

Full-Time Work No Protection From Medical Debt in Families

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WASHINGTON — Medical debt is more common among families with full-time workers than among families whose members work part-time, University of Iowa researchers said at the annual meeting of the American Public Health Association.

“Medical debt can result in credit problems and force people to file for bankruptcy,” said Matthew Levi, a graduate research assistant in the department of community and behavioral health at the university. “These problems can be worsened if an individual stops going in for care and using prescription drugs because untreated problems can prevent a person from returning to work.”

The researchers looked at Urban Institute data from interviews with more than 1,400 residents, some done in person and some by phone. Subjects were located in low-income areas of Des Moines or in surrounding Polk County. Data came primarily from interviews with more than

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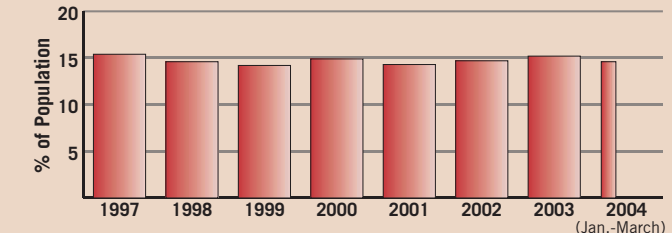
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The researchers did not find a lot of differences in the amount of medical debt reported when comparing the ages of children in the house. But there was a dip in the percentage of debt reported by families with preschool-aged children. “We’re not really sure what that’s about; a lot of children in this sample are Head Start children, so they would be receiving some services and referrals,” Dr. Wallis noted.

DATA WATCH Lack of Health Insurance Coverage Holds Steady



Note: In early 2004, approximately 42 million people were uninsured in the United States. Source: Centers for Disease Control and Prevention

ZOMIG® (zolmitriptan) Tablets ZOMIG-ZMT® (zolmitriptan) Orally Disintegrating Tablets

BRIEF SUMMARY OF PRESCRIBING INFORMATION: **ADVERSE AND USE:** ZOMIG is indicated for the acute treatment of migraine with or without aura in adults. ZOMIG is NOT intended for the prophylactic therapy of migraine or for use in the management of headache or basilar migraine (see CONTRAINDICATIONS). Safety and effectiveness of ZOMIG have not been established for cluster headache, which is present in an older, predominantly male population.

CONTRAINDICATIONS: ZOMIG should not be given to patients with ischemic heart disease (angina pectoris, history of myocardial infarction, or documented silent ischemia) or to patients who have symptoms or findings consistent with ischemic heart disease, coronary artery vasospasm, including Prinzmetal's variant angina, or other significant underlying cardiovascular disease (see WARNINGS). Because ZOMIG may increase blood pressure it should be given to patients with uncontrolled hypertension (see WARNINGS). ZOMIG should not be used within 24 hours of treatment with another 5-HT₁ agonist, or an ergoline-containing or ergot-type medication like dihydroergotamine or methysergide.

ZOMIG should not be administered to patients with hemiplegic or basilar migraine. Concurrent administration of MAO-A inhibitors or use of zolmitriptan with 2 weeks of discontinuation of MAO-A inhibitor therapy is contraindicated (see CLINICAL PHARMACOLOGY). Drug Interactions and PRECAUTIONS: Drug Interactions: ZOMIG is contraindicated in patients who are hypersensitive to zolmitriptan or any of its inactive ingredients.

WARNINGS: ZOMIG should only be used where a clear diagnosis of migraine has been established. Risk of Myocardial Ischemia and/or Interactions and Other Adverse Cardiac Events: ZOMIG should not be given to patients with documented ischemic or vasospastic coronary artery disease (see CONTRAINDICATIONS). It is strongly recommended that zolmitriptan not be given to patients with uncontrolled coronary artery disease (CAD) as indicated by the presence of a history of angina pectoris, hypercholesterolemia, smoker, obesity, diabetes, strong family history of CAD, female with surgical or physiological menopause, or male over 40 years of age unless a cardiovascular evaluation provides satisfactory clinical evidence that the patient is reasonably free of coronary artery and ischemic myocardial disease or other significant underlying cardiovascular disease and the sensitivity of cardiac diagnostic procedures to detect cardiovascular disease or predisposition to coronary artery vasospasm is modest, at best. If, during the cardiovascular evaluation, the patient's medical history, electrocardiographic or other investigations reveal findings indicative of, or consistent with, coronary artery vasospasm or myocardial ischemia, zolmitriptan should not be administered (see CONTRAINDICATIONS). For patients with risk factors predictive of CAD, who are determined to have a satisfactory cardiovascular evaluation, it is strongly recommended that administration of the first dose of zolmitriptan be in the setting of a physician's office or similar medically staffed and equipped facility unless the patient has previously received zolmitriptan. Because cardiac ischemia can occur in the absence of clinical symptoms, consideration should be given to obtaining on the first occasion of use an electrocardiogram (ECG) during the interval immediately following ZOMIG. It is recommended that patients who are hypersensitive to zolmitriptan or who are hypersensitive to ZOMIG and who have or acquire risk factors predictive of CAD, as described above, undergo periodic interval cardiovascular evaluation as they continue to use ZOMIG. The systematic approach described above is intended to reduce the likelihood that patients with unrecognized cardiovascular disease will be exposed to zolmitriptan.

