Chronic Psoriasis May Lead to Diabetes, CVD

BY BETSY BATES
Los Angeles Bureau

PARIS — Chronic cutaneous inflammation associated with psoriasis may trigger a cascade of metabolic events leading to serious systemic diseases, including diabetes and coronary heart disease, Enno Christophers, M.D., asserted at the European Congress on Psoriasis 2004.

A complex interaction of genetics, environmental factors, and age contributes to development of psoriasis and psoriatic flares, said Dr. Christophers, professor of dermatology at the University of Kiel (Germany).

Similarly, multifactorial causes are responsible for diseases found more commonly in people with psoriasis than those with other skin conditions or other adults. Obesity and alcoholism, both elevated in patients with psoriasis, may be environmental contributors.

But in some cases, the inflammatory connection is clear. For example, a recent study found that 30% of patients with psoriasis have evidence of arthritis.

"This is an extremely high figure that we need to memorize," Dr. Christophers said.

Crohn's disease is seen seven times more frequently in psoriasis patients than in patients with other skin diseases.

Evidence is building that chronic inflammation may also lead to development of insulin resistance and Syndrome X, characterized by hypertension, diabetes, adiposity, dyslipidemia, and coronary heart disease.

Patients with psoriasis suffer disproportionately from these conditions. Recent studies have shown that patients with severe psoriasis have a significantly elevated mortality rate from cardiovascular diseases.

In recently completed research, Dr. Christophers and associates at the University of Kiel found that hospitalized psoriasis patients have almost double the body mass index of other skin disease patients or of community controls.

They have sharply increased rates of hypertension and higher rates of diabetes in patients who are in their 40s (comparative *P* less than .001) and those in their 70s (*P* less than .001, with a prevalence of about 25%, compared with about 5% in patients with other skin diseases).

Longstanding systemic inflammation has an impact on endothelial function and lipids, both of which contribute to serious disease, Dr. Christophers stressed. Longstanding cutaneous inflammation may well have the same consequences.

The T-helper 1 response associated with psoriasis activates autoreactive T-cells, and may be compounded by environmental factors and diseases (streptococcal tonsillitis).

Therapies that activate a T-helper 2 response, such as biologics and fumaric acid esters, may dampen inflammation over the long term and protect patients from serious diseases, such as diabetes and heart disease. ■

ZOLOFT is indicated for the treatment of adults with major depressive disorder, social anxiety disorder, panic disorder, posttraumatic stress disorder (PTSD), premenstrual dysphoric disorder (PMDD), obsessive-compulsive disorder (OCD), and is also indicated for pediatric patients (aged 6 to 17 years) with OCD. The most common side effects in adults with major depressive disorder and other premarketing controlled trials for OCD, panic disorder, PTSD, PMDD, and social anxiety disorder include nausea, insomnia, diarrhea, dry mouth, ejaculation failure (primarily ejaculatory delay), somnolence, fatigue, tremor, dyspepsia, libido decreased, increased sweating, anorexia, and agitation. In pediatric patients, the overall profile of adverse events was similar to that of adults. However, the following events were also reported: fever, hyperkinesia, urinary incontinence, aggressive reaction, sinusitis, epistaxis, and purpura.

