REVIEW

Quinagolide – a valuable treatment option for hyperprolactinaemia

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Abstract

Hyperprolactinaemia is characterised by gonadal dysfunction, including infertility and reduced libido and, if left untreated, is associated with an increased risk of long-term complications, such as osteoporosis. The first-line therapy for patients with hyperprolactinaemia is pharmacological intervention with a dopamine agonist. Currently, there are three dopamine agonists available for hyperprolactinaemia therapy: bromocriptine, quinagolide and cabergoline. Bromocriptine has a long history of use; however, a range of 5–18% of patients are reported to show bromocriptine resistance, with only partial lowering of plasma prolactin levels and an absence of tumour shrinkage. The newer dopamine agonists, quinagolide and cabergoline, offer improved efficacy over bromocriptine, with a lower incidence of adverse events. Quinagolide and cabergoline have also demonstrated efficacy in many patients intolerant or resistant to bromocriptine. Thus, the selection of dopamine agonists available provides more than one option for pharmacological intervention of hyperprolactinaemia. This review discusses the clinical use of quinagolide in comparison to other dopamine agonists for hyperprolactinaemia therapy. Quinagolide may improve patient compliance to treatment owing to its reduced side effect profile, simple and rapid titration over just 7 days, once-daily dosing regimen and easy to use starter pack (available in some countries). Quinagolide offers an additional benefit for patients wishing to become pregnant, as it can be used until the point of confirmation of pregnancy. Therefore, as a well tolerated and effective therapy, with a simple dosing regimen, quinagolide should be considered as a first-line therapy in the treatment of hyperprolactinaemia.

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Introduction

Elevated prolactin levels can result from physiological causes, such as pregnancy and stress, and pharmacological causes, including the use of neuroleptics, oestrogens, opiates, antihypertensive drugs, or calcium channel blockers (see (1)). Once physiological and iatrogenic stimuli have been eliminated as causes of elevated prolactin levels, the presence of a micro- or macroprolactinoma is the most likely cause of persistent pathological hyperprolactinaemia (2). These pituitary tumours increase prolactin levels via excessive prolactin production and by attenuation of the normal dopamine inhibition of prolactin secretion through possible disruption of the dopamine delivery pathway from the hypothalamus to the pituitary.

Symptoms of hyperprolactinaemia include signs of gonadal dysfunction, and female patients frequently present with oligomenorrhoea, amenorrhoea and galactorrhoea (3). Pathological hyperprolactinaemia is

also associated with infertility (3) and reduced libido (4) and an increased risk of long-term complications including osteopenia and osteoporosis (5–7). These long-term complications associated with elevated prolactin levels suggest that even patients who are unconcerned by their clinical symptoms or who do not wish to receive therapy in order to restore fertility should be considered for long-term therapeutic intervention.

Pharmacological intervention with dopamine agonists is considered the first-line therapy for patients with prolactinomas, reserving surgery or radiotherapy for patients who demonstrate resistance or intolerance to dopamine agonist therapy. Mimicking the action of dopamine, dopamine agonists, including bromocriptine, quinagolide and cabergoline are able to lower prolactin levels, decrease prolactinoma size and restore ovarian function (see (8)).

Initially, bromocriptine was considered the gold standard for dopamine agonist therapy; however, bromocriptine is associated with a range of side effects,

leaving some patients intolerant to treatment. Bromocriptine administration via the vaginal route may reduce the incidence of side effects and offer an alternative to oral bromocriptine (9, 10). A range of 5–18% of patients have also been reported as resistant to bromocriptine treatment, with only partial lowering of plasma prolactin levels and an absence of tumour shrinkage (11–13) even after administration of high doses of bromocriptine. The newer drugs, quinagolide and cabergoline offer more effective and better tolerated treatment options compared with bromocriptine (14, 15). These more effective dopamine agonists have also shown efficacy in patients resistant or intolerant to bromocriptine (11, 16–24). Thus, the actual selection of dopamine agonists available provides more than one option for pharmacological intervention of hyperprolactinaemia, allowing patients who show resistance or intolerance to one dopamine agonist, such as bromocriptine, to be treated effectively with another, such as quinagolide (11, 16–22). This review discusses the clinical use of quinagolide in comparison to other dopamine agonists as a therapy option for hyperprolactinaemia.

