הודעה על החמרה (מידע בטיחות) בעלון לרופא

(מעודכן 3102.50)

תאריך: **19 ביוני 2013**
שם תכשיר באנגלית: **SIFROL ER Tablets 0.375mg, 0.75mg, 1.5mg**
מספרי רישום: **144-95-33088,144-96-33089, 144-97-33090**
שם בעל הרישום: **מעבדות רפא בע"מ**

ההחמרות מסומנות על רקע צהוב.

ההחמרות המבוקשות		
טקסט חדש	**טקסט נוכחי**	**פרק בעלון**
~~Impulse control disorders and compulsive behaviours Pathological gambling, increased libido and hypersexuality have been reported in patients treated with dopamine agonists for Parkinson's disease, including SIFROL. Furthermore, patients and caregivers should be aware of the fact that other behavioural symptoms of impulse control disorders and compulsions such as binge eating and compulsive shopping can occur. Dose reduction/tapered discontinuation should be considered.~~ Impulse control disorders Patients should be regularly monitored for the development of impulse control disorders. Patients and carers should be made aware that behavioural symptoms of impulse control disorders including pathological gambling, increased libido, hypersexuality, compulsive spending or buying, binge eating and compulsive eating can occur in patients treated with dopamine agonists including SIFROL. Dose reduction/tapered discontinuation should be considered if such symptoms develop.	Impulse control disorders and compulsive behaviours Pathological gambling, increased libido and hypersexuality have been reported in patients treated with dopamine agonists for Parkinson's disease, including SIFROL. Furthermore, patients and caregivers should be aware of the fact that other behavioural symptoms of impulse control disorders and compulsions such as binge eating and compulsive shopping can occur. Dose reduction/tapered discontinuation should be considered	**Special Warnings and Precautions**
Expected adverse reactions The following adverse reactions are expected under the use of SIFROL: abnormal dreams, amnesia, behavioural symptoms of impulse control disorders and compulsions such as binge eating, compulsive shopping, hypersexuality and pathological gambling; cardiac failure, confusion, constipation, delusion, dizziness, dyskinesia, dyspnoea, fatigue, hallucinations, headache, hiccups, hyperkinesia, hyperphagia, hypotension, inappropriate antidiuretic hormone secretion, insomnia, libido disorders, nausea, paranoia, peripheral oedema, pneumonia, pruritus, rash and other hypersensitivity; restlessness, somnolence, sudden onset of sleep, syncope, visual impairment including diplopia, vision blurred and visual acuity reduced, vomiting, weight decrease including decreased appetite, weight increase. Based on the analysis of pooled placebo-controlled trials, comprising a total of 1,778 Parkinson's disease patients on pramipexole and 1,297 patients on placebo, adverse drug reactions were frequently reported for both groups. 67% of patients on pramipexole and 54% of patients on placebo reported at least one adverse drug reaction.	Expected adverse reactions The following adverse reactions are expected under the use of SIFROL: abnormal dreams, amnesia, behavioural symptoms of impulse control disorders and compulsions such as binge eating, compulsive shopping, hypersexuality and pathological gambling; cardiac failure, confusion, constipation, delusion, dizziness, dyskinesia, dyspnoea, fatigue, hallucinations, headache, hiccups, hyperkinesia, hyperphagia, hypotension, insomnia, libido disorders, nausea, paranoia, peripheral oedema, pneumonia, pruritus, rash and other hypersensitivity; restlessness, somnolence, sudden onset of sleep, syncope, visual impairment including diplopia, vision blurred and visual acuity reduced, vomiting, weight decrease including decreased appetite, weight increase. Based on the analysis of pooled placebo-controlled trials, comprising a total of 1,778 Parkinson's disease patients on pramipexole and 1,297 patients on placebo, adverse drug reactions were frequently reported for both groups. 67% of patients on pramipexole and 54% of patients on placebo reported at least one adverse drug reaction.	**Adverse Events**

The adverse drug reactions reported in the table below are those events that occurred in 0.1% or more of patients treated with pramipexole and were reported significantly more often in patients taking pramipexole than placebo, or where the event was considered clinically relevant. The majority of adverse drug reactions were mild to moderate; they usually start early in therapy and most tended to disappear even as therapy was continued.

Within the system organ classes, adverse reactions are listed under headings of frequency (number of patients expected to experience the reaction), using the following categories: very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to < 1/100); rare (≥ 1/10,000 to < 1/1,000); very rare (< 1/10,000).

The most commonly (≥ 5%) reported adverse drug reactions in patients with Parkinson's disease more frequent with pramipexole treatment than with placebo were nausea, dyskinesia, hypotension, dizziness, somnolence, insomnia, constipation, hallucination, headache and fatigue. The incidence of somnolence is increased at doses higher than 1.5 mg pramipexole salt per day (see section 4.2). A more frequent adverse drug reaction in combination with levodopa was dyskinesia. Hypotension may occur at the beginning of treatment, especially if pramipexole is titrated too fast.

