Glitazones & PPI’s May Increase Fracture Risk

Recent reports in the literature warn about an increased risk of fractures in women taking glitazones, a newer class of antidiabetic drugs. Both rosiglitazone (Avandia, Avandamet) and pioglitazone (Actos) have been implicated. The risk of fracture of the arm, hand, ankle and the foot occurs only in women (so far) at a rate of about one fracture per one hundred women taking a glitazone for one year. Researchers do not know if glitazones actually cause fractures but they do appear to be a contributing factor. It is suspected that bone formation is inhibited by glitazones. Women taking this class of drugs who have a history of fractures or are at greatest risk for falls might benefit from monitoring of bone mineral density.

Proton pump inhibitors (PPI’s) such as omeprazole (Losec) are associated with a higher risk of hip fractures (particularly with higher doses taken for more than one year). It is thought that the reduction of gastric acid by the PPI results in less calcium absorption (which requires an acid environment). The increased fracture risk with PPI’s is very small, however the morbidity associated with hip fracture is around 20% in the first year. “Even the smallest increase in risk could be significant in the overall population”. Clinicians recommend that PPI’s be used only when needed at the lowest effective dose. Adequate calcium and vitamin D levels are important when long-term therapy is indicated.

Development of B₁₂ Deficiency with Metformin

A known effect of long-term metformin is the development of vitamin B₁₂ deficiency in some patients. The incidence appears to be related to the dose and duration of metformin use. “Each 1 gram per day increase in metformin dose conferred more than a two-fold increased risk for developing B₁₂ deficiency”. The risk of deficiency almost doubles for patients taking metformin for more than three years. Patients taking more than one gram per day of metformin for three years or more should be monitored for B₁₂ deficiency.

Long-term Bisphosphonate Therapy May Not Be Necessary

Bisphosphonates such as alendronate (Fosamax) and risendronate (Actonel) improve bone density and reduce the risk of fractures in post-menopausal women and men. The drugs have a half-life of over ten years, thus remain in the bone for long periods of time. As a result even when bisphosphonates are discontinued the clinical benefits persist for at least five additional years. Researchers suggest “that five years of a bisphosphonate might be enough for women who have a good response and are at low risk for fractures”. A moderate decline in bone mineral density (BMD) does occur after discontinuation with a slightly higher risk for vertebral fractures. The risk of other types of fractures remains the same as with bisphosphonate treatment. Women who are at an increased risk of fracture (i.e. low BMD, low weight and body mass index, estrogen deficiency, alcoholism, poor nutrition, family history of osteoporosis, prior fracture, etc.) are not good candidates for bisphosphonate discontinuation.

BMD should be closely monitored (annually or every two years) whenever a bisphosphonate is discontinued. “In those with rapid decline in BMD after discontinuation of therapy (e.g. > 8% in one year, > 10% in 2 years or > 5% from baseline), resumption of bisphosphonate therapy or a switch to another osteoporosis agent should be considered”. (Refer to Medical Pharmacies News August 2006—Wisdom of Long-term Bisphosphonate Use Questioned for more information)

Interesting Tidbits...

Lavender & Tea Tree Oils & Gynecomastia ... An endocrinologist, alarmed by the unusual finding of enlarged breasts in preteen boys found that all were using hair products or soap that contained lavender or lavender plus tea tree oil (which have weak estrogenic and/or antiandrogenic activity). The gynecomastia improved when the products were discontinued.

Bisphosphonates & Eye Problems ... Blurred vision, eye pain and inflammation may occur as a rare side effect of bisphosphonates. Any eye problems should be reported to the physician.
Zyram XL 150, 200, 300 & 400 mg tabs
tramadol HCl controlled release
Purdue Pharma (not a benefit of ODB)

Zyram XL is a once-daily analgesic indicated in adults for the management of moderate pain (for several days or more).

**Warnings and Precautions:** Patients over 75 years of age may experience more adverse effects than younger patients. The product should be used with caution in the elderly.

The product should not be used in patients hypersensitive to tramadol or opioids, in pregnancy or lactating mothers, concomitantly with monoamine oxidase inhibitors (MAOI) or within 14 days of therapy with a MAOI, in severe renal or hepatic impairment or in patients with acute intoxication with alcohol, hypnotics, centrally-acting analgescics, opioids or psychotropic drugs. The risk of seizures may be increased in patients taking selective serotonin receptor inhibitors, tricyclic antidepressants and other opioids. Zyram XL may cause psychic and physical dependence.

If Zyram XL is discontinued therapy should be tapered gradually to avoid withdrawal reactions.

**Adverse Effects:** The most commonly reported adverse effects include constipation, dizziness, headache, nausea, somnolence and vomiting. Adverse effects may be reduced by titrating the dose slowly at 7 day intervals.

**Dose & Administration:** The usual initial dose in patients 18 years of age and older is 150 mg once daily, swallowed whole (not chewed, broken or crushed). When higher doses are required, doses should be titrated gradually with an interval of at least 7 days until pain relief is obtained for a duration of 24 hours (with no or tolerable side effects). Patients currently receiving other tramadol products (e.g. Tramacet-Janssen Ortho) may be transferred to Zyram XL at the nearest total daily dose. The maximum recommended dose is 400 mg once daily.

**Availability & Storage:** Zyram XL tablets are white, film-coated, oval-shaped tablets, plain on one side and with the letter “T” followed by strength on the other side. The tablets should be stored at room temperature (15° to 30° C), protected from light, moisture and high humidity.

(Refer to Medical Pharmacies News-Drug News, November 2005 for a review of Tramacet)

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**New Product Briefs**

**Exjade (deferasirox) tablets for oral suspension (Novartis)**...
Exjade is an iron chelating agent indicated in the management of chronic iron overload in patients with transfusion-dependent anemias aged 6 years and older (and in patients aged 2 to 5 who cannot be treated with deferoxamine). The tablets are available in strengths of 125 mg, 250 mg and 500 mg in blisters of 28 tablets.

**Protegol (14% aluminum Cl hexahydrate gel)** Nutimmune Technologies...
Protegol is available in a 35 ml size for the management of axillary hyperhidrosis.

**Zypraxa 20 mg tablets (olanzapine)** Eli Lilly...
New strength (not currently a benefit of ODB)

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**Discontinued**...

**Desocort Cream** (desonide) Galderma
**Dilaudid 3 mg Suppositories** (hydromorphone HCl) Abbott Labs
**Halcion 0.25 mg tablets** (triazolam) Pfizer
**Hycodan Syrup** 1 mg/ml (hydromorphone bitartrate) Bristol Myers Squibb
**Trans-Planter** (salicylic acid) Bristol Myers Squibb
**Trans-Ver-Sal** (salicylic acid) Bristol Myers Squibb
**Westcort Cream** (hydrocortisone-1-valerate) Bristol Myers Squibb
**Zelnorm 6 mg tablets** (tegaserod hydrogen maleate) Novartis

(Consult product monographs for complete information)

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