

Insurer Goes High-Deductible for Its Employees

BY M.R. TRASKA
Contributing Writer

United Healthcare still sells managed care plans to employers, but not to its own workers.

Starting this month, all United Healthcare (UHC) employees have just one major choice for health insurance: a high-deductible plan. Employees will get to choose among different high-deductible packages and will be encouraged to com-

bine those with health savings accounts (HSAs). When combined with high-deductible insurance, HSAs are used to pay out-of-pocket health expenses.

The move into high-deductible plans is a drastic departure from the kind of low out-of-pocket cost, comprehensive benefit package that was once UHC's mainstay. How can the firm reconcile this with managed care?

"They can't," said Greg Scandlen, director of the Center for Consumer Driven

Health Care at the Galen Institute, Alexandria, Va. In his opinion, "these hybrid kinds of PPO-type approaches [that UHC offers] don't really work."

High-deductible plans are not exactly new to UHC. Employees and customers have been offered the plans for several years, and both groups have received the product enthusiastically, according to company executives. In his opinion, "these hybrid kinds of PPO-type approaches [that UHC offers] don't really work."

option previously. He also would not elaborate on specific plan features—for example, whether UHC's plans provide first-dollar coverage for preventive visits as an incentive for patients to get such care.

The move is "a signal that United sees high-deductible HSAs as the wave of the future," said Paul Ginsburg, Ph.D., president of the Center for Studying Health System Change, Washington. He said he sees this move as strong marketing symbolism for United's customers.

Gary Claxton, director of the Health Care Marketplace Project at the Kaiser Family Foundation, Washington, called the change "consistent with a retreat from managed care." In a survey of more than 1,900 employers released last year, the foundation found that fewer than 1% of companies offered high-deductible HSA plans, but 6%

said they were very interested in offering them within 2 years, and 21% said they were somewhat likely to offer them. Of firms with 5,000 or more employees, 22% were very likely to offer the plans within 2 years, and 28% were somewhat likely to do so.

Insurers are starting to plan for those future demands. Blue Cross and Blue Shield plans currently offer HSA-compatible coverage in 34 states for large and small employer groups and in 32 states for individuals. The Blue Cross and Blue Shield Association projects that by 2006, Blue plans will offer HSA-compatible products in all but one state for large employer groups, in 48 states for small employers, and in 44 states for individuals. Even Kaiser Foundation Health Plans, an Oakland, Calif.-based insurer whose main offering is a closed-panel HMO, confirmed that it, too, began to offer a similar high-deductible product last year and planned to combine it with HSAs this year.

"Generally, I'm very concerned" about a significant move into high-deductible plans, said Mila Kofman of Georgetown University Health Policy Institute, Washington.

High out-of-pocket costs can discourage people with chronic diseases, such as diabetes, from getting preventive or maintenance care that would prevent more costly intervention later on. In the longer term, higher deductible plans could actually cost employers more than they save from lowered premiums as more acute illness is treated at later stages, employees end up sicker, and absenteeism increases, Ms. Kofman explained.

Moreover, "I'm not sure that making people pay more out of pocket will make the overall system more efficient," she added. "Insurers haven't been able to figure out who the most efficient providers are, so why do they think that individuals can do any better?"

RISPERDAL® (RISPERIDONE) TABLETS/ORAL SOLUTION

BEFORE PRESCRIBING, PLEASE CONSULT COMPLETE PRESCRIBING INFORMATION OF WHICH THE FOLLOWING IS A BRIEF SUMMARY.

INDICATIONS AND USAGE
RISPERDAL® (risperidone) is indicated for the treatment of schizophrenia.

Monotherapy: RISPERDAL® is indicated for the short-term treatment of acute manic or mixed episodes associated with Bipolar Disorder.

Combination Therapy: The combination of RISPERDAL® with lithium or valproate is indicated for the short-term treatment of acute manic or mixed episodes associated with Bipolar Disorder.

CONTRAINDICATIONS
RISPERDAL® (risperidone) is contraindicated in patients with a known hypersensitivity to the product.

Warnings
Neuroleptic Malignant Syndrome (NMS) A potentially fatal symptom complex sometimes referred to as Neuroleptic Malignant Syndrome (NMS) has been reported in association with antipsychotic drugs. If a patient receives antipsychotic drug treatment after recovery from NMS, the potential reinduction of drug should be carefully considered. The patient should be carefully monitored, since recurrences of NMS have been reported.

