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Final

Core SPC Wording for

SSRIs (Selective serotonin reuptake inhibitors)

(citalopram (SE, NL, UK) , escitalopram (SE) , fluoxetine (PROZAC® and associated names (FR)) (AT, DK, FI, NL, PT, SE, UK) , fluvoxamine (NL, UK) , paroxetine (DK, SE, UK) (Referral: NL&UK), sertraline (PT)); SNRI (serotonin and noradrenaline reuptake inhibitor) (venlafaxine)

and

**Safety and Efficacy in adults - Suicidal behaviour, withdrawal reactions and effects of dose (UK)
as agreed following the PhVWP in October 2005**

SUICIDAL THOUGHTS/BEHAVIOUR

Section 4.4 - Special Warnings and Special Precautions for Use

Suicide/suicidal thoughts: Depression is associated with an increased risk of suicidal thoughts, self harm and suicide (suicide-related events). This risk persists until significant remission occurs. As improvement may not occur during the first few weeks or more of treatment, patients should be closely monitored until such improvement occurs. It is general clinical experience that the risk of suicide may increase in the early stages of recovery.

Other psychiatric conditions for which <SSRI> is prescribed can also be associated with an increased risk of suicide-related events. In addition, these conditions may be co-morbid with major depressive disorder. The same precautions observed when treating patients with major depressive disorder should therefore be observed when treating patients with other psychiatric disorders.

Patients with a history of suicide-related events, those exhibiting a significant degree of suicidal ideation prior to commencement of treatment are known to be at greater risk of suicidal thoughts or suicide attempts, and should receive careful monitoring during treatment. In addition, there is a possibility of an increased risk of suicidal behaviour in young adults.

Patients (and caregivers of patients) should be alerted about the need to monitor for the emergence of such events and to seek medical advice immediately if these symptoms present.

Akathisia/psychomotor restlessness: The use of <SSRI> has been associated with the development of akathisia, characterised by a subjectively unpleasant or distressing restlessness and need to move often accompanied by an inability to sit or stand still. This is most likely to occur within the first few weeks of treatment. In patients who develop these symptoms, increasing the dose may be detrimental.

Section 4.8 - Undesirable effects

Rare: Suicidal thoughts/behaviour (see section 4.4 Special Warnings and Special Precautions for Use)
psychomotor restlessness/akathisia (see section 4.4 Special Warnings and Special Precautions for Use)

WITHDRAWAL REACTIONS

Section 4.2 – Posology and Method of Administration

Withdrawal symptoms seen on discontinuation of SSRI

Abrupt discontinuation should be avoided. When stopping treatment with <SSRI> the dose should be gradually reduced over a period of at least one to two weeks in order to reduce the risk of withdrawal reactions (see section 4.4 Special Warnings and Special Precautions for Use and section 4.8 Undesirable Effects). If intolerable symptoms occur following a decrease in the dose or upon discontinuation of treatment, then resuming the previously prescribed dose may be considered. Subsequently, the physician may continue decreasing the dose, but at a more gradual rate.

Section 4.4 – Special Warnings and Special Precautions for Use

Withdrawal symptoms seen on discontinuation of SSRI treatment

Withdrawal symptoms when treatment is discontinued are common, particularly if discontinuation is abrupt (see section 4.8 Undesirable effects). In clinical trials adverse events seen on treatment discontinuation occurred in approximately X [PRODUCT SPECIFIC %] of patients treated with <SSRI> and X [PRODUCT SPECIFIC %] of patients taking placebo.

The risk of withdrawal symptoms may be dependent on several factors including the duration and dose of therapy and the rate of dose reduction. Dizziness, sensory disturbances (including paraesthesia), sleep disturbances (including insomnia and intense dreams), agitation or anxiety, nausea and/or vomiting, tremor and headache are the most commonly reported reactions [ensure that symptoms include full spectrum seen with all SSRIs]. Generally these symptoms are mild to moderate, however, in some patients they may be severe in intensity. They usually occur within the first few days of discontinuing treatment, but there have been very rare reports of such symptoms in patients who have inadvertently missed a dose. Generally these symptoms are self-limiting and usually resolve within 2 weeks, though in some individuals they may be prolonged (2-3 months or more). It is therefore advised that <SSRI> should be gradually tapered when discontinuing treatment over a period of several weeks or months, according to the patient's needs (see "Withdrawal Symptoms Seen on Discontinuation of <SSRI>", Section 4.2 Posology and Method of Administration).

Section 4.8 – Undesirable Effects

Withdrawal symptoms seen on discontinuation of SSRI treatment

Discontinuation of <SSRI> (particularly when abrupt) commonly leads to withdrawal symptoms. Dizziness, sensory disturbances (including paraesthesia), sleep disturbances (including insomnia and intense dreams), agitation or anxiety, nausea and/or vomiting, tremor and headache are the most commonly reported reactions [ensure that symptoms include full spectrum seen with all SSRIs]. Generally these events are mild to moderate and are self-limiting, however, in some patients they may be severe and/or prolonged. It is therefore advised that when <SSRI> treatment is no longer required, gradual discontinuation by dose tapering should be carried out (see section 4.2 Posology and Method of Administration and section 4.4 Special Warnings and Special Precautions for use).