

Evaluating Central Nervous System Drug Labels For Patient-Reported Outcomes Claims

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Background

- Previous studies (prior to 2003) have suggested that central nervous system (CNS) drugs have had the highest number of patient-reported outcome (PRO) claims used in product approvals.
- This study examined the use of PRO as efficacy endpoints in label claims of recent FDA-approved CNS drugs between 2003 and 2008.

Methods

- Product labels of FDA-approved prescription-only New Molecular Entities (NMEs) from the CNS drug category between January 2003 and October 2008 were reviewed.
- The most recent product label, obtained either from the FDA's Center for Drug Evaluation and Research (CDER) or directly from the manufacturer's website, was used for all the drugs, including the drugs withdrawn from the market.
- Efficacy endpoint data was obtained from the *Clinical Studies* section of the approved product label. Efficacy measures were categorized into PRO, clinician-reported outcomes (CRO) and laboratory measures.

Results

- During the 5-year period, 14 of the 153 FDA-approved NMEs were CNS agents. Table 1 describes the endpoints types by CNS drug subclass.
- Of the 33 efficacy measures used in the CNS product labels, 12 (36.4%) were PRO.
- Of the 12 PRO used, 8 were symptom scales, 2 were global impression scales, 1 scale measured condition-specific health-related quality-of-life, and 1 scale measured functional impairment (Table 2).
- Table 3 describes drug name and the associated PRO endpoint.
- As shown in Figure 1, the percentage of approved CNS drugs using PRO as efficacy endpoints in label claims declined since 2002 (2003-08: 50%; 1997-2002: 75%).

Table 1. Endpoint Types by CNS Subclass

CNS Drug Subclass	Drugs Approved	Type of Endpoint		
		PRO	CRO	Laboratory Measures
Neuromuscular disorders	4	1	5	0
Antipsychotics	2	0	5	0
Antidepressants	2	4	5	0
Sedatives	2	2	0	2
Analgesics	1	1	0	0
Smoking cessation agents	1	3	0	1
CNS stimulant	1	1	2	0
Drug for alcoholism	1	0	1	0
Total	14	12	18	3

Table 2. PRO used in Labels

PRO Type	Names of Scales
Symptom scale	- Patient diary for Parkinson's disease symptoms
	- Subjective measure of patient total sleep time
	- Sleep diary
	- Connor's Parent Rating scale
	- Brief Questionnaire of Smoking Urges
	- Minnesota Nicotine Withdrawal scale
	- Patient self-report
	- Patient diary to report pain
Functional Impairment	- Sheehan Disability scale
Global Impression scale	- Visual Analog Scale of pain Intensity (VASPI)
	- Patient Global Impression (PGI) of change
Condition-specific Health-related Quality of Life	- Fibromyalgia Impact Questionnaire

Figure 1: Drugs Labels with PRO endpoints (1997-2008)

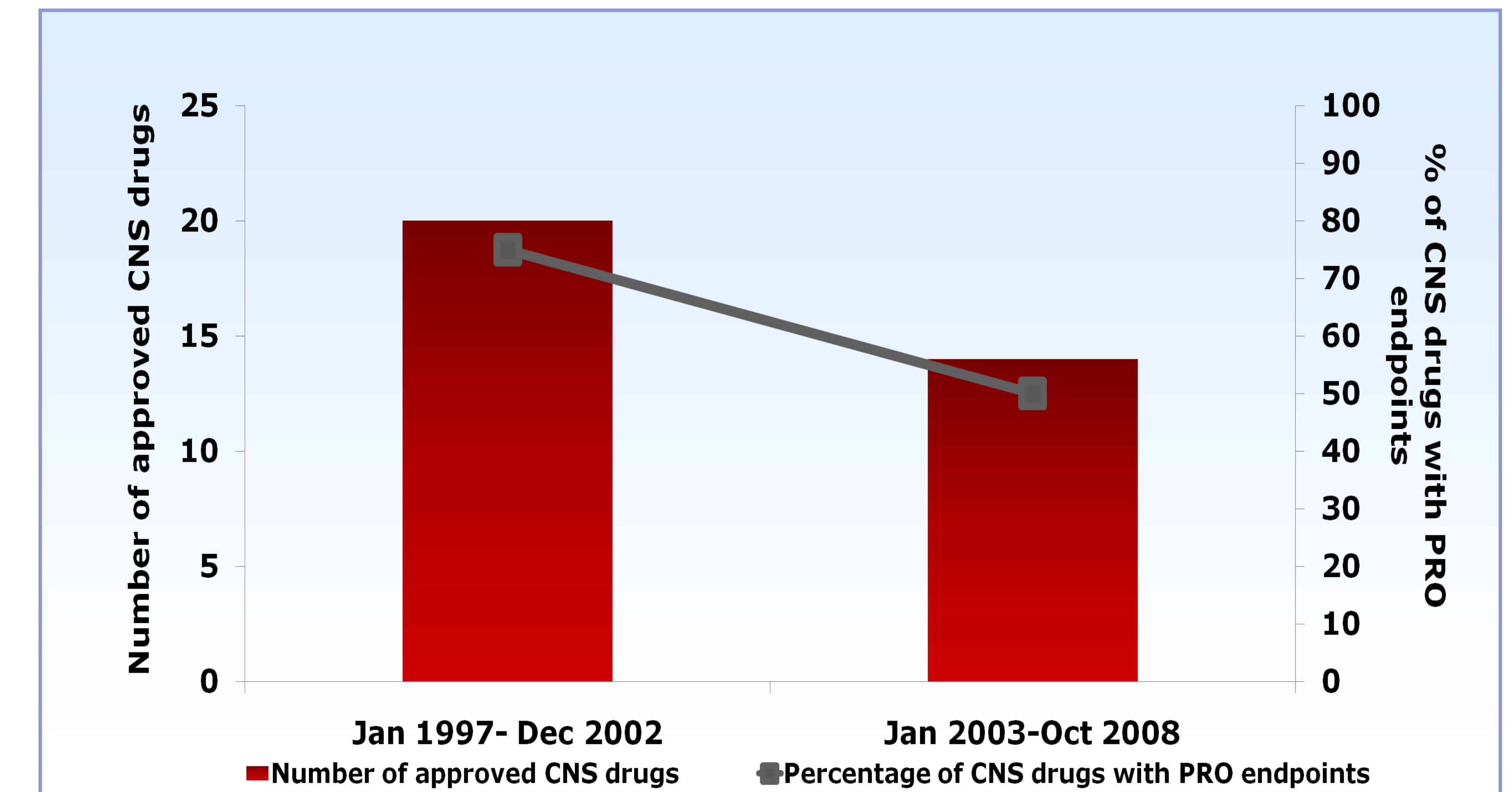


Table 3. Drugs Labels with PRO Endpoints

Generic Name	Brand Name	PRO Endpoints
Rasagiline	Azilect®	Change in disease symptoms
Eszopiclone	Lunesta®	Change in total sleep time
Ramelteon	Rozerem®	Alleviation of insomnia
Lisdexamfetamine dimesylate	Vyvanse™	Reduction in ADHD symptoms
Varenicline	Chantix®	Reduction in smoking urges
Duloxetine hydrochloride	Cymbalta®	Change in symptoms over time
		Functional impairment of daily life
		Reduction in fibromyalgia
Ziconotide	Prialt®	Reduction in pain over time

Conclusions

- The latter half of the past decade has seen a decrease in the number of CNS drugs that have had PRO-based label claims.
- Symptoms scales are the prominent type of PRO used in CNS drug label claims.