Tardive Dyskinesia A syndrome of potentially irreversible, involuntary, dyskinetic movements may develop in patients treated with antipsychotic drugs. Whether antipsychotic drug products differ in their potential to cause tardive dyskinesia is unknown. If signs and symptoms of tardive dyskinesia appear in a patient on RISPERDAL®, drug discontinuation should be considered. However, some patients may require treatment with RISPERDAL® despite the presence of the syndrome.

Cerebrovascular Adverse Events, Including Stroke, in Elderly Patients With Dementia Cerebrovascular adverse events (e.g., stroke, transient ischemic attack), including fatalities, were reported in patients (mean age 85 years; range 75-97) in trials of risperidone in elderly patients with dementia-related psychosis. In placebo-controlled trials, there was a significantly higher incidence of cerebrovascular adverse events in patients treated with risperidone compared to patients treated with placebo. RISPERDAL® has not been shown to be safe or effective in the treatment of patients with dementia-related psychosis.

Hyperglycemia and Diabetes Mellitus Hyperglycemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients with typical antipsychotics including RISPERDAL®. Patients with an established diagnosis of diabetes mellitus who are started on atypical antipsychotics should be monitored regularly for worsening of glucose control. Patients with risk factors for diabetes mellitus who are starting treatment with atypical antipsychotics should undergo fasting blood glucose testing at the beginning of treatment and periodically during treatment.

PRECAUTIONS
General

Orthostatic Hypotension: RISPERDAL® (risperidone) may induce orthostatic hypotension associated with dizziness, tachycardia, and in some patients, syncope, especially during the initial dose titration period, probably reflecting its alpha-adrenergic antagonistic properties. Syncope is reported in 0.2% (2/1007) of RISPERDAL®-treated patients in phase 2/3 studies. The risk of orthostatic hypotension and syncope may be minimized by limiting the initial dose to 2 mg total (either 0.5 or 1 mg BID) in normal adults and 0.5 mg BID in the elderly and patients with renal or hepatic impairment. See DOSAGE AND ADMINISTRATION. Monitoring of orthostatic vital signs should be considered in patients for whom this is of concern. A dose reduction should be considered if hypotension occurs. RISPERDAL® should be used with particular caution in patients with known cardiac dysfunction, including myocardial infarction or ischemia, heart failure, or conduction abnormalities; cerebrovascular disease; and conditions which would predispose patients to hypotension (e.g., dehydration and hypovolemia. Caution: Significant hypotension has been observed with concomitant use of RISPERDAL® and antihypertensive agents.

Seizures: RISPERDAL® should be used cautiously in patients with a history of seizures. **Dysphagia:** Esophageal dysmotility and aspiration have been associated with antipsychotic drug use. Aspiration pneumonia is a common cause of morbidity and mortality in patients with advanced Alzheimer's disease. RISPERDAL® and other antipsychotic drugs should be used cautiously in patients at risk for aspiration pneumonia.

Osteostyrophy and Tumors in Animals: RISPERDAL® CONSTA™ produced osteostyrophy in male and female rats in a 1-year toxicity study and a 2-year carcinogenicity study at a dose of 40 mg/kg administered IM every 2 weeks. RISPERDAL® CONSTA™ produced renal tubular tumors (adenoma, adenocarcinoma) and adrenomedullary pheochromocytomas in male rats in the 2-year carcinogenicity study at 40 mg/kg administered IM every 2 weeks. In addition, RISPERDAL® CONSTA™ produced an increase in a marker of cellular proliferation in renal tissue in males in the 1-year toxicity study and in renal tumor-bearing males in the 2-year carcinogenicity study. **Hyperproliferation:** As with other drugs that antagonize dopamine D₂ receptors, risperidone elevates prolactin levels and the elevation persists during chronic administration. Neural clinical studies not epidemiologic studies conducted to date have shown an association between elevated prolactin levels and the development of hyperproliferative and tumorigenic in humans; the available evidence is considered too limited to be conclusive at this time.