BRIEF SUMMARY. Consult the package insert for complete prescribing information.
CONTRAINDICATIONS: Concomitant use in patients taking either monoamine oxidase inhibitors (MAOIs) or pimozide is contraindicated.
WARNINGS: Cases of serious sometimes fatal reactions have been reported in patients receiving ZOLOFT in combination with an MAOI. ZOLOFT should not be used in combination with an MAOI, or within 14 days of discontinuing treatment with an MAOI. Similarly, at least 14 days should be allowed after stopping ZOLOFT before starting an MAOI. ZOLOFT is contraindicated in patients with a hypersensitivity to sertraline or any of the inactive ingredients in ZOLOFT. Clinical Worsening and Suicide Risk – Adult and pediatric patients with major depressive disorder (MDD) may experience worsening of their depression and/or emergence of suicidal ideation and behavior (suicidality), whether or not they are taking antidepressants; this risk may persist until significant remission occurs. Despite long-standing concern that antidepressants may have a role in inducing worsening of depression and emergence of suicidality in certain patients, their causal role has not been established. **Closely observe patients treated with antidepressants for clinical worsening and suicidality, especially when starting drug therapy, or when dose increases or decreases.** Consider changing the therapeutic regimen or discontinuing the medication in patients whose depression is persistently worse or whose emergent suicidality is severe, abrupt in onset, or was not part of presenting symptoms. Due to possible co-morbidity, observe the same precautions when treating patients with other psychiatric and nonpsychiatric disorders as when treating MDD patients. Anxiety, agitation, panic attacks, insomnia, irritability, hostility (aggressiveness), impulsivity, akathisia (psychomotor restlessness), hypomania, and mania, have been reported in adult and pediatric patients being treated with antidepressants for MDD and other indications, psychiatric or nonpsychiatric. Although the emergence of such symptoms and either the worsening of depression and/or the emergence of suicidal impulses has not been causally linked, consider changing the therapeutic regimen or discontinuing the medication in patients for whom such symptoms are severe, abrupt in onset, or were not part of presenting symptoms. **Alert families and caregivers of patients being treated with antidepressants for MDD or other psychiatric or nonpsychiatric indications to monitor patients for the emergence of both the symptoms described above and the emergence of suicidality, and report such symptoms immediately to health care providers.** Write ZOLOFT prescriptions for the smallest quantity of tablets consistent with good patient management to reduce risk of overdose. If treatment is to be discontinued, medication should be tapered, as rapidly as is feasible, but recognizing that abrupt discontinuation can be associated with certain symptoms (see PRECAUTIONS). ZOLOFT is approved in the pediatric population only for obsessive compulsive disorder. A major depressive episode may be the initial presentation of bipolar disorder. It is generally believed (though not established in controlled trials) that treating such an episode with an antidepressant alone may increase the likelihood of precipitation of a mixed/manic episode in patients at risk for bipolar disorder. Whether any of these symptoms represent such a conversion is unknown. Prior to initiating antidepressant treatment, patients should be adequately screened to determine if they are at risk for bipolar disorder; such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder, and depression. ZOLOFT is not approved for use in treating bipolar depression. **PRECAUTIONS: General—Activation of Mania/Hypomania –** During premarketing testing, hypomania or mania occurred in approximately 0.4% of ZOLOFT-treated patients. **Weight Loss –** Significant weight loss may be an undesirable result of treatment with sertraline for some patients, but on average, patients in controlled trials had minimal, 1 to 2 pound weight loss. **Seizure –** ZOLOFT has not been evaluated in patients with a seizure disorder. ZOLOFT should be introduced with care in patients with a seizure disorder. **Discontinuation of Treatment –** During marketing of ZOLOFT and other SSRIs and SNRIs, spontaneous reports of adverse events occurred upon discontinuation, particularly when abrupt. Symptoms included dysphoric mood, irritability, agitation, dizziness, sensory disturbances (e.g. paresthesias), anxiety, confusion, headache, lethargy, emotional lability, insomnia, and hypomania. These events