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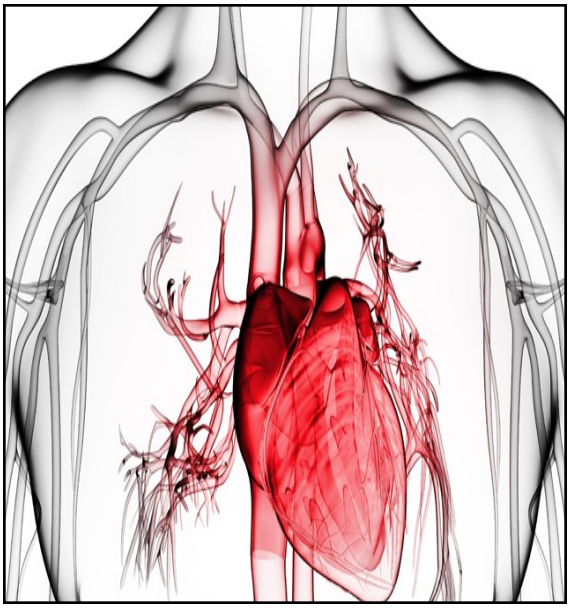
FDA Warns about Azithromycin's Fatal Cardiac Risk

The US Food and Drug Administration (FDA) warned about using *azithromycin* antibiotic as it poses a risk for a potentially fatal irregular heart rhythm and recommended a careful screening of patients using this drug.(1)

Azithromycin, a macrolide-class antibiotic was found to cause abnormal changes in the electrical activity of the heart, that may prolong the QT interval and trigger a rare, associated arrhythmia called torsades de pointes - uncommon and distinctive form of polymorphic ventricular tachycardia (VT) characterized by a gradual change in the amplitude and twisting of the QRS- in people with certain risk factors, according to FDA officials.(1)

The FDA stated that patients at risk for *azithromycin*-induced arrhythmia include those who already have a prolonged QT interval, low blood levels of potassium or magnesium, and abnormal slow heart rate, or who take drugs to treat arrhythmias. Elderly patients and patients with cardiac disease also may be more susceptible to the arrhythmogenic effects of the antibiotic. (2)



FDA notes potential risk of QT prolongation with azithromycin should be placed in appropriate context

The FDA recommends that physicians should consider other treatment options for patients who already are at risk for cardiovascular events and notes that "the potential risk of QT prolongation with *azithromycin* should be placed in appropriate context when choosing an antibacterial drug.(3)

References:
1. *Lowes, Robert. "Azithromycin Poses Fatal Cardiac Risk, FDA Warns."Medscape.com. 12 Mar. 2013. Web. 21 Sept. 2015.*
2. *Lowes, Robert. "FDA Safety Changes: Azithromycin Linked With Fatal Irregular Heart Rhythms." Medscape.org. Web. 21 Sept. 2015.*
3. *"Azithromycin Poses Risk of Potentially Fatal Arrhythmias, FDA Warns."Aafp.org. Web. 21 Sept. 2015.*

Egypt Awaits Two New Hepatitis C Drugs

In July 2015, Adel al-Adawy, the Minister of Health, announced that Harvoni® and Viekira PAK®, two new hepatitis C drugs, will be available by November 2015 at the hepatitis treatment centers.(2)

Hossam Abdel Ghaffar, the spokesperson of the Ministry of Health, announced earlier that the government is negotiating importing a U.S hepatitis C treatment called Harvoni® which is produced by Gilead science, at a low price.(3)

In October 2014, Harvoni® *(sofosbuvir/ledipasvir)* was the first US Food and Drug Administration (FDA) approved interferon- and ribavirin-free treatment for Hepatitis C genotype 1. In December 2014, the FDA also approved Viekira PAK® *(ombitasvir, paritaprevir, and dasabuvir)* as a second HCV treatment for Hepatitis C genotype 1.(1)

The major differences between Sovaldi® *(sofosbuvir)*, Harvoni® and Viekira® are that Sovaldi® is part of a combination therapy that cannot be taken alone. It should be combined with *pegylated interferon* and *ribavirin* and it has been shown to work for genotypes 1, 2, 3, and 4 in just 12 or 24 weeks, depending on the genotype.