Cardiac Events and Fatalities: Serious adverse cardiac events, including acute myocardial infarction, have been reported within a few hours following administration of zolmitriptan. In some cases, death has resulted in patients who had been reported to have no underlying cardiovascular disease. In other cases, the administration of other 5-HT₁ agonists in patients with migraine, the incidence of these events is extremely low. ZOMIG can cause coronary vasospasm. Because of the risk of coronary artery disease, the relationship cannot be excluded. In the cases where there has been known underlying coronary artery disease, the relationship is uncertain. Patients with symptomatic Wolff-Parkinson-White syndrome or arrhythmias associated with other cardiac accessory conduction pathway disorders should not receive ZOMIG.

Pre-marketing experience with zolmitriptan: Among the more than 2,500 patients with migraine who participated in pre-marketing controlled clinical trials of ZOMIG Tablets, no deaths or serious cardiac events were reported.

Post-marketing experience with zolmitriptan: Serious cardiovascular events have been reported in association with the use of ZOMIG Tablets, and in very rare cases, these events have occurred in the absence of known cardiovascular disease. The uncontrolled nature of post-marketing surveillance, however, makes it impossible to determine definitively the proportion of the reported cases that were actually caused by zolmitriptan or to reliably assess the cardiovascular risk associated with zolmitriptan.

Cerebrovascular Events and Fatalities with 5-HT₁ agonists: Cerebral hemorrhage, subarachnoid hemorrhage, stroke, and other cerebrovascular events have been reported with 5-HT₁ agonists. Because zolmitriptan is a 5-HT₁ agonist, it is possible that the cerebrovascular events were primary, the agonist having been administered in the incorrect belief that the symptoms experienced were a consequence of migraine, when they were not. It should be noted that patients with migraine may be at increased risk of certain cerebrovascular events (i.e., stroke, subarachnoid hemorrhage, transient ischemic attack).

Other Vasospasm-Related Events: 5-HT₁ agonists may cause vasospastic reactions other than coronary artery vasospasm such as peripheral and gastrointestinal vasospasm or necrosis have been reported with ZOMIG Tablets; these may present as bloody diarrhea or abdominal pain.

Increase in Blood Pressure: As with other 5-HT₁ agonists, significant elevations in systolic blood pressure have been reported on rare occasions with ZOMIG Tablet use in patients with a history of hypertension; very rarely these increases in blood pressure were associated with significant clinical events. Zolmitriptan is contraindicated in patients with uncontrolled hypertension. In volunteers, an increase of 1 and 3 mm Hg in the systolic and diastolic blood pressure, respectively, was seen at 5 mg. In the headache trials, vital signs were measured only in the small number of patients who were used in the study.

General: As with other 5-HT₁ agonists, sensations of tightness, pain, pressure, and numbness have been reported after treatment with zolmitriptan in the pericardial region. Because zolmitriptan may cause coronary vasospasm, it is possible that the pericardial pain, pressure, or numbness symptoms or signs suggestive of angina following should be evaluated for the presence of CAD or a predisposition to Prinzmetal's variant angina before resuming additional doses of medication, and should be monitored electrocardiographically if resumed and serious or similar symptoms recur. Serious symptoms or signs suggestive of angina or other cardiac events should be reported to the physician. In patients with Raynaud's syndrome or Raynaud's syndrome following the use of any 5-HT₁ agonist are candidates for further evaluation (see WARNINGS). Zolmitriptan should also be administered with caution to patients with diseases that may alter the absorption, metabolism, or excretion of zolmitriptan, such as impaired renal function (see CLINICAL PHARMACOLOGY). For a given dose, zolmitriptan should be administered with caution, the diagnosis of migraine headache should be reconsidered before administration of a second dose.

