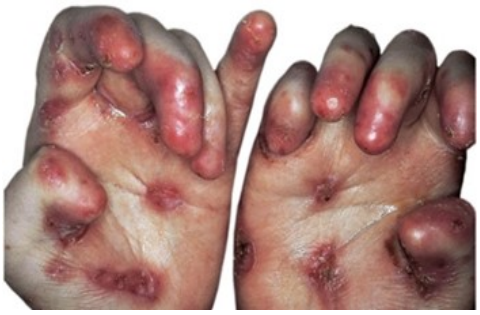
Drug & Poison Information Center Bulletin
Faculty of Pharmacy - Tanta University

JUNE, 2023 | Volume 10, Issue 2

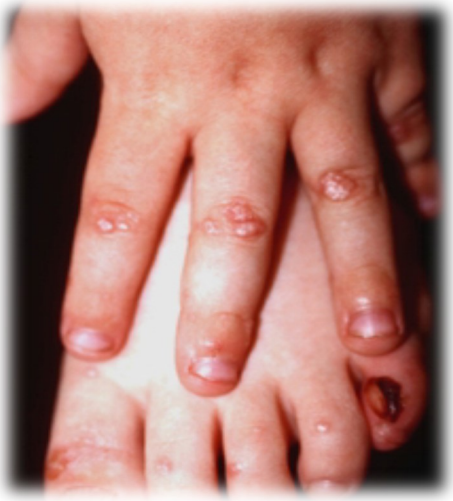
Inside this issue:

Approval of the first-ever topical gene therapy, for rare genetic skin disease

Dystrophic epidermolysis bullosa (DEB) is a rare genetic skin disease that affects the connective tissue in the skin and nails and results from mutation(s) in the COL7A1 gene. This gene encodes type VII collagen (COL7), which is an essential protein that helps strengthen and stabilize the outer and middle layers of the skin. When COL7A1 is deficient, skin layers can separate, causing painful and debilitating blisters and wounds. .DEB usually presents itself at birth and is divided into two major types depending on the inheritance pattern: recessive dystrophic epidermolysis bullosa (RDEB) and dominant dystrophic epidermolysis bullosa (DDEB). Symptoms can vary widely among affected people. Individuals with DDEB typically have mild cases with blistering primarily affecting the hands, feet, knees, and elbows. RDEB cases can be painful and debilitating, often involving widespread



blistering that can lead to vision loss, disfigurement, and other serious medical complications, which could be fatal. Unfortunately, there is no way to stop blisters and wounds from developing on DEB patient skin and the only way is to give patients bandages and helplessly watch as new blisters formed.



FDA approval of first-ever gene therapy for this rare disease:

- On 19th May, 2023, the US Food and Drug Administration (FDA) has approved the first-ever topical gene therapy, which will be used to treat wounds in patients 6 months of age and older who have either recessive or dominant DEB. The therapy, Vyjuvek (beremagene geperpavec, formerly known as B-VEC), uses a non-replicating herpes simplex virus type 1 (HSV -1) vector to deliver the COL7A1 gene directly to skin cells, restoring the COL7 protein fibrils that stabilize skin structure.

- FDA approval of Vyjuvek was based on a randomized, double-blinded, placebo-controlled, 31-patient, phase 3 trial published in the New England Journal of Medicine, which showed that 71% of wounds treated with the gene therapy had complete healing at 3 months compared with 20% of those treated with placebo ($P < .001$). At 6 months, 67% of wounds treated with the gene therapy had complete healing compared with 22% of wounds treated with placebo ($P = .002$). Nearly two thirds of the patients experienced at least one negative outcome. Most were light or medium. The most frequent symptoms, each reported by three patients, were pruritus, chills, and squamous cell carcinoma (SCC). Cases of SCC have been reported in wound sites that have not received Vyjuvek or a placebo. Three individuals experienced three serious side effects that were unrelated to the medication, including cellulitis, diarrhoea, and anaemia.