Quinagolide pharmacology

Quinagolide is selective for D2-type dopamine receptors

Quinagolide (Norprolac, Ferring Pharmaceuticals, Lausanne, Switzerland) is a non-ergot derived dopamine agonist with a chemical structure similar to apomorphine (Fig. 1). Binding of quinagolide or other dopamine agonists to D2 dopamine receptors on the surface of lactotroph cells in the anterior pituitary reduces adenylyl cyclase activity, reduces intracellular cyclic adenosine monophosphate and inhibits prolactin secretion (25). Quinagolide acts specifically and with high affinity on D2-type dopamine receptors and has little affinity, at supra-pharmacological concentrations, for D1-type dopamine receptors (26). Cabergoline is an ergot-derived dopamine agonist, which also demonstrates low affinity for D1-type dopamine receptors and high affinity for D2-type receptors (27). In contrast, the ergot derivative bromocriptine is not a specific D2-type dopamine receptor agonist and can act as an antagonist at D1-type receptors (28).

Both the specificity and the non-ergot nature of quinagolide reduce the risk of side effects, such as nausea and peripheral vasospasm, compared with the less-specific and ergot derivative dopamine agonists, such as bromocriptine (29, 30).

Once-daily dosing of quinagolide

The 22-hour half-life and 24-hour duration of action of quinagolide permit once-daily dosing; the potent prolactin-lowering effect of once-daily quinagolide has

A

B

C

Figure 1 The chemical structures of (A) quinagolide, (B) cabergoline and (C) bromocriptine.

been demonstrated in pharmacological and dose-ranging studies in both healthy volunteers (31) and patients with hyperprolactinaemia (32). Cabergoline is also a long-lasting therapy, with a half-life of 65 h and a duration of action of 7–14 days, which is typically administered once or twice per week (8, 27). In comparison, the half-life of bromocriptine is just 3.3 h (33), with a duration of action of 8–12 h, necessitating multiple daily dosing. The once-daily dosing of quinagolide offers the potential to improve treatment success, in comparison to the conventional multiple-daily dosing with bromocriptine; studies with various pharmacological agents have shown that frequent dosing schedules can reduce patient compliance (34–37). The efficacy of a single evening dose of bromocriptine has been investigated and was shown in one study to provide equivalent control of prolactin levels with a reduced incidence and intensity of side effects compared with a conventional three-times-daily regimen (38).

Initiation of quinagolide therapy

Maintenance dose options and 7-day titration of quinagolide

Quinagolide is available in tablets of 0.025, 0.050, 0.075 and 0.150 mg and is typically taken at a dose of 0.075 mg once daily (32). Patients should be initiated onto quinagolide therapy at a dose of 0.025 mg per day and increased to a dose of 0.075 mg per day with a quick and simple titration over just 7 days. In this titration (available as a starter pack in some countries), patients receive 0.025 mg per day for the first 3 days, followed by 0.050 mg per day for the next 3 days (32). At Day 7, the dose is increased to 0.075 mg per day and is maintained for at least 1 month until an evaluation of clinical effects and prolactin measurements is performed. If necessary, the quinagolide dose can be increased, in stepwise increments, until the dose achieving the optimal patient response is attained, up to a maximum dose of 0.3–0.6 mg per day.

Cabergoline is typically initiated at a dose of 0.25–0.50 mg on a twice-weekly basis. The dose is then adjusted after at least 1 month, according to the serum prolactin levels. The therapeutic dosage is usually 1 mg per week and ranges from 0.25–10.5 mg per week, typically administered in divided doses twice weekly (39). Bromocriptine is initiated at 1.25–2.50 mg in divided doses administered twice a day. The majority of patients with hyperprolactinaemia respond to bromocriptine in divided doses of 7.5 mg daily, but doses of up to 30 mg per day have been used (11). Compared with bromocriptine, the simple titration of quinagolide, at the initiation of treatment, offers the opportunity to improve tolerability and patient compliance.

