Continued brief summary of prescribing information from previous page.

Focalin™ XR (dexmethylphenidate hydrochloride) extended-release capsules

provide the prescribing physician with some basis for estimating the relative contribution of drug and non-drug factors to the adverse event incidence rate in the population studied.

Table 2
Treatment-Emergent Adverse Events[1] Occurring During Double-Blind Treatment – Adults

	Focalin™ XR 20 mg N=57	Focalin™ XR 30 mg N=54	Focalin™ XR 40 mg N=54	Placebo N=53
No. of Patients with AEs				
Total	84%	94%	85%	68%
Primary System Organ Class/ Adverse Event Preferred Term				
Gastrointestinal Disorders	28%	32%	44%	19%
Dry Mouth	7%	20%	20%	4%
Dyspepsia	5%	9%	9%	2%
Nervous System Disorders	37%	39%	50%	28%
Headache	26%	30%	39%	19%
Psychiatric Disorders	40%	43%	46%	30%
Anxiety	5%	11%	11%	2%
Respiratory, Thoracic and Mediastinal Disorders	16%	9%	15%	8%
Pharyngolaryngeal Pain	4%	4%	7%	2%

[1]Events, regardless of causality, for which the incidence was at least 5% in a Focalin XR group and which appeared to increase with randomized dose. Incidence has been rounded to the nearest whole number.

Two other adverse reactions occurring in clinical trials with Focalin XR at a frequency greater than placebo, but which were not dose related were: Feeling jittery (12% and 2%, respectively) and Dizziness (6% and 2%, respectively).

Table 3 summarizes changes in vital signs and weight that were recorded in the adult study (N=218) of Focalin XR in the treatment of ADHD.

Table 3
Changes (Mean ± SD) in Vital Signs and Weight by Randomized Dose During Double-Blind Treatment – Adults

	Focalin™ XR 20 mg N=57	Focalin™ XR 30 mg N=54	Focalin™ XR 40 mg N=54	Placebo N=53
Pulse (bpm)	3.1 ± 11.1	4.3 ± 11.7	6.0 ± 10.1	-1.4 ± 9.3
Diastolic BP (mmHg)	-0.2 ± 8.2	1.2 ± 8.9	2.1 ± 8.0	0.3 ± 7.8
Weight (kg)	-1.4 ± 2.0	-1.2 ± 1.9	-1.7 ± 2.3	-0.1 ± 3.9

Adverse Events with Other Methylphenidate HCl Dosage Forms
Nervousness and insomnia are the most common adverse reactions reported with other methylphenidate products. In children, loss of appetite, abdominal pain, weight loss during prolonged therapy, insomnia, and tachycardia may occur more frequently; however, any of the other adverse reactions listed below may also occur.

Other reactions include:

Cardiac: angina, arrhythmia, palpitations, pulse increased or decreased, tachycardia

Gastrointestinal: abdominal pain, nausea

Immune: hypersensitivity reactions including skin rash, urticaria, fever, arthralgia, exfoliative dermatitis, erythema multiforme with histopathological findings of necrotizing vasculitis, and thrombocytopenic purpura

Metabolism/Nutrition: anorexia, weight loss during prolonged therapy

Nervous System: dizziness, drowsiness, dyskinesia, headache, rare reports of Tourette's syndrome, toxic psychosis

Vascular: blood pressure increased or decreased, cerebral arteritis and/or occlusion

Although a definite causal relationship has not been established, the following have been reported in patients taking methylphenidate:

Blood/Lymphatic: leukopenia and/or anemia

Hepatobiliary: abnormal liver function, ranging from transaminase elevation to hepatic coma

Psychiatric: transient depressed mood, aggressive behavior

Skin/Subcutaneous: scalp hair loss

Very rare reports of neuroleptic malignant syndrome (NMS) have been received, and, in most of these, patients were concurrently receiving therapies associated with NMS. In a single report, a ten-year-old boy who had been taking methylphenidate for approximately 18 months experienced an NMS-like event within 45 minutes of ingesting his first dose of venlafaxine. It is uncertain whether this case represented a drug-drug interaction, a response to either drug alone, or some other cause.

DRUG ABUSE AND DEPENDENCE
Controlled Substance Class
Focalin™ XR (dexmethylphenidate hydrochloride) extended-release capsules, like other methylphenidate products, is classified as a Schedule II controlled substance by Federal regulation.

Abuse, Dependence, and Tolerance
See WARNINGS for boxed warning containing drug abuse and dependence information.

OVERDOSAGE
Signs and Symptoms
Signs and symptoms of acute methylphenidate overdosage, resulting principally from overstimulation of the CNS and from excessive sympathomimetic effects, may include the following: vomiting, agitation, tremors, hyperreflexia, muscle twitching, convulsions (may be followed by coma), euphoria, confusion, hallucinations, delirium, sweating, flushing, headache, hyperpyrexia, tachycardia, palpitations, cardiac arrhythmias, hypertension, mydriasis, and dryness of mucous membranes.

Poison Control Center
The physician may wish to consider contacting a poison control center for up-to-date information on the management of overdosage with methylphenidate.

Recommended Treatment
As with the management of all overdosage, the possibility of multiple drug ingestion should be considered.

When treating overdose, practitioners should bear in mind that there is a prolonged release of dexmethylphenidate from Focalin™ XR (dexmethylphenidate hydrochloride) extended-release capsules.

