ANNEX III

AMENDMENTS TO THE SUMMARIES OF PRODUCT CHARACTERISTICS AND PACKAGE LEAFLETS

AMENDMENTS TO BE INCLUDED IN THE RELEVANT SECTIONS OF THE SUMMARY OF PRODUCT CHARACTERISTICS FOR BROMOCRIPTINE CONTAINING MEDICINAL PRODUCTS

4.2 Posology and method of administration
The following should be reflected as appropriate:
Restriction of maximum dose to 30 mg/day.

4.3 Contra-indications:
…[ ]…
"For long-term treatment: Evidence of cardiac valvulopathy as determined by pre-treatment echocardiography."

4.4 Special warnings and precautions for use:
…[ ]…
"Among patients on bromocriptine, 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 bromocriptine therapy should be contemplated.

In a few patients on bromocriptine, particularly on long-term and high-dose treatment, retroperitoneal fibrosis has been reported. To ensure recognition of retroperitoneal fibrosis at 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.
Bromocriptine medication should be withdrawn if fibrotic changes in the retroperitoneum are diagnosed or suspected."

4.8 Undesirable effects:
The following should be included under cardiac disorders:
"Very rare: cardiac valvulopathy (including regurgitation) and related disorders (pericarditis and pericardial effusion)."

AMENDMENTS TO BE INCLUDED IN THE RELEVANT SECTIONS OF THE PACKAGE LEAFLET FOR BROMOCRIPTINE CONTAINING MEDICINAL PRODUCTS

Section 2 "Before you take [product name]":
Do not take [product name] if you:
…[ ]…
"*- will be treated with [product name] for a long period and have or had fibrotic reactions (scar tissue) affecting your heart.*"

Take special care with [product name]
…[ ]…
"- If you have or had fibrotic reactions (scar tissue) affecting your heart, lungs or abdomen.
In case you are treated with [product name] for a long period, your physician will check before starting treatment whether your heart, lungs and kidneys are in good condition. He/she will also have an echocardiogram (an ultrasound test of the heart) taken before treatment is started. During treatment your physician will pay special attention to any signs which may be related to fibrotic reactions. If necessary he/she will have an echocardiogram taken. If fibrotic reactions occur treatment will have to be discontinued."

Section 4 "Possible side effects":
…[ ]…
"Very rare side effect (affecting less than one person in10.000): heart valve and related disorders e.g. inflammation (pericarditis) or leaking of fluid in the pericardium (pericardial effusion).
The early symptoms may be one or more of the following: difficulty breathing, shortness of breath, chest or back pain and swollen legs. If you experience any one of these symptoms you must tell your doctor immediately."

AMENDMENTS TO BE INCLUDED IN THE RELEVANT SECTIONS OF THE SUMMARY OF PRODUCT CHARACTERISTICS FOR DIHYDROERGOCRYPTINE CONTAINING MEDICINAL PRODUCTS

4.3 Contraindications:
…[ ]…
"For long-term treatment: Evidence of cardiac valvulopathy as determined by pre-treatment echocardiography."

4.4 Special warnings and precautions for use:
…[ ]…
"Among patients on dihydroergocryptine, 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 dihydroergocryptine therapy should be contemplated.

Particularly on long-term and high-dose treatment, retroperitoneal fibrosis has been reported in rare cases. To ensure recognition of retroperitoneal fibrosis at 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. Dihydroergocryptine medication should be withdrawn if fibrotic changes in the retroperitoneum are diagnosed or suspected."

4.8 Undesirable effects:
The following should be included under Cardiac disorders:
"Very rare: cardiac valvulopathy (including regurgitation) and related disorders (pericarditis and pericardial effusion)."

AMENDMENTS TO BE INCLUDED IN THE RELEVANT SECTIONS OF THE PACKAGE LEAFLET FOR DIHYDROERGOCRYPTINE CONTAINING MEDICINAL PRODUCTS

Section 2 "Before you take [product name]":
Do not take [product name] if you:
…[ ]…
"-will be treated with [product name] for a long period andhave or had fibrotic reactions (scar tissue) affecting your heart."

Take special care with [product name]
…[ ]…
"- If you have or had fibrotic reactions (scar tissue) affecting your heart, lungs or abdomen.
In case you are treated with [product name] for a long period, your physician will check before starting treatment whether your heart, lungs and kidneys are in good condition. He/she will also have an echocardiogram (an ultrasound test of the heart) taken before treatment is started. During treatment your physician will pay special attention to any signs which may be related to fibrotic reactions. If necessary he/she will have an echocardiogram taken. If fibrotic reactions occur treatment will have to be discontinued."

Section 4 "Possible side effects":
…[ ]…
"Very rare side effect (affecting less than one person in 10.000): heart valve and related disorders e.g. inflammation (pericarditis) or leaking of fluid in the pericardium (pericardial effusion).
The early symptoms may be one or more of the following: difficulty breathing, shortness of breath, chest or back pain and swollen legs. If you experience any one of these symptoms you must tell your doctor immediately."

AMENDMENTS TO BE INCLUDED IN THE RELEVANT SECTIONS OF THE SUMMARY OF PRODUCT CHARACTERISTICS FOR LISURIDE CONTAINING MEDICINAL PRODUCTS

4.4 Special warnings and precautions for use

…[ ]…

"Lisuride is an ergot derivative. After prolonged use of ergot derivatives, including lisuride inflammatory changes of a fibrotic type have been detected with serous disorders such as pleuritis, pleural effusion, pleural fibrosis, pulmonary fibrosis, pericarditis, pericardial effusions and retroperitoneal fibrosis. Since these changes are of insidious onset, patient should be monitored throughout the treatment, paying special attention to the appearance of signs and symptoms suggestive of an inflammatory disorder of a fibrotic or serous type. If a fibrotic disorder is suspected, the treatment should be halted and the diagnosis confirmed by performance of appropriate tests such as erythrocyte sedimentation rate, determination of serum creatinine and diagnostic imaging procedures (e.g. chest X-ray, echocardiography)."

4.8 Undesirable effects:

The following should be included under Cardiac disorders:

…[ ]…

"Very rare: pericarditis~~,~~ and pericardial effusion.

In patients treated with ergot derivates cardiac valvulopathy (including regurgitation) has been reported."

AMENDMENTS TO BE INCLUDED IN THE RELEVANT SECTIONS OF THE PACKAGE LEAFLET FOR LISURIDE CONTAINING MEDICINAL PRODUCTS

Section 2 "Before you take [product name]":

Take special care with [product name]
…[ ]…
"- If you have or had fibrotic reactions (scar tissue) affecting your heart, lungs or abdomen.
Before treatment your physician may check whether your heart, lungs and kidneys are in good condition. During treatment your physician will pay special attention to any signs which may be related to fibrotic reactions. If necessary he/she will have an echocardiogram taken (an ultrasound test of your heart). If fibrotic reactions occur treatment will have to be discontinued."

Section 4 "Possible side effects":
…[ ]…
"In patients treated with ergot derivatives such as lisuride cases of pericarditis (inflammation of the outer lining of the heart) and pericardial effusion (accumulation of fluid between the outer lining of the heart and the heart itself) have been reported very rarely (affecting less than one person in 10.000).
Also, effects on the heart valve have been observed in patients treated with ergot derivatives. The early symptoms of these effects on the heart may be one or more of the following: difficulty breathing, shortness of breath, chest or back pain and swollen legs. If you experience any one of these symptoms you must tell your doctor immediately."