are generally self-limiting, but serious discontinuation symptoms have been reported. Monitor patients for these symptoms when discontinuing treatment with ZOLOFT. Gradual dose reduction rather than abrupt cessation is recommended whenever possible. If intolerable symptoms occur following a dose reduction or upon discontinuation, resuming the previously prescribed dose may be considered. Subsequently, consider decreasing the dose at a more gradual rate. **Abnormal Bleeding –** Case studies have documented upper gastrointestinal bleeding episodes in patients taking serotonin reuptake inhibitors concurrently with nonselective NSAIDs or aspirin. Bleeding at other sites may be similarly potentiated. Caution patients about bleeding risk associated with concomitant use of ZOLOFT and nonselective NSAIDs, aspirin, or other drugs that affect coagulation. **Weak Uricosuric Effect –** ZOLOFT is associated with a mean decrease in serum uric acid of approximately 7%. The clinical significance of this weak uricosuric effect is unknown. **Use in Patients with Concomitant Illness –** Clinical experience with ZOLOFT in patients with certain concomitant systemic illness is limited. Use cautiously in patients with diseases or conditions that could affect metabolism or hemodynamic responses. In clinical studies, electrocardiograms of 774 patients taking ZOLOFT (excluding those with a recent history of myocardial infarction or unstable heart disease) indicate that ZOLOFT is not associated with the development of significant ECG abnormalities. In patients with chronic mild liver impairment, sertraline clearance was reduced, thus increasing AUC, C_{max}, and elimination half-life. Effects in patients with moderate and severe hepatic impairment have not been studied. Approach the use of sertraline with caution in patients with liver disease, and use a lower or less frequent dose in patients with liver impairment. Since ZOLOFT is extensively metabolized, excretion of unchanged drug in urine is a minor route of elimination. A clinical study has indicated that renal disease does not affect sertraline pharmacokinetics and protein binding. Therefore, no dosage adjustment is needed in patients with renal impairment. **Interference with Cognitive and Motor Performance–**In controlled studies, ZOLOFT did not cause sedation and did not interfere with psychomotor performance. **Hyponatremia –** Several cases of reversible hyponatremia have been reported, mostly in elderly individuals, some of whom were taking diuretics or who were otherwise volume depleted. **Platelet Function –** There have been rare reports of altered platelet function and/or abnormal results from laboratory studies in patients taking ZOLOFT. ***Drug Interactions:*** **Potential Effects of Coadministration of Drugs Highly Bound to Plasma Proteins –** Adverse effects may result from displacement of protein-bound ZOLOFT by other tightly bound drugs, eg, warfarin, digitoxin. Prothrombin time should be carefully monitored when ZOLOFT therapy is initiated or stopped. **Cimetidine –** When administering ZOLOFT with cimetidine, dosage adjustment after the starting dose of 50 mg should be guided by clinical effect. **CNS Active Drugs –** Concomitant use of ZOLOFT with diazepam or desmethyldiazepam may require dosage adjustment. Even though lithium levels were not altered in clinical trials, it is recommended that plasma lithium levels be monitored following initiation of ZOLOFT therapy with appropriate adjustments to the lithium dose. In a controlled study of a single dose (2 mg) of pimozide, 200 mg sertraline (q.d.) co-administration to steady state was associated with a mean increase in pimozide AUC and C_{max} of about 40%, but was not associated with any changes in EKG. Since the highest recommended pimozide dose (10 mg) has not been evaluated in combination with sertraline, the effect on QT interval and PK parameters at doses higher than 2 mg at this time is not known. The risk of using ZOLOFT in combination with other CNS active drugs has not been systematically evaluated. Caution is advised if the concomitant use of ZOLOFT and such drugs is required. There is limited controlled experience regarding the optimal timing of switching from other drugs effective in the treatment of major depressive disorder, OCD, panic disorder, PTSD, PMDD, and social anxiety disorder to ZOLOFT. Caution should be exercised when switching, particularly from long-acting agents. **Drugs Metabolized by P450 3A4 –** In three separate *in vivo* interaction studies, sertraline was coadministered with the cytochrome P450 3A4 substrates, terfenadine, carbamazepine, or cisapride, under steady-state conditions. The