EGYPTIAN DRUG AUTHORITY

هيئة الدواء المصرية

The Egyptian Pharmaceutical Vigilance center

مركز اليقظة الصيدلية المصري

IN THIS ISSUE

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EPVC Mission

Pharmaceutical Vigilance administration is the way through which the processes for authorizing, regulating, monitoring and evaluating the safety of any pharmaceutical product or medical device take place, in addition to disseminating any safety information for public health programs, healthcare professionals, and the Egyptian citizen.

The Pharmaceutical vigilance administration is an integral part of the Central Administration of Pharmaceutical Care that works on the enhancement of the pharmaceutical services to guarantee safe and effective use of medications in Egypt, under the patronage of the Egyptian Drug Authority.

Newsletter

June 2025

Volume 19 Issue 6

Safety Notification: Rare but severe itching after stopping long-term use of oral allergy medicines containing cetirizine or levocetirizine

The Regulatory Authority in US is warning that patients stopping the oral allergy medicines cetirizine or levocetirizine after long-term use may experience rare but severe itching.

These medicines are available in prescription and over-the-counter (OTC) forms. The itching, also called pruritus, has been reported in patients who used these medicines daily, typically for at least a few months and often for years. Patients did not experience itching before starting the medicines. Reported cases were rare but sometimes serious, with patients experiencing widespread, severe itching that required medical intervention. As a result, we are revising the prescription cetirizine and levocetirizine prescribing information to include a new warning about this risk. We will subsequently request that manufacturers add a warning about pruritus to the Drug Facts Label of the OTC versions.

What is cetirizine and levocetirizine?

Cetirizine and levocetirizine are antihistamines that block a molecule called histamine that the body releases during allergic reactions. Both medicines are approved to treat seasonal allergies, called seasonal allergic rhinitis, in adults and children 2 years and older. The medicines are also approved to treat year-round allergies, called perennial allergic rhinitis, and chronic hives, called chronic idiopathic urticaria, in patients 6 months and older.

What should patients and parents/caregivers do?

Patients should contact your health care professional if you develop severe itching after stopping prescription or OTC cetirizine or levocetirizine. Patients should know that itching typically occurred within a few days of stopping these medicines after daily use for a few months to years. Individuals planning on long-term use of cetirizine or levocetirizine, especially for more than a few months, should discuss the benefits and risks with your health care professional, who can provide advice based on your

personal needs.

What should health care professionals do?

Health care professionals should discuss the risk of pruritus after stopping cetirizine or levocetirizine with patients when prescribing or recommending these medicines, especially if planned for chronic use, and with those who indicate they are using OTC versions. Encourage patients to contact you if they experience severe itching after stopping cetirizine or levocetirizine. Effective treatments for pruritus have not been evaluated. However, symptoms resolved in most patients who restarted the medicine and in some who tapered off the medicine after restarting it.

Additional Information for Health Care Professionals

• FDA is warning that patients discontinuing the antihistamine allergy medicines cetirizine or levocetirizine after long-term use may experience severe pruritus. This has been reported in patients using the medicines daily, typically for at least a few months and often years. Patients did not experience itching before starting the medicines. Pruritus developed within a few days after discontinuing long-term daily use of both prescription or over-the-counter (OTC) cetirizine or levocetirizine medicines.

• Encourage patients to contact you patients if they experience severe itching after stopping cetirizine or levocetirizine.

• Effective treatments for pruritus have not been evaluated. Symptoms resolved in most patients who restarted the medicine and in some patients who tapered off the medicine after restarting it.

• When prescribing or recommending these medicines, especially if planned for chronic use, discuss with patients the risk of pruritus after stopping cetirizine or levocetirizine. This risk should also be discussed with patients who indicate they are taking OTC cetirizine or

levocetirizine.

• FDA is adding a warning about the risk of pruritus after stopping long-term use of prescription cetirizine or levocetirizine to the prescribing information for these medicines.

