In This Issue

*Drug overview.... "Koāte®-DVI" P.g 1-4.

*FDA News.... “Zofran and Cipram” P.g 5-6.

*From Our Answered Questions.... “Diclofenac in Children” P.g 6-7.

*Brief Note....”Actonel and Calcid Drug Interaction” P .g 7.

**Drug Overview**

Koāte®-DVI

Koāte®-DVI is indicated for Prevention and treatment of classic hemophilia or (Hemophilia A) (1, 5), in which there is a demonstrated deficiency of activity of the plasma clotting factor, factor -VIII “FVIII”. Koate (antihemophilic factor) -DVI provides a means of temporarily replacing the missing clotting factor in order to control or prevent bleeding episodes, or in order to perform emergency and elective surgery on individuals with hemophilia.

Koate (antihemophilic factor) -DVI contains naturally occurring von Willebrand's factor, which is copurified as part of the manufacturing process.

Koate (antihemophilic factor) -DVI has not been investigated for efficacy in the treatment of von Willebrand's disease, and hence is not approved for such usage. (2, 3, 5)

Koāte-DVI contains purified and concentrated factor VIII. The factor VIII is 300-1000 times purified over whole plasma. Part of the fractionation may be performed by another licensed manufacturer. When reconstituted as directed, Koāte-DVI contains approximately 50-150 times as much factor VIII as an equal volume of fresh plasma. The specific activity, after addition of Albumin (Human), is in the range of 9-22 IU/mg protein. (2)
What is hemophilia-A?

Hemophilia refers to bleeding disorder in which it takes a long time for the blood to clot.

Hemophilia A: (2, 3) is caused by an inherited X-linked recessive trait, with the defective gene located on the X chromosome. Females have two copies of the X chromosome, so if the factor VIII gene on one chromosome doesn't work, the gene on the other chromosome can do the job of making enough factor VIII. Males, however, have only one X chromosome, so if the factor VIII gene on that chromosome is defective, they will have hemophilia A. Thus, most people with hemophilia A are male.

Symptoms: (2, 3)

The severity of symptoms varies. Bleeding is the main symptom of the disease and sometimes, although not always, occurs if an infant is circumcised.

Additional bleeding problems are seen when the infant starts crawling and walking.

Mild cases may go unnoticed until later in life when they occur in response to surgery or trauma. Internal bleeding may happen anywhere, and bleeding into joints is common.

Symptoms may include:

- Bleeding into joints, with associated pain and swelling.
- Blood in the urine or stool.
- Bruising.
- Gastrointestinal tract and urinary tract hemorrhage.
- Nosebleeds.
- Prolonged bleeding from cuts, tooth extraction, and surgery.
- Spontaneous bleeding.
Warning /Precautions on using Koāte-DVI (1, 4, 5, 6)

General

1. Koāte-DVI is intended for treatment of bleeding disorders arising from a deficiency in factor VIII. This deficiency should be proven prior to administering Koāte-DVI.
2. Administer within 3 hours after reconstitution. Do not refrigerate after reconstitution.
3. Administer only by the intravenous route.
4. Filter needle should be used prior to administering.
5. Koāte-DVI contains levels of blood group isoagglutinins which are not clinically significant when controlling relatively minor bleeding episodes. When large or frequently repeated doses are required, patients of blood groups A, B, or AB should be monitored by means of hematocrit for signs of progressive anemia, as well as by direct Coombs' tests.
6. Product administration and handling of the infusion set and needles must be done with caution. Percutaneous puncture with a needle contaminated with blood can transmit infectious viruses including HIV (AIDS) and hepatitis. Obtain immediate medical attention if injury occurs.

