Ultrasound power in the new U-sculpt transducer and the previously cleared larger VDF transducer. This 25 percent power enhancement is designed to increase the efficacy of treatment and improve both the user experience and patient comfort, according to the company.

DEKA Medical, Inc.’s Synchro REPLA:Y, an aesthetic workstation dedicated, but not limited, to high speed stable long-term, or permanent hair reduction, treatment of PFB, treatment of benign pigmented lesions, treatment of wrinkles and photocoagulation of dermatological vascular lesions was FDA cleared this year.

The Synchro REPLA:Y combines hair removal on all Fitzpatrick skin types, vascular and benign pigmented lesions treatments, as well as skin rejuvenation, in a single platform. It utilizes three different light sources: a 755nm Alexandrite laser, a 1064nm Nd:YAG laser, and an intense pulsed light.

HAIR

Women’s Rogaine 5% Minoxidil Topical Aerosol, once-daily use treatment for Female Pattern Hair Loss containing five percent minoxidil in an elegant foam.
formula was officially launched to market after FDA approval in early November. Minoxidil is the only topical ingredient FDA-approved to help regrow hair. Women’s Rogaine 5% Minoxidil Topical Aerosol, penetrates into the scalp, with gentle massaging to reactivate hair follicles and stimulate hair regrowth. Clinical studies show that with once daily use of Women’s Rogaine 5% Minoxidil Topical Aerosol for 24 weeks, 81 percent of women regrew hair, with initial results as early as 12 weeks and new hairs coming in up to 48 percent thicker than before.

PSORIASIS AND PSORIATIC ARTHRITIS

The Dermatologic and Ophthalmic Drugs Advisory Committee (DODAC) to the FDA voted 7 to 0 to support the approval of AIN457 (secukinumab), a selective interleukin-17A (IL-17A) inhibitor, for the treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy (a drug that is absorbed into the bloodstream and distributed to all parts of the body) or phototherapy (light therapy). The DODAC based its recommendation on the safety and efficacy outcomes from 10 psoriasis Phase II/III clinical studies, which included nearly 4,000 patients with moderate-to-severe plaque psoriasis. Novartis submitted a Biologics License Application (BLA) for secukinumab to the FDA in October 2013 and the FDA action date is expected in early 2015.

LEO Pharma Inc., received a new indication for Taclonex (calcipotriene and betamethasone dipropionate) Topical Suspension as a topical combination treatment of plaque psoriasis of the scalp in patients 12 to 17 years. The new indication represents the first indication for adolescent patients aged 12 years and older with scalp plaque psoriasis on the market. Taclonex Topical Suspension is a first-line, once-daily combination product indicated for treatment of both scalp and body plaque psoriasis in adults age 18 and above for up to eight weeks, and now for the treatment of plaque psoriasis of the scalp in pediatric patients 12 to 17 years for the same period.

The FDA approved Celgene’s Otezla (apremilast), an oral, selective inhibitor of phosphodiesterase 4 (PDE4), for the treatment of patients with moderate to severe plaque psoriasis for whom phototherapy or systemic therapy is appropriate. Otezla is the first and only PDE4 inhibitor approved for the treatment of plaque psoriasis. The approval was based primarily on safety and efficacy results from the ESTEEM trials, in which Otezla treatment resulted in significant and clinically meaningful improvements in plaque psoriasis as measured by PASI scores at week 16. Moreover, sPGA scores of clear to almost clear were demonstrated in both studies. Side effects included diarrhea, nausea, upper respiratory tract infection, tension headache, and headache.

Otezla was also approved earlier in the year for the treatment of adults with active psoriatic arthritis (PsA).

This year, Antares Pharma, Inc. announced LEO Pharma’s launch of Otrexup, the first FDA-approved subcutaneous (SC) methotrexate (MTX) product for once weekly self-administration with an easy-to-use, single dose, disposable auto injector. Otrexup is indicated for use in adults who need symptomatic control of severe recalcitrant, disabling psoriasis that is not adequately responsive to other forms of therapy.

ACNE AND ROSACEA

Ranbaxy Laboratories Inc., a wholly owned subsidiary of Ranbaxy Laboratories Limited, launched Absorica...
(isotretinoin) 25 mg and 35 mg capsules into the US healthcare market. The product, licensed by Ranbaxy from Cipher Pharmaceuticals, Inc., is indicated for the treatment of severe recalcitrant nodular acne in patients 12 years of age and older. Due to its high lipophilicity, oral absorption of isotretinoin is enhanced when given with a high-fat meal, however, Absorica, which is formulated using patented Lidose technology, can be given without regards to meals. The fasted AUC0-t of Absorica is approximately 83 percent greater than that of Accutane.

The PicoSure picosecond laser was also approved to treat acne scars. Results from PicoSure clinical studies show a dramatic improvement in the appearance of acne scars in as little as three treatments. In clinical studies, 77 percent of patients achieved greater than 50 percent improvement as graded by the physician.