Binding to Melanin-Containing Tissues: When pigmented rats were given a single oral dose of 10 mg/kg of radiolabeled zolmitriptan, the radioactivity in the eye after 4 hours, the latest time point examined, was 81% of the value measured after 4 hours. This suggests that zolmitriptan and/or its metabolites may bind to the melanin of the eye. Because there could be accumulation in melanin rich tissues over time, this raises the possibility that zolmitriptan could cause toxicity in these tissues after extended use. However, no effects on the retina related to treatment with zolmitriptan were noted in any of the toxicology studies. Although no systematic monitoring of ophthalmologic function was undertaken in clinical trials, and no specific recommendations for ophthalmologic monitoring are offered, prescribers should be aware of the possibility of long-term ophthalmologic effects.

Phenylethanolamines: Phenylethanolamines should be informed that ZOMIG-ZMT contains phenylethylamine (a component of aspartame). Each 2.5 mg orally disintegrating tablet contains 2.81 mg phenylethylamine. Each 5 mg orally disintegrating tablet contains 5.62 mg phenylethylamine.

Information for Patients: See PATIENT INFORMATION at the end of this labeling for the text of the separate leaflet provided for patients. ZOMIG-ZMT Orally Disintegrating Tablets: The orally disintegrating tablet is packaged in a blister. Patients should be instructed not to remove the tablet from the blister until just prior to dosing. The blister pack should be peeled open, and the orally disintegrating tablet placed on the tongue, where it will dissolve and be swallowed with the saliva.

Laboratory Tests: No monitoring of specific laboratory tests is recommended.

Drug Interactions: Ergot-containing drugs have been reported to cause prolonged vasospastic reactions. Because there is a theoretical basis that these effects may be additive, use of ergotamine-containing or ergot-type medications (like dihydroergotamine or methysergide) and zolmitriptan within 24 hours of each other should be avoided (see CONTRAINDICATIONS). MAO-A inhibitors increase the systemic exposure of zolmitriptan. Therefore, the use of zolmitriptan in patients receiving MAO-A inhibitors is contraindicated (see CLINICAL PHARMACOLOGY and CONTRAINDICATIONS). Concurrent use of other 5-HT₁ agonists within 24 hours of zolmitriptan is also contraindicated (see CONTRAINDICATIONS). Following administration of zolmitriptan, the half-life and AUC of zolmitriptan and its active metabolites were approximately doubled (see CLINICAL PHARMACOLOGY). Selective serotonin reuptake inhibitors (SSRIs) (e.g., fluoxetine, fluvoxamine, paroxetine, sertraline) have been reported, rarely, to cause weakness, hyperreflexia, and incoordination when coadministered with 5-HT₁ agonists. If concomitant treatment with zolmitriptan and an SSRI is clinically warranted, appropriate observation of the patient is advised.

Drug/Laboratory Test Interactions: Zolmitriptan may interfere with commonly employed thyroid follicular cell adenomas seen in a rat model of carcinogenesis. Carcinogenesis, Impairment of Fertility: Carcinogenesis: Carcinogenicity studies in rat by gavage were carried out in mice and rats at doses up to 400 mg/kg. Mice were dosed for 85 weeks (males) and 92 weeks (females). The exposure (parental AUC) was 1.1 and 4.2 times exposure in humans receiving the maximum recommended total daily dose of 10 mg/kg and increased 10-fold in the highest dose group. There was no effect of zolmitriptan on tumor incidence. Control, low dose and middle dose rats were dosed for 10-105 weeks; the high dose group was sacrificed after 101 weeks (males) and 86 weeks (females) due to excessive mortality. Aids from an increase in the incidence of thyroid follicular cell adenomas seen in male rats receiving 400 mg/kg/day, an exposure approximately 3000 times that seen in humans after dosing with 10 mg, no tumors were noted.

Mutagenesis: Zolmitriptan was mutagenic in an Ames test, in 2 of 5 strains of *S. typhimurium* tested, in the presence, but not in the absence of metabolic activation. It was not mutagenic in an in vivo mammalian cell mutation (CHO-HGPRT) assay. Zolmitriptan was clastogenic in an in vitro human lymphocyte assay both in the absence and in the presence of metabolic activation; it was not clastogenic in an in vivo mouse micronucleus assay. It was also not genotoxic in an unscheduled DNA synthesis (UDS) assay. Impairment of Fertility: Studies of male and female rats administered zolmitriptan prior to or during mating and up to implantation have shown no impairment of fertility at doses up to 400 mg/kg/day. Exposure at this dose was approximately 3000 times exposure at the maximum recommended human dose of 10 mg/day.

