1.3.1.1 PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

ASPEN-BROMOCRIPTINE 2,5 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet of ASPEN-BROMOCRIPTINE 2,5 mg contains 2,5 mg bromocriptine as bromocriptine mesylate.

Contains sugar: Lactose monohydrate 70,133 mg.

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets

ASPEN-BROMOCRIPTINE 2,5 mg is a white, oval-shaped, bevelled edged tablet, slope-faced towards a score line on one side, flat-faced and plain on the other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

ASPEN-BROMOCRIPTINE 2,5 mg is indicated for :

- *Inhibition of lactation*

  Prevention or suppression of puerperal lactation for medical reasons. ASPEN-BROMOCRIPTINE 2,5 mg is not recommended for the routine suppression of lactation, or for the relief of symptoms of postpartum pain and engorgement, which can be adequately treated with simple analgesics and breast support.

- *Menstrual cycle disorders and female infertility associated with hyperprolactinaemia.*

- *Hyperprolactinaemia in men.*

  Prolactin-related hypogonadism with loss of libido and impotence.

- *Prolactinomas*

  Conservative treatment of prolactin-secreting pituitary micro-adenomas or macro-adenomas.

  Prior to surgery to reduce tumour size to facilitate removal or after surgery if prolactin level is still elevated.

- *Certain cases of acromegaly as adjunctive therapy.*

  ASPEN-BROMOCRIPTINE 2,5 mg has been used in a number of specialised units, as an adjunct to surgery and/or radiotherapy, to reduce circulating growth hormone levels in the management of acromegalic patients.

- *Parkinsonism*.

  Idiopathic and postencephalitic Parkinson's disease, either in monotherapy or in combination with other anti-Parkinsonian medicines.

  ASPEN-BROMOCRIPTINE 2,5 mg may improve tremor, rigidity, bradykinesia and the other Parkinsonian symptoms at all stages of the disease. ASPEN-BROMOCRIPTINE 2,5 mg has been of benefit to patients showing severe "on-off" reactions (swing response) and other forms of deteriorating response to levodopa. Combination with

levodopa may achieve increased anti-Parkinsonian effects allowing a reduction in the dosage of either compound.

ASPEN-BROMOCRIPTINE 2,5 mg may also be combined with anticholinergic and/or other anti-Parkinsonian drugs. Parkinson's disease may require comparatively high doses of bromocriptine.

- *Other*

There is insufficient evidence of efficacy of ASPEN-BROMOCRIPTINE 2,5 mg in the treatment of premenstrual symptoms and benign breast disease. The use of ASPEN-BROMOCRIPTINE 2,5 mg in patients with these conditions is therefore not recommended.

4.2 Posology and method of administration

Posology

Adults

ASPEN-BROMOCRIPTINE 2,5 mg should always be taken with food.

Inhibition of lactation for medical reasons

a) On the first day, ½ (half) tablet with food in the morning and evening, followed by 1 tablet twice a day for 14 days. To prevent the onset of lactation, treatment should be instituted within a few hours of parturition or abortion, but not before vital signs have stabilised. Milk secretion may occur 2 or 3 days after treatment has been withdrawn. This can be stopped by resuming treatment at the same dosage for a further week.

Female infertility associated with hyperprolactinaemia and menstrual cycle disorders

The patient should be instructed to take half a tablet at bedtime for three days, followed by one tablet at bedtime for a further three days. Thereafter, the patient should take one tablet twice a day with meals. If necessary, the dose may be increased to one tablet three times a

day with meals. If further increases in the dosage are required, it may be increased by another tablet daily at two to three day intervals. The majority of patients should respond to a dose of 7,5 mg per day, but doses of up to 30 mg per day have been used. Treatment may have to be continued for the duration of several menstrual cycles to prevent a relapse

Hyperprolactinaemia in men with prolactin-related loss of libido and impotence:

1,25 mg (½ tablet) 2 or 3 times daily, gradually increasing to 5 to 10 mg per day.

Prolactinomas

The usual starting dose is half a tablet two to three times daily, gradually increasing to several tablets daily as required to keep plasma prolactin adequately suppressed.

