The Technical committee new decision regarding the use of Meclizine in pregnancy

What is meclizine?

Meclizine is an antihistamine that reduces the effects of natural chemical histamine in the body.

Meclizine is used to treat or prevent nausea, vomiting, and dizziness caused by motion sickness. It is also used to treat symptoms of vertigo (dizziness or spinning sensation) caused by disease that affects your inner ear.

On 07/10/2010 the Technical committee at CAPA (the Central administration for Pharmaceutical affairs) has required the Marketing authorization holders to add this warning on the external package:

“Products containing meclizine should not be used during the first trimester of pregnancy”

However on 25/06/2015 the Technical committee has decided to cancel the previous decision.

Cancelling the previous decision was based on EPVC committee recommendations just to ensure that this sentence is added to the internal leaflets only of the pharmaceutical products containing meclizine.

“It should be used in pregnancy only if it is clearly needed (Pregnancy Category B) and under the supervision of a physician”.

It is important to mention that Meclizine should not be used in infants under 2 years, and used only under medical supervision for Children (2-12 years) according to EPVC recommendations and technical committee decision on 05/02/2015.
The Technical Committee decision regarding Propylene glycol in medicinal products for children

Propylene glycol (CH₈O₂) is a commonly used drug solubilizer in topical, oral, and injectable medications. It is used as stabilizer for vitamins, and as a water-miscible cosolvent. Propylene glycol has been used for over 50 years in a large variety of applications. As a pharmaceutical additive, propylene glycol is generally regarded as safe.

However, Propylene glycol is known to be potentially toxic in some patients that are not able to adequately metabolise and eliminate this excipient. These patients are mainly infants and children below the age of 4 years, pregnant women, patients with hepatic or renal failure, and patients treated with disulfiram or metronidazole.

The technical committee at CAPA (the central administration for pharmaceutical affairs) has decided on 25/06/2015

1. The modification of the safety limits of propylene glycol which is used in the pharmaceutical products as follows:

<table>
<thead>
<tr>
<th>Safety limits</th>
<th>neonates up to 28 days (or 44 weeks post menstrual age for pre-terms)</th>
<th>1 month (29 days) up to 4 years</th>
<th>5 years up to 17 years and adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Safety limits</td>
<td>1 mg/kg</td>
<td>50 mg/kg</td>
<td>500 mg/kg</td>
</tr>
</tbody>
</table>

2. Performing tests on the raw materials to confirm the absence of Diethylene glycol & Triethylene glycol

The previous decision came after the Pharmacovigilance committee recommendations on 04/06/2015

References:

EMA - Background review for the excipient propylene glycol (Click here)
Ceftriaxone – Mastocytosis infant case died due to uncontrolled bleeding – In Cairo

The regional center in Cairo received a yellow card concerning 18 months old male infant who died due to Generalized uncontrolled bleeding within 24 hrs following administration of IV bolus Ceftriaxone 500mg for gastroenteritis. The infant was previously diagnosed with Bullous Mastocytosis and had been stabilized by adequate interventions in the hospital.

It is worth to be mentioned that the center also received another yellow card concerning 35 days old jaundiced female neonate taking IM Ceftriaxone therapy who suffered from bleeding so Ceftriaxone therapy was immediately stopped and she was referred to a pediatric Hospital which reported very high INR (<10) and internal bleeding. She was survived by Blood transfusion, Plasma and Ringer solution. Then she was referred to incubator.

Background:
Ceftriaxone is used mostly in hospital practice for neonatal sepsis, meningitis and ophthalmia neonatorum. Its broad spectrum of activity, once daily dosing and good penetration into CSF are features favoring its use. However, there are not many reports on its efficacy or safety in neonates.

Three cephalosporins Cefoperazone, Cefotetan and Ceftriaxone can cause bleeding tendencies. The mechanism is reduction of Prothrombin levels through interference with vitamin K metabolism.

Mastocytosis is a rare and heterogeneous disease characterized by the presence of excessive numbers of mast cells in various organs, mainly the skin and the bone marrow. Systemic symptoms are related to mast cell degranulation. Although heparin is one of the mediators released by mast cells, spontaneous bleeding has been very rarely reported in mastocytosis.