Potential for Cognitive and Motor Impairment: Somnolence was a commonly reported adverse event associated with RISPERDAL® treatment, especially when ascertained by direct questioning of patients. This adverse event is dose related. Patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that RISPERDAL® therapy does not affect their ability. **Preipria:** Rare cases of priapism have been reported.

Thrombotic Thrombocytopenic Purpura (TTP): A single case of TTP was reported in a 28-year-old female patient receiving RISPERDAL® in a large, open premarketing evaluation (approximately 10 mg daily administered IM, twice daily, and being subsequently recovered after receiving plasmapheresis. The relationship to RISPERDAL® therapy is unknown.

Antiemetic Effect: Risperidone has an antiemetic effect in animals; this effect may also occur in humans, and may mask signs and symptoms of overdose with anti-nausea drugs or of conditions such as intestinal obstruction, Rye's syndrome, and brain tumor.

Body Temperature Regulation: Disruption of body temperature regulation has been attributed to antipsychotic agents. Caution is advised when prescribing for patients who will be exposed to temperature extremes.

Suicide: The possibility of a suicide attempt is inherent in schizophrenia, and close supervision of high risk patients should accompany drug therapy. **Use in Patients With Concomitant Illness:** Clinical experience with RISPERDAL® in patients with certain concomitant systemic illnesses is limited. Caution is advisable in using RISPERDAL® in patients with conditions that could affect metabolism or hemodynamic responses.

Because of the risks of orthostatic hypotension and QT prolongation, caution should be observed in cardiac patients (see WARNINGS and PRECAUTIONS). Increased plasma concentrations of risperidone and 9-hydroxyrisperidone occur in patients with severe renal impairment and in patients with severe hepatic impairment. A lower starting dose should be used in such patients.

Information for Patients: Physicians are advised to consult full prescribing information to review issues to be discussed with patients for whom they prescribe RISPERDAL®. **Phenylethanolamine:** Phenylethanolamine is a component of aspartame. Each 2 mg RISPERDAL® M-TAB™ Orally Disintegrating Tablet contains 0.56 mg phenylethanolamine, each 1 mg RISPERDAL® M-TAB™ Orally Disintegrating Tablet contains 0.28 mg phenylethanolamine, and each 0.5 mg RISPERDAL® M-TAB™ Orally Disintegrating Tablet contains 0.14 mg phenylethanolamine.

Drug Interactions: The interactions of RISPERDAL® and other drugs have not been systematically evaluated. Given the primary CNS effects of risperidone, caution should be used when RISPERDAL® is taken in combination with other centrally acting drugs and alcohol. Because of its potential for inducing hypotension, RISPERDAL® may enhance the hypotensive effects of other therapeutic agents with this potential. RISPERDAL® may antagonize the effects of levodopa and dopamine agonists. Chronic administration of clozapine with risperidone may decrease the clearance of risperidone.

Carbamazepine and Other Enzyme Inducers: In a drug interaction study in schizophrenic patients, 11 subjects received risperidone titrated to 6 mg/day for 3 weeks, followed by concurrent administration of carbamazepine for an additional 3 weeks. During co-administration, risperidone plasma concentrations were decreased by pharmacologically active metabolite, 9-hydroxyrisperidone, were decreased by about 50%. Plasma concentrations of carbamazepine did not appear to be affected. The dose of risperidone may need to be titrated accordingly for patients receiving carbamazepine, particularly during initiation or discontinuation of carbamazepine therapy. Co-administration of other known enzyme inducers (e.g., phenytoin, rifampin, and phenobarbital) with risperidone may cause similar decreases in the combined plasma concentrations of risperidone and 9-hydroxyrisperidone, which could lead to decreased efficacy of risperidone therapy.

Fluoxetine: Fluoxetine (20 mg QD) has been shown to increase the plasma concentration of risperidone 2.5-2.8 fold, while the plasma concentration of 9-hydroxyrisperidone was not affected. When concurrent fluoxetine is initiated or discontinued, the physician should be aware of RISPERDAL®. The effects of discontinuation of concomitant fluoxetine therapy on the pharmacokinetics of risperidone and 9-hydroxyrisperidone have not been studied.