On the other hand, Harvoni® combines two active constituents in one pill that is taken once daily in 12 weeks of treatment for the majority of the patients. Viekira PAK® is a 3D treatment combining *ombitasvir, paritaprevir*, and *dasabuvir*. The PAK contains *ritonavir* that helps to elevate the blood levels of *paritaprevir*. Viekira PAK® is used for 12 to 24 weeks with or without *ribavirin*.(1)

Al-Adawy announced that Harvoni® and Viekira PAK® will be available at the hepatitis treatment centers

References:
1. *"HCV Advocate Newsletter." HCV Advocate. Ed. Alan Franciscus. 2015. Web. 18 Sept. 2015.*
2. *2 New Hepatitis C Drugs to Be Available in November in Egypt. (2015, July 8). Retrieved September 18, 2015, from http://www.thecairopost.com/news/158838/news/2-new-hepatitis-c-drugs-to-be-available-in-november-in-egypt*
3. *"Egypt Negotiates Importing Hepatitis C Drug Harvoni at Lower Price." The Cairo Post. 18 May 2015. Web. 18 Sept. 2015.*

"A contraindication for concomitant use of repaglinide and clopidogrel has been added to the product monographs."

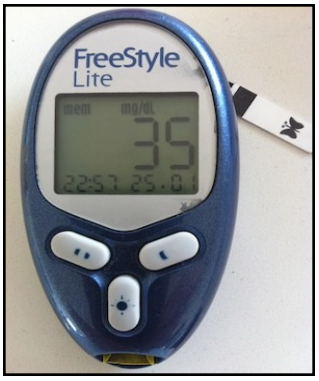
Concomittant Use of Repaglindine and Clopidogrel May Lead to Hypoglycemia

Health Canada has declared that a contraindication for concomitant use of *repaglinide* and *clopidogrel* has been added to the product monographs of these drugs. (1)

Novo Nordisk Canada and Health Canada have reviewed new safety information determining that coadministration of *repaglinide* and *clopidogrel* may lead to a significant drug-drug interaction. (2) *Clopidogrel*, a CYP2C8 inhibitor, may inhibit the metabolism of *repaglinide*, potentially increasing its systemic exposure and the risk of hypoglycemia.(1)

Key messages(3):

- Co-administration of *repaglinide* and *clopidogrel* (a CYP2C8 inhibitor) may lead to a significant decrease



This drug-drug interaction potentially increases the risk of hypoglycemia

in blood glucose levels.

- The concomitant use of *repaglinide* and *clopidogrel* is now contraindicated.
- The prescriber information for GLUCONORM® (*repaglinide*) has been updated. The prescriber information for PLAVIX® (*clopidogrel*) is currently being updated. The prescriber information for the generic products will be updated.

References:

1. *"Concomitant Use of Repaglinide and Clopidogrel Contraindicated in Canadian Labeling: Update." Wolters Kluwer. 15 Aug. 2015. Web. 13 Sept. 2015.*
2. *"Warning on Concomitant Use of Clopidogrel and Repaglinide." The Pharmaletter. 1 Aug. 2015. Web. 13 Sept. 2015.*
3. *"Gluconorm (repaglinide) - New Contraindication for Concomitant Use with Clopidogrel." Healthy Canadians. Health Canada, 31 July 2015. Web. 13 Sept. 2015.*

"Praulent® is approved for use in adjunct to diet and maximally tolerated statin therapy in adult patients."

A New Class of Drugs Gains FDA Approval for the Treatment of LDL Cholesterol

On July 2015, Praulent® gained the US Food and Drug Administration (FDA) approval for treatment of High LDL Cholesterol in adult patients.

Praulent® a new proprotein convertase subtilisin kexin type 9 (PCSK9) inhibitors

Praulent® is considered the first cholesterol-lowering treatment approved in a new class of drugs known as *proprotein convertase subtilisin kexin type 9* (PCSK9) *inhibitors*.[1]

Praulent® is an antibody that targets a specific protein, called PCSK9. This protein reduces the number of receptors found on the liver that eliminate LDL cholesterol from the blood. By blocking the ability of PCSK9, more receptors will be available to remove LDL cholesterol from the blood, consequently; it will lower the cholesterol level.[2]

Praulent® is approved for use in adjunct to diet, and maximally tolerated statin therapy in adult patients require additional lowering of LDL cholesterol level, such as patients who suffer from heterozygous familial hypercholesterolemia (HeFH) or from atherosclerotic cardiovascular disease such as stroke or heart attack.[2]

