



bi-monthly newsletter focusing on migraine awareness and education.

HEADquarters Migraine Management Newsletter

NEWS BULLETIN: Serotonin Syndrome & Medication warnings

Special Edition July 2006

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Drugs affected by the FDA ruling

Greetings!

As you may recall, our February/March newsletter featured an article about serotonin syndrome. On July 19, the US FDA issued a public health advisory bulletin regarding the "Combined Use of 5- Hydroxytryptamine Receptor Agonists (Triptans), Selective Serotonin Reuptake Inhibitors (SSRIs) or Selective Serotonin/Norepinephrine Reuptake Inhibitors (SNRIs)."

Based on new information received, the US FDA has requested that all manufacturers of triptan medications, SSRI and SNRI antidepressant medications update their prescribing information to warn of the possibility of serotonin syndrome when triptans and these antidepressant medications are taken together.

Of 27 reports of serotonin syndrome occurring in the setting of triptans taken with either an SSRI or SNRI antidepressant reviewed by the FDA, two were life-threatening, and 13 cases required hospitalization. Some of the cases were people who had tolerated a triptan and an SSRI antidepressant previously. In 8 cases, the problems arose from adding a third serotonergic medication to the triptan/SSRI or SNRI combination or from dose increases.

Now—should you panic? Of course not. As mentioned in our last newsletter about this, the likelihood of this happening is low. Even the FDA is not counseling panic. What it is recommending to doctors is this:

Physicians prescribing a triptan, SSRI or SNRI should:

- keep in mind that triptans are often used intermittently and that either the triptan, SSRI or SNRI may be prescribed by a different physician
- weigh the potential risk of serotonin syndrome with the expected benefit of using a triptan with an SSRI or SNRI
- discuss the possibility of serotonin syndrome with patients if a triptan and an SSRI or SNRI will be used together
- follow patients closely if a triptan and an SSRI or SNRI are used together, particularly during treatment initiation, with dose increases, or with the addition of another serotonergic medication
- instruct patients who take a triptan and an SSRI or SNRI together to seek medical attention immediately if they experience the symptoms of serotonin syndrome

Serotonin Syndrome & Medication warnings

Drugs affected by the FDA ruling: SSRIs, SNRIs, and Combination Drug with an SSRI

Drug Containing an SSRI

Zoloft (sertraline)
 Celexa (citalopram) Lexapro (escitalopram)
 Luvox (fluvoxamine)
 Paxil (paroxetine)
 Prozac, Sarafem (fluoxetine)
 Symbyax (olanzapine & fluoxetine)

Triptans

Amerge (naratriptan)
 Axert (almotriptan)
 Frova (frovatriptan)
 Imitrex (sumatriptan)
 Maxalt and Maxalt-MLT (rizatriptan)
 Relpax (eletriptan)
 Zomig (zolmitriptan)

SNRIs

Cymbalta (duloxetine)
 Effexor (venlafaxine)

Other medications that can contribute to serotonin syndrome:

Tricyclic antidepressants

Elavil (amitriptyline)
 Pamelor (nortriptyline)
 Sinequan (doxepin)
 Tofranil (imipramine)
 Anafranil (clomipramine)
 Vivactil (protriptyline)

MAO Inhibitor antidepressants

Marplan (isocarboxazid)
 Nardil (phenelzine)
 Parnate (tranylcypromine)
 Eldepryl, Deprenyl (selegiline)
 Manerix (moclobemide)

Plant MAO Inhibitors

St. John's Wort (*Hypericum perforatum*)
 Yohimbe (used for erectile dysfunction)
 Syrian Rue (*Peganum harmala*)--hallucinogen
 Ayahuasca (*Banisteropsis caapi*)-- hallucinogen

Antibiotics/Antivirals

www.fda.gov/cder/drug/advisory/SSRI_SS200607.htm

What Should You Do?

Of course, it is more important than ever to make sure that all your doctors—and your pharmacist— know all the medications that you are taking. We recommend that you **keep a list of your medications** and take it to appointments to keep your health care providers updated. This is also why **keeping a headache diary** is so important— keeping track of what you have taken for a migraine attack can be invaluable if you start having odd symptoms a day or so later. (The majority of the cases reviewed by the FDA had symptoms within one day of taking the medication combination; a few were delayed reactions.)