Concerns related to adverse effects:

- Antibody formation: The development of factor VIII antibodies has been reported with antihemophilic factors; monitor for signs of formation of antibodies to factor VIII; may occur at anytime but more common in young children with severe hemophilia.
- Hypersensitivity reactions: Allergic hypersensitivity reactions (including anaphylaxis) may occur.
- Koāte-DVI is made from human plasma. Products made from human plasma may contain infectious agents, such as viruses, and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent that can cause disease. There is also the possibility that unknown infectious agents may be present in such products.
- Hepatitis B vaccination is essential for patients with hemophilia A; vaccination is recommended at birth or at the time of diagnosis. Hepatitis A vaccination is also recommended for hemophilia patients who are hepatitis A seronegative. (6,7)
- **Pregnancy Category C**: (1, 5)
  
  Animal reproduction studies have not been conducted with Koāte-DVI. It is also not known whether Koāte-DVI can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Koāte-DVI should be given to a pregnant woman only if clearly needed.

- **Lactation**:

  Excretion in breast milk unknown/use caution

- ** Pediatric Use**:

  Koāte-DVI has not been studied in pediatric patients. Koāte-HP, solvent/detergent treated Antihemophilic Factor (Human), has been used extensively in pediatric patients.

  Spontaneous adverse event reports with Koāte-HP for pediatric use were within the experience of those reports for adult use.

- **Storage**: (5, 8)

  - **Koāte®-DVI**: To be stored under refrigeration, 2°C to 8°C. "AVOID FREEZING".
  - Freezing should be avoided as breakage of the diluent bottle might occur.
  - **Koāte®-DVI**: Lyophilized powder may also be stored at room temperature of 25°C for ≤6 months.
  - Protect the product from light.
  - If refrigerated, the dried concentrate and diluent should be warmed to room temperature before reconstitution.
  - Use within 3 hours of reconstitution.
  - Do not refrigerate after reconstitution, precipitation may occur.

**References**:

1. www.rxlist.com/koate-drug.htm
2. www.hemophilia.org/NHFWeb/MainPgs/MainNHF.aspx?menuid=182&contentid=47&rptname=bleeding
4. dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?id=47439#s27
5. Lexicomp online database
6. www.talecris-pi.info/inserts/Koate_DVI.pdf
8. www.talecris-pi.info/inserts
On Sep, 2011, FDA Notified Health Care Professionals and Patient about Two Drugs That Affect Heart Rhythm and May Induce Arrhythmia:

1- Zofran (ondansetron): Drug Safety Communication - Risk of Abnormal Heart Rhythms:
   o Ongoing safety review and labeling changes for the anti-nausea drug Zofran (ondansetron) and generics. Ondansetron may increase the risk of developing prolongation of the QT interval of the electrocardiogram, which can lead to an abnormal and potentially fatal heart rhythm, including Torsade de Pointes. Patients at particular risk for developing Torsade de Pointes include those with underlying heart conditions, such as congenital long QT syndrome, those who are predisposed to low levels of potassium and magnesium in the blood, and those taking other medications that lead to QT prolongation.

   RECOMMENDATION:
   o The labels are being revised to include a warning to avoid use in patients with congenital long QT syndrome because these patients are at particular risk for Torsade.
   o Recommendations for ECG monitoring in patients with electrolyte abnormalities (e.g., hypokalemia or hypomagnesemia), congestive heart failure, bradyarrhythmias, or in patients taking other medications that can lead to QT prolongation, are being included in the labels.

   (Ondansetron is available in Egyptian market as Zofran, Danofran & Danset)

   Reference: FDA.gov

2- Celexa (citalopram hydrobromide): Drug Safety Communication - Abnormal Heart Rhythms Associated With High Doses:
   o The antidepressant citalopram hydrobromide should no longer be used at doses greater than 40 mg per day because it can cause abnormal changes in the electrical activity of the heart. Changes in the electrical activity of the heart (prolongation of the QT interval of the electrocardiogram [ECG]) can lead to an abnormal heart rhythm (including Torsade de Pointes), which can be fatal. Patients at particular risk for developing prolongation of the QT interval include those with underlying heart conditions and those who are predisposed to low levels of potassium and magnesium in the blood.
   o Studies did not show a benefit in the treatment of depression at doses higher than 40 mg per day.
RECOMMENDATION:
o Citalopram causes dose-dependent QT interval prolongation. Citalopram should no longer be prescribed at doses greater than 40 mg per day.
o Citalopram should not be used in patients with congenital long QT syndrome. Patients with congestive heart failure, bradyarrhythmias, or predisposition to hypokalemia or hypomagnesemia because of concomitant illness or drugs, are at higher risk of developing Torsade de Pointes.