Certain cases of acromegaly as adjunctive therapy

Initially 1,25 mg (½ tablet) 2 or 3 times daily, gradually increasing to 10 mg to 20 mg daily, depending on clinical response and side effects. Growth hormone levels must be determined from time to time to establish the correct dose of ASPEN-BROMOCRIPTINE 2,5 mg.

Parkinson's Disease

In order to ensure optimal tolerability, treatment should be started with a low dose of 1,25 mg (½ tablet) per day, given preferably in the evening, over the first week. ASPEN-BROMOCRIPTINE 2,5 mg should be titrated slowly in order to provide each patient with the minimal effective dose. The increase in daily dosage should be gradual, by increments of 1,25 mg a day every week. The daily dosage is divided into two or three single doses. An adequate therapeutic response may be reached within 6 to 8 weeks. Otherwise, the dose may be further increased by increments of 2,5 mg a day every week.

Should undesirable reactions occur during the titration phase, the daily dose is to be reduced

and maintained constant for at least a week. If the adverse reactions disappear, the dose can be increased again. The usual therapeutic range for monotherapy is 10 mg to 40 mg bromocriptine a day. In some patients higher doses are required.

Elderly population

There is no clinical evidence that ASPEN-BROMOCRIPTINE 2,5 mg poses a special risk to the elderly.

Hepatic impairment

In patients with impaired hepatic function, the speed of elimination may be retarded and plasma levels may increase, requiring dose adjustment.

Paediatric population

Safety and efficacy have not been established in children (see section 4.3).

Method of administration

For oral administration.

4.3 Contraindications

ASPEN-BROMOCRIPTINE 2,5 mg is contraindicated in:

- Patients with hypersensitivity to bromocriptine or other ergot alkaloids or to any excipients in ASPEN-BROMOCRIPTINE 2,5 mg (see section 6.1).
- Patients with eclampsia or uncontrolled hypertension should not receive ASPEN-BROMOCRIPTINE 2,5 mg. ASPEN-BROMOCRIPTINE 2,5 mg should not be used in the postpartum and in the puerperal woman with high blood pressure, coronary artery disease or symptoms and/or history of serious psychotic disorders.
- In patients with a history of psychotic disorders, hepatic disease or severe angina

and myocardial infarction.

- Long-term treatment: Evidence of cardiac valvulopathy as determined by pre-treatment echocardiography.
- Pregnancy: Toxaemia of Pregnancy (see section 4.4)
- In children as safety and efficacy has not been established in children (see section 4.2).

4.4 Special warnings and precautions for use

ASPEN-BROMOCRIPTINE 2,5 mg may cause somnolence or rare episodes of sudden onset of sleep, particularly in patients with Parkinson's disease. Patients should be cautioned about operating hazardous machinery, including motor vehicles, while taking ASPEN-BROMOCRIPTINE 2,5 mg.

Patients who have experienced somnolence and/or an episode of sudden sleep onset must not drive or operate machines (see section 4.7). Furthermore, a reduction of dosage or termination of therapy may be considered.

ASPEN-BROMOCRIPTINE 2,5 mg is contraindicated for use in the suppression of lactation or other non-life-threatening indications in patients with severe coronary artery disease, or symptoms and/or a history of serious mental disorders (see section 4.3)

Caution is required when ASPEN-BROMOCRIPTINE 2,5 mg is being given to patients with a history of psychotic disorders, severe cardiovascular disease, peptic ulcer, or gastrointestinal bleeding.

A few cases of gastrointestinal bleeding and gastric ulcer have been reported. If this occurs, ASPEN-BROMOCRIPTINE 2,5 mg should be withdrawn. Patients with a history of evidence of peptic ulceration should be closely monitored when receiving the treatment.

Since, especially during the first few days of treatment, hypotensive reactions may occasionally occur and result in reduced alertness, particular care should be exercised when driving a vehicle or operating machinery (see section 4.8).

