## Self-Medication Ubiquitous in Chinese Immigrants

BY ROBERT FINN

San Francisco Bureau

SAN FRANCISCO — The use of traditional Chinese medicine is nearly universal among Chinese immigrants living in San Francisco, Amy Wu and Samuel LeBaron, M.D., reported in a poster session at the annual meeting of the American Academy of Family Physicians.

In a survey of 198 patients, self-medication with herbs was the most frequent form of traditional Chinese medicine (TCM), used by 93% of the patients within the past 12 months. Overall, 68% reported self-medication with topical preparations, 33% reported using herbal medications prescribed by a TCM doctor, and 7% reported using topicals prescribed by a TCM doctor.

Also, 14% of the patients reported using acupuncture, 12% massage therapy, 11% tai chi, 7% qigong, and 5% other modalities.

In a parallel study, Ms. Wu (a third-year

medical student) and family physician Dr. LeBaron of Stanford (Calif.) University found that of 17 physicians serving those patients, 24% said they asked about TCM rarely, 58% sometimes, and 18% usually.

Since conducting this study, "I find that I'm asking all my Chinese patients now about their use of TCM, which I had not done before," Dr. LeBaron said in an interview. "More than half of them say yes. They've already been using it for whatever ailment brought them in."

He acknowledged that he would advise some patients to be cautious in using TCM, including such those with renal or liver disease, patients on multiple medications, or those on medications with many known interactions, such as coumadin.

He described a patient being treated by an oncologist for prostate cancer, and who was also being treated by a TCM doctor with acupuncture and herbal medicine. "I actually brought the list of medications to the TCM doctor—who is well trained in Western medicine—and vice versa, I took the list of herbal preparations to the oncologist, so both of them could see what was going on and make comparisons," he said. "I also consulted with a pharmacist. So there's a lot of double checking that we should do."

"We have to put it in perspective too and realize that most likely with our Western medical treatments we're causing far more complications than our patients are getting from TCM. So while we should be cautious about it, we probably should be focusing the majority of our attention on the very Western drugs that we ourselves are using," Dr. LeBaron said.

### BENICAR® Tablets (olmesartan medoxomil)/BENICAR HCT® Tablets (olmesartan medoxomil-hydrochlorothiazide)

hough any chloride deficit is generally mild and usually does not require spe-ic treatment except under extraordinary circumstances (as in liver disease or all disease), chloride replacement may be required in the treatment of meta-

orate merapy is water restriction, rather than administration of sall except in a nstances when the hyponatremia is life-threatening. In actual salt depletion, ppropriate replacement is the therapy of choice. Hyperuricemia may occur or frank gout may be precipitated in certain patients eceiving thiazide therapy.

In diabetic patients dosage adjustments of insulin or oral hypoglycemic agents may be required. Hyperglycemia may occur with thiazide diuretics. Thus latent diabetes mellitus may become manifest during thiazide therapy. The antihypertensive effects of the drug may be enhanced in the post-sympathectomy patient.

If progressive renal impairment becomes evident consider withholding or discontinuing diuretic therapy.

Thiazides have been shown to increase the urinary excretion of magnesium; this may result in hypomagnesemia.

Thiazides may decrease urinary calcium excretion. Thiazides may cause intermit-tent and slight elevation of serum calcium in the absence of known disorders of calcium metabolism. Marked hypercalcemia may be evidence of hyperpara-thyroidism. Thiazides should be discontinued before carrying out tests for para-thyroid function.

Increases in cholesterol and triglyceride levels may be associated with thiazide diuretic therapy.

Impaired Renal Function
As a consequence of inhibiting the renin-angiotensin-aldosterone system, changes in renal function may be anticipated in susceptible individuals treated with olinesartan medoxomil. In patients whose renal function may depend upon the activity of the renin-angiotensin-aldosterone system (e.g., patients with severe congestive heart failure), treatment with angiotensin converting enzyme inhibitors and angiotensin receptor antagonists has been associated with oliguria and/or progressive azotemia and (rarely) with acute renal failure and/or death. Similar results may be anticipated in patients treated with olimesartan medoxomil. (See CLINICAL PHARMACOLOGY, Special Populations in the full prescribing information.)

information.) In Studies of ACE inhibitors in patients with unilateral or bilateral renal artery stenosis, increases in serum creatinine or blood urea nitrogen (BUN) have be reported. There has been no long-term use of olmesartan medoxomil in patie with unilateral or bilateral renal artery stenosis, but similar results may be

Information for Patients

Pregnancy: Female patients of childbearing age should be told about the consequences of second and third trimester exposure to drugs that act on the reninangiotensin system and they should be told also that these consequences do no appear to have resulted from intrauterine drug exposure that has been limited to the first trimester. These patients should be asked to report pregnancies to their physicians as soon as possible.

