



# Clini



# News

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Drug Information Center - Al Jazeera Hospital

## Top five questions:

### *Q1: What is Nitrendipine? Does it have any skin reaction?*

**Answer:** Nitrendipine is a Calcium Channel Blocker dihydropyridine.

It has been used in SYST-EUR 2 study to prove reduction in the risk of cardiovascular complication in older patients (> 60 years) with isolated systolic hypertension. As a CCB it may have some, but rare skin reactions. Verapamil, nifedipine, and diltiazem have all been associated with the occurrence of Stevens-Johnson syndrome, erythema multiform and exfoliative dermatitis (each less than 1 case per 1 million prescriptions). Diltiazem was associated with toxic epidermal necrolysis (TEN) (0.09 cases per million prescriptions).

### *Q2: Which one of the Statins is suitable for use during breast-feeding?*

**Answer:** All Statins are not recommended to use during breast-feeding, as all of them are excreted in the breast milk and all have the potential for serious adverse effects on the baby. This is not the only class of lipid lowering drugs that should be avoided, Fibrates has the same contraindication, and however Cholestyramine use is controversial.

### *Q3: Which one of the following drugs (Carbamazepine – Gabapentin) is the preferable treatment for Diabetic neuropathy in a patient who is currently on the following drugs; Amiodarone, Digoxin and Warfarin?*

**Answer:** Gabapentin, which has no reported interaction with Warfarin, may be preferable, while Carbamazepine had an interaction with Warfarin with moderate severity and fair documentation leading to decreased anticoagulant effect of Warfarin, the probable Mechanism is by increased Warfarin metabolism.

### *Q4: What is the oral anti-fungal of choice for the treatment of allergic fungal sinusitis?*

**Answer:** The primary treatment of allergic fungal sinusitis is (surgical intervention+ systemic corticosteroids), alternatively Itraconazole, in a dose of 200 mg twice daily for 12 months can be used.

### *Q5: can Amiodarone induce SIADH?*

**Answer:** Drug- induced SIADH has been reported with Chlorpropamide, Carbamazepine, Cyclophosphamide, NSAIDs and SSRIs. However in the literature there are 2 case reports linking Amiodarone with this syndrome, although the mechanism of SIADH and associated hyponatremia secondary to Amiodarone is unclear.

## Natural Products- Drug Interactions:

The myth that natural products are completely safe is constantly promoted in advertising and creates a need for responsible public education.

The health care professional should be vigilant and seeks for information before prescribing, taking medical history or counseling a patient on natural products.

The following table has some of the natural products that are available in UAE, their beneficial uses, Cautions and some documented drug interactions.

Natural product	Clinical uses	Caution and documented drug interactions
Echinacea	Immunomodulator in the treatment of common cold and Influenza	Its immunomodulating effect makes it contraindicated in patients receiving immunosuppressant therapy.
Garlic	Hyperlipidemia, Hypertension and other cardiovascular indications	There are many reports of postoperative bleeding and spontaneous spinal epidural hematoma. It should be discontinued at least 10 days prior to elective surgery. Avoid combination with Anticoagulants
Ginkgo (Ginkgo biloba)	Alzheimer's disease, intermittent Claudication	-It inhibits platelet aggregation & increases INR when combined with Warfarin as it inhibits Warfarin metabolism( avoid combination) -it may causes subdural hematoma , subarchnoid hemorrhage have occurred when used alone or in combination with Aspirin ( avoid combination)
Ginseng	Improves well-being, enhance immune system and boasts energy	Combination with Insulin or Oral hypoglycemic may induce hypoglycemia
Glucosamine	Used alone or in combination with Chondroitin for osteoarthritis	It reduces Glucose tolerance and should be used only under medical supervision and monitoring in case of diabetic patients
St. John's wort	Mild to moderate depression	Induces Failure in the treatment of the following drugs: -Cyclosporin (organ rejection) -Protease inhibitors anti AIDS treatment -Oral contraceptives If combined with TCADs and SSRIs it may induce serotonin syndrome like adverse effects.

## Treatment options for elevated plasma Homocysteine level:

**Homocysteinemia**; is a condition of elevated levels of Homocysteine and its metabolites, which is produced due to disorder in Methionine metabolism.

This happens when there is disruption in any of the three interrelated pathways of Methionine metabolism;

§Deficiency in the cystathionine B- synthase enzyme **CBS**

§Defective methylcobalamin synthesis

§Abnormality in methylene tetrahydrofolate reductase **MTHFR**

The three different cofactors (vitamins) that are necessary for the completion of Methionine metabolism are Folate, Methylcobalamin, Pyridoxal -5- phosphate (Folic acid, B12 and B6 respectively).

