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Inside this issue:

U.S. FDA grants emergency use authorization for Novavax COVID-19 vaccine

Novavax, Inc. a biotechnology company dedicated to developing and commercializing next-generation vaccines for serious infectious diseases, announced that the Novavax COVID-19 vaccine, adjuvanted (NVX-CoV2373) has received expanded emergency use authorization (EUA) from the U.S. Food and Drug Administration (FDA) to provide a two-dose primary series for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS -CoV-2) in adolescents aged 12 through 17.

The FDA EUA decision was based on data from the ongoing pediatric expansion of the Phase 3 PREVENT-19 trial of 2,247 adolescents aged 12 through 17 years across 75 sites in the U.S., to evaluate the safety and effectiveness of the Novavax COVID-19 vaccine, adjuvanted. In pediatric expansion, the vaccine achieved its primary efficacy endpoint with clinical efficacy of 78.29% (95% CI: 37.55%, 92.45%) overall at a time when the Delta variant was the predominant circulating SARS-CoV-2 strain in the U.S. The efficacy analysis was supported by assessment of antibody titers that were shown to be higher in adolescents than in young adults.

Clinical data:

Safety data from the pediatric expansion showed the vaccine to be generally well-tolerated. Serious and severe adverse reactions (AR) were low in number and balanced between vaccine and placebo groups, and not considered related to the vaccine. Local and systemic reactogenicity was generally lower than or similar to adults, after the first and second dose. No new safety signal was observed through the placebo-controlled portion of the study. Among participants 12 through 17 years of age, identified ARs following administration of any dose of the Novavax COVID-19 vaccine, adjuvanted were injection site pain/tenderness (75.0%), headache (56.9%), fatigue/malaise (57.9%), muscle pain (49.0%), nausea/vomiting (19.9%), joint pain (16.2%), fever (16.9%), injection site swelling (8.0%), and injection site redness (7.5%). Most were mild-to-moderate in severity and lasted less than two days.

Contraindications:

Do not administer the Novavax COVID-19 Vaccine, adjuvanted to individuals with a known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the Novavax COVID-19 vaccine, adjuvanted.

Warnings and precautions:

Management of acute allergic reactions: An acute anaphylactic reaction occurs following administration of the Novavax COVID-19 vaccine, adjuvanted. Appropriate medical treatment to manage immediate allergic reactions must be immediately available in the event according to the Centers for Disease Control and Prevention (CDC) guidelines.

Myocarditis and pericarditis:

Clinical trials data provide evidence for increased risks of myocarditis and pericarditis following administration of the Novavax COVID-19 vaccine, adjvanted.

Syncope (fainting):

May occur in association with administration of injectable vaccines. Procedures should be in place to avoid injury from fainting.

Altered immunocompetence:

Immuno-compromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the Novavax COVID-19 vaccine, adjuvanted.

Limitations of vaccine effectiveness:

The Novavax COVID-19 vaccine adjuvanted may not protect all vaccine recipients. Additional adverse reactions, some of which may be serious, may become apparent with more widespread use of the Novavax COVID-19 vaccine, adjuvanted.

Reporting adverse events and vaccine administration errors:

The vaccination provider enrolled in the federal COVID-19 Vaccination Program is responsible for mandatory reporting of the following to the Vaccine Adverse Event Reporting System (VAERS):

- Vaccine administration errors whether or not associated with an adverse event,
- Serious adverse events (irrespective of attribution to vaccination),
- Cases of Multisystem Inflammatory Syndrome (MIS), in adults and children, and cases of COVID-19 that results in hospitalization or death.

The reports should include the words "Novavax COVID-19 vaccine, adjuvanted EUA" in the description section of the report.

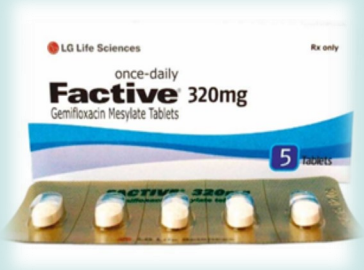
References:

- *U.S. FDA Grants Emergency Use Authorization for Novavax COVID-19 Vaccine, Adjuvanted for Adolescents Aged 12 Through 17. Available at: https://www.drugs.com/clinical_trials/u-s-fda-grants-emergency-authorization-novavax-covid-19-vaccine-adjuvanted-adolescents-aged-12-20326.html. Accessed in August, 2022.*
- *Novavax Nuvaxovid™ COVID-19 Vaccine Granted Expanded Provisional Approval in New Zealand for Adolescents Aged 12 Through 17. Available at: https://www.nasdaq.com/press-release/novavax-nuvaxovidtm-covid-19-vaccine-granted-expanded-provisional-approval-in-new-0. Accessed in August, 2022.*

By: Marwa Elsayed, PGCPD.

