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

July 2023

Volume 14 **Issue 7**

Drug Safety Update

Direct-acting oral anticoagulants (DOACs): Pediatric formulations; reminder of dose adjustments in patients with renal impairment

Risk minimization materials are available to support the safe use of new pediatric formulations of rivaroxaban and dabigatran etexilate. In addition, we ask healthcare professionals to consult the current advice to ensure that all patients with renal impairment receive an appropriate dose of DOAC medicines.

Advice for healthcare professionals:

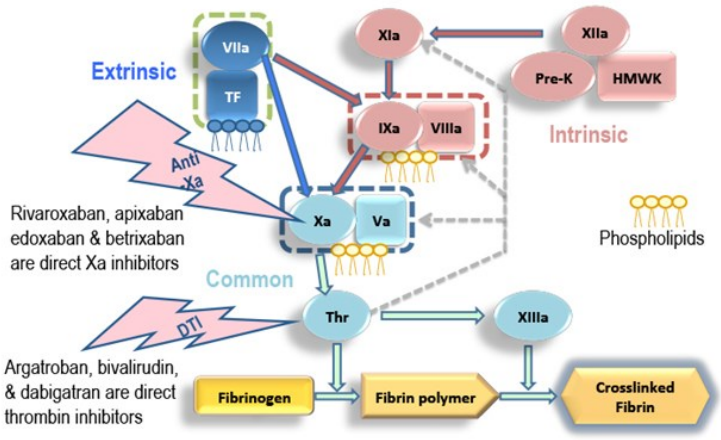
• for paediatric use of these medicines, counsel parents and caregivers about the reconstitution and dosing of dabigatran granules and rivaroxaban granules to reduce the risk of medication errors; highlight the new instructions for use and other educational materials to support safe use in children

• ensure all patients with renal impairment receive an appropriate DOAC dose and monitor renal function during treatment to ensure dose remains appropriate

• report suspected adverse drug reactions associated with DOACs on a Yellow Card, including thromboembolic or haemorrhagic events

Advice for healthcare professionals to give to patients and carers:

• DOACs are a group of medicines that help to prevent blood clots from forming – they are used to prevent strokes, heart attacks and other issues associated with blood clots



• parents and caregivers of children and adolescents prescribed these medicines should read and follow the Instructions for Use (IFU) booklet provided for instructions on how to prepare and administer these medicines

• all patients with renal impairment who are taking DOACs will be reviewed regularly to make sure they are taking the correct dose

• if patients or carers have any concerns about these medicines, they should talk to their healthcare professional

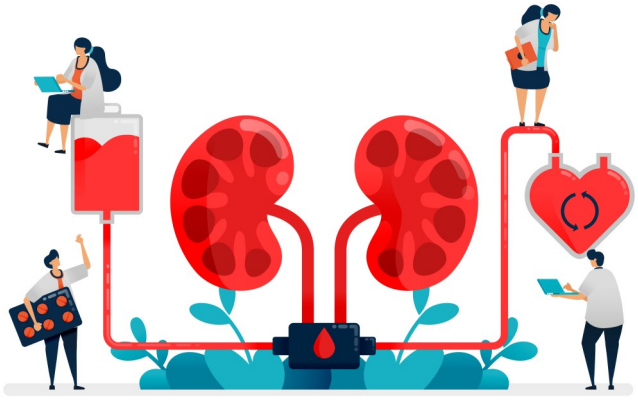
References:

MHRA: *(Click here)*

"Ca acetate caused muscle cramps to a fifth degree kidney failure patient compared to Ca carbonate being used as a phosphate binder "

The regional center in Cairo a case of a male patient in his eighties, suffered from chronic kidney failure of fifth degree, and on hemodialysis. He received three sessions of hemodialysis per week, and each session lasted for about 4 hours. He used to administer (Ca carbonate 500 mg) with a dose of two tablets twice daily, for about 7 years with no adverse effect. He administered (Ca acetate 700 mg) with a dose of one tablet three times per day (within the meal), as a phosphate binder to decrease phosphorus level and increase Calcium. After 3 days of drug administration he suffered from symptoms like seizure, pain and cramps that started in his right arm extended to the left arm then the legs.
The reaction was considered serious and caused hospitalization and disabling.

Ca acetate was stopped and replaced by (Ca Carbonate 500 mg) with a dose of two tablets twice daily without any adverse events. After that he re- administered Ca acetate (the available drug at that time) and after the third dose he suffered from cramps and pain all over his arms and legs. The drug was stopped and after 5 days the patient recovered gradually.