There is insufficient evidence of efficacy of ASPEN-BROMOCRIPTINE 2,5 mg in the treatment of premenstrual symptoms and benign breast disease. The use of ASPEN-BROMOCRIPTINE 2,5 mg in patients with these conditions is therefore not recommended.
Serious adverse events, including hypertension, myocardial infarction, seizures, stroke or psychiatric disorders have been reported in postpartum women treated with ASPEN-BROMOCRIPTINE 2,5 mg for inhibition of lactation. In some patients the development of seizures or stroke was preceded by severe headache and/or transient visual disturbances (see section 4.8).
Patients with severe cardiovascular disorders or psychiatric disorders taking ASPEN-BROMOCRIPTINE 2,5 mg for the indication of macro-adenomas should only take it if the perceived benefits outweigh the potential risks (see section 4.3).
Hypotension may occur especially at initiation of therapy.
Particular caution is required in patients who have recently been treated or are on concomitant therapy with medicines that can alter blood pressure.

A reduction in blood pressure can occur during ASPEN-BROMOCRIPTINE 2,5 mg therapy, and ambulant patients should have their blood pressure checked during the first few days of treatment. Postural hypotension may be a problem and should be treated symptomatically.

Blood pressure should be carefully monitored, especially during the first days of therapy.

Concomitant use of bromocriptine, as in ASPEN-BROMOCRIPTINE 2,5 mg with vasoconstrictors such as sympathomimetics or ergot alkaloids including ergometrine or methylergometrine during the puerperium is not recommended.

If hypertension, suggestive chest pain, severe progressive or unremitting headache, or any signs of CNS toxicity develop, treatment should be discontinued immediately, and the patient should be evaluated promptly.

Before hyperprolactinaemia with or without amenorrhoea is treated, the patient should be assessed, and the possibility of a pituitary adenoma ruled out, as the tumour may progress during treatment despite clinical improvement of the patient.

Treatment of women suffering from amenorrhoea and galactorrhoea with ASPEN-BROMOCRIPTINE 2,5 mg will result in ovulation.

Hyperprolactinaemia may be idiopathic, medicines induced, or due to hypothalamic or pituitary disease. The possibility that hyperprolactinaemic patients may have a pituitary tumour should be recognised and complete investigation at specialised units to identify such patients is advisable. ASPEN-BROMOCRIPTINE 2,5 mg will effectively lower prolactin levels in patients with pituitary tumours but does not obviate the necessity for radiotherapy or surgical intervention where appropriate in acromegaly

Before treatment of patients with acromegaly, patients should be assessed and only treated with ASPEN-BROMOCRIPTINE 2,5 mg if an alternative to conventional therapy is required. Patients treated for acromegaly have been reported to have gastrointestinal bleeding.

Acromegaly patients with a history of peptic ulceration should receive alternative treatment. If ASPEN-BROMOCRIPTINE 2,5 mg therapy is required, the patient must be closely observed and asked to report any gastrointestinal side effects immediately.

Since patients with macro-adenomas of the pituitary might have accompanying hypopituitarism due to compression or destruction of pituitary tissue, one should make a complete evaluation of pituitary functions and institute appropriate substitution therapy prior to administration of ASPEN-BROMOCRIPTINE 2,5mg. In patients with secondary adrenal insufficiency, substitution with corticosteroids is essential.
The evolution of tumour size in patients with pituitary macro-adenomas should be carefully monitored and if evidence of tumour expansion develops, surgical procedures must be considered
If in adenoma patients, pregnancy occurs after the administration of ASPEN-BROMOCRIPTINE 2,5 mg , careful observation is mandatory. Prolactin-secreting adenomas may expand during pregnancy. In these patients, treatment with ASPEN -BROMOCRIPTINE 2,5 mg often results in tumour shrinkage and rapid improvement of the visual fields defects. In severe cases, compression of the optic or other cranial nerves may necessitate emergency pituitary surgery.

Visual field impairment is a known complication of macroprolactinoma. Effective treatment with ASPEN-BROMOCRIPTINE 2,5 mg leads to a reduction in hyperprolactinaemia and often to resolution of the visual impairment. In some patients, however, a secondary deterioration of visual fields may subsequently develop despite normalised prolactin levels and tumour shrinkage, which may result from traction on the optic chiasm which is pulled down into the now partially empty sella. In these cases the visual field defect may improve on reduction of bromocriptine dosage while there is some elevation of prolactin and some tumour re-expansion. Monitoring of visual fields in patients with macroprolactinoma is

therefore recommended for an early recognition of secondary field loss due to chiasmal herniation and adaptation of medicine dosage.