Clinical experience with quinagolide

Efficacy in reduction of prolactin levels and prolactinoma size

Once-daily quinagolide therapy in women with hyperprolactinaemia has been shown to effectively reduce prolactin levels and prolactinoma size and to relieve the associated symptoms, with particular respect to restoration of gonadal function and fertility (11, 15–21, 30, 32, 40–47) (Table 1). For example, treatment of 41 women with hyperprolactinaemia for 12–52 weeks with quinagolide reduced prolactin levels and resolved menstrual cycle irregularities in the majority of patients; amenorrhoea was resolved in 19 of the 25 women with this condition at week 12, and in 24 women at the end of the study. During this study, the prolactin levels were normalised in 71% of patients at a quinagolide dose of ≤ 0.1 mg per day. However, further dose increases of up to 0.5 mg per day following the 12-month study period resulted in normal prolactin levels in 95% of the patients (42). Another study evaluated the outcome of 40 patients with hyperprolactinaemia under quinagolide for 2–72 months. Of these 40 patients, 11 had microadenomas and 12 had macroadenomas. Quinagolide treatment reduced prolactin levels in all patients, where normalisation of prolactin levels was observed in 82% of the patients with no observable tumour at baseline, 73% of patients with microadenomas and 67% of patients with macroadenomas (18).

While elevated prolactin levels are encountered mostly in young females, men can also suffer from hyperprolactinaemia, typically leading to hypogonadism and symptoms including decreased libido, erectile dysfunction and abnormal semen analysis. In a study of the effects of chronic quinagolide treatment on sexual and gonadal function in male patients with hyperprolactinaemia, 14 men (13 with macroprolactinoma; one with microprolactinoma) were treated with quinagolide for 6–24 months (4). Analysis of the semen of these patients at baseline revealed reduced sperm count and motility, abnormal sperm morphology and decreased viability. Treatment with quinagolide effectively reduced the prolactin levels, with normalisation observed within 3 months in 13 of the 14 men. Analysis of the semen after 1 year of quinagolide treatment revealed increases in sperm number (from $5600 \pm 111 \text{ mm}^3$ to $20\,564 \pm 587 \text{ mm}^3$), motility at 1 h (from $24.8 \pm 0.1\%$ to $52.6 \pm 0.5\%$) and normal morphology (from $53.8 \pm 2.5\%$ to $62.2 \pm 2.4\%$). In addition, tumour mass was reduced by at least 30% in 8 of the 13 men with a macroprolactinoma. The authors concluded that normalisation of prolactin levels with quinagolide improves gonadal and sexual function and fertility in male patients with hyperprolactinaemia resulting from a prolactinoma (4). In a prospective, unblinded, multicenter trial, 26 patients with macroadenomas received once-daily quinagolide for 24 weeks

Table 1 Summary of a series of studies investigating the use of quinagolide.

	Ref	No. of patients	Duration	Outcomes at the end of the study				
				Normalisation of PRL levels (% of patients)	Prolactinoma size (% of cases)	Regular menstrual cycles (% of patients)	Fertility	Galactorrhoea
Efficacy of quinagolide	[42]	41	12–52 weeks	71% with a once-daily dose ≤ 0.1 mg	–	96	Pregnancies occurred within 12 months in 4/11 (36%) infertile W	Resolved in 92%
	[18]	40	2–72 months	No tumour: 82% Micro: 73% Macro: 67%	Micro: reduced in 55% Macro: reduced in 75%	–	–	–
	[4]	14 (male)	6–24 weeks	93%	Reduced by $\geq 30\%$ in 62% of macro	–	Increase sperm number, motility at 1 hour, and normal morphology	–
	[48]	26	24 weeks	58%	Macro: reduced in 81%	73	Sexual function improved in 71% of affected males	–
Quinagolide vs bromocriptine	[40]	45	24 weeks	81 vs 70%	–	Restored with both drugs	Restored with both drugs	Reduced
	[15]	22	6 months	91 vs 43%	–	In 91 vs 82	67 vs 25% of patients who wanted to become pregnant did so	–
Quinagolide in bromocriptine-resistant patients	[11]	28	1 year	43%	–	In 40	Nine pregnancies in seven women within 1.8 ± 0.5 years; libido and potency improved in men	–
	[30]	24	24 weeks	67%	–	(94%) patients with normalised PRL levels	(94%) patients with normalised PRL levels	–
	[43]	20	3–20 months	70%	–	70	57% of patients complaining of infertility became pregnant	Resolved in 71%
Quinagolide vs cabergoline	[51]	20	12 weeks	75 vs 90% ($P < 0.05$)	–	Similar efficacy between drugs	Similar efficacy between drugs	Similar efficacy between drugs
	[21]	39	12 months	Micro: 100 vs 96% Macro: 88 vs 88%	Micro: reduced by $> 80\%$ in 22 vs 30% Macro: reduced by 25 vs 31%	–	–	–

Macro, macroadenoma; micro, microadenoma; PRL, prolactin; W, women.