Background:

The role of Ca acetate and Ca carbonate in hemodialysis:
Most patients with end-stage renal disease develop hyperphosphatemia because their dietary intake exceeds phosphorus elimination by intermittent thrice-weekly dialysis.
National Kidney Foundation Kidney Disease Outcome and Quality Initiative (K/DOQI) Bone Metabolism and Chronic Kidney Disease Guidelines recommend that serum phosphorus levels be maintained between 3.5 and 5.5 mg/dL.
Calcium carbonate is widely used as an oral phosphorus binder to control hyperphosphatemia in hemodialysis patient
In adults, calcium acetate binds phosphorus more effectively than calcium carbonate, while reducing the frequency of hypercalcemic events (1).

"Ca acetate caused muscle cramps to a fifth degree kidney failure patient compared to Ca carbonate being used as a phosphate binder " (Continued)

Recommended doses of Ca acetate and Ca carbonate in hemodialysis

The recommended doses of calcium acetate required for control of serum phosphorus fall within the 1500 to 2000 mg of elemental calcium intake per day recommended by the K/DOQI guidelines (2).

Patients with serum phosphorus levels between 4.5 and 5.0 mg/dL received an initial dose of 1 gelcap per meal; those with phosphorus levels between 5.1 and 6.0 mg/dL started with 2 gelcaps per meal and those with phosphorus levels > 6.0 mg/dL were administered a starting dose of 3 gelcaps per meal

Ca acetate VS Ca carbonate in hemodialysis

- Significantly less elementary calcium was ingested with calcium acetate than with calcium carbonate: 750 (375-1,500) vs. 1,200 (0-3,000) mg calcium/day, $P < 0.0001$. With calcium carbonate serum calcium increased significantly. The number of episodes of hyperphosphatemia or hypercalcemia did not differ between treatments. Intact plasma parathyroid hormone (PTH) decreased significantly with both phosphate binders

We conclude that hyperphosphatemia can be controlled effectively by both calcium acetate and calcium carbonate in hemodialysis patients. The oral load of elementary calcium is reduced significantly by binding phosphorus with calcium acetate instead of calcium carbonate; nevertheless, hypercalcemic episodes remain equally frequent with both phosphate binders (3).

- In a Meta-Analysis comparing the two preparations for Hyperphosphatemia of Hemodialysis Patients, calcium acetate showed better efficacy and with a higher incidence of intolerance compared with calcium carbonate. There are insufficient data to establish the comparative superiority of the two calcium-based phosphate binders on all -cause mortality and cardiovascular end-points in hemodialysis patients (4).

Ca acetate and muscle cramps

- A randomized control trial was conducted in four phases with calcium acetate or calcium carbonate involving sixty-four patients on hemodialysis showed that calcium acetate has similar effect on serum phosphate levels as compared to calcium carbonate in patients on maintenance hemodialysis. However, calcium acetate results in lesser frequency of hypercalcemia as compared to calcium carbonate. Tolerance to both drugs was similar, though patients complained of more muscle cramps while taking calcium acetate (5).

- In present study, calcium carbonate and calcium acetate were compared regarding their phosphate binding properties and hypercalcemic effects and tolerance. The protocol was designed in such a way that comparable doses (in grams) of each salt were given during each phase of the study. In this content, the daily amount of calcium prescribed was always lower with calcium acetate. The study dropout ratio for each compound was low and without statistical difference statistically. Tolerance and side effects were also comparable, although upper GI intolerance and muscle cramp were seen in two patients in acetate group (6).

"Ca acetate caused muscle cramps to a fifth degree kidney failure patient compared to Ca carbonate being used as a phosphate binder " (Continued)

Labeled information:

(Ca acetate) tablets SPC (7)

Composition:

700 mg Ca acetate equivalent to 177.3 mg elemental Ca.

Usual dose:

2 Tablets Calcium acetate 700 mg 4 times dail (corresponding to 1,419 mg calcium) or 3 tablets Calcium acetate 700 mg 3 times daily (corresponding to 1,597 mg calcium).

Possible side effects:

Calcium acetate tablets may cause high levels of calcium in the blood (hypercalcaemia), which can lead to the following symptoms:

- nausea (feeling sick) or vomiting (being sick),
- constipation,
- anorexia lack of appetite.

(Ca carbonate) tablets SPC (8)

Composition:

Calcimate 500 mg Ca Carbonate equivalent to 200 mg elemental Ca

Dose:

Adults and older people 1,000 mg of calcium corresponding to 5 tablets per day.

Possible side effects:

Metabolism and nutrition disorders:

Uncommon: hypercalcemia, hypercalciuria.

Gastrointestinal disorders

Rare: nausea, vomiting, diarrhea, abdominal pain, constipation, flatulence, abdominal distension.

Contraindications:

Severe renal impairment

Recommendations for Healthcare Professionals:

The dose of either Ca acetate or Ca carbonate should be detected based on the levels of phosphate.