Aqua Pharmaceuticals’ Acticlate (doxycycline hyclate USP) Tablets, 150 mg and 75 mg, was FDA approved as an oral antibiotic for acne. Acticlate is a tetracycline-class antibacterial indicated for the treatment of a number of infections, including adjunctive therapy in severe acne. Acticlate 150 mg tablets have two functional scores, providing several dosing options to physicians and patients. The Acticlate film-coated, round 75 mg tablets and oval-shaped, dual-scored 150 mg tablets are designed to be small and easy to swallow. Utilization of the latest manufacturing technology has allowed 150 mg of doxycycline to be formulated in a substantially reduced tablet size for Acticlate, according to Aqua Pharmaceuticals.

Valeant Pharmaceuticals’ Supplemental New Drug Application (sNDA) application for Retin-A Micro (tretinoin) Gel microsphere 0.08% was FDA approved for the topical treatment of acne vulgaris.

ANTIFUNGAL/ANTIBACTERIAL THERAPIES

Syneron Medical Ltd. launched a new handpiece featuring a new 5-millimeter spot size for the Gentle Pro Nd:YAG Laser Series. This new FDA-cleared handpiece expands the functionality of the GentleYAG Pro and GentleMax Pro Nd:YAG laser to treat onychomycosis in addition to its existing capabilities for hair removal and for the treatment of vascular and pigmented lesions. With its precision 5mm handpiece, the Gentle Pro Nd:YAG Laser raises the temperature under the nail to a level that’s inhospitable to fungus in order to increase the appearance of clear nails.

The FDA approved Anacor Pharmaceuticals’ New Drug Application for Kerydin (tavaborole) topical solution, 5%, the first oxaborole antifungal approved for the topical treatment of onychomycosis of the toenails due to Trichophyton rubrum or Trichophyton mentagrophytes. Kerydin is a clear, colorless, alcohol-based solution applied with a dropper to the infected toenail once daily for 48 weeks. Debridement of the nail is not required during the treatment period. Due to its topical application, Kerydin has low systemic absorption and has not demonstrated systemic side effects.

Kerydin’s efficacy and safety were evaluated in two multicenter, double-blind, randomized, vehicle-controlled trials. Kerydin or vehicle was applied once daily for 48 weeks in subjects with 20-60 percent clinical involvement of the target toenail, without dermatophytomas or lunula involvement. A total of 1,194 subjects (795 Kerydin, 399 Vehicle) 18 to 88 years of age, participated in these two trials. The primary efficacy endpoint
was complete cure at Week 52 plus mycological cure (negative KOH wet mount and negative fungal culture). In the first trial, 6.5 percent of subjects treated with Kerydin reached the primary endpoint, compared to 0.5 percent of subjects treated with vehicle. In the second trial, 9.1 percent of subjects treated with Kerydin reached the primary endpoint, compared to 1.5 percent for vehicle. Common adverse reactions occurring in at least one percent of subjects treated with Kerydin included application site exfoliation, ingrown toenail, application site erythema, and application site dermatitis.

Valeant Pharmaceuticals International, Inc.’s Jublia (efinaconazole 10% topical solution) was FDA approved as the first topical triazole for the treatment of onychomycosis of the toenails. Jublia is applied daily to the nail with a novel bottle that has a built-in flow-through brush applicator. It dries quickly and there is no need to remove excess product. In addition, there are no concerns for systemic side effects. In two positive pivotal studies published last year, 17.8 percent and 15.2 percent of patients treated with Jublia were completely cured compared to only 3.3 percent and 5.5 percent of patients treated with vehicle, respectively.

Dalvance (dalbavancin), a new antibacterial drug used to treat adults with skin infections, was approved for the treatment of acute bacterial skin and skin structure infections (ABSSSI) caused by certain susceptible bacteria like Staphylococcus aureus (including methicillin-susceptible and methicillin-resistant strains) and Streptococcus pyogenes. The treatment is administered intravenously. Dalvance’s safety and efficacy were evaluated in two clinical trials with a total of 1,289 adults with ABSSSI. Results showed Dalvance was as effective as vancomycin for the treatment of ABSSSI. The most common side effects identified in the clinical trials were nausea, headache and diarrhea. In the trials, more participants in the Dalvance group had elevations in one of their liver enzyme tests. The Dalvance drug label provides recommendations on dosage adjustment in patients with renal impairment.

Quinnova Pharmaceuticals LLC, an affiliate of Exeltis, launched its FDA-approved Ecoza (econazole nitrate) topical foam 1%. Ecoza Foma is indicated for the treatment of interdigital tinea pedis caused by Trichophyton rubrum, Trichophyton mentagrophytes, and Epidermophyton floccosum in patients 12 years of age and older. Proven to kill fungi that cause interdigital tinea pedis when applied once-daily for four weeks, its unique, alcohol-free foam delivery helps protect and restore skin, penetrating quickly and drying rapidly without the greasy residue that is common among other creams and gels.