(48). Macroadenoma size decreased in 21 patients, regular menses were restored in 11 of 15 premenopausal women and sexual function improved in five of seven affected males (48).

Thus, together, these studies suggest that quinagolide is an effective therapy for the treatment of both male and female patients with hyperprolactinaemia and is able to alleviate the symptoms associated with elevated prolactin levels and to produce significant tumour shrinkage after 6–12 months of treatment in at least 61–80% of cases.

Efficacy of quinagolide compared with bromocriptine

Quinagolide has been shown to be at least as effective as bromocriptine in the treatment of hyperprolactinaemia. For example, one double-blind, randomized study of 47 women with long-standing hyperprolactinaemia compared once-daily quinagolide administration with twice-daily bromocriptine treatment (40). In this study, 81% of patients achieved normal prolactin levels after 24 weeks of quinagolide treatment compared with 70% of bromocriptine-treated patients. However, there was no significant difference between the treatment groups with respect to the prolactin levels at the end of the study. Both drugs were able to restore menses and fertility and reduce the incidence of galactorrhoea (40).

In another double-blind, randomized study that compared once-daily quinagolide with twice-daily bromocriptine, 22 women with hyperprolactinaemia were treated for 6 months (15). At the end of the study, the prolactin levels did not differ between treatment groups. However, prolactin levels returned to normal in 10 of the 11 patients in the quinagolide group, while in the bromocriptine group, four patients discontinued the study owing to side effects and normal prolactin levels were observed in three of the seven remaining patients. Regular menses were restored in 10 of the 11 women receiving quinagolide and nine of 11 patients receiving bromocriptine. While barrier contraception was recommended to patients in this study, two of the three women who wanted to conceive in the quinagolide group became pregnant within three ovulations as compared with one of four women in the bromocriptine group (15).

Quinagolide has also demonstrated efficacy in patients who are resistant to bromocriptine therapy (11, 16–21, 30, 40, 43, 49). Bromocriptine-resistance may be defined by the persistence of elevated prolactin levels and the absence of alleviation of clinical symptoms despite daily long-term administration of 15–30 mg of bromocriptine (50). In a study of 28 patients with bromocriptine-resistant prolactinomas treated with quinagolide for 1–3 years, restoration of normal prolactin levels and gonadal function

occurred in 12 patients after 1 year of quinagolide treatment. During the 3 year follow-up period, nine pregnancies were observed in seven women (11). A double-blind, randomized study in 24 female patients with hyperprolactinaemia, 23 of whom were previously treated with bromocriptine, revealed a decrease in prolactin levels in all patients and normalisation of prolactin levels in 16 patients after 24 weeks. Regular menstruation and ovulation were restored in 15 of the 16 patients with normalised prolactin levels (30). These 15 patients received ongoing treatment with quinagolide for a total of 24 months. At 24 months, prolactin levels were normalised in all 15 patients, regular menses and ovulation were restored in 13 patients and galactorrhoea was relieved in 11 of the 14 patients presenting with galactorrhoea at baseline (30).

In another prospective trial, 20 women with persistent hyperprolactinaemia received quinagolide for 3–20 months (43). Prolactin levels decreased in all patients after 3 months of treatment, with an average decrease from baseline of 85% by the end of the study. Of the 20 women in this study, 19 had previously been treated with bromocriptine. Normal prolactin levels were restored in 13 patients after 3 months and in 14 patients at the end of the study, in accord with restoration of normal menses. Of the seven patients in this study complaining of infertility at baseline, four became pregnant and delivered healthy babies (43). A similar efficacy of quinagolide, in bromocriptine-resistant patients, was also reported in another smaller study (16).

