ANNEX III

AMENDMENTS TO THE SUMMARY OF PRODUCT CHARACTERISTICS AND PACKAGE LEAFLET

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

The following should be reflected as appropriate (the new text is shown in bold and underlined and text to be deleted is shown strikethrough):

4.1 Therapeutic indications

[Invented name] 400 mg film-coated tablets are indicated for **the treatment of the following bacterial infections in patients of 18 years and older (see section 4.4, 4.8 and 5.1):**

- **Acute bacterial sinusitis (ABS)**
- **Acute exacerbations of chronic bronchitis (AECB)**

Moxifloxacin should be used to treat adequately diagnosed ABS and AECB only when it is considered inappropriate to use antibacterial agents that are commonly recommended for the initial treatment of these infections or when these have failed to resolve the infection.

- Community acquired pneumonia, except severe cases

Moxifloxacin should be used only when it is considered inappropriate to use antibacterial agents that are commonly recommended for the initial treatment of this infection.

(…)

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2 Posology and method of administration

(…)

Duration of administration

(…)

Acute **bacterial** sinusitis 7 days

(…)

4.4 Special warnings and precautions for use:

- Moxifloxacin has been shown to prolong the QTc interval on the electrocardiogram in some patients. In the analysis of ECGs obtained in the clinical trial program, QTc prolongation with moxifloxacin was 6 msec ± 26 msec, 1.4% compared to baseline. **As women tend to have a longer baseline QTc interval compared with men, they may be more sensitive to QTc-prolonging medications. Elderly patients may also be more susceptible to drug-associated effects on the QT interval.**
  Medication that can reduce potassium levels should be used with caution in patients receiving moxifloxacin.
  Moxifloxacin should be used with caution in patients with ongoing proarrhythmic conditions **(especially women and elderly patients)**, such as acute myocardial ischaemia or QT prolongation as this may lead to an increased risk for ventricular arrhythmias (incl. torsade de pointes) and cardiac arrest (see also section 4.3)..

  (…)

- Cases of fulminant hepatitis potentially leading to liver failure **(including fatal cases)** have been reported with moxifloxacin (see section 4.8).
(…)

- **Cases of bullous skin reactions like Stevens-Johnson syndrome or toxic epidermal necrolysis have been reported with moxifloxacin (see section 4.8). Patients should be advised to contact their doctor immediately prior to continuing treatment if skin and/or mucosal reactions occur.**

(…)

- **Antibiotic associated diarrhoea (AAD) and antibiotic-associated colitis (AAC), including pseudomembranous colitis and *Clostridium difficile*-associated diarrhoea, has been reported in association with the use of broad spectrum antibiotics including moxifloxacin and may range in severity from mild diarrhoea to fatal colitis. Therefore it is important to consider this diagnosis in patients who develop serious diarrhoea during or after the use of moxifloxacin. If AAD or AAC is suspected or confirmed, ongoing treatment with antibacterial agents, including moxifloxacin, should be discontinued and adequate therapeutic measures should be initiated immediately. Furthermore, appropriate infection control measures should be undertaken to reduce the risk of transmission. Drugs inhibiting peristalsis are contraindicated in patients who develop serious diarrhoea.**
- **Moxifloxacin should be used with caution in patients with myasthenia gravis because the symptoms can be exacerbated.**

(…)

4.7 Effects on ability to drive and use machines

(…) However, fluoroquinolones including moxifloxacin may result in an impairment of the patient's ability to drive or operate machinery due to CNS reactions (e.g. dizziness, see section 4.8) **or acute and short lasting loss of consciousness (syncope, see section 4.8).**
(…)

4.8 Undesirable effects:
(…)

System Organ Class	**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
Cardiac and Vascular Disorders	(…)	(…)	Ventricular tachyarrhythmias Syncope **(i.e., acute and short lasting loss of consciousness)** Hypertension Hypotension	(…)

