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

July 2026

Volume 20 Issue 7

Use Label Update / Safety Communication: ACE Inhibitors and Risk of Delayed-Onset Angioedema

The regulatory authority in UK issued a Drug Safety Update on 16 June 2026 highlighting an important safety concern regarding ACE inhibitors (Angiotensin-Converting Enzyme inhibitors). The update emphasizes the critical distinction between two types of angioedema associated with these medicines — bradykinin-mediated and histamine-mediated — as treatment strategies differ significantly between the two types. Failure to recognize this distinction may result in ineffective treatment and potentially fatal outcomes.

ACE inhibitors are among the most widely prescribed medicines globally and in Egypt, used for the management of hypertension, heart failure, diabetic nephropathy, and chronic kidney disease. Commonly used agents include enalapril, lisinopril, captopril, ramipril, and perindopril.

Background

Angioedema is a sudden, localized swelling of the deep dermis, subcutaneous tissue, or mucous membranes. When it affects the tongue, lips, throat, or larynx, it constitutes a medical emergency due to the risk of life-threatening airway obstruction.

ACE inhibitor-induced angioedema is estimated to occur in 0.1 –0.7% of patients treated with these medicines. However, its clinical significance is disproportionate to its frequency due to the potential for fatal airway compromise.

Two distinct pathophysiological mechanisms exist:

1. Histamine-mediated Angioedema

•Occurs as part of a classical allergic/anaphylactic reaction

•Usually accompanied by urticaria, pruritus, and other anaphylactic features

•Responds well to standard treatment: adrenaline, antihistamines, and corticosteroids

2. Bradykinin-mediated Angioedema

The mechanism responsible for ACE inhibitors-induced angioedema

•ACE inhibitors block the degradation of bradykinin, leading to its accumulation in tissues

•Bradykinin causes vasodilation and increased vascular permeability, resulting in localized oedema

•Critically: Does not reliably respond to standard anaphylaxis treatment including adrenaline, antihistamines, or corticosteroids

•Usually occurs WITHOUT urticaria or pruritus

•May present after prolonged use — MHRA data confirms approximately 50% of cases occurred 30 days or more after treatment initiation, and cases have been reported after years of uneventful therapy

Fatal cases, though rare, have been reported and involved airway compromise

The following medicines associated with ACE inhibitor-induced bradykinin-mediated angioedema:

Enalapril, Lisinopril, Captopril, Ramipril, Perindopril,

Management

1. Recognition

Healthcare professionals must consider ACE inhibitor-induced bradykinin-mediated angioedema in any patient presenting with angioedema who is currently taking — or has recently stopped — an ACE inhibitor, even if the patient has been on the medicine for a long period without prior problems.

Key distinguishing features suggesting bradykinin-mediated angioedema:

•Absence of urticaria or pruritus

•No other features of anaphylaxis

•Patient is on ACE inhibitor therapy

•Delayed onset (days, weeks, months, or even years after starting treatment)

2. Immediate Action

•Secure the airway as the first priority

•Do NOT rely on adrenaline, antihistamines, or corticosteroids as primary treatment — these are ineffective for bradykinin-mediated angioedema

•Discontinue the ACE inhibitor permanently

•Refer to specialist care (ear, nose and throat / anaesthesia / intensive care) urgently if airway is compromised

3. Long-term Management

•The ACE inhibitor must be permanently discontinued in any patient who develops angioedema

•If antihypertensive therapy must be continued, switch to an alternative class such as angiotensin receptor blockers (ARBs) — noting that cross-reactivity with ARBs is possible but rare

Document the reaction clearly in the patient's medical record

•Inform the patient of the risk and advise them to disclose this history to any future healthcare providers

4. Label Update

MHRA is currently implementing updates to the Summary of Product Characteristics (SmPC) and Patient Information Leaflets (PIL) for all ACE inhibitor products to strengthen warnings regarding delayed-onset angioedema and the potential ineffectiveness of standard anaphylaxis treatments.