Withdrawal of gemifloxacin
The story behind

Gemifloxacin is a synthetic broad-spectrum antibacterial agent that belongs to the fluoroquinolone class of antibiotics and is available in an oral formulation as the mesylate salt. Gemifloxacin drug substance was originally discovered by LG Life Sciences Ltd and subsequently developed by SmithKline Beecham (later GSK) and Oscient Pharmaceutical Co. for the treatment of urinary and respiratory tract bacterial infections. Gemifloxacin which was approved by FDA in April 2003 (Factive®, Oscient Pharmaceutical Co.), has been launched in the U.S. in September 2004.



⇒ Its currently approved indications in the US include:

- Acute exacerbation of chronic bronchitis (AECB).
- Community acquired pneumonia (CAP) of mild to moderate severity including multi-drug resistant strains *Streptococcus pneumoniae* (MDRSP).

⇒ The recommended dose in both indications is one 320 mg tablet administered once daily for 5 days with the possibility to extend treatment to 7 days in cases of CAP due to known or suspected MDRSP.

In late 2006, Menarini International Operations Luxembourg acquired exclusive rights to register gemifloxacin in all the European countries. In 2009, The European Medicines Agency (EMA) has been formally notified by Menarini International Operations Luxembourg of its decision to withdraw its application for a centralized marketing authorization for the medicine Factive® (gemifloxacin), 320 mg film-coated tablets. The application was withdrawn because the Committee for Medicinal Products for Human Use (CHMP) of the EMA concluded that the evidence presented did not allow the committee to determine that Factive® had a favorable benefit-risk balance at the time.

CHMP benefit-risk assessment:

A-Claimed benefits:

Gemifloxacin showed a good in-vitro activity against most of the important bacteria causing community acquired respiratory infections. But for the two proposed indications, they found that:

- **Community acquired pneumonia:** The data provided by the applicant showed that five-day treatment is not enough, and seven-day treatment is needed for mild to moderate CAP.

- **Acute exacerbation of chronic bronchitis**: This indication is not supported due to the lack of superiority studies and deficiencies of the conducted studies.

B-Risks:

- The most common adverse effect of gemifloxacin is rash. Rash is less common with 5 days treatment than with 7 days treatment but since five-day gemifloxacin is inadequate for treatment of CAP, the frequency of rashes and of other adverse effects associated with seven days therapy must be used to assess benefit-risk.
- Gemifloxacin is a more potent mutagenic than other fluoroquinolones and appears to provide only a lower margin of safety than cipro- or moxifloxacin for therapeutic treatment.
- The use of lower chain alcohols with alkyl mesylate (product excipient) during the synthesis of gemifloxacin mesylate can lead to the formation of the potentially genotoxic alkyl mesylates and it is seen as a major risk to the quality of the product.

Balance:

The risk-benefit relationship for use of 7 days gemifloxacin to treat mild to moderate CAP is not considered to be favorable. The risk-benefit relationship for 5 days gemifloxacin to treat AECB cannot be considered favorable without a demonstration of superiority against placebo or against an active comparator.

Conclusion: The two requested indications of gemifloxacin were not approved by EMA's CHMP.

In 2022, The Egyptian Drug Authority (EDA) took a decision to refuse to register any new gemifloxacin generics and withdraw its all products in the Egyptian market for the same reasons as EMA and due to the availability of safer fluoroquinolones antibiotics.

References:

- *European Medicines Agency Pre-authorisation Evaluation of Medicines for Human Use Procedure No. EMEA/H/C/995. Available at: https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/european-medicines-agency-pre-authorisation-procedural-advice-users-centralised-procedure_en-0.pdf. Accessed in August, 2022.*
- *Iannini P. B. (2007). The safety profile of moxifloxacin and other fluoroquinolones in special patient populations. Current medical research and opinion, 23(6), 1403–1413.*

By: Mohamed K. Talaat, PharmD.

A promising novel gene therapy for hemophilia B significantly reduces bleeding, a Phase 1-2 clinical trial shows

In a new study published in the New England Journal of Medicine, researchers from University College London, Royal Free Hospital, and Freeline Therapeutics reported that the investigational gene therapy FLT180a can significantly reduce the bleeding risk in hemophilia B patients with a single gene therapy injection. Hemophilia B is an inherited, X-linked, recessive disorder that results in deficiency of functional plasma coagulation factor IX which leads to bleeding and hemorrhage. Current treatments of hemophilia B necessitates that hemophilia B patients injects themselves regularly, usually weekly, with recombinant Factor IX for life.

⇒ The study reported that normal factor IX levels can be achieved in patients with severe or moderately severe hemophilia B with the use of relatively low vector doses of FLT180a. FLT180a is a liver-directed, adeno-associated virus (AAV) gene therapy designed to normalize levels of the factor IX protein that is needed for coagulation. AAV gene therapy delivers a functional copy of this gene directly to patient tissues to compensate for one that is not working properly. It leads to the synthesis of factor IX proteins and a one-time gene therapy infusion can achieve long-lasting effects, the authors of study said.