Symptomatic Hypotension: A patient receiving BENICAR HCT® should be cautioned that light-headedness can occur, especially during the first days of therap and that it should be remorted to the prescribing on bysician. The natients should

and that it should be reported to the prescribing physician. The patients should be cauand that it should be reported to the prescribing physician. The patients should be told that if syncope occurs, BENIGAR HCT® should be discontinued until the physician has been consulted.

All patients exhauld be the prescribing the prescribing the prescribed by the prescribing the physician has been consulted.

All patients should be cautioned that inadequate fluid intake, excessive perspira-tion, diarrhea or vomiting can lead to an excessive fall in blood pressure, with the same consequences of light-headedness and possible syncope.

Ulmesartan medoxomil
No significant drug interactions were reported in studies in which olmesartan medoxomil was co-administered with hydrochlorothiazide, digoxin or warfarin in healthy volunteers. The bioavailability of olmesartan was not significantly altered by the co-administration of antacids [AI(OH)\_MG(OH)\_2]. Olmesartan medoxomil in ot metabolized by the cytochrome P450 system and has no effects on P450 earymes; thus, interactions with drugs that inhibit, induce or are metabolized by those enzymes are not expected.

 $\label{thm:continuity} \textit{Hydrochlorothiazide} \\ \text{When administered concurrently the following drugs may interact with thiazide} \\$ 

 $\label{lem:condition} \textit{Antidiabetic Drugs (oral agents and insulin)} - \textit{dosage adjustment of the antidiabetic drug may be required.}$ Other Antihypertensive Drugs – additive effect or potentiation

Confestyramine and Colestipol Resins – absorption of hydrochlorothiazide is impaired in the presence of anionic exchange resins. Single doses of either cholestyramine or colestipol resins bind the hydrochlorothiazide and reduce its absorption from the gastrointestinal tract by up to 85 and 43 percent, respectively Corticosteroids, ACTH – intensified electrolyte depletion, particularly hypokalemia Pressor Amines (e.g., Norepinephrine) – possible decreased response to pressor amines but not sufficient to preclude their use.

Skeletal Muscle Relaxants, Non depolarizing (e.g., Tubocurarine) – possible increased responsiveness to the muscle relaxant.

Lithium – should not generally be given with diuretics. Diuretic agents reduce the renal clearance of lithium and add a high risk of lithium toxicity. Refer to the pack age insert for lithium preparations before use of such preparation with olmesartan medoxomil-hydrochlorothiazide.

medoxomil-hydrochlorothiazide.

Non-steroidal Anti-inflammatory Drugs – in some patients the administration of a non-steroidal anti-inflammatory gent can reduce the diuretic, natriuretic and anti-hypertensive effects of loop, posassium-sparing and thiazide duretics. Therefore, when olmesartan medoxomil-hydrochlorothiazide tablets and non-steroidal anti-inflammatory agents are used concomitantly, the patients should be observed closely to determine if the desired effect of the diuretic is obtained.

Carcinogenesis, Mulagenesis, Impairment of Fertility
Olmesartan medoxomil-hydrochlorothiazide
No carcinogenicity studies with olmesartan medoxomil-hydrochlorothiazide been conducted.

been conducted.

Olmesartan medoxomil-hydrochlorothiazide in a ratio of 20:12.5 was negative in the Salmonella-Escherichia coll'mammalian microsome reverse mutation test up to the maximum recommended plate concentration for the standard assays. Olmesartan medoxomil and hydrochlorothiazide were tested individually and in combination ratios of 40:12.5, 20:12.5 and 10:12.5, for clastogenic activity in the in vitro Chinese hamster lung (CHL) chromosomal aberration assay. A positive response was seen for each component and combination ratio. However, no synergism in clastogenic activity was detected between olmesartan medoxomil and hydrochlorothiazide at any combination ratio. Olmesartan medoxomil-hydrochlorothiazide in a ratio of 20:12.5, administered orally, tisetd negative in the in vivor mouse bone marrow erythrocyte micronucleus assay at administered doses of up to 3144 mg/kg.

No studies of impairment of fertility with olmesartan medoxomil-hydrochlorothiazide have been conducted.