References

1. ***MHRA :*** *Click here*
2. ***NIH:*** *Click here*
3. ***NIH:*** *Click here*
4. ***Pubmed :*** *Click here*

Local Case Safety Report: Medication Error and Potential drug Interaction Leading to Neuropsychiatric Manifestations in an Alzheimer's Disease Patient

The Cairo Regional Pharmacovigilance Center received an Individual Case Safety Report

(ICSR) concerning suspected adverse drug reactions in a 65-year-old female patient with a medical history of Alzheimer's disease and no reported previous medications

The patient had been receiving memantine hydrochloride 10 mg once daily and donepezil hydrochloride 10 mg once daily since February 2026 for the management of Alzheimer's disease.

On 30 March 2026, quetiapine fumarate 25 mg once daily at bedtime was prescribed for depression. The following day, the patient developed delusion and emotional distress. The case also involved medication error due to inappropriate memantine titration and a potential drug interaction between donepezil and quetiapine, which was associated with a reported **reduced therapeutic response** . The patient had not recovered at the time of reporting as the drugs doses were not changed.

Background:

Delusion

- Delusions are false beliefs based on incorrect inference about external reality that persist despite the evidence to the contrary; these beliefs are not ordinarily accepted by other members of the person's culture or subculture.

Psychological Distress

Psychological distress is described as the non-specific mental symptoms of depression, anxiety, personality traits, and multiple psychological (e.g., burnout), somatic, and behavioral problems. It results from complex dynamics (social, psychological, neurochemical, etc.) associated with overwhelming and sustained stress and painful experiences.

Memantine hydrochloride

It is a voltage-dependent, moderate-affinity uncompetitive N-methyl-D-aspartate receptor antagonist. It modulates the effects of pathologically elevated tonic levels of glutamate that may lead to neuronal dysfunction, and it is used to treat moderate to severe Alzheimer's disease.

Titration Dose

The recommended starting dose is 5 mg per day, which is stepwise increased over the first 4 weeks of treatment reaching the recommended maintenance dose as follows:

- Week 1 (day 1-7): The patient should take 5 mg film-coated per day for 7 days.
- Week 2 (day 8-14): The patient should take one 10 mg film-coated tablet per day for 7 days.
- Week 3 (day 15-21): The patient should take one 15 mg film-coated per day for 7 days.
- Week 4 (day 22-28): The patient should take one 20 mg film-coated per for 7 days.
- The maximum daily dose is 20 mg per day.

Donepezil hydrochloride

Donepezil hydrochloride is a specific and reversible inhibitor of acetylcholinesterase, the predominant cholinesterase in the brain. It is indicated for the symptomatic treatment of mild to moderately severe Alzheimer's dementia.

Method of Administration:

Adults/Elderly people:

Treatment is initiated at 5 mg/day (once-a-day dosing). The 5 mg/day dose should be maintained for at least one month in order to allow the earliest clinical responses to treatment to be assessed and to allow steady-state concentrations of donepezil hydrochloride to be achieved. Following a one-month clinical assessment of treatment at 5 mg/day, the dose of Donepezil can be increased to 10 mg/day (once-a-day dosing). The maximum recommended daily dose is 10 mg. Doses greater than 10 mg/day have not been studied in clinical trials.

Quetiapine fumarate

Quetiapine is an atypical antipsychotic agent. Quetiapine and the active human plasma metabolite, norquetiapine interact with a broad range of neurotransmitter receptors. Quetiapine and norquetiapine exhibit affinity for brain serotonin (5HT2) and dopamine D1- and D2- receptors. It is this combination of receptor antagonism with a higher selectivity for 5HT2 relative to D2- receptors, which is believed to contribute to the clinical antipsychotic properties and low extrapyramidal side effect (EPS) liability of Quetiapine compared to typical antipsychotics.