Labeled information:
According to Ceftriaxone Summary of product Characteristics (SmPC):

[1] It was stated under section 4.8 Undesirable effects: Blood and lymphatic system disorders that: “Ceftriaxone has rarely been associated with prolongation of prothrombin time, however, bleeding and bruising due to hypoprothrombinaemia may be more prevalent in patients with renal or hepatic impairment, malnourished patients or those with low vitamin K levels and patients receiving prolonged ceftriaxone therapy.”.

[2] It was stated under section 4.3 Contraindications that: Ceftriaxone is contraindicated in: Hyperbilirubinaemic newborns and preterm newborns should not be treated with ceftriaxone. In vitro studies have shown that ceftriaxone can displace bilirubin from its binding to serum albumin and bilirubin encephalopathy can possibly develop in these patients.

Recommendations for Healthcare Professionals:
1. Cephalosporins may cause bleeding due to hypoprothrombinaemia and should be used with caution in patients with renal or hepatic impairment, malnourished patients or those with low vitamin K levels and also in patients receiving prolonged cephalosporin
therapy who are at increased risk of developing hypoprothrombinaemia.

2. **Ceftriaxone is contraindicated in:**
   - Premature newborns up to a corrected age of 41 weeks (weeks of gestation + weeks of life),
   - Full-term newborns (up to 28 days of age) with jaundice, or who are hypoalbuminaemic or acidic because these are conditions in which bilirubin binding is likely to be impaired.

3. **Regular** blood counts (haemoglobin, erythrocyte, leucocyte and platelet counts and screening for prolongation of prothrombin time) should be carried out during treatment.

**References:**
1. Ceftriaxone – Safety in neonates: [Click here].
2. Pharmacology for Nursing Care, 8th Edition by Richard A. Lehne [Click here].
3. Ncbi.nlm.nih.gov: [Click here].
4. Ceftriaxone SmPC [Click here].

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**Cefdinir125mg/5ml suspension - Case of rectal bleeding to 4 months infant in Alexandria**

The regional center in Alexandria received a yellow card concerning a 4 months male infant who suffered from massive rectal bleeding after receiving Cefdinir125mg/5ml suspension (3ml/24 hr) as prescribed by the physician for chest infection management.

Cefdinir monohydrate suspension contains an extended-spectrum, semisynthetic cephalosporin, for oral administration. Cefdinir should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria.

Trade names for cefdinir125mg/5ml suspension in the Egyptian market: Cefdin®, Dinar®, Denrocef®, Omnicef®, Cednir®, Eglyn®, Cefathird®, Ramedinir, Maxdinir®, Merbactadin®, Bacticefdin®.

**Labeled information:**
According to Cefdinir suspension Summary of product Characteristics (SmPC) it was stated under section (Pediatric Use) that:
*(Safety and efficacy in neonates and infants less than 6 months of age have not been established)*
*And was stated under section (adverse drug reaction) that there is some Rare but important or life-*
threatening ADRs including: Bloody diarrhea, hemorrhagic colitis, melena, bleeding tendency, upper GI bleeding

**Recommendations for Healthcare Professionals:**

- Cefdinir Safety and efficacy in neonates and infants less than 6 months of age have not been established (Also there is no doses recommended for pediatric less than 9 kg wt)
- There is potential association of cefdinir with “bloody stool”
- The total daily dose in Pediatric Patients for all infections is 14 mg/kg dose (Age 6 Months Through 12 Years), up to a maximum dose of 600 mg per day. Once-daily dosing for 10 days is as effective as twice daily dosing.
  - Cefdinir for oral suspension should be administered twice daily in skin infections.
  - Cefdinir for oral suspension USP may be administered with or without food.

**References:**

1. Drugs.com- cefdinir SmPC (Click here)
2. Up to date (Click here)
3. The American board of family medicine (Click here)

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**Gluten- and Casein - free diets for Autistic spectrum disorder**

**The Egyptian pharmaceutical vigilance regional center in Sohag** had received a report about (aggravation of mental behavior disorder (*autism*) and GIT disturbance after administration of milk derivative products by autistic patient)

*Autism:* is a complex neurobehavioral disorder that includes impairments in social interaction and developmental language and communication skills combined with rigid, repetitive behaviors.

*Gluten* is found in wheat, rye, and barley.

*Casein* is found in milk and other dairy products.

**(BCM7)** is a peptide called beta-casomorphin-7, this peptide is released on digestion from A1 beta-casein.

*By search in Scientific websites and references, it was found:*

*According to the FDA:*

“It has been reported that casein can be broken down into casomorphin, a peptide fragment with opioid qualities, which has been suggested to increase the release of histamine. It is also thought that casomorphin is responsible for aggravating the symptoms of autism and because casein and gluten are so similar, many children with autism spectrum disorders are on a casein and gluten-free diet”.