In addition to the genetic predisposition Homocysteinemia may be prevalent due to nutritional and environmental factors such as;

§Chronic renal failure

§Hypothyroidism

§Malignancies

§Methotrexate treatment

§Smoking

Whatever the cause is Homocysteinemia is considered as an independent risk factor for all types of vascular diseases such as cerebrovascular accidents, coronary artery disease **CAD** and peripheral vascular disease.

Of the risk for CAD in the general population, 10% has been estimated as being attributable to Homocysteinemia.

Several mechanisms have been suggested as a possible cause of accelerated vascular disease induced by Homocysteinemia, these include;

§Endothelial cell damage

§Smooth muscle proliferation

§Lipid peroxidation

§Upregulation of prothrombotic factors (XII, V)

§Downregulation of antithrombotic factors or endothelial derived Nitric Oxide.

Although there are no firm therapeutic guidelines, Consideration should be given to the treatment as a primary prevention measure for patients whose baseline level > 14micromol/ liter. Treatment as a secondary prevention measure in patients with established CAD should be considered at level of = or > 11 micromol / liter (this level has been associated with an increase in cardiovascular events).

**Treatment:** include daily doses of **folic acid (400- 800mcg and as high as 8-10 mg can be used), and possibly in addition to Vitamin B6 (100 – 500mg) and Vitamin B12 (0.2 – 1 mg)**

**In one study** that had been done by researchers from Switzerland and the US\*, in attempt to assess the improvement of the clinical outcome after percutaneous coronary intervention **PCI**, Combination therapy with Folic acid, Cyanocobalamin B12 and Pyridoxine B6 were used. A total of 553 patients who had undergone angioplasty of one significant coronary stenosis were randomized to receive (**Folic acid 1 mg/ day + Cyanocobalamin 400mcg/day + pyridoxine 10 mg / day**) (n = 272), or placebo (n = 281) for 6 months.

The primary outcome measure was a composite endpoint of major adverse events (death, non fatal MI and repeated revascularization)

At the end of treatment, Homocysteine levels were significantly lower in the active

treatment group (7.5 micromol / liter), compared with placebo group (10.1 micromol/ l). There was significantly lower incidence of major adverse events in the active treatment group, relative to the placebo group at 6 months (11.4% vs 18.9 % Of patients) and at one year (15.4 % vs 22.8%) after the initiation of treatment.

Moreover, adjustments for multiple risk factors did not significantly affect this association.

There are a number of clinical trials that will further assess the efficacy of Folic acid and vitamins B6 and B12 still underway.

*\* The Swiss Heart Study: a randomized controlled trial. JAMA 2002; 288: p 973-9*

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### **Drugs safety updates:**

#### **New Risperdal safety information:**

Following discussion with FDA, Janssen Pharmaceutica has sent out a **Safety Alert** to highlight emerging safety information pertaining to cerebrovasculr events in elderly patients receiving Risperdal (Risperidone) for dementia.

The company examined data from 4 placebo- controlled dementia trials in elderly patients taking Risperdal within the approved dosage range for 4-12 weeks.

Overall, they found 29 cases of CVAs, including 4 fatal cases, in 764 patients who received Risperdal compared with only 7 cases (1 fatal) in 466 patients who received placebo. In addition, a review of the company's global post marketing database revealed a total of 37 spontaneous reports of CVAs associated with Risperdal, of which 16 were fatal. The prescribing information for Risperdal will be updated to include the new information.

#### **Heat Stroke reported with the use of Diphenhydramine, Haloperidol, Pseudoephedrine, Thioridazine and Imipramin**

5 patients developed heat stroke during a heat wave while using medications known to induce or worsen hyperthermia; these included Diphenhydramine, Haloperidol, Imipramine, Thioridazine and Pseudoephedrine (therapeutic indications, dosages and duration of treatment not stated)

one of the cases a 51 year old man had been receiving Diphenhydramine and Haloperidol when he was admitted with a temperature of 42 c. he developed rhabdomyolysis and was hospitalized for 21 days before discharge.

The WHO adverse drug reactions database contained 6 reports of malignant hyperpyrexia associated with Imipramine (Tofranil)

In hot climate country like U.A.E, the pharmacist should advise any patient who is utilizing these medications to avoid long standing in the open air and to avoid being dehydrated by ingesting adequate amount of fluid.



*All references are available upon request at "Drug Information Center", Al- Jazeira Hospital, Abu Dhabi. Ext.518.*