Offisearian medoxomil was not carcinogenic when administered by dietary administration to rats for up to 2 years. The highest dose tested (2000 mg/kg/day) was, on a mg/m² basis, about 480 times the maximum recommended human dose (MRHD) of 40 mg/day. Two carcinogenicity studies conducted in mice, a 6-month gavage study in the p53 knockout mouse and a 6-month dietary

dministration study in the Hras2 transgenic mouse, at doses of up to 1000 mg/kg/day about 120 times the MRHD), revealed no evidence of a carcinogenic effect of Imesartan medoxomil.

olmesartan medoxomil. Both olmesartan tested negative in the *in vitro* Syrian hamster embryo cell transformation assay and showed no evidence of genetic toxicity in the Ames (bacterial mutagenicity) test. However, both were shown to induce chromosomal aberrations in cultured cells *in vitro* (Chinese hamster lung) and both tested positive for thymidine kinase mutations in the *in vitro* mouse lymphoma assay. Olmesartan medoxomil tested negative *in vivo* for mutations in the MutaMouse intestine and kidney, and for clastogenicity in mouse bone marrow ssay. Olmesartan medoxomii testeu ilegative ili vivo ioi ilibatatisuuse intestine and kidney, and for clastogenicity in mouse bone marrucleus test) at oral doses of up to 2000 mg/kg (olmesartan not test

levels as high as 1000 mg/kg/day (240 times the MRHD) in a study in which dos-ing was begun 2 (female) or 9 (male) weeks prior to mating.

rygrochlorothiazide
Two-year feeding studies in mice and rats conducted under the auspices of the National Toxicology Program (NTP) uncovered no evidence of a carcinogenic potential of hydrochlorothiazide in female mice (at doses of up to approximately 600 mg/kg/day) or in male and female rats (at doses of up to approximately 100 mg/kg/day). The NTP, however, found equivocal evidence for hepatocarcino genicity in male mice.

Hydrochlorothiazide was not genotoxic *in vitro* in the Ames mutagenicity assay of Salmonella typhimurium strains TA 98, TA 100, TA 1535, TA 1537 and TA 1538, or in the Chinese Hamster Ovary (CHO) test for chromosomal aberrations. It was in the clinitese rainised to vary (vch) jest for clinicipsushila abertatoris. It was on ord genotoxic in vivo in assays using mouse germinal cell chromosomes, inese hamster bone marrow chromosomes, or the *Drosophila* sex-linked reces e lethal trait gene. Positive test results were obtained in the *in vitro* CHO Sister romatid Exchange (clastogenicity) assay, the Mouse Lymphoma Cell (muta-nicity) assay and the *Aspergillus nidulans* non-disjunction assay.

genicity) assay and the Asperijanus mutuans nonruspinction assay. Hydrochlorothiazide had no adverse effects on the fertility of mice and rats of either sex in studies wherein these species were exposed, via their diet, to doses of up to 100 and 4 mg/kg, respectively, prior to mating and throughout gestation

## Pregnancy Pregnancy Categories C (first trimester) and D (second and third trimesters) (See WARNINGS: Fetal/Neonatal Morbidity and Mortality.)

Nursing Mothers
It is not known whether olmesartan is excreted in human milk, but olmesartan is secreted at low concentration in the milk of lactating rats. Because of the potential for adverse effects on the nursing infant, a decision should be made whether to discontinue nursing or discontinue unusing or discontinue the drug to the mother.

of the drug to the mother.

Thiazides appear in human milk. Because of the potential for adverse effects o
the nursing infant, a decision should be made whether to discontinue nursing
or discontinue the drug, taking into account the importance of the drug to the

Pediatric Use Safety and effectiveness in pediatric patients have not been established.

Safety and effectiveness in periodic patients have not been assumed.

Geriatric USE

Clinical studies of BENICAR HCT® did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal or cardiac function and of concomitant diseases or other drug therapy. Olmesartan and hydrochlorothiazide are substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired repel function.

AUVENDE HEALTIUMS

Offmearatan medoxomil-hydrochlorothiazide

Olmesartan medoxomil-hydrochlorothiazide has been evaluated for safety in 1243

hypertensive patients. Treatment with ofmearatan medoxomil-hydrochlorothiazide

was well tolerated, with an incidence of adverse events similar to placebo. Events

generally were mild, transient and had no relationship to the dose of olmesartan

medoxomil-hydrochlorothiazide.

nedoxomin-hydrochiorotinazide. In the clinical trials, the overall frequency of adverse events was not dose-related. Analysis of gender, age and race groups demonstrated no differences between ofmesartan medoxomil-hydrochiorothazida and placebo-treated patients. The rate of withdrawals due to adverse events in all trials of hypertensive patients was 2.0% (25/1243) of patients treated with olmesartan medoxomil-hydrochiorothiazide and 2.0% (7/342) of patients treated with placebo.

allo 2.0% (17942) to patients used to man process.