• We will also request that manufacturers add a warning about pruritus after stopping use of cetirizine and levocetirizine to the Drug Facts Label of the OTC versions. We will follow up when

additional information becomes available

References

1. FDA: (click here)

Safety Reminder: Importance of Rabies Vaccination and Associated Adverse Events

Background:

Rabies is a viral zoonotic disease that affects the central nervous system and is almost invariably fatal once clinical symptoms appear. However, rabies is entirely preventable through prompt and appropriate post-exposure prophylaxis (PEP) and, where applicable, pre-exposure vaccination.

Importance of Vaccination:

Rabies vaccination is a critical public health intervention.

Pre-exposure prophylaxis is recommended for individuals at continual, frequent, or increased risk of exposure (e.g., veterinarians, animal handlers, laboratory personnel, travelers to endemic areas).

Post-exposure prophylaxis, including timely administration of rabies vaccine and, when indicated, rabies immunoglobulin (RIG), is essential to prevent disease progression following suspected exposure.

Vaccination Schedule:

Pre-exposure: 3 doses administered intramuscularly on Days 0, 7, and 21 or 28.

Post-exposure (unvaccinated individuals): RIG on Day 0, with vaccine administered on Days 0, 3, 7, and 14.

Post-exposure (previously vaccinated): 2 vaccine doses on Days 0 and 3; RIG not required.

Safety and Adverse Events:

While rabies vaccines are generally safe and effective, healthcare professionals and recipients should be informed of potential adverse events. Monitoring and prompt management of adverse events following immunization (AEFIs) are critical components of pharmacovigilance.

Common (Mild) Reactions:

Local: Injection site pain, erythema, swelling, or pruritus.

Systemic: Fever, headache, malaise, myalgia, dizziness.

Uncommon to Rare (Moderate to Severe) Reactions:

Gastrointestinal: Nausea, vomiting.

Neurological: Paresthesia, neuropathy (very rare).

Allergic: Urticaria, rash.

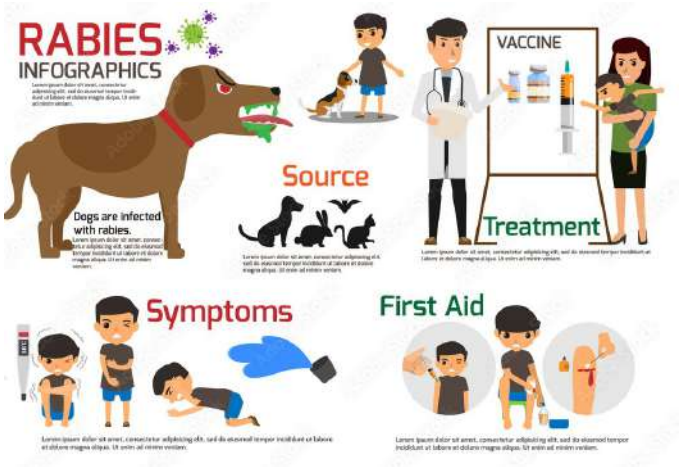
Serious adverse events:

Anaphylaxis: Requires immediate medical intervention; extremely rare.

Guillain-Barré Syndrome (GBS): Rare neurological event;

Recommendations for Healthcare Providers (from the national committee for causality assessment of AEFIs :

1. Observe all vaccine recipients for a minimum of 30 minutes post-vaccination.
2. Ensure full adherence to the recommended dosing schedule to achieve optimal protection.
3. In case of adverse events, pre and post symptomatic treatment should be maintained. However all doses should be completed
4. Maintain cold chain requirements for all vaccine storage and handling.
5. Promptly report any suspected AEFIs to the national pharmacovigilance center.



Conclusion:

Rabies remains a public health threat with devastating outcomes if not managed appropriately. Rabies vaccination is a safe and indispensable tool in the prevention of this fatal disease. Health professionals must continue to advocate for timely vaccination, maintain vigilance in adverse event monitoring, and ensure accurate reporting.

References

1. ***WHO:*** (click here)
2. ***Centers for Disease Control and Prevention (CDC :*** (click here)
3. ***FDA:*** (click here)
4. ***PubMed :*** (click here)

This topic is a participation from the expanded program of immunization

Paracetamol induced hepatotoxicity

1. Reason for publishing:

On May 29, 2025, the Regional Center of Pharmacovigilance in Cairo received a report about a 46-year-old male patient with no significant medical or drug history. He was taking a daily dose of paracetamol ranging from 4 to 5 grams for joint pain (multiple trade names), with the possibility of increasing the dose based on his pain levels.