⇒ The trial was a multicenter, open-label, phase 1-2 trial, and it involved ten male patients with severe or moderately severe hemophilia B receiving varying doses FLT180a to assess its safety and efficacy. After 26 weeks, patients were enrolled in a long-term follow-up study for 15 years. The primary end points were safety and efficacy, as assessed by factor IX levels at week 26.

⇒ Concerning the gene therapy's efficacy, the results showed that the treatment led to a sustained increase in Factor IX protein production, which resulted in less excessive bleeding with no longer need for required weekly injections of Factor IX protein. These results reported in all study patients except one who required a return to factor IX prophylaxis due to a failure in the immunosuppression regimen caused by a delay in the recognition of an immune response at approximately 22 weeks after treatment, the authors report.

⇒ However, immunosuppression was needed to prevent the patients' bodies from rejecting the vector gene therapy. Immunosuppression consisted of administering glucocorticoids with or without tacrolimus.

The therapy was generally well tolerated, with no infusion reactions or discontinuations of infusions. As of the study cutoff, no inhibitors of factor IX were detected.

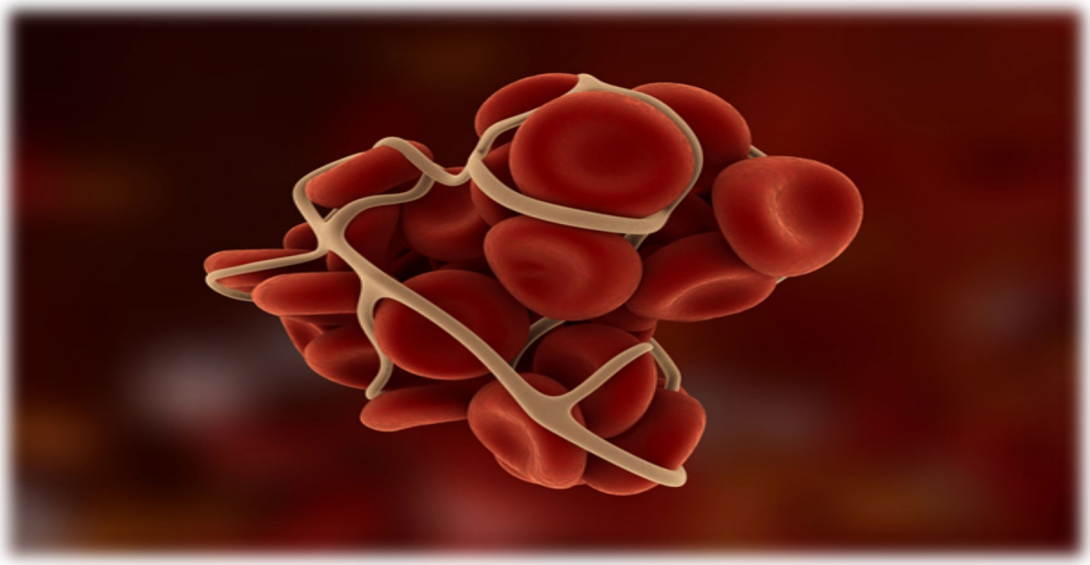
Reported adverse effects:

Approximately 10% were related to FLT180a and 24% to immunosuppression. Increases in liver aminotransferase levels were the most common FLT180a-related adverse events, with late increases in aminotransferase levels were reported among patients who had received prolonged tacrolimus beyond the tapering of glucocorticoid treatment. A serious adverse event of arteriovenous fistula thrombosis occurred in the patient with high factor IX levels.

The authors noted in the limitations of the study that further study is needed to understand FLT180a dose and immunosuppression regime, what is the best way to monitor aminotransferase levels in patients receiving gene therapy for hemophilia patients, when to intervene to treat elevations in aminotransferase levels.

References:

- *Phase 1–2 Trial of AAVS3 Gene Therapy in Patients with Hemophilia B Abstract at New England journal of Medicine. Available at: https://www.nejm.org/doi/full/10.1056/NEJMoa2119913?query=featured_home. Accessed in August, 2022.*
- *No More Injections After One-Off Gene Therapy in Hemophilia B at Medscape.com: Available at: https://www.medscape.com/viewarticle/977751#vp_2. Accessed in August, 2022*
- *Gene therapy reduces bleeding in haemophilia B at the British Society of Haemophilia. Available at: https://b-s-h.org.uk/about-us/news/gene-therapy-reduces-bleeding-in-haemophilia-b/. Accessed in August, 2022.*



By: Amr Noweir, B.Sc.

Contact us

Facebook: Drug and Poison Information Center-Faculty of Pharmacy-Tanta

Hotline: 090071020

Phone: 040/3331577-333600711

Email: Tanta_DPIC@pharm.tanta.edu.eg

We are on the web

https://pha.tanta.edu.eg/units/Drug%20Information/Default.aspx

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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