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Nursing Mothers: It is not known whether zolmitriptan is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when zolmitriptan is administered to a nursing woman. Lactating rats dosed with zolmitriptan had milk levels equivalent to maternal plasma levels at 1 hour and 4 times higher than plasma levels at 4 hours.

Pediatric Use: Safety and effectiveness of ZOMIG in pediatric patients have not been established. ZOMIG is not recommended for use in patients under 18 years of age. Postmarketing experience with other triptans includes a limited number of reports that describe pediatric patients who have experienced clinically serious adverse events that are similar in nature to those reported rarely in adults.

Geriatric Use: Although the pharmacokinetic disposition of the drug in the elderly is similar to that seen in younger adults, there is no information about the safety and effectiveness of zolmitriptan in this population because patients age 65 were excluded from the controlled clinical trials. (see CLINICAL PHARMACOLOGY: Special Populations)

ADVERSE REACTIONS: Serious cardiac events, including myocardial infarction, have occurred following the use of ZOMIG Tablets. These events are extremely rare and most have been reported in patients with risk factors predictive of CAD. Events reported, in association with drugs of this class, have included coronary artery vasospasm, transient myocardial ischemia, myocardial infarction, ventricular tachycardia, and ventricular fibrillation (see CONTRAINDICATIONS, WARNINGS, and PRECAUTIONS).

Incidence in Controlled Clinical Trials: Among 2,633 patients treated with ZOMIG Tablets in the active and placebo controlled trials, no patients withdrew for reasons related to adverse events, but as patients treated a single headache in these trials, the opportunity for discontinuation was limited. In a long-term, open label study where patients were allowed to treat multiple migraine attacks for up to 1 year, 8% (157 of 2,028) withdrew from the trial because of adverse experiences. The most common events were parosmia, asthenia, nausea, dizziness, pain, chest or neck tightness or heaviness, somnolence and warm sensation. Table 1 lists the adverse events that occurred in 2% of the 2,074 patients in any one of the ZOMIG 1 mg, ZOMIG 2.5 mg or ZOMIG 5 mg Tablets dose groups of the controlled clinical trials. Only events that were more frequent in a ZOMIG Tablets group compared to the placebo groups are included. The events chest reflex experience gained under closely monitored conditions of clinical trials in a highly selected patient population. In actual clinical practice or in other clinical trials, these frequencies may not apply, as the conditions of use, reporting behavior, and the kinds of patients treated may differ. Several of the adverse events appear dose related, notably parosmia, sensation of heaviness or tightness in chest, neck, jaw, and throat, dizziness, somnolence, and possibly asthenia and nausea.

Table 1. Adverse Experience Incidence in Five Placebo-Controlled Migraine Clinical Trials: Events Reported by 2% Patients Treated With ZOMIG Tablets

Adverse Event Type	Placebo (n=401)	ZOMIG 1 mg (n=163)	ZOMIG 2.5 mg (n=498)	ZOMIG 5 mg (n=1072)
ATYPICAL SENSATIONS	6%	12%	12%	18%
Hypesthesia	1%	1%	1%	2%
Parosmia (all types)	2%	5%	7%	9%
Sensation warm/heat/hotness/pressure	4%	2%	2%	2%
PAIN AND PRESSURE SENSATIONS	7%	13%	14%	22%
Chest-pain/tightness/pressure and/or heaviness	1%	2%	3%	4%
Pain-in/around/low-pain/highness/pressure	1%	1%	2%	5%
Heaviness other than chest or neck	1%	1%	2%	5%
Pain-in/around/low-pain/highness/pressure	0%	2%	2%	2%
Other-pressure/tightness/heaviness	0%	2%	2%	2%
DIGESTIVE	2%	5%	16%	14%
Dyspepsia	1%	3%	5%	3%
Dysphagia	0%	0%	0%	2%
Diarrhea	4%	4%	4%	6%
NEUROLOGICAL	10%	11%	17%	21%
Dizziness	4%	6%	8%	10%
Somnolence	0%	0%	0%	2%
Vertigo	0%	0%	0%	2%
OTHER				
Asthenia	3%	5%	3%	9%
Palpitations	1%	0%	<1%	2%
Myalgia	<1%	1%	1%	2%
Nausea	<1%	1%	1%	2%
Sweating	1%	0%	2%	3%

ZOMIG is generally well tolerated. Across all doses, most adverse reactions were mild and transient and did not lead to long-lasting effects. The incidence of adverse events in controlled clinical trials was not affected by gender, weight, or age of the patients; use of prophylactic medications; or presence of aura. There were insufficient data to assess the impact of race on the incidence of adverse events.