After four months of chronic medication administration, he developed jaundice and elevated liver enzyme levels. These reactions were considered serious, with liver function tests reaching 24000 U/L. The reactions resolved after the withdrawal of the suspected medications and appropriate corrective treatment.

2. Background:

Paracetamol is an analgesic and antipyretic drug that is used to temporarily relieve mild-to-moderate pain and fever. It can be used as a standalone treatment for mild pain or in combination with other analgesics for more severe pain.

Mechanism of action: According to its FDA labeling, acetaminophen's exact mechanism of action has not been fully established - despite this, it is often categorized alongside NSAIDs (nonsteroidal anti-inflammatory drugs) due to its ability to inhibit the cyclooxygenase (COX) pathways. It is thought to exert central actions which ultimately lead to the alleviation of pain symptoms.

Hepatotoxicity (Liver toxicity)

Liver toxicity, also known as drug-induced liver injury (DILI) or toxic hepatitis, is a condition where the liver is damaged by exposure to certain substances, including medications, herbal remedies, or toxins. It can manifest in various ways, from mild, asymptomatic liver test abnormalities to acute liver failure. Acute hepatotoxicity may result from intentional or unintentional overdose in adult and pediatric patients. In pediatric patients, unintentional overdose can be a result of accidental ingestion, supratherapeutic dosing, more frequent administration than recommended, and use of multiple acetaminophen-containing products; hepatotoxicity has also been rarely reported with recommended dosages.Spontaneous resolution occurs with or without treatment in ~65% of cases; although, some cases may progress to acute liver failure leading to liver transplantation or death; a mortality rate of ~0.4% has been reported.

Mechanism: Dose-related; direct toxic effect through formation of toxic metabolite, N-acetyl-p-benzoquinoneimine (NAPQI) that binds to cellular proteins, including mitochondrial proteins.

Toxic free radicals, including peroxynitrite, may also cause damage inside the mitochondria.

Onset: Rapid. Nonspecific symptoms (eg, nausea, vomiting, abdominal pain) may occur within the first 24 hours post-ingestion, followed by resolution of nonspecific symptoms and initial increases in serum AST and ALT within 24 to 72 hours. Marked increases in AST and ALT occur within 72 to 96 hours post-ingestion, along with a return of nonspecific symptoms and additional symptoms (eg, jaundice, encephalopathy, coagulopathy, lactic acidosis).

Risk factors:

Dose:

Pediatric: Toxicity is likely to occur with single ingestions >150 mg/kg or when the maximum daily acetaminophen dose is >75 mg/kg/day (maximum of 5 daily doses) up to 4,000 mg/day from all sources.

Adult: Toxicity is likely to occur with single ingestions >250 mg/kg or >12,000 mg over a 24-hour period. Asymptomatic elevation of ALT may occur following maximal therapeutic doses of acetaminophen (4,000 mg/day) for ≥4 days.

Multiple acetaminophen-containing products:

An unintentional overdose may occur in adult and pediatric patients who take multiple acetaminophen or acetaminophen-containing combination products.

Chronic alcohol ingestion:

Patients with chronic alcohol use disorder who take therapeutic doses of acetaminophen are NOT at an increased risk of hepatotoxicity. In contrast, patients with chronic alcohol use disorder who ingest repeated supratherapeutic doses of acetaminophen are at an increased risk for hepatotoxicity.

Concomitant medications and herbal products:

Although use of products that induce CYP2E1 enzymes (eg, carbamazepine, phenobarbital, phenytoin, isoniazid, rifampin) have been postulated to predispose to acetaminophen hepatotoxicity by enhanced production of NAPQI, there is little evidence, aside from case reports, that drug interactions increase the risk of liver injury.

Nutritional status: Malnutrition and fasting may increase the risk.