results of these studies indicated that sertraline did not increase plasma concentrations of terfenadine, carbamazepine, or cisapride. These data indicate that sertraline's extent of inhibition of P450 3A4 activity is not likely to be of clinical significance. Results of the interaction study with cisapride indicate that sertraline 200 mg (q.d.) induces the metabolism of cisapride (cisapride AUC and C_{max} were reduced by about 35%). **Drugs Metabolized by P450 2D6 –** Many antidepressants, eg, the SSRIs, including sertraline, and most tricyclic antidepressants inhibit the biochemical activity of the drug metabolizing isozyme cytochrome P450 2D6 (debrisoquin hydroxylase), and, thus, may increase the plasma concentrations of coadministered drugs that are metabolized by P450 2D6. This potential interaction is of greatest concern in those drugs metabolized primarily by 2D6 and which have a narrow therapeutic index, eg, the tricyclic antidepressants (TCAs) and the Type 1C antiarrhythmics propafenone and flecainide. The extent to which this interaction is an important clinical problem depends on the extent of the inhibition of P450 2D6 by the antidepressant and the therapeutic index of the coadministered drug. Antidepressants vary in their extent of clinically important 2D6 inhibition; sertraline at lower doses has a less prominent inhibitory effect on 2D6 than some others in the class. Nevertheless, even sertraline has the potential for clinically important 2D6 inhibition. Consequently, concomitant use of a drug metabolized by P450 2D6 with ZOLOFT may require lower doses than usually prescribed for the other drug. Whenever ZOLOFT is withdrawn from co-therapy, an increased dose of the coadministered drug may be required. **Sumatriptan –** Rare reports describe weakness, hyperreflexia, and incoordination following combined SSRI-sumatriptan treatment. Combined therapy warrants appropriate patient observation. **TCAs –** Caution is indicated in the coadministration of TCAs with ZOLOFT, because sertraline may inhibit TCA metabolism. The extent to which SSRI-TCA interactions may pose clinical problems depends on the degree of inhibition and the pharmacokinetics of the SSRI involved. Plasma TCA concentrations may need to be monitored, and the dose of TCA may need to be reduced, if a TCA is co-administered with ZOLOFT. **Hypoglycemic Drugs –** In a placebo-controlled trial in normal volunteers, concomitant use of ZOLOFT and tolbutamide caused a decrease in the clearance of tolbutamide, which may have been due to a change in the metabolism of the drug. The clinical significance of this is unknown. **Atenolol –** ZOLOFT (100 mg) administered to 10 healthy males had no effect on the beta-adrenergic blocking ability of atenolol. **Digoxin –** In another study, administration of ZOLOFT for 17 days (including 200 mg/day for the last 10 days) did not change serum digoxin levels or digoxin renal clearance. **Microsomal Enzyme Induction –** ZOLOFT was shown to induce hepatic microsomal enzymes, as determined by a decrease in antipyrine half-life. This small change reflects a clinically insignificant change in hepatic metabolism. **Electroconvulsive Therapy (ECT) –** There are no clinical studies establishing the risks or benefits of the combined use of ECT and ZOLOFT. **Alcohol –** Although ZOLOFT did not potentiate the cognitive and psychomotor effects of alcohol in clinical studies, the concomitant use of ZOLOFT and alcohol is not recommended. ***Carcinogenesis, Mutagenesis, Impairment of Fertility:*** Lifetime carcinogenicity studies carried out in mice and rats showed a dose-related increase of liver adenomas in male mice receiving sertraline at 10-40 mg/kg (0.25-1.0 times the MRHD on a mg/m² basis). No increase was seen in female mice or in rats of either sex receiving the same treatments, nor was there an increase in hepatocellular carcinomas. There was an increase in follicular adenomas of the thyroid in female rats receiving sertraline at 40 mg/kg. While there was an increase in uterine adenocarcinomas in rats receiving sertraline at 10-40 mg/kg, this effect was not clearly drug related. Sertraline had no genotoxic effects, with or without metabolic activation, based on laboratory assays. A decrease in fertility was seen in one of two rat studies at a dose of 80 mg/kg (4 times the maximum human dose on a mg/m² basis). ***Pregnancy—Pregnancy Category C:*** There are no adequate and well-controlled studies in pregnant women. ZOLOFT should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. **Pregnancy-Nonteratogenic Effects –** Neonates exposed to ZOLOFT and other SSRIs or SNRIs, late in the third trimester have developed complications