Core Safety Profile

Active substance: Quinagolide
Pharmaceutical form(s)/strength: Tablet, 25 mikrogram + 50 mikrogram, 75 mikrogram and 150 mikrogram
P-RMS: SE/H/PSUR/0027/002
Date of FAR: 13.02.2013
4.3 Contraindications

Severely impaired hepatic or renal function. Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Hyperprolactinaemia may be physiological (pregnancy, lactation) as well as be due to other causes among others tumours in hypothalamus or pituitary gland and a number of drugs. Therefore it is important that the specific cause to a hyperprolactinaemia is explained as far as possible and that causal therapy is initiated.

Since orthostatic hypotension may result in syncope in rare cases, it is recommended to check blood pressure both lying and standing during the first days of therapy and following dosage increases. Moreover, orthostatic blood pressure changes with reflex increases in heart rate might be relevant for patients with severe heart diseases.

In women suffering from prolactin-related fertility disorders, fertility may be restored by treatment with QUINAGOLIDE. Women of child-bearing age who do not wish to conceive should therefore be advised to practice a reliable method of contraception.

In a few cases, including patients with no previous history of mental illness, treatment with QUINAGOLIDE has been associated with the occurrence of acute psychosis, usually reversible upon discontinuation. Particular caution is required in patients who have had psychotic episodes in their previous history.

To date no data is available with the use of QUINAGOLIDE in patients with impaired renal or hepatic function.

QUINAGOLIDE has been associated with somnolence. Other dopamine agonists have been associated with sudden sleep onset episodes, particularly in patients with Parkinson’s disease. Patients must be informed of this and advised to be cautious while driving or operating machines during treatment with QUINAGOLIDE.

Patients who have experienced somnolence must not drive or operate machines. Furthermore, a reduction of dosage or termination of therapy may be considered.

No interaction studies have been performed with quinagolide and caution is therefore recommended if QUINAGOLIDE is combined with other medicinal products (see section 4.5).

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

The tolerability of QUINAGOLIDE may be reduced by alcohol.

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 Quinagolide. Dose reduction/tapered discontinuation should be considered if such symptoms develop.
A limited number of elderly patients have been treated for pituitary adenomas and rheumatoid arthritis with quinagolide at doses ranging from 50 – 300 µg/day. The duration of treatment ranged from 6 – 93 months and the treatment was well-tolerated.

A limited number of children aged 7-17 years have been treated with QUINAGOLIDE for prolactinoma, at doses ranging from 75 – 600 µg/day. The duration of treatment ranged from 1 – 5 years and the treatment was well-tolerated.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed and no interactions between QUINAGOLIDE and other drugs have so far been reported. On theoretical grounds, a reduction of the prolactin-lowering effect could be expected when drugs (e.g. neuroleptic agents) with strong dopamine antagonistic properties are used concomitantly.

As the potency of quinagolide for 5-HT1 and 5-HT2 receptors is some 100 times lower than that for D2 receptors, an interaction between QUINAGOLIDE and 5-HT1a receptors is unlikely. However, care should be taken with concomitant use of medication interfering with these receptors.

Due to limited data available with respect to the enzyme(s) involved in the metabolism of quinagolide, potential pharmacokinetic interactions are difficult to predict. Data is also lacking regarding the potential for quinagolide to affect the pharmacokinetics of other medicinal products, e.g. via enzyme inhibition. Caution is therefore recommended if QUINAGOLIDE is combined with other medicinal products, in particular with drugs known to be potent inhibitors of drug-metabolising enzymes.

The tolerability of QUINAGOLIDE may be reduced by alcohol.

4.6 Pregnancy and lactation

Pregnancy: Animal data provide no evidence that QUINAGOLIDE has any embryotoxic or teratogenic potential, but clinical experience in pregnant women is limited. In patients wishing to conceive, QUINAGOLIDE should be discontinued when pregnancy is confirmed, unless there is a medical reason for continuing therapy. No increased incidence of abortion has been observed following withdrawal of the drug at this point. If pregnancy occurs in the presence of a pituitary adenoma and QUINAGOLIDE treatment has been stopped, close supervision throughout pregnancy is essential.

Lactation: Breast-feeding is usually not possible since QUINAGOLIDE suppresses lactation. If lactation should continue during treatment, breast-feeding cannot be recommended because it is not known whether quinagolide passes into human breast milk.

4.7 Effects on ability to drive and use machines

Treatment with QUINAGOLIDE may, in some patients, impair the ability to react during the first days of treatment. This has to be taken into consideration when sharpened alertness is demanded, e.g. when driving. Patients being treated with QUINAGOLIDE and presenting with somnolence and/or sudden sleep onset episodes must be advised not to drive or engage in activities where impaired alertness may put themselves or others at risk of serious injury or death (e.g. operating machines) until these episodes or the somnolence have ceased.

See also section 4.4.
4.8 Undesirable effects

Most adverse reactions are dose-dependent and transient. The adverse reactions are seldom sufficiently serious to require discontinuation of treatment.

<table>
<thead>
<tr>
<th>MedDRA Organ Class</th>
<th>Very common (≥1/10)</th>
<th>Common (≥1/100 to &lt;1/10)</th>
<th>Rare (≥1/10,000 to &lt;1/1,000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolism and nutrition disorders</td>
<td>-</td>
<td>Anorexia</td>
<td>-</td>
</tr>
<tr>
<td>Psychiatric disorders</td>
<td>-</td>
<td>Insomnia</td>
<td>Reversible acute psychosis</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td>Dizziness, headache</td>
<td>-</td>
<td>Somnolence</td>
</tr>
<tr>
<td>Vascular disorders</td>
<td>-</td>
<td>Orthostatic hypotension</td>
<td>-</td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastenal disorders</td>
<td>-</td>
<td>Nasal congestion</td>
<td>-</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>Nausea, vomiting</td>
<td>Abdominal pain, constipation, diarrhoea</td>
<td>-</td>
</tr>
<tr>
<td>Musculoskeletal, connective tissue and bone disorders</td>
<td>-</td>
<td>Muscular weakness</td>
<td>-</td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
<td>Fatigue</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

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 Quinagolide. (See section 4.4. ‘Special warnings and precautions for use’).

Orthostatic hypotension reported following use of QUINAGOLIDE, rarely can result in syncope.

The risk of hypersensitive reactions could not be excluded.

4.9 Overdose

Limited experience of overdose. It would be expected to cause nausea, vomiting, headache, dizziness, drowsiness, hypotension, hallucinations. Treatment of overdose should be symptomatic. If justified stomach wash-out or carbon.