Recommendations:

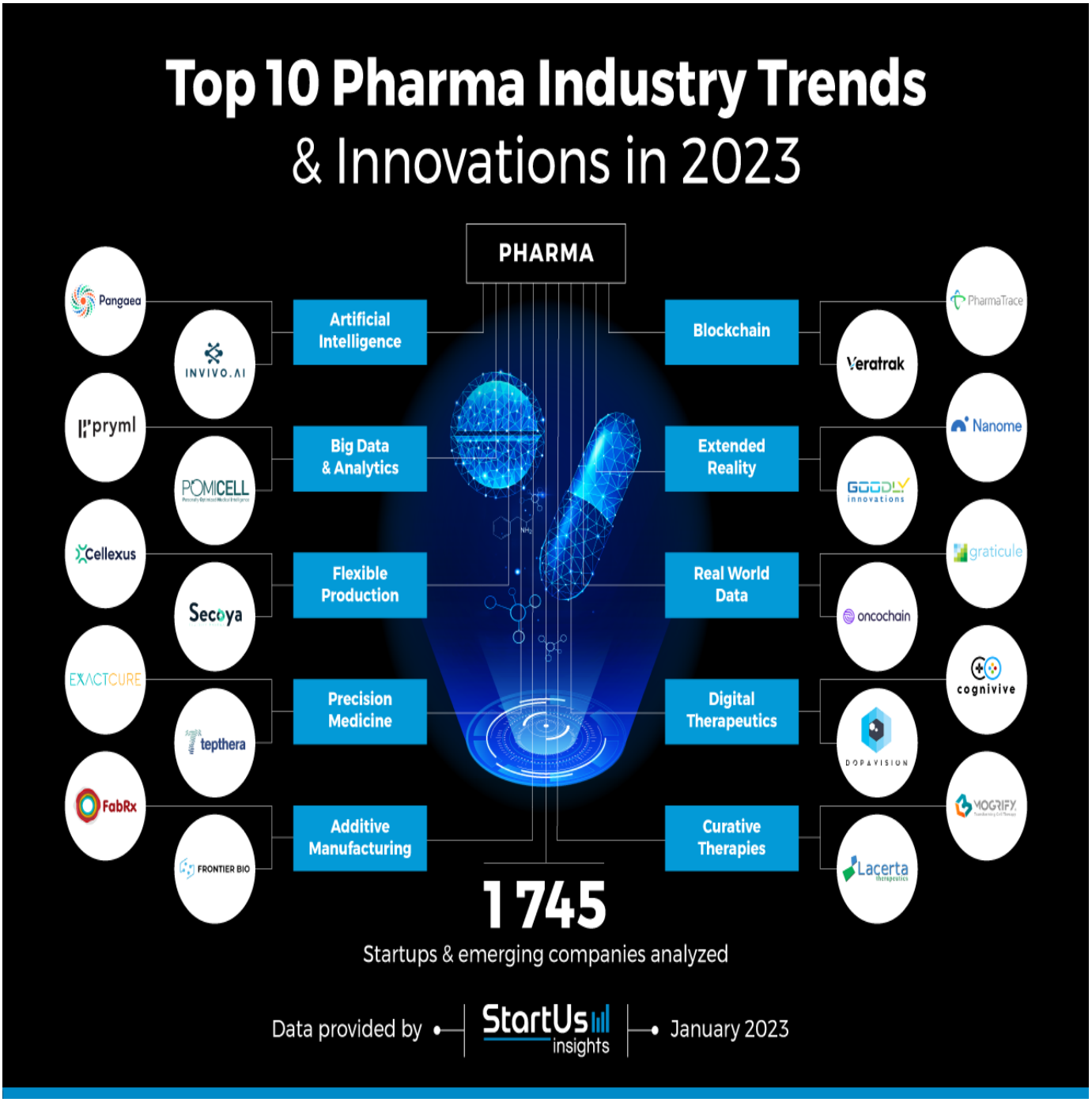
Vyjuvek is evenly applied to a wound once a week by a healthcare professional with the following precautions for patients and caregivers:

- **Avoid** direct contact with treated wounds and dressings of treated wounds for 24 hours following application. **Clean** any area that is accidentally exposed.
- **Wash** hands and wear protective gloves when changing wound dressings.
- **Disinfect** the bandages used for the first dressing with a viricidal agent, such as 70% isopropyl alcohol, 6% hydrogen peroxide, or <0.4% ammonium chloride, and dispose of them in a separate, sealed plastic bag in household waste.
- **Subsequent** used dressings and cleaning materials should be disposed of in sealed plastic bags in household waste.