In some patients with prolactin-secreting adenomas treated with ASPEN-BROMOCRIPTINE 2,5 mg, cerebrospinal fluid rhinorrhea has been observed. The data available suggest that this may result from shrinkage of invasive tumours

Bromocriptine has been associated with somnolence and episodes of sudden sleep onset, particularly in patients with Parkinson's disease. Sudden onset of sleep during daily activities, in some cases without awareness or warning signs, has been reported. Patients must be informed of this and advised to exercise caution while driving or operating machines during treatment with bromocriptine. Patients who have experienced somnolence and/or an episode of sudden sleep onset must refrain from driving or operating machines (see section 4.7). Furthermore, a reduction of dosage or termination of therapy may be considered.

When women of child-bearing age are treated with ASPEN-BROMOCRIPTINE 2,5 mg for conditions not associated with hyperprolactinaemia the lowest effective dose should be used. This is in order to avoid suppression of prolactin to below normal levels, with consequent impairment of luteal function. If treatment continues for more than 6 months, post-ovulatory progesterone and plasma prolactin levels should be assessed.

If the patient shows symptoms of a pronounced enlargement of a prolactinoma, the ASPEN-BROMOCRIPTINE 2,5 mg therapy can be reinstated, or surgery may be considered appropriate.

High doses of ASPEN-BROMOCRIPTINE 2,5 mg should only be used for the indications of acromegaly and Parkinson’s.

All female patients who receive ASPEN-BROMOCRIPTINE 2,5 mg therapy for more than 6 months at a time should have regular gynaecological assessments, annually for pre-

menopausal patients and 6 monthly for post-menopausal patients. The assessment should include cervical and endometrial cytology.

Patients receiving ASPEN-BROMOCRIPTINE 2,5 mg for long periods should have periodic liver function tests.

Among patients on ASPEN-BROMOCRIPTINE 2,5 mg, particularly on long-term and high-dose treatment, pleural and pericardial effusions, as well as pleural and pulmonary fibrosis and constrictive pericarditis have occasionally been reported. Patients with unexplained pleuropulmonary disorders should be examined thoroughly and discontinuation of ASPEN-BROMOCRIPTINE 2,5 mg therapy should be contemplated.

In a few patients on ASPEN- BROMOCRIPTINE 2,5 mg, particularly on long-term and high-dose treatment, retroperitoneal fibrosis has been reported. To ensure recognition of retroperitoneal fibrosis at an early reversible stage it is recommended that its manifestations (e.g. back pain, oedema of the lower limbs, impaired kidney function) should be watched in this category of patients. ASPEN-BROMOCRIPTINE 2,5 mg medication should be withdrawn if fibrotic changes in the retroperitoneum are diagnosed or suspected.

ASPEN-BROMOCRIPTINE 2,5 mg has been associated with retroperitoneal fibrosis as well as pleural thickening and effusions. Patients with unexplained pleuropulmonary disorders should be examined thoroughly and discontinuation of ASPEN-BROMOCRIPTINE 2,5 mg should be contemplated.

Attention should be paid to the signs and symptoms of

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Constrictive pericarditis should be excluded if such symptoms appear.

Appropriate investigations such as erythrocyte sedimentation rate, chest X-ray and serum creatinine measurements should be performed if necessary to support a diagnosis of a fibrotic disorder. It is also appropriate to perform baseline investigations of erythrocyte sedimentation rate or other inflammatory markers, lung function/chest X-ray and renal function prior to initiation of therapy.

These disorders can have an insidious onset and patients should be regularly and carefully monitored while taking ASPEN- BROMOCRIPTINE 2,5 mg for manifestations of progressive fibrotic disorders. ASPEN-BROMOCRIPTINE 2,5 mg should be withdrawn if fibrotic or serosal inflammatory changes are diagnosed or suspected.

Impulse control disorders

Patients should be regularly monitored for the development of impulse control disorders. Patients and caregivers 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 ASPEN-BROMOCRIPTINE 2,5 mg. Dose reduction/tapered discontinuation should be considered if such symptoms develop.