In a placebo-controlled clinical trial, the following adverse events reported with olmesartan medoxomil-hydrochlorothiazide occurred in >2% of patients, and more aften on the almesartan medoxomil-hydrochlorothiazide combination than olmesartan medoxomil-hydrochlorothiazide more often on the olmesartan medoxomil-h on placebo, regardless of drug relationship:

	Olmesartan/ HCTZ (N=247) (%)	Placebo (N=42) (%)	Olmesartan (N=125) (%)	HCTZ (N=88) (%)
Gastrointestinal				
Nausea	3	0	2	1
Metabolic				
Hyperuricemia	4	2	0	2
Nervous System				
Dizziness	9	2	1	8
Desnivatavu				
Respiratory				
Upper Respiratory Tract Infection	7	0	6	7

The following adverse events were also reported at a rate of >2%, but were as, or more, common in the placebo group: headache and urinary tract infection.

Other adverse events that have been reported with an incidence of greater than 1.0%, whether or not attributed to treatment, in the more than 1200 hypertensive patients treated with olmesartan medoxomil-hydrochlorothiazide in controlled or open-label trials are listed below.

m-label trials are listed below.

Body as a Whole: chest pain, back pain, peripheral edema
Central and Peripheral Nervous System: vertigo
Gastrointestinat: abdominal pain, dyspensia, gastroenterilis, diarrhea
Liver and Biliary System: SGOT increased, GGT increased, SGPT increased
Metabolic and Nutritionat: hypertipemia, creatine phosphokinase increased,
hypertyl-cenia
Musculoskelata: arthritis, arthralgia, myalgia
Respiratory System: coughing
Skin and Appendages Disorders: rash
Urinary System: hematuria
lai eddem was renorted in 2/1043 poliante conidera structure.

Urinary System: hematuria
Facial edema was reported in 2/1243 patients receiving olmesartan medoxomil-hydrochlorothiazide. Angioedema has been reported with angiotensin II receptor

antagunists.

Offinesartan medoxomil

Other adverse events that have been reported with an incidence of greater than 0.5%, whether or not attributed to treatment, in more than 3100 hypertensive patients treated with offinesartan medoxomil monotherapy in controlled or openlabel trials are tachycardia and hypercholesterolemia.

Hydrochlorothiazide
Other adverse experiences that have been reported with hydrochlorothiazide, without regard to causality, are listed below:

Body as a Whole: weakness Digestive: pancreatitis, jaundice (intrahepatic cholestatic jaundice), sialadeni-tis, cramping, gastric irritation Hematologiic: aplastic anemia, agranulocytosis, leukopenia, hemolytic anemia, thrombocytopenia

ingurcation unazue. Creatinine, Board Urea Nitrogen: Increases in blood urea nitrogen (BUN) and serum creatinine of 550% were observed in 1.3% of patients. No patients were discontinued from clinical trials of olmesartan medoxomil-hydrochlorothiazide of to increased BUN or creatinine.

Hemoglobin and Hematocrit: A greater than 20% decrease in hemoglobin and hematocrit was observed in 0.0% and 0.4% (one patient), respectively, of olmesartan medoxomil-hydrochlorothiazide patients, compared with 0.0% and 0.0%, respectively, in placebo-treated patients. No patients were discontinued due to anemia.

Post-Marketing Experience: The following adverse reactions have been reported in post-marketing experience:

t-marketing experience:
Body as a Whole: Asthenia, angioedema
Gastrointestina: Vomitting
Musculoskeletal: Rhabdomyolysis
Urogenital System: Acute renal failure, increased blood creatinine levels
Skin and Appendages: Alopecia, pruritus, urticaria

OVENUOSHOE

Olmesartan medoxomil

Limited data are available related to overdosage in humans. The most likely manifestations of overdosage would be hypotension and tachycardia; bradycardia could be encountered if parasympathetic (vagal) stimulation occurs. If symptomatic hypotension should occur, supportive treatment should be initiated. The dialyzability of olmesartan is unknown.