requiring prolonged hospitalization, respiratory support, and tube feeding. Complications can arise immediately upon delivery. Reports include respiratory distress, cyanosis, apnea, seizures, temperature instability, feeding difficulty, vomiting, hypoglycemia, hypotonia, hypertonia, hyperreflexia, tremor, jitteriness, irritability, and constant crying. This is consistent with a direct toxic effect of SSRIs and SNRIs or, possibly, a drug discontinuation syndrome. In some cases, the clinical picture is consistent with serotonin syndrome. Consider carefully the potential risks and benefits when treating a pregnant woman with ZOLOFT during the third trimester. **Labor and Delivery –** The effect of ZOLOFT on labor and delivery in humans is unknown. **Nursing Mothers –** It is not known whether sertraline or its metabolites are excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when ZOLOFT is administered to a nursing woman. ***Pediatric Use –*** *In over 600 pediatric patients aged 6 to 17 years, drug exposure was generally similar to that of adults, when plasma concentrations were adjusted for weight. The effectiveness of ZOLOFT in pediatric patients with major depressive disorder, panic disorder, PTSD, PMDD, or social anxiety disorder has not been established. Subjects who completed 34 weeks of sertraline treatment (10 weeks placebo-controlled + 24 weeks open-label, n=68) had weight gain that was similar to that expected using data from age-adjusted peers. Regular monitoring of weight and growth is recommended. The risks, if any, that may be associated with ZOLOFT's use beyond 1 year in children and adolescents with OCD have not been systematically assessed. There are no studies that directly evaluate the effects of long-term use of sertraline on the growth, development, and maturation of children and adolescents. Although there is no affirmative finding for such effects, the potential of sertraline to have adverse effects with chronic use is not known.* **Geriatric Use –** Geriatric studies of ZOLOFT in major depressive disorder in patients 65 years of age revealed no overall differences in pattern of efficacy or adverse reactions relative to younger patients except for urinary tract infection (incidence 2% and greater than placebo). As with all medications, greater sensitivity of some older individuals cannot be ruled out. As with other SSRIs, ZOLOFT has been associated with cases of clinically significant hyponatremia in elderly patients. **ADVERSE REACTIONS: Incidence in Placebo-Controlled Clinical Trials—Most Common Treatment-Emergent Adverse Events:** The most common adverse events reported in adult patients receiving ZOLOFT (N=2799; N=2394 for placebo) for the treatment of major depressive disorder/other, OCD, panic disorder, PTSD, PMDD, and social anxiety disorder combined in controlled trials (incidence 2% or more for ZOLOFT and greater than placebo): **Autonomic Nervous System Disorders –** ejaculatory failure ([primarily ejaculatory delay; denominator used for male patients only] 14% [n=1118] vs 1% [n=926]), mouth dry (14% vs 8%), sweating increased (7% vs 2%). **Central & Peripheral Nervous System Disorders –** somnolence (13% vs 7%), dizziness (12% vs 7%), headache (25% vs 23%), paresthesia (2% vs 1%), tremor (8% vs 2%). **Disorders of Skin and Appendages –** rash (3% vs 2%). **Gastrointestinal Disorders –** anorexia (6% vs 2%), constipation (6% vs 4%), diarrhea/loose stools (20% vs 10%), dyspepsia (8% vs 4%), nausea (25% vs 11%), vomiting (4% vs 2%). **General –** fatigue (12% vs 7%). **Psychiatric Disorders –** agitation (5% vs 3%), anxiety (4% vs 3%), insomnia (21% vs 11%), libido decreased (6% vs 2%), nervousness (5% vs 4%). **Special Senses –** vision abnormal (3% vs 2%). ***Adverse Events in Pediatric Patients:*** In pediatric patients, the overall profile was similar to that of adults. However, the following events were also reported from controlled trials (n=281 treated with ZOLOFT) (incidence of 2% and at least twice that of placebo): fever, hyperkinesia, urinary incontinence, aggressive reaction, sinusitis, epistaxis, and purpura. ***Associated with Discontinuation of Treatment:*** The adverse events associated with discontinuation of ZOLOFT treatment (incidence at least twice that for placebo and at least 1% for ZOLOFT) in major depressive disorder and other premarketing controlled trials are agitation, diarrhea, dry mouth, ejaculation failure (primarily ejaculatory delay), headache, insomnia, nausea, somnolence, and tremor; in OCD are diarrhea, dizziness, ejaculation failure (primarily ejaculatory delay), insomnia, nausea, and somnolence; in panic disorder are agitation, diarrhea, dyspepsia, ejaculation