Important precautions

When dose reduction or discontinuation of this medicines is necessary, the dose should be gradually reduced. Rapid dose reduction or discontinuation may cause a neuroleptic malignant syndrome . In addition, rapid dose reduction or discontinuation of dopamine receptor agonists may cause drug withdrawal syndrome (characterized by apathy, anxiety, depression, fatigue, sweating, pain, etc.).

Dopamine dysregulation syndrome (DDS) is an addictive disorder that has been observed in some patients treated with ASPEN-BROMOCRIPTINE 2,5 mg Patients affected exhibit the compulsive abuse of dopaminergic medicines, using higher doses than are necessary for the adequate control of motor symptoms from Parkinson's disease. In some cases, this may result in severe dyskinesia.

Elderly

Clinical studies for bromocriptine did not include sufficient numbers of subjects ages 65 and above to determine whether the elderly respond differently from younger subjects. However, other reported clinical experiences, including post-marketing reporting of adverse events have identified no difference in response or tolerability between elderly and younger patients.

Even though no variation in efficacy or adverse reaction profile in elderly patients taking bromocriptine has been observed, greater sensitivity in some elderly individuals cannot be categorically ruled out. In general, dose selection for an elderly patient should be cautious, starting at the lower end of the dose range, reflecting the greater frequency of decreased hepatic, renal or cardiac function, and of concomitant disease or other medicinetherapy in this population.

Paediatric population

Safety and efficacy has not been established in children (see section 4.2 and 4.3).

Excipients

ASPEN-BROMOCRIPTINE 2,5 mg contains lactose.

Patients with the rare hereditary conditions of galactose intolerance e.g. galactosaemia,

Lapp lactase deficiency, glucose-galactose malabsorption or fructose intolerance should not take ASPEN-BROMOCRIPTINE 2,5 mg.

4.5 Interaction with other medicines and other forms of interaction

Caution is required in patients who are on concomitant therapy with, or have recently been treated with medicines that can alter blood pressure.

Bromocriptine is both a substrate and an inhibitor of CYP3A4 (see section Pharmacokinetic properties). Caution should therefore be used when co-administering medicines which are strong inhibitors and/or substrates of this enzyme (azole antimycotics, HIV protease inhibitors). The concomitant treatment of acromegalic patients with bromocriptine and octreotide led to increased plasma levels of bromocriptine.

Since ASPEN-BROMOCRIPTINE 2,5 mg exerts its therapeutic effect by stimulating central dopamine receptors, dopamine antagonists such as antipsychotics (phenothiazines, butyrophenones and thioxanthenes), but also metoclopramide and domperidone may reduce its activity.

Although there is no conclusive evidence of an interaction between ASPEN-BROMOCRIPTINE 2,5 mg and other ergot alkaloids e.g. ergometrine and methylergometrine, the concomitant use of these medications is not recommended (see section 4.4)

Tolerability to ASPEN-BROMOCRIPTINE 2,5 mg may be reduced by alcohol.

4.6 Fertility, pregnancy and lactation

Women of child-bearing potential

Women of childbearing age who do not wish to conceive should therefore be advised to practice a reliable method of contraception

Pregnancy

If the patient does not wish to fall pregnant, appropriate contraceptive measures should be taken.

If the patient wishes to fall pregnant, the ASPEN-BROMOCRIPTINE 2,5 mg therapy should be discontinued once pregnancy has been confirmed, unless a medical reason exists for continuing therapy.

Rapid expansion of pituitary tumours sometimes occurs during pregnancy and this may also occur in patients who have been able to conceive as a result of bromocriptine therapy.

As a precautionary measure, patients should be monitored to detect signs of pituitary enlargement so that bromocriptine may be reintroduced if necessary. Based on the outcome of more than 2 000 pregnancies, the use of bromocriptine to restore fertility has not been associated with an increased risk of abortion, premature delivery, multiple pregnancy or malformation in infants. Because this accumulated evidence suggests a lack of teratogenic or embryopathic effects in humans, maintenance of bromocriptine treatment during pregnancy may be considered where there is a large tumour or evidence of expansion.

If the patient falls pregnant whilst receiving treatment for a pituitary adenoma, and the ASPEN-BROMOCRIPTINE 2,5 mg therapy is stopped, the patient should be observed closely throughout the pregnancy.