References:

- *US Food and Drug Administration . FDA Approves First Topical Gene Therapy for Treatment of Wounds in Patients with Dystrophic Epidermolysis Bullosa. Available at: https://www.fda.gov/news-events/press-announcements/fda-approves-first-topical-gene-therapy-treatment-wounds-patients-dystrophic-epidermolysis-bullosa. Published on 19th may 2023. Accessed on 22th may 2023.*
- *Alicia Ault. FDA OKs First-Ever Topical Gene Therapy, for Rare Skin Disease. Available at: https://www.medscape.com/viewarticle/992226#vp_1. Published on 19th may 2023. Accessed on 22th may 2023.*

By: Bassant Maher, M.Sc.



FDA approves new treatment for common symptom of dry eye disease

The (FDA) has approved a drug to target the excessive tear evaporation associated with dry eye disease.

The drug, MIEBO (perfluorohexyloctane ophthalmic solution, formerly known as NOV03), is a semifluorinated alkane that works to reduce tear evaporation by forming a monolayer on the tear film.

MIEBO is the only FDA-approved treatment specifically targeting excessive tear evaporation, which affects 86% of people with dry eye disease, according to Bausch + Lomb, which developed the drug with its German partner, Novaliq GmbH.

Excessive evaporation of tears damages the ocular surface over time through inflammation and increased surface desiccation. The development and progression of dry eye disease (DED) often are associated with meibomian gland dysfunction (MGD), a condition that affects the oil glands on the eyelid. The glands produce oil that prevents the eye's water layer from evaporating too rapidly; when the glands are impaired, evaporation of tears increases.

MIEBO clinical data:

The FDA approval of MIEBOTM was based on results from two 57-day, multi-center, randomized, double-masked, saline-controlled studies, GOBI and MOJAVE, which enrolled a total of 1,217 patients with a history of (DED) and clinical signs of (MGD), a major cause of development and disease progression. An estimated 86% of people with DED have excessive tear evaporation whereby MGD is the major contributor. In the GOBI and MOJAVE phase 3 pivotal studies, MIEBO met both primary sign and symptoms efficacy endpoints.

Reported side effects:

The most common side effects with MIEBO were blurred vision and eye redness; both affected up to 3% of the participants. Patients are encouraged to report negative side effects of prescription drugs to the FDA. Visit: www.fda.gov/medwatch.

Important safety information:

- ◊ *Patients should remove contact lenses before using MIEBOTM and wait for at least 30 minutes before reinserting.*
- ◊ *It is important for patients to use MIEBO exactly as prescribed.*
- ◊ *It is not known if MIEBOTM is safe and effective in children under the age of 18.*

In 2019, Bausch + Lomb obtained an exclusive license for the commercialization and development of the drug in the United States and Canada. The drug is expected to be commercially available in the second half of this year, according to the company.

References:

- ◊ *FDA Approves New Treatment for Common Symptom of Dry Eye Disease. Available at: https://www.medscape.com/viewarticle/992296?src=. Accessed in May, 2022.*
- ◊ *Bausch + Lomb and Novaliq Announce FDA Approval of MIEBOTM (Perfluorohexyloctane Ophthalmic Solution) for the Treatment of the Signs and Symptoms of Dry Eye Disease. Available at: https://www.novaliq.com/press-releases/2023/05/19/bausch-lomb-and-novaliq-announce-fda-approval-of-miebotm-perfluorohexyloctane-ophthalmic-solution-for-the-treatment-of-the-signs-and-symptoms-of-dry-eye-disease/. Accessed in May, 2022.*

By: Marwa Elsayed, PGCPD.

Antibiotics use: Shorter is better

In prescribing antibiotics to patients, one of the most frequently debated points is... "What is the appropriate duration of use for this antibiotic?".

◊ The usual durations for using antibiotics range from 7 to 14 days. It is noteworthy that this period is based on the idea that a week is composed of 7 days, making the duration of use one to two weeks. However, how did one week become the standard unit of use for most antibiotics?.

◊ For the first time in 2008, Dr. Louis Rice published a scientific article in the Clinical Infectious Diseases Journal, which is the official journal of the Infectious Diseases Society of America with an impact factor of 20, about rational antibiotic administration in an era of antimicrobial resistance.