Drug interaction between Quetiapine fumarate and donepezil hydrochloride

A published case report in 2017 described an 84-year-old man with probable dementia with Lewy bodies - protein inclusions containing disaggregated oligomers of many cellular proteins- who developed neuroleptic malignant syndrome (NMS) following treatment with donepezil, olanzapine, and subsequently quetiapine. The patient was initially hospitalized with fever and altered consciousness due to respiratory infection and acute kidney injury. Donepezil was discontinued on admission, and quetiapine was initiated for nocturnal restlessness. Within 72 hours, he developed worsening consciousness

Local Case Safety Report: Medication Error and Potential drug Interaction Leading to Neuropsychiatric Manifestations in an Alzheimer's Disease Patient

,fever, tachycardia, diaphoresis, severe rigidity, tremors, and myoclonus, with elevated creatine phosphokinase (CPK) levels, consistent with NMS. Quetiapine was immediately discontinued, and supportive treatment was initiated. The patient's condition gradually improved, with normalization of CPK levels and recovery of consciousness. At a three-month follow-up, he remained clinically stable with improved functional status. The authors suggested that the cumulative effects of donepezil and antipsychotics (olanzapine and quetiapine) may have contributed to the development of NMS, emphasizing the importance of careful monitoring when these agents are used in elderly patients with dementia.

A key pharmacodynamic interaction involves the concurrent use of acetylcholinesterase inhibitors (AChEIs)—such as Donepezil—and anticholinergic drugs, which have opposing effects and lead to pharmacological antagonism. Many drugs with anticholinergic properties—including atypical antipsychotics like Quetiapine, as well as certain antidepressants, antihistamines, bronchodilators, and medications for urinary incontinence—are commonly prescribed to Alzheimer's patients, especially those with behavioral and psychotic symptoms. Co-administration of quetiapine with donepezil may result in pharmacodynamic antagonism due to their opposing cholinergic and anticholinergic effects, with a potential impact on the therapeutic effects of donepezil. Lastly, cardiovascular side effects, including potential rhythm disturbances and QT interval changes, should also be considered when managing these patients.

Labeled information:

According to Summary of product Characteristics (SmPC) of memantine hydrochloride, Posology and method of administration stated that: "Treatment should be initiated and supervised by a physician experienced in the diagnosis and treatment of Alzheimer's dementia. Therapy should only be started if a caregiver is available who will regularly monitor the intake of the medicinal product by the patient and the recommended starting dose is 5 mg per day, which is stepwise increased over the first 4 weeks of treatment reaching the recommended maintenance''

There is no data regarding drug interaction between Quetiapine fumarate and donepezil hydrochloride in Summary of product Characteristics (SmPC) of both drugs

Conclusion:

This case highlights the importance of adherence to the recommended titration schedule for memantine and the need for careful evaluation of concomitant medications in patients with Alzheimer's disease. Although no established interaction between donepezil and quetiapine is described in the SmPCs, the concomitant use warrants clinical vigilance, particularly in elderly patients receiving multiple medications. Prompt recognition and reporting of suspected adverse drug reactions and medication errors are essential to improving patient safety and contribute to signal detection.

Recommendations for Healthcare Professionals:

Patients with Alzheimer's disease may be at increased risk of adverse drug reactions and drug–drug interactions due to advanced age, polypharmacy, and disease-related changes in the central nervous system.

1. Adhere to the recommended titration schedule when initiating memantine therapy to minimize medication errors.
2. Review all concomitant medications for potential interactions before prescribing antipsychotics to patients with Alzheimer's disease.
3. Closely monitor new or worsening neuropsychiatric symptoms after initiating or modifying treatment.
4. Reassess the benefit-risk profile of antipsychotic therapy regularly and prescribe the lowest effective dose for the shortest appropriate duration.
5. Educate caregivers to promptly report changes in cognition, behavior, or mental status.
6. Report suspected adverse drug reactions as a result of medication errors or potential drug interactions to the pharmacovigilance center to support continuous safety monitoring.

References

1. **Delusion**(click here)
2. **Psychological Distress** (click here)
3. **Memantine hydrochloride SPC** (click here).
4. **Donepezil hydrochloride SPC** (click here).
5. **Quetiapine fumarate SPC** (click here).
6. **Published case report** (click here).