Finally, treatment with once-daily quinagolide in 21 patients with prolactinomas resistant to bromocriptine was evaluated according to the prolactin levels at baseline (49). In the 10 patients with the highest prolactin levels at baseline ($948 \pm 538 \mu\text{g/l}$), prolactin levels decreased by 48% overall (49); however, no reduction in tumour size was observed. In the 11 patients with mean baseline prolactin levels of $468 \pm 160 \mu\text{g/l}$, normoprolactinaemia was obtained in all patients after 1–6 months of treatment with quinagolide and tumour size decreased by at least 25% in 6 patients (49). Other studies have reported an improved tolerance with quinagolide in patients previously intolerant to bromocriptine (17). In a study in which quinagolide efficacy was investigated in 20 bromocriptine-intolerant patients, quinagolide reduced prolactin levels in patients with macroprolactinomas (–91%) after 1 year of therapy. Decreases in tumour size were also observed (–74%) and were correlated with the decrease in prolactin levels ($P < 0.01$) (17).

Thus, these studies demonstrate that quinagolide is able to improve prolactin levels and the associated clinical symptoms in patients who demonstrate resistance or intolerance to previous dopamine agonist therapy with bromocriptine.

Efficacy of quinagolide compared with cabergoline

Several studies have investigated the efficacy of quinagolide and cabergoline in patients with hyperprolactinaemia (21, 51–53). In a randomized, cross-over study, 20 patients with hyperprolactinaemia received once-daily quinagolide or twice-weekly cabergoline for 12 weeks, with the two treatment phases separated by a wash-out period of 12 weeks with placebo (51). In this study, a higher percentage of patients with hyperprolactinaemia achieved normal prolactin levels with cabergoline compared with quinagolide (90 vs 75%; $P < 0.05$). However, clinical efficacy was similar between treatments in terms of improvement of symptoms, such as amenorrhoea, oligomenorrhoea, galactorrhoea and impotence, and there was no difference in the occurrence of side-effects (51).

Another study investigated the treatment of 39 patients with prolactinomas with once-daily quinagolide and twice-weekly cabergoline (21). Of the 39 patients, 23 patients had microprolactinomas and 16 had macroprolactinomas. Treatment with quinagolide for 12 months was followed by a 12-month wash-out period and then cabergoline treatment was given for a further 12-month period. The 12-month withdrawal of dopamine agonist therapy was introduced in this protocol in order to evaluate the recurrence of hyperprolactinaemia. After treatment with quinagolide for the first 12 months, prolactin levels normalised in 100% of patients with microprolactinomas and in 88% of patients with macroprolactinomas. Tumour volume, assessed by magnetic resonance imaging, was reduced by more than 80% in 22% of patients with microprolactinomas and 25% of patients with macroprolactinomas. At the end of the wash-out period, prolactin levels had increased in all patients, but were significantly lower than the prolactin levels measured at baseline before initiation of quinagolide therapy ($P = 0.01$). After 12 months of cabergoline treatment, prolactin levels normalised in 96% of patients with microprolactinoma and 88% with macroprolactinoma. Tumour volume reductions of more than 80% were noted in 30% and 31% of patients with micro- and macroprolactinomas, respectively. After 12 months of withdrawal from cabergoline treatment, recurrence of hyperprolactinaemia was observed in all patients with macroprolactinomas and 19 of the 23 patients with microprolactinomas. Therefore, in this study, quinagolide and cabergoline normalised prolactin levels in the majority of patients after 12 months of treatment, but recurrence of hyperprolactinaemia was observed in all patients with macroprolactinomas withdrawn from cabergoline and quinagolide (21). In another randomized cross-over study, 12 patients received either once-daily quinagolide (0.075 mg) or twice-weekly cabergoline (0.5 mg) for 12 weeks (53). Treatment with the second dopamine agonist was

initiated after the recurrence of hyperprolactinaemia; nine patients completed both treatment cycles. In this study, the clinical effects were similar with both cabergoline and quinagolide and, interestingly, only one patient remained resistant to both dopamine agonists (53). In a study of 26 children or adolescents with prolactinomas, 16 were considered resistant or intolerant to bromocriptine (52). Quinagolide therapy allowed normalization of prolactin values in five of these 16 cases. Subsequent treatment with cabergoline allowed further prolactin normalisation in six of the remaining 10 cases (52). This study suggests that while some patients show resistance to dopamine agonist therapy, those resistant to one therapy may be treated effectively with another dopamine agonist; however a small proportion of patients still appear to be resistant to pharmacotherapy with bromocriptine, quinagolide and cabergoline.