*Indian Journals.com* “There is strong evidence that links this casein and its opioid derivative with
heart disease, mental disorders such as autism and schizophrenia, type-1 diabetes and a number of other autoimmune disorders.

**NCBI (National Center for Biotechnology Information):**

“There is limited evidence for a number of novel treatments, particularly magnesium with pyridoxine, omega-3 fatty acids, the gluten free casein -free diet, and low-frequency repetitive trans cranial magnetic simulation. Zinc and L-carnosine are potential novel treatments supported by basic research but not clinical studies.

**Milk Proteins and Human Health, Sydney, 22 May 2011**

“BCM7 has long been considered a risk factor for autism but the hypothesis remains controversial. Trials with animals show that BCM7 crosses the blood-brain barrier and leads to autistic type behavior. Milk elimination trials in humans have produced positive results but are often criticized for lack of double blind protocols. Many autistic children suffer from digestive complaint which may make them susceptible to BCM7 absorption. There are theoretical ground to suspect that BCM7 reaching the brain will affect the seratoninergic system with implications for neurological development”

**Drugs .com**

Your child's caregiver may suggest that your autistic child **not eat foods with gluten and casein.**

**However by search, other scientific websites revealed that this relation can not proved and large scale, good quality randomised controlled trials are needed.**

**References:**
- FDA ([Click here](#)).
- Drugs.com ([Click here](#)).
- NCBI: ([Click here](#)).
- Onlinelibrary.wiley.com ([Click here](#)).
- indianjournals ([Click here](#)).
- An Address to the General Practitioners Conference, Sydney, 22 May 2011 ([Click here](#)).
Study shows new drug effectively blocks malaria

Approximately 200 million malaria cases occur around the world every year, and approximately 500,000 people die from malaria. Many of these deaths are African children. Malaria infects the body through a parasite known as Plasmodium falciparum (Pf). Even though the disease is treatable with antimalarial drugs, many times the drugs are harsh and the body develops resistance to them. In 2011, it was found that basigin, a human protein, is needed for Pf strains to invade red blood cells. This step is crucial to the life cycle of the parasite. Many antibodies treat malaria by blocking the parasite and protein interaction, and now the researchers have created a nontoxic antibasigin drug (Ab-1). This drug effectively treated the blood infection in mice. The new study used mice as its test subjects. There were no obvious side effects to the treatments, which hints that it may be safe and effective for humans to use the drug. Because basigin has also been suggested as being part of the progression of cancer and graft-versus-host disease for transplant patients, basigin-blocking drugs have already been shown to be safe and effective for humans. They are currently in clinical use.

Reference
Vaccine News Daily: (Click Here)

FDA approves new chronic hepatitis C infection treatment

The U.S. Food and Drug Administration (FDA) approved a Drug to be used as treatment for hepatitis C virus (HCV) genotype 3 infections. This is the first drug that has shown efficacy and safety adequate to treating genotype 3 HCV infections. These demonstrations have shown that The drug does not require a co-administration of ribavirin or interferon,. Hepatitis C, a viral disease, inflames the liver and may develop into liver failure or reduced liver function. Many people with HCV infections do not show any symptoms until they develop liver damage, which can take years. People who have chronic HCV infections develop cirrhosis, or scarred livers with poor functioning, over time.

Reference
Vaccine News Daily: (Click Here)
CDC connects weak immune systems to measles complications.

The Centers for Disease Control and Prevention (CDC) recently published an update about a measles-related death in the U.S., saying a weak immune system was a serious contributor to the death. The CDC has used this opportunity to warn the general public that measles is more serious for people who have under-developed or weakened immune systems, emphasizing that measles is potentially life-threatening for these individuals.

Measles is highly contagious, even before the rash starts, and is easily spread when an infected person breathes, coughs, or sneezes. If not protected, a person can get measles just by walking into a room where someone with the disease has been in the past couple of hours. Those with compromised immune systems can have more serious, more severe, and sometimes deadly symptoms of pneumonia, diarrhea, middle ear infections, and even serious brain infections. In these cases, measles symptoms appear differently.

Reference
Vaccine News Daily: (Click Here)

New vaccine patch protects against flu in humans.