EPVC hosts an awareness session at 6th October University Hospital July 2026

The Egyptian Drug Authority is pleased to build up collaboration and partnership with hospitals for providing awareness visits and session for healthcare providers about the role of PV in achieving safety of medications and patients regarding using pharmaceutical products.

As part of this; PVGA conducted an official visit to 6th October University Hospital, The visit was attended by Prof. Samir Osman, Vice Dean of Education and Student Affairs, Faculty of Pharmacy; Prof. Heba Helmy, Vice Dean of Education and Student Affairs, Faculty of Medicine; and Dr. Ahmed Essam, Head of the Clinical Pharmacy Department.

This visit designed to integrate students of faculty of medicine into the field of pharmacovigilance by fostering the reporting culture and the role of HCG in ensuring patient safety by achieving medication safety

During the visit, multiple engaging awareness sessions were delivered covering "The Pharmacovigilance Landscape in Egypt" & "Reporting Cycle and Channels" & "Medicines adverse reactions" & "adverse Events following immunization" and "substandard/ falsified medicines".

The event also featured an interactive workshop utilizing a game-based learning approach, to maximize participant engagement that successfully engaged by 55 of academic staff members, teaching assistants, and students dedicated to enhancing medication safety.

Vigitest Competition 2026 – Vigitest Competition 2026 – Round 4 with Live Pharmacovigilance Challenge

Following the successful launch of **Vigitest in 2026 round 1**, and **Round 2 of the Vigitest competition we are heading to conduct R4 dynamic live format for 2026** concurrently with R3 in same time for more leveling up moments
Stay tuned for live rounds that test your PV expertise in real-time.

How to Join Vigitest 2026

1. Register your participation by submitting your name through the Google Form linked below.
   Scan the QR code or tap the link below, follow the instruction and answer the questions.

   Or

   copy the link:
   https://docs.google.com/forms/d/e/1FAIpQLSetBbvH_U8JDZnJZzDIHm2383ZgJVgzwqrfQcjSh-AiEQBVYQ/viewform?usp=dialog

2. Once registered, you will receive an **invitation email one day before the competition**, including:
   - Exact **date and time** of your competition round

Instructions on accessing the live platform
Compete with peers, and keep the Vigitest legacy alive live!
Don't miss the opportunity to be part of the **Vigitest Game 2026** – where knowledge meets action!

EPVC Tips On Pharmacovigilance

Herbal Medicines Are Medicines Too

Some Many people choose herbal medicines because they are natural, but natural does not always mean safe. Like all medicines, herbal products can cause side effects, interact with other medicines, or may not be suitable for everyone.

Before taking any herbal medicine, tell your doctor or pharmacist about all the medicines, vitamins, and supplements you are using. This is especially important if you are pregnant or breastfeeding, have a chronic medical condition, or take medicines such as blood thinners, diabetes medications, or medicines for high blood pressure.

It is also important to use herbal products from reliable sources and follow the recommended dose. Taking more than the recommended amount or combining several herbal products may increase the risk of unwanted effects.

If you experience any unexpected symptoms after using a herbal medicine, stop using it only after consulting a healthcare professional (unless it is a medical emergency), and report the side effect to your national pharmacovigilance center or discuss it with your healthcare provider.

Remember: Herbal medicines can provide benefits when used appropriately, but using them safely starts with being informed and communicating openly with your healthcare provider.

Safe use of herbal medicines begins with informed choices.

You can report any ADR on:

Email: pv.followup@edaegypt.gov.eg

Hotline: 15301

Website: (click Here)

Or report through your pharmacy / product distributor / company hotline — they are required to forward it to EDA.

Why Your Report Matters

Every report _ to us counts when it comes to the safety of medicines and patients worldwide

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*

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.

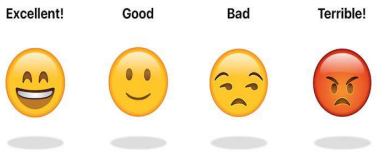
What is the Egyptian Pharmaceutical Vigilance Center?

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

Communication information

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هيئة الدواء المصرية (الرعاية الصيدلية)