Drug Information Bulletin

Drug Information Centre (DIC)
Indian Pharmaceutical Association
Bengal Branch
Tele fax: 033 24612776, E-mail: ipabengal.dic@gmail.com
Web Site: http://www.ipabengal.org
Contact: 09830136291

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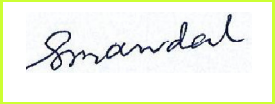
Content

Editorial

Wishing you all a happy "Durgotsab"!

The U.S. FDA has learned that some Ranitidine products contain a nitrosamine impurity called N-nitrosodimethylamine (NDMA) at low levels. NDMA is classified as a possible human carcinogen (a substance that could cause cancer) based on results from laboratory tests. NDMA is a known environmental contaminant and found in water and foods, including meats, dairy products, and vegetables.

Some of the companies manufacturing and marketing products of Ranitidine voluntarily recalled/hold their products, but some other companies are continuing selling their products in USA and the same status in India. The regulators and the manufacturers are investigating the same. As there is no limit test for NDMA in Ranitidine or its products in USP of IP they are trying to know if it is more than the limit prescribed for food. In the meantime is noted that the method published by USFDA for testing Angiotensin II Receptor Blocker (ARBs) for nitrosamine impurities. That method is not suitable for testing Ranitidine because heating the sample generates NDMA. Therefore a suitable method is require to be developed and included in the monograph of Ranitidine in Pharmacopoeias. In the meantime a stringent pharmacovigilance require to be in place to identify and ADR if developed.



Dr. Subhash C. Mandal
Editor
E mail: subhash.mandaldr@gmail.com
Mob. 9830136291

New Drug: Safinamide tablets, for oral use

Initial U.S. Approval: 2017 in the Brand name XADAGO

INDICATIONS AND USAGE: XADAGO is a monoamine oxidase type B (MAO-B) inhibitor indicated as adjunctive treatment to levodopa/carbidopa in patients with Parkinson's disease (PD) experiencing "off" episodes Limitations of Use: XADAGO has not been shown to be effective as monotherapy for the treatment of PD.

DOSAGE AND ADMINISTRATION: • Start with 50 mg administered orally once daily at the same time of day; after two weeks, the dose may be increased to 100 mg once daily, based on individual need and tolerability • Hepatic Impairment: Do not exceed 50 mg once daily in patients with moderate hepatic impairment; contraindicated in patients with severe hepatic impairment.

DOSAGE FORMS AND STRENGTHS: Tablets: 50 mg and 100 mg.

CONTRAINDICATIONS: XADAGO is contraindicated in patients with: • Concomitant use of the following drugs: o Other monoamine oxidase inhibitors or other drugs that are potent inhibitors of monoamine oxidase (e.g., linezolid) o Opioid drugs (e.g., tramadol, meperidine and related derivatives); selective norepinephrine reuptake inhibitors; tri-or tetra-cyclic or triazolopyridine antidepressants; cyclobenzaprine; methylphenidate, amphetamine, and their derivatives; St. John's wort o Dextromethorphan • A history of a hypersensitivity to safinamide • Severe hepatic impairment (Child-Pugh C: 10-15).

WARNINGS AND PRECAUTIONS: • May cause or exacerbate hypertension • May cause serotonin syndrome when used with MAO inhibitors, antidepressants, or opioid drugs • May cause falling asleep during activities of daily living • May cause or exacerbate dyskinesia; consider levodopa dose reduction • May cause hallucinations and psychotic behavior • May cause problems with impulse control/compulsive behaviors • May cause withdrawal-emergent hyperpyrexia and confusion.

ADVERSE REACTIONS: Most common adverse reactions (incidence on XADAGO 100 mg/day at least 2% greater than placebo) were dyskinesia, fall, nausea, and insomnia to report SUSPECTED ADVERSE REACTIONS, contact US WorldMeds, LLC, Inc. at 1-888-492-3246 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS: • Selective Serotonin Reuptake Inhibitors: Monitor patients for serotonin syndrome • Sympathomimetic Medications: Monitor patients for hypertension • Tyramine: Risk of severe hypertension • Substrates of Breast Cancer Resistance Protein (BCRP): Potential increase in plasma concentration of BCRP substrate.

Source: USFDA

Indian situation: CDSCO has approved Safinamide methane sulphonate bulk drug and Safinamide tablets 50, 100mg For the treatment of adult patients with idiopathic Parkinson's disease (PD) as addon therapy to a stable dose of Levodopa (Ldopa) alone or in combination with other Parkinson's disease (PD) medicinal products in mid to late stage fluctuating patients with effect from 09.09.2019.

Statement alerting patients and health care professionals of NDMA found in samples of ranitidine

Director - Center for Drug Evaluation and Research, Janet Woodcock M.D. released the statement on 13.09.2019

The U.S. Food and Drug Administration has learned that some ranitidine medicines, including some products commonly known as the brand-name drug Zantac, contain a nitrosamine impurity called N-nitrosodimethylamine (NDMA) at low levels. NDMA is classified as a probable human carcinogen (a substance that could cause cancer) based on results from laboratory tests. NDMA is a known environmental contaminant and found in water and foods, including meats, dairy products, and vegetables.

The FDA has been investigating NDMA and other nitrosamine impurities in blood pressure and heart failure medicines called Angiotensin II Receptor Blockers (ARBs) since last year. In the case of ARBs, the FDA has recommended numerous recalls as it discovered unacceptable levels of nitrosamines.

When the agency identifies a problem, it takes appropriate action quickly to protect patients. The FDA is evaluating whether the low levels of NDMA in ranitidine pose a risk to patients. FDA will post that information when it is available.