Flu vaccines delivered using microneedles that dissolve in the skin can protect people against infection even better than the standard needle-delivered vaccine, according to new research. The authors of the study say their dissolvable patch - the only vaccination system of its kind - could make vaccination easier, safer, and less painful. According to the World Health Organization, immunization prevents an estimated 2-3 million deaths every year. The continued threat of pandemics such as H1N1 swine flu and emerging infectious diseases such as Ebola makes vaccine development and mass vaccination a priority for global healthcare. Most vaccines are injected under the skin or into the muscle using needles. While this is an effective delivery method, it requires medical personnel with technical skills and brings the risk of needle-related diseases and injuries. The new microneedle patch is made of dissolvable material, eliminating needle-related risks. It is also easy to use without the need for trained medical personnel, making it ideal for use in developing countries, where healthcare resources are limited.

Reference
Science Daily: (Click Here)
Experimental MERS vaccine shows promise in animal studies

A two-step regimen of experimental vaccines against Middle East respiratory syndrome (MERS) prompted immune responses in mice and rhesus macaques, report National Institutes of Health scientists who designed the vaccines. Vaccinated mice produced broadly neutralizing antibodies against multiple strains of the MERS coronavirus (MERS-CoV), while vaccinated macaques were protected from severe lung damage when later exposed to MERS-CoV. The findings suggest that the current approach, in which vaccine design is guided by an understanding of structure of viral components and their interactions with host cells, holds promise for developing a similar human MERS vaccine regimen.

The three prime-boost regimens that elicited the most robust immune responses in mice were then tested in groups of macaques and were found to elicit similar immune system responses. A separate group of 18 macaques (12 vaccinated, six unvaccinated) were exposed to MERS-CoV 19 weeks after the vaccinated animals received the boost injection. Although macaques do not develop overt MERS disease, the researchers observed that unvaccinated animals experienced lung abnormalities indicative of pneumonia that were more profound and longer lasting than those seen in the vaccinated animals. The team is now working on refining the vaccine candidates and may eventually test a second-generation vaccine candidate in clinical trials.

Reference
Science Daily: (Click Here)

Strong diabetes and TB connection discovered

Researchers discovered a strong connection between tuberculosis (TB) and diabetes in the nation’s tropical region.
Though there has been improvements in antibiotics and sanitation, TB continues to be one of the leading bacterial killers around the world.
The research built on previous studies conducted in developing countries, which still have TB at endemic status. The earlier studies also showed a connection between TB and diabetes.
The latest study showed that patients who have diabetes have a higher likelihood of developing TB when compared to the general population.
If a person has diabetes, they are up to seven times more likely to contract TB compared to the general population. You can have TB your whole life and not know it, but if you suffer from diabetes and your immune system is not functioning well, it can flare up

Reference
Vaccine News Daily: (Click Here)
What is Pharmacovigilance

According to the WHO, Pharmacovigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine-related problem.

What is the Egyptian Pharmaceutical Vigilance Center

With the increasing demand for patient’s safety which is becoming more stringent, the regulatory authorities are facing an increased demand for patient welfare and safety. Thus, The Egyptian Pharmaceutical Vigilance Center (EPVC) is constructed within The Central Administration of Pharmaceutical Affairs (CAPA) Ministry of Health to be responsible for the collection and evaluation of information on pharmaceutical products marketed in Egypt with particular reference to adverse reactions. Furthermore, EPVC is taking all appropriate measures to:

1. Encourage physicians and other healthcare professionals to report the suspected adverse reactions to EPVC.

2. Necessitate the pharmaceutical companies to systematically collect information on risks related to their medical products and to transmit them to EPVC.

3. Provide information to end-users through adverse drug reaction news bulletins, drug alerts and seminars.

A call for reporting

Please remember that you can report suspected adverse reaction of medicines to EPVC, and adverse reaction following immunization to NORCB using the following communication information:

51 Wezaret El Zeraa Street, Agouza, Giza P.O. Box: 354 Dokki
Phone: +202 – 37 480 478 ext. 118
Fax: +202 – 37480472
Email: pmsdep@yahoo.com

Communications information

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Email: pv.center@eda.mohealth.gov.eg

National Organization for Research & Control of Biologicals
Post Marketing Surveillance and Adverse Event Following Immunization Department
51 Wezaret El Zeraa Street, Agouza, Giza P.O. Box: 354 Dokki
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