◊ In the article, Dr. Rice discussed the factors that increase antimicrobial resistance (AMR), and noted that: The most viable strategy for reducing antimicrobial selective pressure is to treat infections only for as long as is necessary. Shortening courses would not only benefit patients appropriately treated with narrow-spectrum antimicrobial agents but would also reduce exposure associated with patients treated inappropriately or patients given more antibiotics than they truly need. However, he mentioned that what may hinder the short-term use of antibiotics includes:

1- Doctor's preference for using antibiotics for a longer period, even after the patient's improvement, just to ensure that the patient will remain in good condition, based on the assumption that increasing the use of antibiotics will not harm the patient if it does not benefit them.

2- The lack of sufficient studies on the ideal duration of antibiotic use in different infectious diseases.

◊ But this was in 2008, and since then, many studies have been published on this topic since the attention was drawn to the significant role of increasing the duration of antibiotic use in AMR, to study the effect of prolonged use of antibiotics. In a multihospital cohort study conducted by Vaughn et al., in 2019 to examine predictors and outcomes associated with excess duration of antibiotic treatment. They reported that 67.8% of patients received excess antibiotic therapy and each excess day of treatment was associated with a 5% increase in the odds of antibiotic-associated adverse events.

Now, we will mention some studies that have compared the prolonged or short-term use of antibiotics in some types of bacterial infections:

- In a systematic review and meta-analysis conducted by Royer et al., in 2018, they included 19 RCTs comprising 2867 patients. They concluded that shorter courses of antibiotics can be safely utilized in hospitalized patients with common infections to achieve clinical and microbiologic resolution without adverse effects on mortality or recurrence.
- Also, Dinh et al., in 2021 reported that discontinuing β-lactam treatment after 3 days was non-inferior to 8 days of treatment.
- Moreover, Molina et al., in 2022 reported that 7-day treatment plan of infections by Enterobacterales achieved outcomes similar to those of 14-day plans.

- Change is scary, and medicine is a conservative profession but it is time for the medical community to support changing our old habits and help to transform how we use and protect the rapidly eroding societal trust that is effective antimicrobial therapy.
- Finally and not least, let our new slogan be when using antibiotics as stated by the famous JAMA journal in its article: ***"The New Antibiotic Mantra, Shorter is better"***

Infections for Which Short-Course Therapy Has Been Shown to Be Equivalent in Efficacy to Longer Therapy

	Treatment Days	
	Short	Long
Community-acquired pneumonia	3-5	7-10
Nosocomial pneumonia	≤8	10-15
Pyelonephritis	5-7	10-14
Intraabdominal infection	4	10
Acute exacerbation of chronic bronchitis and COPD	≤5	≥7
Acute bacterial sinusitis	5	10
Cellulitis	5-6	10
Chronic osteomyelitis	42	84

Spellberg B, JAMA Intern Med. 2016 ;176(9):1254-1255.

References:

- *Rice LB. The Maxwell Finland Lecture: for the duration-rational antibiotic administration in an era of antimicrobial resistance and clostridium difficile. Clin Infect Dis. 2008;46(4):491-496.*
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- *Spellberg B. The New Antibiotic Mantra-"Shorter Is Better". JAMA Intern Med. 2016;176(9):1254-1255.*
- *Hanretty AM, Gallagher JC. Shortened Courses of Antibiotics for Bacterial Infections: A Systematic Review of Randomized Controlled Trials. Pharmacotherapy. 2018;38(6):674-687.*

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Vision

The vision of Tanta University DPIC is to improve national healthcare service through provision of evidence-based, unbiased, patient oriented drug information services & adverse drug reporting system.

Mission

* Responding to drug inquiries related to the use of the drug and providing the health care professionals and patients with drug information related to the patient's care to achieve the optimal use of the drug in addition to the provision of other toxicological managing information.
* Educational activities to support the rational optimal use of drugs as well, supporting research activities.
* Continuous medical education and training courses in various fields of pharmacy for students, undergraduates, postgraduate students, and researchers.
* Issuing a Drug Information Bulletin periodically to take a look at medical & pharmaceutical news.
* Supporting the National Pharmaceutical Vigilance Program by following up and monitoring side effects and problems related to use of pharmaceutical preparations within regional hospitals.
* Contributing to the establishment of various treatment protocols and prescription booklet services in regional hospitals.

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