System Organ Class	Adverse Drug Reaction
Infections and infestations	
Uncommon	pneumonia
Endocrine disorders	
Uncommon	inappropriate antidiuretic hormone secretion[1]
Psychiatric disorders	
Common	abnormal dreams, behavioural symptoms of impulse control disorders and compulsions; confusion, hallucinations, insomnia,
Uncommon	binge eating[1], compulsive shopping, delusion, hyperphagia[1], hypersexuality, libido disorder, paranoia, pathological gambling, restlessness
Nervous system disorders	
Very common	dizziness, dyskinesia, somnolence
Common	headache
Uncommon	amnesia, hyperkinesia, sudden onset of sleep, syncope
Eye disorders	
Common	visual impairment

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Nervous system disorders	
Very common	dizziness, dyskinesia, somnolence
Common	headache
	amnesia,

	including diplopia, vision blurred and visual acuity reduced
Cardiac disorders	
Uncommon	cardiac failure[1]
Vascular disorders	
Common	hypotension
Respiratory, thoracic, and mediastinal disorders	
Uncommon	dyspnoea , hiccups
Gastrointestinal disorders	
Very common	nausea
Common	constipation, vomiting
Skin and subcutaneous tissue disorders	
Uncommon	hypersensitivity, pruritus, rash
General disorders and administration site conditions	
Common	fatigue, peripheral oedema
Investigations	
Common	weight decrease including decreased appetite
Uncommon	weight increase
Unknown	urinary retention

[1] This side effect has been observed in post-marketing experience. With 95 % certainty, the frequency category is not greater than uncommon, but might be lower. A precise frequency estimation is not possible as the side effect did not occur in a clinical trial database of 2,762 patients with Parkinson's Disease treated with pramipexole.

Somnolence
Pramipexole is commonly associated with somnolence and has been associated uncommonly with excessive daytime somnolence and sudden sleep onset episodes (see also section 4.4).

Libido disorders
Pramipexole may uncommonly be associated with libido disorders (increased or decreased).

~~Impulse control disorders and compulsive behaviours Patients treated with dopamine agonists for Parkinson's disease, including SIFROL, especially at high doses, have been reported as exhibiting signs of pathological gambling, increased libido and hypersexuality, generally reversible upon reduction of the dose or treatment discontinuation. See also section 4.4.~~

Impulse control disorders
Pathological gambling, increased libido, hypersexuality, compulsive spending or buying, binge eating and compulsive eating can occur in patients treated with dopamine agonists including SIFROL (see section 4.4).

In a cross-sectional, retrospective screening and case-control study including 3,090 Parkinson's disease patients, 13.6% of all patients receiving

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Uncommon	weight increase

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Impulse control disorders and compulsive behaviours
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dopaminergic or non-dopaminergic treatment had symptoms of an impulse control disorder during the past six months. Manifestations observed include pathological gambling, compulsive shopping, binge eating, and compulsive sexual behaviour (hypersexuality). Possible independent risk factors for impulse control disorders included dopaminergic treatments and higher doses of dopaminergic treatment, younger age (≤ 65 years), not being married and self-reported family history of gambling behaviours. Cardiac failure In clinical studies and post-marketing experience cardiac failure has been reported in patients with pramipexole. In a pharmacoepidemiological study pramipexole use was associated with an increased risk of cardiac failure compared with non-use of pramipexole (observed risk ratio 1.86; 95% CI, 1.21-2.85). Rhabdomyolysis Rhabdomyolysis (incidence unknown): characterized by myalgia, feelings of weakness, increased CK (CPK), and increased blood and urine myoglobin, may occur. Patients should be closely monitored. If any abnormality is observed, administration should be discontinued and appropriate measures taken.	In a cross-sectional, retrospective screening and case-control study including 3,090 Parkinson's disease patients, 13.6% of all patients receiving dopaminergic or non-dopaminergic treatment had symptoms of an impulse control disorder during the past six months. Manifestations observed include pathological gambling, compulsive shopping, binge eating, and compulsive sexual behaviour (hypersexuality). Possible independent risk factors for impulse control disorders included dopaminergic treatments and higher doses of dopaminergic treatment, younger age (≤ 65 years), not being married and self-reported family history of gambling behaviours. Cardiac failure In clinical studies and post-marketing experience cardiac failure has been reported in patients with pramipexole. In a pharmacoepidemiological study pramipexole use was associated with an increased risk of cardiac failure compared with non-use of pramipexole (observed risk ratio 1.86; 95% CI, 1.21-2.85).	