Treatment consists of appropriate supportive measures. The patient must be protected against self-injury and against external stimuli that would aggravate overstimulation already present. Gastric contents may be evacuated by gastric lavage as indicated. Before performing gastric lavage, control agitation and seizures if present and protect the airway. Other measures to detoxify the gut include administration of activated charcoal and a cathartic. Intensive care must be provided to maintain adequate circulation and respiratory exchange; external cooling procedures may be required for hyperpyrexia.

Efficacy of peritoneal dialysis for Focalin overdosage has not been established.

Focalin™ XR is a trademark of Novartis AG

This product is covered by US patents including 5,837,284, 5,908,850, 6,228,398, 6,355,656, and 6,635,284.

REFERENCE
American Psychiatric Association. Diagnosis and Statistical Manual of Mental Disorders. 4th ed. Washington DC: American Psychiatric Association 1994.

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PD Guidelines: Therapy Do's and Don't Bother's

BY AMY ROTHMAN SCHONFELD
Contributing Writer

SAN DIEGO — Use of alternative therapies in the management of Parkinson's disease is supported only by weak data, according to one of four new practice parameters issued by the American Academy of Neurology at its annual meeting.

Considering that 60%-70% of PD patients turn to alternative therapies, the parameter provides the evidence a clinician needs to answer patient inquiries about their use.

AAN's review also found only weak evidence that exercise or speech therapy improves motor function. There was insufficient evidence to show that patients with PD derive any benefit from acupuncture, biofeedback, chiropractic, Mucuna pruriens (a nutritional supplement derived from a tropical legume, also known as velvet bean, that contains levodopa), or the Alexander technique (a form of movement therapy emphasizing correct posture and the proper positioning of the head with regard to the spine), according to the parameters, the 100th set to be issued by the AAN, which is known for the rigor of its guidelines. An estimated 80% of the AAN membership uses the academy's various practice parameters in their clinical practice. The goals of the parameters are not to dictate decision making but rather to provide neurologists with the information they need to make evidence-based judgments.

Treating Parkinson's-induced psychosis, the leading reason for nursing home placement in PD, can lessen 1-year mortality from 100% to 28%.

The four new guidelines address the diagnosis and prognosis of new-onset PD, neuroprotective strategies and alternative therapies, treatment of PD with motor fluctuations and dyskinesia, and evaluation and treatment of depression, psychosis, and dementia in PD.

For each parameter, the Quality Standards Subcommittee selected a committee composed of movement disorder specialists, a general neurologist, and, in the case of the nonmotor-symptom parameter, psychiatrists. Each committee surveyed the literature published from 1996 to January 2005, and scientifically rigorous studies were selected. For the treatment of PD with motor fluctuations and dyskinesia parameter, 730 articles were initially identified but only 29 met criteria for inclusion, explained coauthor Dr. Rajesh Pahwa of the University of Kansas, Kansas City.

The use of selegiline, levodopa, or a dopamine agonist for the initiation of treatment for PD is supported by the highest level of data.

For neuroprotection, the panel found that levodopa may be considered for the initial treatment of PD because it does not accelerate disease progression and is safe. However, the neuroprotective value of other medications is unproven. Good evidence is available to discount any protective effects from vitamin E (2,000 U).

For motor fluctuations, the panel recommended that entacapone and rasagiline should be offered, while pergolide, pramipexole, ropinirole, and tolcapone may be considered to reduce "off time" in PD. Only weak evidence is available to support the use of subcutaneous apomorphine, cabergoline, or selegiline, and the panel disregarded the use of sustained-release carbidopa/levodopa or bromocriptine.

The panel also updated the evidence on deep brain stimulation (DBS) for motor fluctuations, a matter that it last addressed 7 years ago. Level C evidence was found for DBS of the subthalamic nucleus, while there is insufficient evidence to make any recommendations about DBS of the globus pallidus interna or ventral intermediate nucleus of the thalamus.

For the first time, the AAN established a practice parameter for nonmotor PD symptoms, reflecting current thought that almost all PD patients are affected with one or more of these problems and that they have serious consequences. For instance, psychosis is the strongest marker for placement of a PD patient in a nursing home and, if untreated, leads to 100% mortality within a year, said coauthor Dr. Jill M. Miyasaki of the University of Toronto. With treatment, mortality falls to 28%. The panel examined whether effective screening tools and treatments were available for these conditions. While these parameters looked only at depression, psychosis, and dementia, new guidelines in preparation will address other nonmotor features of PD, including other behavioral issues, constipation, lightheadedness, and bladder problems.

The guidelines also will help investigators identify gaps in knowledge that may guide future research. For instance, more evidence is needed to determine whether DBS of areas other than the subthalamic nucleus is effective for treating motor fluctuations. There is also a need for head-to-head comparisons of medications.

The parameters are available in the April 11 issue of Neurology (2006;66:968-1002) and on the AAN's Web site (www.aan.com/professionals/practice/guideline/index.cfm). The AAN has also made available guideline summary sheets for clinicians and a separate set for patients and families.

The guidelines "scored an 'A,' " commented Robin A. Elliott, executive director of the Parkinson's Disease Foundation. Mr. Elliott was particularly appreciative of the patient summary sheets. Noting that only one-third of PD patients are treated by a movement disorders specialist, Mr. Elliott said the parameters "will empower larger groups of doctors to become expert in PD." ■