This drug is available in two different doses (75 mg and 150 mg). Both doses are available in a single 1 milliliter (mL) injection. It is given in a single-dose by syringe or prefilled pen that patients self-administer every two weeks.[1]

References:

1. *"Sanofi and Regeneron Announce FDA Approval of Praluent® (alirocumab) Injection, the First PCSK9 Inhibitor in the U.S., for the Treatment of High LDL Cholesterol in Adult Patients." Sanofi - Media - Press Nasdaq. 24 July 2015. Web. 18 Sept. 2015.*
2. *"FDA Approves Praluent to Treat Certain Patients with High Cholesterol." U.S. Food and Drug Administration. 24 July 2015. Web. 18 Sept. 2015.*

Codeine Not to Be Used in Children below 12 Years for Cough and Cold

The Coordination Group for Mutual Recognition and Decentralized Procedures Human (CMDh) has agreed upon new measures to minimize the risk of serious side effects, with *codeine*-containing medicines when used for cough and cold in children.[1]

Codeine for cough and cold in children below 12 years is now contraindicated, and not recommended with compromised respiratory function in children between 12 and 18 years.[2, 3]

Codeine is also contraindicated in women during breastfeeding and patients known to be CYP2D6 ultra -rapid metabolizers.[3]

Since the way *codeine* is converted into morphine is unpredictable in children below 12 years,

the available data explains that this population is at special risk of morphine-induced side effects. [3]
The safety of using *codeine*-containing medicines to treat coughs and colds in children younger than 18 years is under investigation, because of the potentiality of serious adverse effects, including slowed or difficult breathing.[2]
The international guidelines call attention to the fact that cough associated with viral infections may be satisfactorily managed with fluids and increased ambient humidity. The evidence that *codeine* is effective in children is limited, and in the case of chronic cough, treatment should be directed at the underlying disease. [3]
Healthcare professionals are encouraged to report adverse events or adverse effects related to the use of these products to MedWatch, the FDA's safety information and adverse event reporting program.[2]

New measures to minimize the risk of serious side effects, with *codeine*-containing medicines

References:

1. *"Codeine Not to Be Used in Children below 12 Years for Cough and Cold." PharmAround. Web. 8 Sept. 2015.*
2. *FDA Reviewing Safety of Codeine for Cough in Kids under 18. Medscape. Jul 01, 2015.*
3. *"Codeine Not to Be Used in Children below 12 Years for Cough and Cold." European Medicines Agency. 24 Apr. 2015. Web. 8 Sept. 2015.*

FDA Strengthens NSAID Warning for Heart and Stroke Risks

The US Food and Drug Administration (FDA) strengthened an existing warning that there is an increased heart attack and stroke risk for the use of *non-steroidal anti-inflammatory drugs* (*NSAIDs*). [1]
The first boxed warning regarding *NSAIDs* heart risk was added by the FDA back in 2005 and no modifications were made ever since that date. *NSAIDs* are used to reduce fever and pain in minor aches like headache, toothache, backaches, cramps...etc. Common over the counter *NSAIDs* include ibuprofen and naproxen along with other medications. However, over the years many studies revealed the mechanism of *NSAIDs* heart risk which is possibly attributed to the decreased prostacyclins. [1,2]
The new recommendations issued by the FDA include the following:

- The risk of heart attack and stroke may increase even with the short-term use, and the risk begins within few weeks of *NSAIDs* intake.
- The risk is correlated with higher doses and longer treatment durations for *NSAIDs*.
- In general, the risk is greater in patients with history of heart disease. However, patients with no history of any heart conditions might be at risk.
- The new label indicates that there is no enough information whether the risk is higher or lower for one *NSAID* compared with the others.
- Patients are at increased risk for heart failure with *NSAIDs* use.[2]

These new recommendations have been issued following a comprehensive review of new safety information including observational studies, a large combined analysis of clinical trials, and other scientific publications. FDA will require drug manufacturers of *NSAIDs* products to update their labels with these new recommendations issued by the FDA. [1]

References:

"FDA Strengthens Warning of Heart Attack and Stroke Risk for Non-Steroidal Anti-Inflammatory Drugs.". FDA, 9 July 2015. Web.
"FDA Strengthens Warning That NSAIDs Increase Heart Attack and Stroke Risk." Harvard Health Publications. Harvard University, 13 July 2015. Web.

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