Breastfeeding

Since bromocriptine inhibits lactation, it should not be administered to mothers who elect to breastfeed.

Fertility

Fertility may be restored by treatment with bromocriptine.

4.7 Effects on ability to drive and use machines

ASPEN-BROMOCRIPTINE 2,5 mg has a major influence on the ability to drive and use machines.

Since adverse reactions such as dizziness, drowsiness and visual disturbances have been reported in patients receiving ASPEN-BROMOCRIPTINE 2,5 mg, patients should not drive, use machinery or perform any tasks that require concentration, until they are certain that ASPEN-BROMOCRIPTINE 2,5 mg does not adversely affect their ability to do so (see section 4.4 and/or 4.8).
Hypotensive reactions may be disturbing in some patients during the first few days of treatment and particular care should be exercised when driving vehicles or operating machinery.

Patients being treated with bromocriptine and presenting with somnolence and/or sudden sleep 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 such recurrent episodes and somnolence have resolved (see also section 4.4).

4.8 Undesirable effects

a) Summary of the safety profile

The occurrence of side effects can be minimised by gradual introduction of the dose or a dose reduction followed by a more gradual titration. If necessary, initial nausea and/or vomiting may be reduced by taking ASPEN-BROMOCRIPTINE 2,5 mg during a meal and by

the intake of a peripheral dopamine antagonist, such as domperidone, for a few days, at least one hour prior to the administration of ASPEN-BROMOCRIPTINE 2,5 mg.

b) Tabulated list of adverse reactions

System organ class	**Frequent**	**Less frequent**	**Frequency unknown** (cannot be estimated from the available data)
Psychiatric disorders		Confusion, psychomotor agitation, hallucinations, psychotic disorders, insomnia	Dopamine dysregulation syndrome
Nervous system disorders	Headache, drowsiness	Dizziness, dyskinesia, somnolence, paresthesia, excess daytime somnolence and sudden sleep onset	Seizure, delusions, confusion, dystonia in Parkinsonism, muzziness, syncope
Eye disorders		Visual disturbances, blurred vision	
Ear and labyrinth disorders		Tinnitus	
Cardiac disorders		Tachycardia, bradycardia, dysrhythmia, cardiac valvulopathy (including regurgitation) and related disorders (pericarditis and pericardial effusion).	Myocardial infarction, arrhythmias, exacerbation of angina

Vascular disorders		Hypotension including orthostatic hypotension (which may in very rare instances lead to collapse), reversible pallor of the fingers and toes	Hypertension, stroke, hypotension, postural hypotension, prolonged severe hypotension arrhythmias, erythromelalgia.
Respiratory, thoracic and mediastinal disorders	Nasal congestion	Pleural effusion, pleural and pulmonary fibrosis, pleuritis, dyspneoa	
Gastrointestinal disorders	Nausea, constipation	Vomiting, dry mouth, diarrhoea, abdominal pain, retroperitoneal fibrosis, gastrointestinal ulcer, gastrointestinal haemorrhage	Gastrointestinal bleeding in acromegaly patients
Skin and subcutaneous tissue disorders		Allergic skin reactions, hair loss	
Musculoskeletal and connective tissue disorders		Leg cramps	
Renal and urinary disorders			Micturition
General disorders and administrative site conditions		Fatigue, peripheral oedema	
Investigations			Altered liver function tests

c) Description of selected adverse reactions

Psychosis, with hallucinations, delusions and confusion occurs, particularly at high doses, used to treat Parkinsonism, but has also been reported with low doses.

In some patients the occurrence of seizures or stroke was preceded by severe headache and/or transient visual disturbances.

Nausea, dizziness, vomiting and orthostatic hypotension are frequently experienced during the first few days of treatment, but should not be serious enough to warrant discontinuation of treatment.

Many of the side effects are dose dependent and if they persist can be controlled by reducing the dose temporarily.
Patients receiving daily doses of bromocriptine of 20 mg or more have reported episodes of cold induced reversible pallor of the fingers and toes, especially patients who have previously exhibited Raynaud's phenomenon.

Post-partum women
In extremely rare cases (in postpartum women treated with bromocriptine for the prevention of lactation) serious adverse events including hypertension, myocardial infarction, convulsion, stroke or mental disorders have been reported, although the causal relationship is uncertain. In some patients the occurrence of convulsion or stroke was preceded by severe headache and/or transient visual disturbances (see section 4.4 Special warnings and precautions for use).

