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Drugs

Information for Healthcare Professionals: Selective Serotonin Reuptake Inhibitors (SSRIs), Selective Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs), 5-Hydroxytryptamine Receptor Agonists (Triptans)

Update: The issues described in this communication have been addressed in product labeling (see Drugs@FDA¹)

FDA ALERT [7/2006]: Potentially Life-Threatening Serotonin Syndrome with Combined Use of SSRIs or SNRIs and Triptan Medications

There is the potential for life-threatening serotonin syndrome (a syndrome of changes in mental status, autonomic instability, neuromuscular abnormalities, and gastrointestinal symptoms) in patients taking 5-hydroxytryptamine receptor agonists (triptans) and selective serotonin reuptake inhibitors (SSRIs) or selective serotonin/norepinephrine reuptake inhibitors (SNRIs) concomitantly (see drug names at the bottom of this sheet). This information is based on reports of serotonin syndrome occurring in patients treated with triptans and SSRIs/SNRIs, and the biological plausibility of such a reaction in persons receiving two serotonergic medications. The FDA recommends that patients treated concomitantly with a triptan and an SSRI/SNRI be informed of the possibility of serotonin syndrome (which may be more likely to occur when starting or increasing the dose of an SSRI, SNRI, or triptan) and be carefully followed.

This information reflects FDA's preliminary analysis of data concerning this drug. FDA is considering, but has not reached a final conclusion about this information. FDA intends to update this sheet when additional information or analyses become available.

To report any unexpected adverse or serious events associated with the use of these drugs, please contact the FDA MedWatch program using the contact information at the bottom of this page.

Considerations

- Weigh the potential risk of concomitant SSRI/SNRI and triptan use with the benefit expected from using each drug, prior to prescribing these drugs together.
- When prescribing an SSRI or a triptan, physicians should discuss the possibility of serotonin syndrome with patients if an SSRI and a triptan will be used concomitantly. Healthcare providers should keep in mind that triptans are often used intermittently, and that the SSRI, SNRI, or triptan may be prescribed by a different healthcare provider.
- Healthcare providers should be alert to the highly variable signs and symptoms of serotonin syndrome. Serotonin syndrome symptoms may include mental status changes (e.g., agitation, hallucinations, coma), autonomic instability (e.g., tachycardia, labile blood pressure, hyperthermia), neuromuscular aberrations (e.g. hyperreflexia, incoordination) and/or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea).
- If concomitant treatment with an SSRI or SNRI and triptan is clinically warranted, the patient should be carefully observed, particularly during treatment initiation and dose increases.

Data Summary

The FDA has reviewed 27 reports of serotonin syndrome reported in association with concomitant SSRI or SNRI and triptan use. Two reports described life-threatening events and 13 reports stated that the patients required hospitalization. Some of the cases occurred in patients who had previously used concomitant SSRIs or SNRIs and triptans without experiencing serotonin syndrome. The reported signs and symptoms of serotonin syndrome were highly variable and included respiratory failure, coma, mania, hallucinations, confusion, dizziness, hyperthermia, hypertension, sweating, trembling, weakness, and ataxia. In 8 cases, recent dose increases or addition of another serotonergic drug to an SSRI/triptan or SNRI/triptan combination were temporally related to symptom onset. The median time to onset subsequent to the addition of another serotonergic drug or dose increase of a serotonergic drug was 1 day, with a range of 10 minutes to 6 days.

Serotonin syndrome following concomitant SSRI or SNRI and triptan use is biologically plausible. SSRIs, SNRIs, and triptans independently increase serotonin levels. Therefore, it is expected that concomitant use of SSRIs or SNRIs and triptans would result in higher serotonin levels than the serotonin levels observed with the use of SSRIs, SNRIs, or triptans alone, potentially leading to serotonin syndrome.

SSRIs	SNRIs	Triptans
<ul style="list-style-type: none"> • Celexa (citalopram) • Fluvoxamine • Lexapro (escitalopram) • Paxil (paroxetine) • Prozac (fluoxetine) • Zoloft (sertraline) 	<ul style="list-style-type: none"> • Cymbalta (duloxetine) • Effexor (venlafaxine) 	<ul style="list-style-type: none"> • Amerge (naratriptan) • Axert (almotriptan) • Frova (frovatriptan) • Imitrex (sumatriptan) • Maxalt and Maxalt-MLT (rizatriptan) • Relpax (eletriptan) • Zomig and Zomig ZMT (zolmitriptan)

Additional Information

[Antidepressant Use in Children, Adolescents, and Adults](#)²

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