Other Events: In the paragraphs that follow, the frequencies of less commonly reported adverse clinical events are presented. Because the reports include events from both open and uncontrolled studies, the rate of ZOMIG in their causation cannot be reliably determined. Furthermore, variability associated with adverse event reporting, the terminology used to describe adverse events, etc., limit the value of the quantitative frequency estimates provided. Event frequencies are calculated as the number of patients who used ZOMIG Tablets (n=2,633) and reported an event divided by the total number of patients exposed to ZOMIG Tablets. All reported events are included except those already listed in the previous table, those too general to be informative, and those not numerically associated with the use of the drug. Events are further classified into body system categories and enumerated in order of decreasing frequency using the following definitions: Infrequent adverse events are those occurring in 1/100 to 1/1,000 patients and rare adverse events are those occurring in fewer than 1/1,000 patients.

Allergic sensitivities: Infrequent with hypersensitivity. General: Infrequent were allergic reactions, chills, facial edema, fever, malaise and photosensitivity. Cardiovascular: Infrequent were arrhythmias, hypertension and syncope. Rare were bradycardia, erythrocytosis, postural hypotension, gastroenteritis, larynx dysfunction and tinnitus. Rare were anoxia, constipation, gastritis, hematemesis, pancreatitis, nausea and ulcer. Hemetic: Infrequent was ecchymosis. Rare were cyanosis, thrombocytopenia, eosinophilia and leukopenia. Metabolic: Infrequent was edema. Rare were hyperglycemia and alkaline phosphatase increase. Musculoskeletal: Infrequent were back pain, leg cramps and tenosynovitis. Rare were arthralgia, asthenia, ataxia and twitching. Neurological: Infrequent were agitation, anxiety, depression, emotional lability and insomnia. Rare were akathisia, amnesia, apathy, ataxia, dystonia, euphoria, hallucinations, cerebellar ataxia, hyperkinesia, hypotonia, hyperreflexia and instability. Respiratory: Infrequent were bronchitis, bronchospasm, epistaxis, hiccup, laryngitis, and yawn. Rare were apnea and voice alteration. Skin: Infrequent were pruritus, rash and urticaria. Special Senses: Infrequent were dry eye, eye pain, hyperacusis, ear pain, parosmia, and tinnitus. Rare were diplopia and lacrimation. Urteral: Infrequent were hematuria, cystitis, polyuria, urinary frequency, urinary urgency. Rare were micturition and dyspareunia.

The adverse experiences profile seen with ZOMIG-ZMT Tablets was similar to that seen with ZOMIG Tablets.

Postmarketing Experience with ZOMIG Tablets: The following section enumerates potentially important adverse events that have occurred in clinical practice and which have been reported spontaneously to various surveillance systems. The events enumerated represent reports arising from both domestic and non-domestic use of oral zolmitriptan. The events enumerated include all except those already listed in the ADVERSE REACTIONS section above or those too general to be informative. Because the reports cite events reported spontaneously from worldwide postmarketing experience, frequency of events and the role of zolmitriptan in their causation cannot be reliably determined.

Cardiovascular: Coronary artery vasospasm; transient myocardial ischemia, angina pectoris, and myocardial infarction.

Digestive: Very rare gastrointestinal ischemic events including ischemic colitis, ischemic ileitis, and gastrointestinal infarction or necrosis have been reported; these may be open and uncontrolled studies, the rate of ZOMIG in their causation cannot be reliably determined.

Neurological: As with other acute migraine treatments including other 5-HT₁ agonists, there have been rare reports of headache.

General: As with other 5-HT₁ agonists, there have been very rare reports of anaphylaxis or anaphylactoid reactions in patients receiving ZOMIG. There have been firm reports of hypersensitivity reactions, including angioedema.

DRUG ABUSE AND DEPENDENCE: The abuse potential of ZOMIG has not been assessed in clinical trials.

OVERDOSAGE: There is no experience with clinical overdose. Volunteers receiving single 50 mg oral doses of zolmitriptan commonly experienced sedation. The elimination half-life of ZOMIG is 15 hours (see CLINICAL PHARMACOLOGY), and therefore monitoring of patients after overdose with ZOMIG should continue for at least 3 to 4 hours or until symptoms or signs persist. There is no specific antidote to zolmitriptan. In the highest doses tested in humans, there was no increase in the maximum recommended total daily dose of 10 mg/day, ensuring adequate oxygenation and ventilation, and monitoring and support of the cardiovascular system. It is unknown what effect hemodialysis or peritoneal dialysis has on the plasma concentrations of zolmitriptan.

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