System Organ Class	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
Hepatobiliary Disorders	(…)	(…)	(…)	Fulminant hepatitis potentially leading to life-threatening liver failure **(incl. fatal cases,** see section 4.4)
Skin and Subcutaneous Tissue Disorders		(…)		Bullous skin reactions like Stevens-Johnson syndrome or toxic epidermal necrolysis (potentially life-threatening, **see section 4.4)**
Musculoskeletal, Connective Tissue and Bone Disorders		(…)	(…)	Tendon rupture (see section 4.4) Arthritis Muscle rigidity **Exacerbation of symptoms of myasthenia gravis (see section 4.4)**

There have been very rare cases of the following side effects reported following treatment with other fluoroquinolones, which might possibly also occur during treatment with moxifloxacin: transient loss of vision, hypernatraemia, hypercalcaemia, haemolysis, **rhabdomyolysis,** photosensitivity reactions (see section 4.4).

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

The following should be reflected as appropriate (the new text is shown in bold and underlined and text to be deleted is shown strikethrough):

1. WHAT [INVENTED NAME] 400 MG FILM-COATED TABLETS ARE AND WHAT THEY ARE USED FOR

~~[Invented name] is an antibiotic belonging to the quinolone family.~~ [Invented name] contains moxifloxacin as the active ingredient which belongs to a group of antibiotics called fluoroquinolones. [Invented name] works by killing bacteria that cause infections~~, if they are caused by bacteria that are susceptible to the active ingredient moxifloxacin.~~

[Invented name] is used in **patients of 18 years** and older for treating the following bacterial infections **when caused by bacteria against which moxifloxacin is active: infection of the sinuses, sudden worsening of long term inflammation of the airways or infection of the lungs (pneumonia) acquired outside the hospital (except severe cases)**.

[Invented name] should only be used to treat these infections when usual antibiotics cannot be used or have not worked.

(…)

2. BEFORE YOU TAKE [INVENTED NAME] 400 MG FILM-COATED TABLETS

(…)

Before taking [Invented name] 400 mg film-coated tablets

- [Invented name] can change your heart's ECG, **especially if you are female, or if you are elderly**. If you are currently taking any medicine that decrease your blood potassium levels, consult your doctor before taking [Invented name]. If you experience palpitations or irregular heart beat during the period of treatment, you should inform your doctor immediately. He/she may wish to perform an ECG to measure your heart rhythm.

(…)

- **If you suffer from myasthenia gravis taking [Invented name] may worsen the symptoms of your disease. If you think you are affected consult your doctor immediately.**

(…)

When taking [Invented name] 400 mg film-coated tablets

(…)

- [Invented name] may cause a rapid and severe inflammation of the liver which could lead to life-threatening liver failure (**including fatal cases**, see section *4. Possible side effects*). Please contact your doctor before you continue the treatment if you develop signs such as rapidly feeling unwell and/or being sick associated with yellowing of the whites of the eyes, dark urine, itching of the skin, a tendency to bleed or liver induced disease of the brain (symptoms of a reduced liver function or a rapid and severe inflammation of the liver).
- **If you develop a skin reaction or blistering and/or peeling of the skin and/or mucosal reactions (see section *4. Possible side effects*) contact your doctor immediately before you continue the treatment.**

(…)

Driving and using machines

[Invented name] may make you feel dizzy or light-headed **or you might faint for a short period**. If you are affected in this way do not drive or operate machinery.

(…)

3. HOW TO TAKE [INVENTED NAME] 400 MG FILM-COATED TABLETS

(…)

-Sudden worsening of chronic bronchitis (acute exacerbation of chronic bronchitis) 5 - 10 days

(…)

4. POSSIBLE SIDE EFFECTS

(…)

Liver

(…)

Very rare: Fulminant inflammation of the liver potentially leading to life-threatening liver failure (**incl. fatal cases**)

(…)

Muscular and Joint System

(…)

Very rare: Rupture of tendon, inflammation of joints, muscle rigidity, **worsening of the symptoms of myasthenia gravis**

(…)

Furthermore, there have been very rare cases of the following side effects reported following treatment with other quinolone antibiotics, which might possibly also occur during treatment with [Invented name]:

transient loss of vision, increased blood sodium levels, increased blood calcium levels, increased breakdown of red blood cells, **muscle reactions with muscle cell damage**, increased sensitivity of the skin to sunlight or UV light.

(…)