SKIN CANCER

The FDA granted accelerated approval to Keytruda (pembrolizumab) for treatment of patients with advanced or unresectable melanoma who are no longer responding to other drugs. Keytruda is the first approved drug that blocks a cellular pathway known as PD-1, which restricts the body’s immune system from attacking melanoma cells. Keytruda is intended for use following treatment with ipilimumab, a type of immunotherapy. For melanoma patients whose tumors express a gene mutation called BRAF V600, Keytruda is intended for use after treatment with ipilimumab and a BRAF inhibitor. Keytruda’s efficacy was established in 173 clinical trial participants with advanced melanoma whose disease progressed after prior treatment. All participants were treated with Keytruda 2mg/kg or 10 mg/kg. In the half of the participants who received Keytruda at the 2 mg/kg dose, approximately 24 percent had their tumors shrink. This effect lasted at least 1.4 to 8.5 months and continued beyond this period in most patients. A similar percentage of patients had their tumor shrink at the 10 mg/kg dose.
GlaxoSmithKline plc received FDA approval of Mekinist (trametinib) for use in combination with Tafinlar (dabrafenib) for the treatment of patients with unresectable melanoma or metastatic melanoma with BRAF V600E or V600K mutations. The approval of the combination is based on the demonstration of response rate and median duration of response in a Phase I/II study. The combination was approved through the FDA’s Accelerated Approval program and reviewed under a Priority Review designation.

PEDIATRIC DERMATOLOGY

Pierre Fabre Dermatologie was awarded marketing authorization from the FDA for Hemangeol (propranolol hydrochloride), which is the first and only approved treatment for “proliferating infantile hemangioma requiring systemic therapy.” Hemangeol was studied in infants five weeks to five months old (at therapy initiation) with a proliferative infantile hemangioma requiring systemic treatment in a randomized, double blind placebo controlled, multi-dose and multi-center adaptive Phase II/III trial, which compared four propranolol treatment protocols (1 or 3mg/kg/day for three or six months) versus placebo. The treatment protocol of 3mg/kg/day dose for the duration of six months had a 60.4 percent success rate versus 3.6 percent in the placebo group (p< 0.0001) reaching the primary endpoint: complete or nearly-complete resolution of the target hemangioma. In the study, 11.4 percent of patients needed to be retreated after stopping the treatment.

OTHER APPROVALS

The FDA granted orphan drug designation status for Galderma’s trifarotene molecule for the treatment of congenital ichthyosis. Trifarotene is a selective agonist of the gamma retinoic acid receptor (RARγ), which is currently in clinical development for use in other more common dermatological conditions. In addition to studying treatments for lamellar ichthyosis and other congenital ichthyoses, Galderma is also exploring the treatment of other rare skin diseases.

The FDA approved a labeling change that allows Galen US Incorporated’s Synera (lidocaine and tetracaine) topical patch to be used at home to help prevent needle stick pain associated with superficial IVs and superficial dermatological procedures. It combines lidocaine and tetracaine with warming technology in a simple-to-use peel-and-stick patch. In a randomized, double-blind, placebo-controlled study, 59 percent of children aged three to 17 years reported no pain upon the needle stick compared with only 20 percent among children who were given a patch with no numbing medications. Synera is approved for use in adults and children as young as three years old.

Impavido (miltefosine) was approved to treat leishmaniasis, a disease caused by Leishmania, a parasite which is transmitted to humans through sand fly bites. The disease occurs primarily in people who live in the tropics and subtropics. Impavido is an oral medicine approved to treat the three main types of leishmaniasis: visceral leishmaniasis, cutaneous leishmaniasis, and mucosal leishmaniasis. It is intended for patients 12 years of age and older.

The FDA approved XOMA Corporation’s IL-1 beta antibody gevokizumab for the treatment of pyoderma gangrenosum (PG) under an orphan drug designation. The FDA grants orphan drug designation to those drugs that treat rare diseases, which inflict fewer than 200,000 patients in the US. Once a corporation becomes designated, they have seven years to market themselves with tax credits for clinical research costs, the ability to apply for grant funding and waive the Prescription Drug User Fee Act.

Xolair (omalizumab) was FDA approved for the treatment of chronic idiopathic urticaria (CIU) for patients 12 years of age and older who remain symptomatic despite treatment with H1-antihistamine therapy. Xolair is jointly developed by Genentech and Novartis Pharma AG and is co-promoted by Novartis Pharmaceuticals Corporation with Genentech in the United States.

Sitavig (50mg acyclovir) Muco-Adhesive Buccal Tablet is now available from Innocutis for the treatment of recurrent herpes labialis, offering a unique vehicle and delivery system. Sitavig, licensed from BioAlliance Pharma, uses proprietary Lauriad delivery technology to deliver a high and sustained concentration of acyclovir in saliva and labial mucosa. Sitavig 50mg reduces the occurrence of vesicular lesions, primary or non-primary, and prevents and delays the recurrence of the next herpes episode. Sitavig 50mg buccal tablet is an alternative option to systemic antiviral treatment for patients with recurrent HL when applied within one hour of occurrence of prodromal symptoms.

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