Age: Pediatric patients are less susceptible, whereas elderly patients are at a higher risk.

Paracetamol induced hepatotoxicity

Delay to treatment with N-acetylcysteine (NAC): Most patients with acetaminophen overdose who receive treatment with NAC within 8 hours of ingestion will not develop hepatotoxicity.

Labeled information:

According to Paracetamol Summary of product Characteristics (SmPC) it was stated under section (4.9 Overdose) that: "Excessive ingestion of high doses of paracetamol can lead to signs of intoxication with a latency of 24 to 48 hours. Patients may develop hepatic dysfunction, hepatocellular necrosis and hepatic coma (which can be fatal).

The following symptoms of overdose with paracetamol may occur:

During phase 1, which lasts between 12 and 14 hours after overdose, patients may often experience nausea, vomiting, sweating, sleepiness and discomfort.

During phase 2, after 24 to 48 hours, there is a subjective improvement in the symptoms, but the first signs of hepatic injury appear: mild abdominal pain, hepatomegaly, increased levels of transaminases and bilirubin, prolonged prothrombin time and oliguria.

During phase 3, after 48 hours, levels of transaminases reach their maximum, jaundice, coagulopathy, hypoglycemia and progression to hepatic coma".

Paracetamol related DHPC:

According to DHPC regarding Paracetamol – Reminder of proper use and risks associated with

overdose published by EDA in June 2025:

In adults, significant toxicities can be expected from a cumulative intake of 10 grams, in

children from 150 mg/kg. In the presence of risk factors, toxicity can already be observed

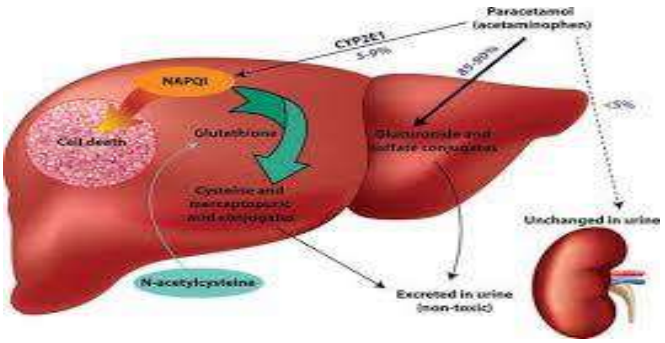
with lower doses, as well as in the case of chronic use of the usual maximum daily dose (4

grams). Any suspicion of overdose requires immediate medical attention.

Recommendations

Read the medication instructions carefully and follow your doctor's prescription and/or the recommendations from his pharmacist.

Discuss with them the dangers of misuse of medications which could lead to irreversible damage, in some cases.



Risk of hepatotoxicity is higher in patients taking chronic high dose, or use of more than one acetaminophen-containing product

Paracetamol may be taken every 4 to 6 hours. Leave at least 4 hours between doses and Do not take more than the recommended dose

Do not take more than four doses in 24 hours.

The medicinal product should be used with caution (dose adjustment, intervals of administration adjustment or under medical supervision) particularly in patients with hepatocellular disorders, renal insufficiency and gilbert syndrome (hepatic inability to uptake unconjugated bilirubin from blood due to hepatic insufficiency), chronic dehydration, severe hemolytic anemia and chronic malnutrition.

Caution during administration of paracetamol with drugs that induces hepatic enzymes and long term oral anti-coagulants that could cause hepatic injury.

References

1. ***Paracetamol SmPC*** (click here).
2. ***Paracetamol Info:*** (click here).
3. ***NCBI Drug induced hepatotoxicity*** (click here).
4. ***Drug-Induced Hepatotoxicity*** (click here).
5. ***EDA DHPC Paracetamol – Reminder of proper use and risks associated with overdose*** (click here).
6. ***Acetaminophen (paracetamol): Drug information*** (click here).

Egyptian Pharmaceutical Vigilance Center (EPVC) VigiFlow expansion project:

EPVC The Egyptian Pharmaceutical Vigilance Centre (EPVC) expresses gratitude to the Ministry of Health and Population (MoHP) in collaboration with the National Tuberculosis Control Program, General Administration of Chest Diseases and General Authority for Health Insurance for enhancing pharmacovigilance practices among the affiliated organizations.