No lethality was observed in acute toxicity studies in mice and rats given single oral doses up to 2000 mg/kg olmesartan medoxomil. The minimum lethal oral dose of olmesartan medoxomil in dogs was greater than 1500 mg/kg.

uuse or oimesartan medoxomii in dogs was greater than 1500 mg/kg. Hydrochlorothiazide
The most common signs and symptoms of overdose observed in humans are those caused by electrolyte depletion (hypokalemia, hypochloremia, hypo-natremia) and dehydration resulting from excessive diuresis. If digitalish has also been administered, hypokalemia may accentuate cardiac arrhythmias. The degree to which hydrochlorothiazide is removed by hemodialysis has not been established. The oral LD<sub>50</sub> of hydrochlorothiazide is greater than 10 g/kg in both mice and rats. DOSAGE AND ADMINISTRATION

DOSAGE AND ADMINISTRATION
The usual recommended starting dose of BENICAR® (olmesartan medoxomil) is
20 mg once daily when used as monotherapy in patients who are not volumecontracted. For patients requiring further reduction in blood pressure after 2
weeks of therapy, the dose may be increased to 40 mg. Doses above 40 mg do
not appear to have greater effect. Twice-daily dosing offers no advantage over the

same total dose given once daily. No initial dosage adjustment is recommended for elderly patients, for patients with moderate to marked renal impairment (creatinine clearance <40 mL/min) or with moderate to marked hepatic dysfunction (see CLINICAL PHARMACOLOGY. Special Populations in the full prescribing information). For patients with possible depletion of intravascular volume (e.g., patients treated with diuretics, particularly those with impaired renal function), BENICAR® should be initiated under close medical supervision and consideration should be given to use of a lower starting dose (see WARNINGS, Hypotension in Volume- or Salt-Depleted Patients).

Patients).

Hydrochlorothiazide is effective in doses between 12.5 mg and 50 mg once daily. The side effects (see WARNINGS) of BENICAR® are generally rare and independent of dose; those of hydrochlorothiazide are most bypically dose-dependent (primarily hypokalemia). Some dose-independent phenomena (e.g., pancreatitis) do occur with hydrochlorothiazide are most working of oliesartan medoxomil and hydrochlorothiazide will be associated with both sets of dose-independent side effects.

To minimize dose-independent side effects, it is with the sets of dose-independent side effects.

To minimize dose-independent side effects, it is usually appropriate to begin com-bination therapy only after a patient has failed to achieve the desired effect with

Replacement Therapy BENICAR HCT® (olmesartan medoxomil-hydrochlorothiazide) may be substituted

Tor its tritated components.

Dose Tittation by Clinical Effect

BENICAR HCT® is available in strengths of 20 mg/12.5 mg, 40 mg/12.5 mg

and 40 mg/25 mg. A patient whose blood pressure is inadequately controlled

by BENICAR® or hydrochlorothiazide alone may be switched to once daily

BENICAR HCT® (ofmesartan medoxomil-hydrochlorothiazide).

Dosing should be individualized. Depending on the blood pressure response, the
dose may be titrated at intervals of 2-4 weeks.

dose may be titrated at Intervals of 2-4 weeks.

If blood pressure is not controlled by BENICAR® alone, hydrochlorothiazide may be added starting with a dose of 12.5 mg and later titrated to 25 mg once daily. If a patient is taking hydrochlorothiazide, BENICAR® may be added starting with a dose of 20 mg once daily and titrated to 40 mg, for inadequate blood pressure control. If large doses of hydrochlorothiazide have been used as monotherapy and volume depletion or hyponatremia is present, caution should be used when adding BENICAR® or switching to BENICAR HCT® as marked decreases in blood pressure may occur (see WARNINGS, Hypotension in Volume- or Salt-Depleted Patients). Consideration should be given to reducing the dose of hydrochlorothiazide Patients). Consideration should be given to 12.5 mg before adding BENICAR®.

to 12.5 mig before adough Schildar HCT® is related to the dose of both com-ponents over the range of 10 mg/12.5 mg to 40 mg/25 mg (see CLINICAL PHAR-MACOLORY, Clinical Trials in the full prescribing information). The dose of BENICAR HCT® is one tablet once daily. More than one tablet daily is not RENICAR HCT® may be administered with other antihypertensive agents

ICHAN IN 19 may be annulmistered with other alterpreters we agents.

Bents with Renal Impairment

usual regimens of therapy with BENICAR HCT® may be followed provided the with creatinine clearance is >30 mL/min. In patients with more severe renal imment, loop diuretics are preferred to thiazides, so BENICAR HCT® is not

### No dosage adjustment is necessary with hepatic impairment (see CLINICAL PHARMACOLOGY, Special Populations in the full prescribing information)

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