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 ASPEN-BROMOCRIPTINE 2,5 mg (see section 4.4).

Vascular disorders:

Hypotension including orthostatic hypotension (which may in very rare instances lead to collapse)

Reversible pallor of fingers and toes induced by cold (especially in patients who have a history of Raynaud's phenomenon).

A syndrome resembling Neuroleptic Malignant Syndrome has been reported on withdrawal of bromocriptine.

Other Adverse Reactions

Drug withdrawal syndrome*

Apathy, anxiety, depression, fatigue, sweating, pain, etc.

*When any abnormalities are observed, appropriate measures should be taken such as resuming administration or returning the dose to the level prior to reduction.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to:

SAHPRA: https://www.sahpra.org.za/health-products-vigilance/

Aspen Pharmacare:

E-mail: Drugsafety@aspenpharma.com

Tel: 0800 118 088

4.9 Overdose

Symptoms

Overdosage with ASPEN-BROMOCRIPTINE 2,5 mg is likely to result in vomiting and other symptoms which could be due to over stimulation of dopaminergic receptors and might include nausea, dizziness, hypotension, postural hypotension, tachycardia, drowsiness, somnolence, lethargy, confusion and hallucinations. General supportive measures should be undertaken to remove any unabsorbed material and maintain blood pressure if necessary. There have been isolated reports of children who accidentally ingested bromocriptine. Vomiting, somnolence and fever were reported as adverse events. Patients recovered either spontaneously within a few hours or after symptomatic treatment.

Treatment

Treatment is symptomatic and supportive. In the case of overdose, administration of activated charcoal is recommended and in the case of very recent oral intake, gastric lavage may be considered.

The management of acute intoxication is symptomatic; metoclopramide may be indicated for the treatment of emesis or hallucinations.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and Class: A 21.12 Hormone inhibitors

Pharmacotherapeutic group: Dopamine agonist

ATC code: Dopamine agonist (ATC code N04B C01), prolactin inhibitor (ATC code G02C B01)

Mechanism of action

Bromocriptine, an ergot derivative, is a dopaminergic receptor stimulant. Dopamine, a neurotransmitter, has an effect on hypothalamic function, in particular it has an effect on

prolactin secretion and can regulate growth hormone secretion. Bromocriptine inhibits the secretion of prolactin by the pituitary. Bromocriptine lowers elevated circulating growth hormone levels in acromegalics.

These effects are due to stimulation of dopamine receptors.

As a specific inhibitor of prolactin secretion, bromocriptine can be used to prevent or suppress physiological lactation.

In Parkinson's disease, bromocriptine acts as a specific dopamine receptor agonist, thus restoring the neurotransmitter balance in the corpus striatum.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Croscarmellose sodium, lactose monohydrate, magnesium stearate, microcrystalline cellulose

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store at or below 25 °C in a well-closed container.

Protect from light and moisture.

Keep in original packaging until required for use.

6.5 Nature and contents of container

30, 90 or 100 tablets are packed in a clear amber round glass bottle with a white metal cap

with permaseal liner and glossy coated pulp liner beneath, together with coiler rayon and a leaflet.

30, 90 or 100 tablets are packed in a white round high-density polyethylene bottle, with a white polypropylene cap with induction heat seal liner, together with rayon and either a polypropylene or high-density polyethylene desiccant disk or a silica gel bag. The bottle is packed into a unit carton together with a leaflet.

Not all packs and pack sizes are necessarily marketed.

6.6 Special precautions for disposal

No special requirements.

7.HOLDER OF THE CERTIFICATE OF REGISTRATION

PHARMACARE LIMITED

Healthcare Park

Woodlands Drive

Woodmead 2191

8. REGISTRATION NUMBER

30/21.12/0459

9. DATE OF FIRST AUTHORISATION

21 October 1998

10. DATE OF REVISION OF TEXT

28 August 2021

Die Afrikaanse Professionele Inligting is op versoek beskikbaar. Mediese Blitslyn: 0800 118 088.

Namibia: NS2 10/21.12/0569

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