In line with this, EPVC was pleased to deliver a training program over days for qualifying all healthcare providers for entry into the national database VigiFlow, and within the framework of national efforts to achieve excellence and expansion in the field of pharmacovigilance by 2025 to support focal points at various healthcare institutions.

First: EPVC team provided 3 lectures and 2 workshops for 90 pharmacists and nurses working in chest centers inside Cairo, Qalyubia and Dakahlia on pharmacovigilance principles and how to record the adverse drug reactions of TB medications on VigiFlow database that served as a starting point for activating the role of healthcare providers as an integrated team in recording adverse effects that will be followed by a comprehensive training plan for all governorates.

Second: EPVC team provided 5 hybrid lectures for 25 pharmacists working in General Administration of Chest Diseases and healthcare institutions affiliated with the Health Insurance Organization (HIO) to expand the participation of institutions, hospitals, and centers into VigiFlow entry.Additionally, EPVC extends its sincere appreciation to all organizations that have collaborated with us in the expansion of the VigiFlow system. We commend their ongoing commitment to enhancing the reporting of monthly cases continuously within the national database. Their dedication is instrumental in strengthening pharmacovigilance efforts across the country.

In particular, EPVC proudly recognizes the following organizations for their outstanding ICSR entry rate on VigiFlow during the month of May:

- Giza Health Directorate
- Cairo Health Directorate
- Menofia Health Directorate
- Nasser Institute

EPVC Tips

On Pharmacovigilance

Restriction of injection in an inflamed tissue

Injecting medicine or vaccines into inflamed tissue is generally restricted or avoided due to several important reasons:

1. Poor Absorption: Inflamed tissue often has impaired blood flow, which can lead to poor drug absorption and reduced therapeutic effect.
2. Tissue Damage: Inflammation makes tissue more fragile and vulnerable, increasing the risk of tissue necrosis or damage.
3. Spread of Infection: If the inflammation is due to infection, injecting into the area could introduce pathogens deeper, worsening the infection or spreading it systemically.
4. Increased Pain: Inflamed areas are highly sensitive, and injection can cause severe pain and discomfort.
5. Unreliable Drug Distribution: Inflammation can alter the local pH and enzyme activity, potentially affecting drug stability and action.
6. Clinical Recommendation:
7. Always choose a non-inflamed, healthy site for injections (especially intramuscular or subcutaneous).
8. If inflammation is present at a commonly used site (e.g., deltoid or gluteus), stop all routes of injection and refer to a dermatologist

References

1. WHO: (click here).

Visit EDA website to find all medicine- related news, updates and alerts *Click here*

You will find all EPVC Newsletters and DHPCs here

You will also find all alerts regarding counterfeited and falsified products released by Central Administration of Operations *here*

The Egyptian Pharmaceutical Vigilance center

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One report counts

A call for reporting

Please remember that you can report safety information of medicines to EPVC using the following communication information:

What is Pharmacovigilance

Pharmacovigilance (PV) is defined as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug- related problem.

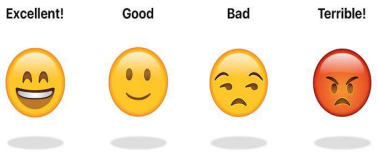
What is the Egyptian Pharmaceutical Vigilance Center?

With the increasing demand for patient's safety which is becoming more stringent, . The Egyptian Pharmaceutical Vigilance Center was established to be responsible for the safety monitoring of the pharmaceutical products throughout its lifecycle and it is the regulatory authority regarding Pharmacovigilance and its applications .

EPVC monitors the safety of all types of pharmaceutical products, including human medicines, biological products, supplements, cosmetics, veterinary medicines, medical devices, Biocides and pesticides

Participate with us

We invite you to take a quick survey on how much our communication with you is effective
We value your feedback! Help us enhance our communication by taking a quick survey. Your insights are crucial in ensuring we meet your expectations.
Survey Link: (Click Here)



Thank you for your valuable input

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