

## ciprofloxacin

### RECOMMENDED CHANGES TO THE PRODUCT INFORMATION

The following changes to the product information of medicinal products containing the active substance ciprofloxacin are recommended:

#### Summary of product characteristics

- Section 4.4

A warning should be revised as follows (new wording in bold):

- ✓ Cytochrome P450

Ciprofloxacin inhibits CYP1A2 and thus may cause increased serum concentration of concomitantly administered substances metabolised by this enzyme (e.g. theophylline, clozapine, olanzapine, ropinirole, tizanidine, duloxetine, **agomelatine**). Co-administration of ciprofloxacin and tizanidine is contra-indicated. Therefore, patients taking these substances concomitantly with ciprofloxacin should be monitored closely for clinical signs of overdose, and determination of serum concentrations (e.g. of theophylline) may be necessary (see section 4.5).

- ✓ Vision disorders

If vision becomes impaired or any effects on the eyes are experienced, an eye specialist should be consulted immediately.

- ✓ Paediatric population

The use of ciprofloxacin in children and adolescents should follow available official guidance.

[...]

Treatment should be initiated only after a careful benefit/risk evaluation, due to possible adverse events related to joints and/or surrounding tissue (**see section 4.8**).

- Section 4.5

Warnings should be added as follows:

#### Agomelatine

In clinical studies, it was demonstrated that fluvoxamine, as a strong inhibitor of the CYP450 1A2 isoenzyme, markedly inhibits the metabolism of agomelatine resulting in a 60-fold increase of agomelatine exposure. Although no clinical data are available for a possible interaction with ciprofloxacin, a moderate inhibitor of CYP450 1A2, similar effects can be expected upon

concomitant administration (see 'Cytochrome P450' in section 'Special warnings and precautions for use').

Zolpidem

Co- administration ciprofloxacin may increase blood levels of zolpidem, concurrent use is not recommended.

- Section 4.8

The following adverse reaction(s) should be added under the SOC of Psychiatric disorders with a frequency "unknown": Mania, hypomania.

The following adverse reaction(s) should be added under the SOC of Skin and Subcutaneous Tissue Disorders with a frequency "unknown": DRESS.

Antibiotic associated diarrhea incl pseudomembranous colitis should be removed from SOC Infections and Infestations to the SOC Gastrointestinal disorders.

### **Package leaflet**

[Add sections as relevant, ensuring that the above proposed changes to the SmPC are adequately reflected, in lay terms, in the package leaflet]

The following should be added in

- ✓ Section 2. What you need to know before you use ciprofloxacin:

Warnings and precautions

If your eyesight becomes impaired or if your eyes seem to be otherwise affected, consult an eye specialist immediately

Other medicines and ciprofloxacin

Ciprofloxacin can increase the level of the following substances in the blood:

Agomelatine,

Zolpidem

- ✓ Section 4 Possible side effects When taking [Product]

Unknown frequency: Feeling highly excited (mania) or feeling great optimism and over-activity (hypomania), serious hypersensitivity reaction called DRESS (Drug Reaction with Eosinophilia and Systemic Symptoms)