Ca acetate was shown in different studies to be more effective as phosphate binder than Ca carbonate thus its dose must be adjusted carefully based on frequent electrolyte analysis.

Muscle cramps is one of the complications that has been observed in Ca acetate administration rather than Ca carbonate, thus follow up with the patient is recommended.

References:

1. **Introduction to phosphorous binders:** *(Click here)*
2. **Recommended dose of Ca acetate**: *(Click here)*
3. **Ca acetate vs Ca carbonate:** *(Click here)*
4. **Ca acetate vs Ca carbonate:** *(Click here)*
5. **Ca acetate vs Ca carbonate and incidence of muscle cramps:** *(Click here)*
6. **Ca acetae and muscle cramps:** *(Click here)*
7. **Ca acetate SPC:** *(Click here)*
8. **Ca carbonate SPC:** *(Click here)*

Together for Safe Medicine Initiative Progress

We are happy to announce that we are planning for sharing with you the registration link for 4th wave of the Initiative "Together for Safe Medicine" for all Pharmacists who are interested to participate with us from community and governmental pharmacists all over Egypt after celebrating the Success of the first three waves of the Central Administration of pharmaceutical care Initiative "Together for Safe Medicine" on 25 May 2023 where Professor Dr. **Ayman ElKhattib** and Dr **Shereen Abd ElGawad** "Head of Central Administration of pharmaceutical care sector" had Rewarded the top achievers' pharmacists of the three waves who attended the celebration and the Pharmacovigilance team responsible for Initiative by giving them a shield of distinction as an appreciation of their valuable efforts in applying, practicing, and spreading the science of Pharmacovigilance and increasing the ADRs reporting rate through their community and governmental Pharmacies trying to improve Drug safety in the Egyptian Market.

Egyptian Pharmaceutical Vigilance Center (EPVC) Vigiflow expansion project Trainings for Raising Reporting Awareness

In the context of the vision and mission of the Egyptian Pharmaceutical Vigilance Center (EPVC) in spreading awareness of pharmacovigilance and the culture of reporting side effects among Healthcare professionals to promote the safe and effective use of different pharmaceutical products and to promote the pharmaceutical care, the center conducted training on pharmacovigilance organized by Alexandria main University Hospital on 20 June 2023, attendees were 37 HCPs as 24 pharmacists, 12 nurses, and 1 Physician had attended from different healthcare units from four hospitals of Alexandria university as El Mowassat University Hospital, Alexandria Main University Hospital, New University Hospital, Smouha University Hospital For Pediatrics and Pediatric Surgeries.

The training included a lecture and workshop on the basics of Pharmacovigilance, its importance, and how to report adverse events and other safety information related to the different pharmaceutical products such as medicines, vaccines, biological products, and medical devices, and the shared HCPs showed much interest and sharing in the workshop and discussed very important Safety issues Concerning medicines, vaccines ADRs and showed their tendency for Reporting Serious ADRs as soon as possible.

EPVC Tips On Pharmacovigilance

Management of Pharmaceutical Household Waste

Limiting Environmental Impacts of Unused or Expired Medicine

Pharmaceutical household waste from expired or unused medicine does not only offer zero therapeutic benefit, but also contributes to environmental pollution when disposed of via improper routes. Medicines discarded in sinks and flushed down toilets enter sewage waters and, if not filtered out, leak into aquatic systems. Disposal of unused or expired medicines via solid household waste can also result in pharmaceutical residues entering the environment if this waste is illegally dumped, or destined for landfills. In addition to environmental risks, unused or expired medicine not only constitutes wasted healthcare resources, but also presents a possible public health risk of accidental or intentional misuse and poisoning if extracted from waste bins. Preventing pharmaceutical household waste and ensuring the effective collection and environmentally sound treatment of unavoidable waste is thus an important policy objective.

Visit EDA website to find all any 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

The Egyptian Pharmaceutical Vigilance center
مركز اليقظة الصيدلية المصري

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

EPCV would like to thank **El Mansoura International Hospital** for their good practice regarding reporting ICSRs and we are looking forward to more fruitful participation

One report counts

A call for reporting

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

Communication information

The Egyptian Drug Authority (EDA)
Pharmaceutical Care Administration
The Egyptian Pharmaceutical Vigilance Center (EPVC)

Address: 21 Abd El Aziz AlSoud Street. El-Manial, Cairo, Egypt, PO Box: 11451
Hotline: 15301
Fax: +202 – 23610497
Email: pv.followup@edaegypt.gov.eg
Reporting link: www.edaegypt.gov.eg
https://sites.google.com/view/epvc-reporting/healthcare-professional-public-adverse-drug-event-reporting/reporting-other-adverse-drug-event-cases

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