

Številka: 1472-0042/2010
Datum : 16.11.2010

Javna agencija Republike Slovenije
za zdravila in medicinske pripomočke
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VSEM IMETNIKOM DOVOLJENJ ZA PROMET Z
ZDRAVILI, KI VSEBUJEJO TAMOKSIFEN

Zahteva za predložitev spremembe tipa IB – dopolnitev povzetka glavnih značilnosti zdravila in navodila za uporabo za zdravila, ki vsebujejo tamoksifen

Spoštovani,

V septembru 2010 je delovna skupina za farmakovigilanco (PhVWP) ocenila podatke o kliničnem odzivu pri zdravljenju s tamoksifenom zaradi genske variacije CYP2D6, oz. podatke o kliničnem odzivu pri sočasni uporabi tamoksifena z inhibitorji encima CYP2D6. Na osnovi ocene podatkov je zaključila, da je treba informacije v povzetku glavnih značilnosti zdravila in v navodilih za uporabo zadevnih zdravil ustrezno dopolniti.

Imetnike dovoljenj za promet z zadevnimi zdravili, ki še niso predložili vloge za spremembo prosimo, da Javni agenciji RS za zdravila in medicinske pripomočke v skladu s Pravilnikom o dovoljenju za promet z zdravilom za uporabo v humani medicini (Uradni list RS, št. 59/2006) in obvestilom JAZMP glede nove Uredbe Komisije (ES) št.1234/2008 z dne 24.11.2008 o pregledu sprememb pogojev dovoljenj za promet z zdravili za uporabo v humani medicini in zdravili za uporabo v veterinarski medicini predložijo spremembo tipa IB najkasneje v 30 dneh od objave obvestila. Dodatne informacije in podporna dokumentacija v vlogi niso potrebne.

V nadaljevanju vam podajamo odobreno originalno besedilo spremembe, objavljeno je tudi na spletni strani Vodij agencij za zdravila <http://www.hma.eu/222.html>.

S spoštovanjem,


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SUMMARY OF PRODUCT CHARACTERISTICS

Section 4.4

In the literature it has been shown that CYP2D6 poor metabolisers have a lowered plasma level of endoxifen, one of the most important active metabolites of tamoxifen (see section 5.2).

Concomitant medications that inhibit CYP2D6 may lead to reduced concentrations of the active metabolite endoxifen. Therefore, potent inhibitors of CYP2D6 (e.g.

paroxetine, fluoxetine, quinidine, cinacalcet or bupropion) should whenever possible be avoided during tamoxifen treatment (see section 4.5 and 5.2).

Section 4.5

Pharmacokinetic interaction with CYP2D6 inhibitors, showing a 65-75% reduction in plasma levels of one of the more active forms of the drug, i.e. endoxifen, has been reported in the literature. Reduced efficacy of tamoxifen has been reported with concomitant usage of some SSRI antidepressants (e.g. paroxetine) in some studies. As a reduced effect of tamoxifen cannot be excluded, co-administration with potent CYP2D6 inhibitors (e.g. paroxetine, fluoxetine, quinidine, cinacalcet or bupropion) should whenever possible be avoided (see section 4.4 and 5.2).

Section 5.1

CYP2D6 polymorphism status may be associated with variability in clinical response to tamoxifen. The poor metaboliser status may be associated with reduced response. The consequences of the findings for the treatment of CYP2D6 poor metabolisers have not been fully elucidated (see sections 4.4, 4.5 and 5.2)

CYP2D6 genotype

Available clinical data suggest that patients who are homozygote for non-functional CYP2D6 alleles, may experience reduced effect of tamoxifen in the treatment of breast cancer.

The available studies have mainly been performed in postmenopausal women (see sections 4.4 and 5.2)

Section 5.2

Tamoxifen is metabolised mainly via CYP3A4 to N-desmethyl-tamoxifen, which is further metabolised by CYP2D6 to another active metabolite endoxifen. In patients who lack the enzyme CYP2D6 endoxifen concentrations are approximately 75% lower than in patients with normal CYP2D6 activity. Administration of strong CYP2D6 inhibitors reduces endoxifen circulating levels to a similar extent.

PACKAGE LEAFLET

Take special care

- Co-administration with the following drugs should be avoided because a reduction of the effect of tamoxifen cannot be excluded: *paroxetine, fluoxetine (e.g. antidepressants), bupropion (antidepressant or aid to smoking cessation), quinidine (for example used in the treatment of cardiac arrhythmia) and cincalet/cinacalcet (for treatment of disorders of the parathyroid gland).*

Taking other medicines

- *Please inform your doctor if you are taking, or have recently taken any other medicines, even those you have bought without prescription. In particular, you should inform your doctor if you are taking:*
 - *paroxetine, fluoxetine (e.g. antidepressants)*
 - *bupropion (antidepressant or aid to smoking cessation)*
 - *quinidine (for example used in the treatment of cardiac arrhythmia)*
 - *cinacalcet (for treatment of disorders of the parathyroid gland)*