Lithium: Risperidone oral doses of risperidone (3 mg BID) did not affect the exposure (AUC) or peak plasma concentrations (C_{max}) of lithium (n=13). **Valproate:** Repeated oral doses of risperidone (4 mg QD) did not affect the pre-dose or average plasma concentrations exposure (AUC) of valproate (1000 mg daily in three divided doses) compared to placebo (n=21). However, there was a 20% increase in valproate peak plasma concentration (C_{max}) after concomitant administration of risperidone.

Drugs that Inhibit CYP 2D6 and CYP 3A4 Isozymes: Risperidone is metabolized to 9-hydroxyrisperidone by cytochrome P₄₅₀2D6, an enzyme that is polymorphic in the population and that can be inhibited by a variety of psychotropic and other drugs (see CLINICAL PHARMACOLOGY). Drug interactions that reduce the metabolism of risperidone to 9-hydroxyrisperidone would increase the plasma concentrations of risperidone and lower the concentrations of 9-hydroxyrisperidone. Analysis of clinical studies involving a modest number of poor metabolizers (n=7) does not suggest that poor and extensive metabolizers have different rates of adverse effects. No comparison of effectiveness in the two groups has been made. In vitro studies showed that drugs metabolized by CYP 2D6 isozyme, including 1A1, 1A2, 1C9, 1C19, 1C2, and 11A4, are only weak inhibitors of risperidone metabolism.

Drugs Metabolized by CYP 2D6: In vitro studies indicate that risperidone is a relatively weak inhibitor of CYP 2D6. Therefore, RISPERDAL® is not expected to decrease the clearance of drugs that are metabolized by this enzymatic pathway. However, clinical data to confirm this expectation are not available.

Carcinogenesis, Mutagenesis, Impairment of Fertility Carcinogenesis: Carcinogenicity studies were conducted in Swiss albino mice and Wistar rats. Risperidone was administered by oral gavage to mice at doses of 0.1, 0.3, 1, 3, 10, and 30 mg/kg for 12 months to mice and for 25 months to rats. These doses are equivalent to 0.2, 0.75 and 3 times the maximum human dose (16 mg/day) on a mg/kg basis and 0.4, 1.5, and 5 times the maximum human dose (mice) and 0.4, 1.5, and 5 times the maximum human dose (rats) on a mg/m² basis. There were no statistically significant increases in the incidence of adenomas, endocrine pancreatic adenomas and mammary gland adenocarcinomas. These findings are considered to be proclinal mediated. The incidence of uterine leiomyomas was increased in female rats. The incidence of uterine leiomyomas in rodents is unknown. See Hyperproliferation under PRECAUTIONS, GENERAL.

Mutagenesis: No evidence of mutagenicity potential for risperidone was found. **Impairment of Fertility:** Risperidone (0.16 to 5 mg/kg) was shown to impair mating, but not pregnancy, in Wistar rats. There was no statistically significant effect on the number of pups and increase in the number of dead pups at birth (Day 0), and a decrease in birth weight in pups of drug-treated dams were observed. In addition, there was an increase in deaths by Day 1 among pups of drug-treated dams, regardless of whether or not the dams were cross-fostered to control dams. There was no effect on the number of pups born to control dams and survival from Day 1 to 4 of 6 times the maximum recommended human dose (MRHD) on a mg/m² basis and in one Segment II study in New Zealand rabbits (0.315 mg/kg or 0.4 to 1.6 times the MRHD on a mg/m² basis). The incidence of malformations was not increased compared to control in offspring of rats or rabbits given 0.4 to 1.6 times the MRHD on a mg/m² basis. In three reproductive studies in rats (two Segment II and a multigeneration study), there was an increase in pup deaths during the first 4 days of lactation at doses of 0.15 mg/kg or 0.1 to 1.6 times the MRHD on a mg/m² basis. This increase was not observed in offspring of dams that received the fetuses or pups or effects on the dams. There was no no-effect dose for increased rat pup mortality. In one Segment II study, there was an increase in stillborn rat pups at a dose of 2.5 mg/kg or 1.5 times the MRHD on a mg/m² basis. In a cross-fostering study in Wistar rats, pups were affected on the fetus or pup, as evidenced by a decrease in the number of live pups and an increase in the number of dead pups at birth (Day 0), and a decrease in birth weight in pups of drug-treated dams were observed. In addition, there was an increase in deaths by Day 1 among pups of drug-treated dams, regardless of whether or not the dams were cross-fostered to control dams. 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