Safety

Tolerability

As a non-ergot derivative, quinagolide is unlikely to cause side effects such as peripheral vasospasm, erythromelalgia, and pleuropulmonary or retroperitoneal fibrosis that occasionally occur with ergot derivatives, such as bromocriptine (29). The specificity of quinagolide for D2-type dopamine receptors is also likely to result in fewer side effects compared with dopamine agonists, such as bromocriptine that also act on D1-type dopamine receptors.

Indeed, quinagolide has shown better tolerability compared with bromocriptine; in one double-blind, randomized 6-month study in 22 women with persistent hyperprolactinaemia, quinagolide was significantly better tolerated compared with bromocriptine ($P = 0.025$) (15). While cabergoline is able to act on D1-type dopamine receptors, it has only a low affinity for these receptors and demonstrates a high affinity for D2-type receptors (54). Cabergoline has also been used effectively to treat hyperprolactinaemia with a low incidence of side effects (14, 39, 55–58). The better tolerability of cabergoline compared with bromocriptine (14) may be related not only to the high affinity for D2-type receptors, but also to the longer half-life of cabergoline, which results in fewer changes in drug concentration in the blood.

As mentioned above, quinagolide has also been used effectively and safely in patients demonstrating bromocriptine intolerance (15, 18, 22); cabergoline has also shown efficacy in these patients (39, 57). In studies with quinagolide, the most frequently reported side effects tend to be nausea and headache, but with most reported as mild to moderate in intensity, often transient and occurring within the first few weeks of treatment (15, 30, 40, 42, 43). Quinagolide has a good safety profile, with, for example, no reported

changes in blood biochemistry, haematology, blood pressure or pulse rate (15, 30, 40, 43, 48).

Thus, the newer and more specific dopamine agonists, quinagolide and cabergoline, offer safe and effective treatment options that are better tolerated than bromocriptine and show efficacy in bromocriptine-intolerant patients. In some countries, these more specific dopamine D2 'superagonists' have replaced bromocriptine in the medical management of hyperprolactinaemia.

Treatment during pregnancy

Bromocriptine does not appear to be a teratogen during early pregnancy and is not associated with any detrimental effect on pregnancy or foetal development (59–63) or any increase in spontaneous abortions, ectopic or multiple pregnancies or preterm deliveries (59–61). However, it is recommended that patients with microprolactinomas suspend treatment with bromocriptine once pregnancy has been confirmed to avoid any potential harmful effects (64).

The 22-hour half life of quinagolide allows this dopamine agonist to be used until the point of confirmed pregnancy. This allows patients who wish to become pregnant to continue quinagolide therapy for hyperprolactinaemia whilst trying to conceive. It is generally recommended to withdraw dopamine agonist therapy during pregnancy in patients with prolactinomas. There are limited published data detailing quinagolide use during pregnancy; however, no teratogenic effects during early pregnancy have been reported (11, 15, 18, 40, 42, 43). In the author's personal experience, a normal outcome was observed in a series of 30 pregnancies. Indeed, a multicentre prospective analysis of the pregnancies outcome in women treated with quinagolide must be undertaken.

It is recommended that patients cease cabergoline use at least 1 month prior to trying to conceive owing to the long half-life of this agent. However, cabergoline has demonstrated a good safety record in the small number (approximately 300) of cases in which this dopamine agonist was taken during early pregnancy (58, 65) and there have been no reported teratogenic effects or an increase in the rate of spontaneous abortion (57, 58, 65–67).

Conclusion

The importance of treating hyperprolactinaemia and the need for continual therapy must not be underestimated in order to resolve symptoms and prevent the development of long-term complications associated with elevated prolactin levels. Bromocriptine has been available for the treatment of hyperprolactinaemia for over 25 years and as such, this generic and inexpensive dopamine agonist is often chosen as the

first-line therapy option. However, the newer and more selective dopamine agonists, quinagolide and cabergoline offer more effective and better tolerated treatment options for patients compared with bromocriptine. In addition, quinagolide may improve patient compliance to treatment owing to its reduced side effect profile, simple and rapid titration over just 7 days, once-daily dosing regimen and easy to use starter pack (available in some countries). Quinagolide offers an additional benefit for patients wishing to become pregnant, as it can be used until the point of confirmation of pregnancy. In summary, this well tolerated and effective therapy, with a simple dosing regimen should be considered as a first-line therapy in the treatment of hyperprolactinaemia.

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