What you should **not** do is abruptly stop your SSRI or SNRI antidepressant. Many of these medications have withdrawal syndromes, and need to be tapered and discontinued gradually. Furthermore, they were prescribed for you in the first place, and likely for a good reason. Always talk to your prescribing physician before making any changes in your medication regimen.

To review, early symptoms of serotonin syndrome (and “minor diagnostic criteria”) are agitation, nervousness, insomnia, rapid heart rate, rapid breathing, difficulty breathing, nausea, diarrhea, impaired coordination, dilated pupils, and high or low blood pressure. Remember—some of these are also going to occur during a headache: for example, pain can increase blood pressure a little. Some of these are also symptoms of anxiety, which occurs more commonly in headache sufferers than in the general population. (See our next newsletter for more on anxiety.)

Later, and more serious symptoms, of serotonin syndrome are fever, sweating, confusion, a change in mood like elation, semi-coma or even deterioration to coma, tremors, chills, muscular rigidity, serious difficulty breathing, brisk reflexes, and myoclonus (a form of muscle hyperreactivity.)

What you should also not do is panic if you just have some nausea or diarrhea. Although these can be some of the earlier symptoms of a serotonin syndrome, these are also migraine symptoms for a lot of people. The things that make a serotonin syndrome dangerous are high fever, high blood pressure, coma (obviously), and muscle rigidity that can lead to respiratory difficulty or collapse. The thing that a neurologist will look for in the diagnosis of a serotonin syndrome in addition to these is a muscular abnormality called clonus.

As always, educate yourself, and you will be ahead of the game.

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Empowering headache sufferers to help themselves

Zyvoxid (linezolid)
 Norvir (ritonavir)

Antiemetics

Zofran (ondansetron)
 Kytril (granisetron)
 Reglan (metoclopramide)

Other antidepressants

Desyrel (trazadone)
 Remeron (mirtazepine)
 nefazadone, (formerly available as Serzone)

Stimulants

amphetamine, methamphetamine
 Adderall, Dexedrine
 Desoxyn
 Pondimin* (fenfluramine)
 Redux* (dexfenfluramine)
 Meridia (sibutramine)

Drugs of Abuse

MDMA/Ecstasy
 methamphetamine
 cocaine
 LSD
 "foxy methoxy" (5-methoxydiisopropyltyptamine)

Miscellaneous

L-tryptophan
 Parlodel (bromocriptine)
 Sinemet (L-dopa)
 reserpine
 dextromethorphan
 Demerol, Dispadol (meperidine, pethidine)
 Ultram, Tramal (tramadol)
 Duragesic, Sublimaze (fentanyl)
 Talwin (pentazocine)
 lithium
 Buspar (buspirone)
 Ergots/ergotamine
 ginseng

*removed from the US market in 1997

One more reason not to panic:

This is the DSM-IV Diagnostic Criteria for the diagnosis of a caffeine-induced mental disorder:

1. *Caffeine-Induced Organic Mental Disorder 305.90 Caffeine Intoxication*
 1. *Recent consumption of caffeine, usually in excess of 250 mg.*
 2. *At least five of the following signs:*
 1. *restlessness*
 2. *nervousness*
 3. *excitement*
 4. *insomnia*
 5. *flushed face*
 6. *diuresis*
 7. *gastrointestinal disturbance*
 8. *muscle twitching*
 9. *rambling flow of thought and speech*
 10. *tachycardia or cardiac arrhythmia*

- 11. *periods of inexhaustibility*
- 12. *psychomotor agitation*
- 3. *Not due to any physical or other mental disorder, such as an Anxiety Disorder.*

One No-Doz® tablet contains 200 mg of caffeine. Each Excedrin® tablet you take contains 65 mg of caffeine. If you drink any coffee at all, and take two Excedrin® a day, you have gotten more than 250 mg of caffeine a day.

Does any of this sound similar to the symptoms of serotonin syndrome? Yes. This is why you should not panic, but be informed. Oh, and this much caffeine is really not a lot better for you than too much serotonin. It is unlikely to land you in the hospital, but it might just give you a headache.

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