(Citalopram is available in Egyptian market as Cipram, Sedopram, Citalo, Cipramax, Depram, Talopram, Ramdeep, Puracit & Citalomep)

Reference: FDA.gov

From our answered questions

*Use of Diclofenac Sodium (Voltaren) in Children*

In UK (1, 2):
- In children 1 to 12 years old the licensed UK oral diclofenac sodium for juvenile idiopathic arthritis in a dose 1 to 3 mg/kg daily in divided doses.
- Suppositories not licensed for use in children under 6 years EXCEPT for use in children over 1 year for juvenile idiopathic arthritis in a dose 1 to 2 mg/kg daily in divided doses for a maximum of 4 days.
- Solid dose forms containing more than 25 mg and the parenteral route not licensed for use in children although parenteral has been used.
- The BNFC suggests slightly different doses of diclofenac sodium:
  - For the management of rheumatic disease, including juvenile idiopathic arthritis by oral route in children from 6 months of age in a dose 3 to 5 mg/kg daily, in 2 or 3 divided doses, maximum of 150 mg daily.
  - And for relief of pain and inflammation by oral and rectal in children from 6 months of age in a dose 0.3 to 1 mg/kg given three times daily and by deep intramuscular (gluteal) injection instead may be given a similar dose once or twice daily, in children 2 years of age and older for up to 2 days.
In USA (3, 4):

- Safety and efficacy not established in children.
- Diclofenac sodium is indicated for children in juvenile idiopathic arthritis in a dose 2-3 mg/kg/day divided 2-4 times/day; maximum dose: 200 mg/day.
- A good results with oral diclofenac obtained in a limited number of children 3–16 years of age for the management of juvenile rheumatoid arthritis.

N.B:

- Diclofenac potassium (Cataflam) tablets not licensed for use in children under 14 years (2).
- However, Cataflam Oral Drops are particularly suitable for paediatric use because they enable the dosage to be individually tailored to bodyweight within the recommended range (5).

References:
1- BNF For children 2009
2- Martindale 36th edition 2009
3- Lexicomp online database
4- http://www.drugs.com/monograph/diclofenac-sodium.html
5- http://www.medical-explorer.com/drugs-c/cataflam_1.html

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**Brief Note**

**Drug interaction between Actonel (Risedronate -Bisphosphonate Derivatives) and Calcid (Calcium Salts)**

**Actonel** is used for osteoporosis in postmenopausal women and osteoporosis in men. Postmenopausal women (and older men) should take adequate supplemental elemental calcium and vitamin D if dietary intake is inadequate.

Concern about these combination that calcium Salts may decrease the serum concentration of Bisphosphonate Derivatives. The likely primary mechanism of this interaction is binding of the bisphosphonate derivative to calcium ions to form a nonabsorbable (or very poorly absorbable) chelate. Only oral preparations of calcium salts and bisphosphonate derivatives are expected to participate in this interaction.

→ Patient should avoid administration of oral calcium supplements within 30 minutes after Risedronate administration.

References:
1- Uptodate database.
2- Lexicomp online database.
3- www.drugs.com
Our Vision
The pharmacist working in Kasr Alainy Drug Information Center (KDIC) provides accurate, unbiased, relevant, evidenced based and timely information about drugs and drug related problems to assist the center users in optimizing health outcomes.

Our Mission
Pharmacists in the KDIC are part of the health care team working through the Clinical Pharmacology and Pharmacy committee, to provide useful service and the pharmaceutical information needed for the hospitals' patients.

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