failure (primarily ejaculatory delay), insomnia, nausea, nervousness, and somnolence; in PTSD are headache and nausea; in PMDD (daily dosing) are diarrhea, nausea, and nervousness; in PMDD (luteal phase dosing) are hot flushes, insomnia, nausea, and palpitation, and in social anxiety disorder are abdominal pain, anxiety, ejaculation failure (primarily ejaculatory delay), fatigue, headache, insomnia, and nausea. **Sexual Dysfunction with SSRIs:** Although sexual desire, sexual performance, and sexual satisfaction may change as a manifestation of psychiatric disorders, some evidence suggests that SSRIs may cause untoward sexual experiences. Reliable estimates of such untoward experiences are difficult to obtain, due to physician and patient reluctance; accordingly, product labeling is likely to underestimate their actual incidence. There are no adequate, well-controlled studies of sexual dysfunction with sertraline. Priapism has been reported with all SSRIs. Physicians should routinely inquire about possible sexual side effects in patients taking SSRIs. ***Other Events Observed During the Premarketing Evaluation of ZOLOFT:*** During premarketing assessment, multiple doses of ZOLOFT were administered to over 4000 adult subjects. Events are further categorized by body system and listed in order of decreasing frequency. Note: frequent=events occurring in at least 1/100 patients; infrequent=1/1000 patients; rare=less than 1/1000 patients. It is important to emphasize that although the events reported occurred during treatment with ZOLOFT, they were not necessarily caused by it. **Autonomic Nervous System Disorders –** *Frequent:* impotence; *Infrequent:* flushing, increased saliva, cold clammy skin, mydriasis; *Rare:* pallor, glaucoma, priapism, vasodilation. **Body as a Whole – General Disorders –** *Rare:* allergic reaction, allergy. **Cardiovascular –** *Frequent:* palpitations, chest pain; *Infrequent:* hypertension, tachycardia, postural dizziness, postural hypotension, periorbital edema, peripheral edema, hypotension, peripheral ischemia, syncope, edema, dependent edema; *Rare:* precordial chest pain, substernal chest pain, aggravated hypertension, myocardial infarction, cerebrovascular disorder. **Central and Peripheral Nervous System Disorders –** *Frequent:* hypertonia, hypoesthesia; *Infrequent:* twitching, confusion, hyperkinesia, vertigo, ataxia, migraine, abnormal coordination, hypoesthesia, leg cramps, abnormal gait, nystagmus, hypokinesia; *Rare:* dysphasia, coma, dyskinesia, hypotonia, ptosis, choreoathetosis, hyperreflexia. **Disorders of Skin and Appendages –** *Infrequent:* pruritus, acne, urticaria, alopecia, dry skin, erythematous rash, photosensitivity reaction, maculopapular rash; *Rare:* follicular rash, eczema, dermatitis, contact dermatitis, bullous eruption, hypertrichosis, skin discoloration, pustular rash. **Endocrine Disorders –** *Rare:* exophthalmos, gynecomastia. **Gastrointestinal Disorders –** *Frequent:* appetite increased; *Infrequent:* dysphagia, tooth caries aggravated, eructation, esophagitis, gastroenteritis; *Rare:* melena, glossitis, gum hyperplasia, hiccup, stomatitis, tenesmus, colitis, diverticulitis, fecal incontinence, gastritis, rectum hemorrhage, hemorrhagic peptic ulcer, proctitis, ulcerative stomatitis, tongue edema, tongue ulceration. **General –** *Frequent:* back pain, asthenia, malaise, weight increase; *Infrequent:* fever, rigors, generalized edema; *Rare:* face edema, aphthous stomatitis. **Hearing and Vestibular Disorders –** *Rare:* hyperacusis, labyrinthine disorder. **Hematopoietic and Lymphatic –** *Rare:* anemia, anterior chamber eye hemorrhage. **Liver and Biliary System Disorders –** *Rare:* abnormal hepatic function. **Metabolic and Nutritional Disorders –** *Infrequent:* thirst; *Rare:* hypoglycemia, hypoglycemia reaction. **Musculoskeletal System Disorders –** *Frequent:* myalgia; *Infrequent:* arthralgia, dystonia, arthrosis, muscle cramps, muscle weakness. **Psychiatric Disorders –** *Frequent:* yawning, other male sexual dysfunction, other female sexual dysfunction; *Infrequent:* depression, amnesia, paranoia, teeth-grinding, emotional lability, apathy, abnormal dreams, euphoria, paranoid reaction, hallucination, aggressive reaction, aggravated depression, delusions; *Rare:* withdrawal syndrome, suicide ideation, libido increased, somnambulism, illusion. **Reproductive –** *Infrequent:* menstrual disorder, dysmenorrhea, intermenstrual bleeding, vaginal hemorrhage, amenorrhea, leukorrhea; *Rare:* female breast pain, menorrhagia, balanoposthitis, breast enlargement, atrophic vaginitis, acute female mastitis. **Respiratory System Disorders –** *Frequent:* rhinitis; *Infrequent:* coughing, dyspnea, upper respiratory tract infection, epistaxis, bronchospasm, sinusitis; *Rare:* hyperventilation, bradypnea, stridor, apnea, bronchitis, hemoptysis, hypoventilation, laryngismus, laryngitis. **Special Senses –** *Frequent:* tinnitus; *Infrequent:* conjunctivitis, earache, eye pain, abnormal accommodation; *Rare:* xerophthalmia, photophobia, diplopia, abnormal lacrimation, scotoma, visual field defect. **Urinary System Disorders –** *Infrequent:* micturition frequency, polyuria, urinary retention, dysuria, nocturia, urinary incontinence; *Rare:* cystitis, oliguria, pyelonephritis, hematuria, renal pain, strangury. **Laboratory Tests:** Asymptomatic elevations in serum transaminases (SGOT [or AST] and SGPT [or ALT]) have been reported infrequently (approximately 0.8%). Hepatic enzyme elevations usually occurred within the first 1 to 9 weeks of treatment and promptly diminished upon drug discontinuation. ZOLOFT therapy was associated with small mean increases in total cholesterol (approximately 3%) and triglycerides (approximately 5%), and a small mean decrease in serum uric acid (approximately 7%) of no apparent clinical importance. The safety profile observed with ZOLOFT treatment in patients with major depressive disorder, OCD, panic disorder, PTSD, and social anxiety disorder is similar. ***Other Events Observed During the Postmarketing Evaluation of ZOLOFT:*** Reports of adverse events received since market introduction that are not listed above and that may have no causal relationship with ZOLOFT include: acute renal failure, anaphylactoid reaction, angioedema, blindness, optic neuritis, cataract, increased coagulation times, bradycardia, AV block, atrial arrhythmias, QT-interval prolongation, ventricular tachycardia (including torsade de pointes-type arrhythmias), hypothyroidism, agranulocytosis, aplastic anemia and pancytopenia, leukopenia, thrombocytopenia, lupus-like syndrome, serum sickness, hyperglycemia, galactorrhea, hyperprolactinemia, neuroleptic malignant syndrome-like events, extrapyramidal symptoms, oculogyric crisis, serotonin syndrome, psychosis, pulmonary hypertension, severe skin reactions, which potentially can be fatal, such as Stevens-Johnson syndrome, vasculitis, photosensitivity and other severe cutaneous disorders, rare reports of pancreatitis, and liver events — clinical features (which in the majority of cases appeared to be reversible with discontinuation of ZOLOFT) occurring in one or more patients include: elevated enzymes, increased bilirubin, hepatomegaly, hepatitis, jaundice, abdominal pain, vomiting, liver failure and death. **DRUG ABUSE AND DEPENDENCE: Controlled Substance Class –** ZOLOFT is not a controlled substance. Premarketing clinical experience with ZOLOFT did not reveal any tendency for a withdrawal syndrome or any drug-seeking behavior. Physicians, however, should carefully evaluate patients for history of drug abuse and observe them for signs of ZOLOFT misuse or abuse. **OVERDOSAGE:** Reports of death attributed to overdoses of ZOLOFT alone have been extremely rare. Any overdosage should be treated aggressively by ensuring an adequate airway, oxygenation, and ventilation. Gastric lavage with appropriate airway protection, may be indicated. Induction of emesis is not recommended.

Zoloft® (sertraline HCl)

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S. aureus May Contribute to Psoriasis Severity

PARIS — Patients colonized with certain enterotoxic strains of *Staphylococcus aureus* had significantly worse Psoriasis Area and Severity Index scores than did patients not colonized with these bacterial strains, raising the possibility that antibiotics might have an adjunctive role in treatment, Austrian dermatologists reported at the European Congress on Psoriasis 2004.

Nordwig S. Tomi, M.D., and Elisabeth Aberer, M.D., of Karl Franzens University in Graz, Austria, took sample swabs from the lesional skin and nares of 25 patients with psoriasis for evidence of *S. aureus* colonization and identification of enterotoxins A, B, C, or D.

Samples from 15 of 25 patients grew positive cultures; these samples were from the nares alone in 1 patient, skin only in 4 patients, and skin and nares in 10. Sixty percent of the strains produced *S. aureus* enterotoxins.

Four patients had enterotoxin B, two had enterotoxin C, one had D, and combinations of A plus D and B plus C were found in one patient each. The Psoriasis Area and Severity Index score was significantly higher ($P = .001$) in patients with enterotoxin-producing staphylococcal strains, the investigators reported in a poster presentation at the meeting.

—Betsy Bates