Patients should be able to trust that their medicines are as safe as they can be and that the benefits of taking them outweigh any risk to their health. Although NDMA may cause harm in large amounts, the levels the FDA is finding in ranitidine from preliminary tests barely exceed amounts you might expect to find in common foods.

Ranitidine is an over-the-counter (OTC) and prescription drug. Ranitidine is an H2 (histamine-2) blocker, which decreases the amount of acid created by the stomach. Over-the-counter ranitidine is approved to prevent and relieve heartburn associated with acid ingestion and sour stomach. Prescription ranitidine is approved for multiple indications, including treatment and prevention of ulcers of the stomach and intestines and treatment of gastroesophageal reflux disease.

The agency is working with international regulators and industry partners to determine the source of this impurity in ranitidine. The agency is examining levels of NDMA in ranitidine and evaluating any possible risk to patients. The FDA will take appropriate measures based on the results of the ongoing investigation. The agency will provide more information as it becomes available.

The FDA is not calling for individuals to stop taking ranitidine at this time; however, patients taking prescription ranitidine who wish to discontinue use should talk to their health care professional about other treatment options. People taking OTC ranitidine could consider using other OTC medicines approved for their condition. There are multiple drugs on the market that are approved for the same or similar uses as ranitidine.

Consumers and health care professionals should report any adverse reactions with ranitidine to the FDA's MedWatch program to help the agency better understand the scope of the problem:

- Complete and submit the report online at www.fda.gov/medwatch/report.htm
- Download and complete the appropriate form, then submit it via fax at 1-800-FDA-0178

The FDA, an agency within the U.S. Department of Health and Human Services, protects the public health by assuring the safety, effectiveness, and security of human and veterinary drugs, vaccines and other biological products for human use, and medical devices. The agency also is responsible for the safety and security of our nation's food supply, cosmetics, dietary supplements, products that give off electronic radiation, and for regulating tobacco products.

Source: USFDA

Indian regulatory measures: CDSCO has released a statement on 23.09.2019 directing all the State and UT Drugs Controllers to communicate to the manufacturers of Ranitidine APU and formulations under their jurisdiction to verify their products and take appropriate measures to ensure patient safety. DCGI also requested to let his office know the action taken.

Source: CDSCO

Different test methods show different levels of NDMA in Ranitidine Medicines

FDA is continuing to test ranitidine products from multiple manufacturers and is assessing the potential impact on patients who have been taking ranitidine. In addition, the agency has asked manufacturers of ranitidine to conduct their own laboratory testing to assess levels of NDMA in their ranitidine products and to send samples of ranitidine products to FDA to be tested by our scientists.

FDA observed the testing method used by a third-party laboratory uses higher temperatures. The higher temperatures generated very high levels of NDMA from ranitidine products because of the test procedure. FDA published the method for testing angiotensin II receptor blockers (ARBs) for nitrosamine impurities. That method is not suitable for testing ranitidine because heating the sample generates NDMA.

FDA recommends using an LC-HRMS testing protocol to test samples of ranitidine. FDA's LC-HRMS testing method does not use elevated temperatures and has shown the presence of much lower levels of NDMA in ranitidine medicines than reported by the third-party laboratory. International regulators using similar

LC-MS testing methods have also shown the presence of low levels of NDMA in ranitidine samples.

FDA will test ranitidine oral solution products and has begun testing samples of other H2 blockers and proton-pump inhibitors to help inform this ongoing investigation. To date, the agency's early, limited testing has found unacceptable levels of NDMA in samples of ranitidine. The agency will provide more information as it becomes available.

Source: USFDA News Release

NHSRC redesignated as WHO Collaborating Centre for Medical Devices

The National Health Systems Resource Centre (NHSRC) has been redesignated as a WHO collaborating centre for priority medical devices and health technology policy, an official statement said on Thursday.

The mandate of the division of healthcare technology at NHSRC is to draw up technical specifications for technologies procured under National Health Mission, draft policies for medical device maintenance and management, undertake evaluations of health product innovations and support the ministry on issues related to diagnostics initiative, National Dialysis Program among others.

In the past, NHSRC as a collaborating centre has supported WHO in formulating technical specifications for medical devices such as oxygen concentrators and resuscitation devices and continues to support evaluation of innovations for WHO's compendium on innovative devices, the statement said.

"This year in collaboration with WHO's country office, NHSRC developed a guidance document for the health ministry's free diagnostics initiative to further strengthen the agenda of universal access to affordable diagnostics," said the statement.

NHSRC also works with WHO on development of technical specification of blood pressure measuring devices, in vitro diagnostics and devices for cancer and cardiovascular diseases.

"Such global collaborations in the area of health technology will ensure that scientific and technological advances, research and development as well as innovative technologies play a substantial supportive role in healthcare and enable us to reach the public health goals and achieve universal health coverage," the statement said.

Source: ET Health World

Bhutan works to reach malaria-free status

The country of Bhutan is making rapid progress in reducing local cases of malaria and hopes to achieve malaria-free status from the World Health Organization in the coming years. In addition to increased access to screening and mosquito nets, the national effort has involved coining a local word for "larvae" and working in ways that respect the Buddhist culture's deep reverence for all life.

Source: BBC

EU approves GW's Cannabinoid Epidyolex for severe epileptic seizures

GW Pharma's Epidyolex, an oral cannabidiol solution, was approved by the European Commission as a treatment for patients with seizures resulting from Lennox Gastaut syndrome or Dravet syndrome. The approval is indicated for patients ages 2 years and older, and will be used as an adjunctive therapy with clobazam.

Source: PharmaTimes online (UK)