הודעה על החמרה (מידע בטיחות) בעלון לרופא

(מעודכן 05.2013)

תאריך: 22/06/2017

שם תכשיר באנגלית ומספר הרישום: Retrovir IV for infusion- 100 74 28753 00

שם בעל הרישום: GlaxoSmithKline (ISRAEL) Ltd

טופס זה מיועד לפרוט ההחמרות בלבד !

ההחמרות המבוקשות		
טקסט חדש	**טקסט נוכחי**	**פרק בעלון**
[…] *Weight and metabolic parameters*: An increase in weight and in levels of blood lipids and glucose may occur during antiretroviral therapy. Such changes may in part be linked to disease control and life style. For lipids, there is in some cases evidence for a treatment effect, while for weight gain there is no strong evidence relating this to any particular treatment. For monitoring of blood lipids and glucose reference is made to established HIV treatment guidelines. Lipid disorders should be managed as clinically appropriate. **[…]**	**[…]** ---- **[…]**	**Special warnings and precautions for use**
As a general rule, when deciding to use antiretroviral agents for the treatment of HIV infection in pregnant women and consequently for reducing the risk of HIV vertical transmission to the newborn, the animal data (see section 5.3) as well as the clinical experience in pregnant women should be taken into account. In the present case, the use in pregnant women of zidovudine, with subsequent treatment of the newborn infants, has been shown to reduce the rate of maternal-foetal transmission of HIV. A large amount of data on pregnant women (more than 3000 outcomes from first trimester and more than 3000 outcomes from second and third trimester exposure) indicate no malformative toxicity. Retrovir can be used during pregnancy if clinically needed. The malformative risk is unlikely in humans	The use of Retrovir in pregnant women over 14 weeks of gestation, with subsequent treatment of their newborn infants, has been shown to significantly reduce the rate of maternal-foetal transmission of HIV based on viral cultures in infants. The results from the pivotal U.S. placebo-controlled study indicated that Retrovir reduced maternal-foetal transmission by approximately 70%. In this study, pregnant women had CD4 cell counts of 200 to 1818/mm^3 (median in treated group 560/mm^3) and began treatment therapy between weeks 14 and 34 of gestation and had no clinical indications for Retrovir therapy; their newborn infants received Retrovir until 6-weeks old. A decision to reduce the risk of maternal transmission of HIV should be based on	**Pregnancy**:

based on the mentioned large amount of data. Zidovudine has been associated with reproductive toxicity findings in animal studies (see section 5.3). The active ingredients of Retrovir may inhibit cellular DNA replication and zidovudine has been shown to be a transplacental carcinogen in one animal study. The clinical relevance of these findings is unknown. Placental transfer of zidovudine has been shown to occur in humans. Mitochondrial dysfunction: nucleoside and nucleotide analogues have been demonstrated in vitro and in vivo to cause a variable degree of mitochondrial damage. There have been reports of mitochondrial dysfunction in HIV-negative infants exposed in utero and/or post-natally to nucleoside analogues (see section 4.4).	the balance of potential benefits and potential risk. Pregnant women considering the use of Retrovir during pregnancy for prevention of HIV transmission to their infants should be advised that transmission may still occur in some cases despite therapy. The efficacy of zidovudine to reduce the maternal-foetal transmission in women with previously prolonged treatment with zidovudine or other antiretroviral agents or women infected with HIV strains with reduced sensitivity to zidovudine is unknown. It is unknown whether there are any long-term consequences of in utero and infant exposure to Retrovir. Based on the animal carcinogenicity/mutagenicity findings a carcinogenic risk to humans cannot be excluded (see section 5.3). The relevance of these findings to both infected and uninfected infants exposed to Retrovir is unknown. However, pregnant women considering using Retrovir during pregnancy should be made aware of these findings. A large amount of data on pregnant women (more than 3000 exposed outcomes) indicate no malformative nor feto/neonatal toxitcity. Retrovir can be used during pregnancy if clinically needed. Studies in pregnant rats and rabbits given zidovudine orally at dosage levels up to 450 and 500 mg/kg/day respectively during the major period of organogenesis have revealed no evidence of teratogenicity. There was, however, a statistically significant increase in foetal resorptions in rats given 150 to 450 mg/kg/day and in rabbits given 500 mg/kg/day. A separate study, reported subsequently, found that rats given a dosage of 3000 mg/kg/day, which is very near the oral median lethal dose (3683 mg/kg), caused marked maternal toxicity and an increase in the incidence of foetal malformations. No evidence of teratogenicity was observed in this study	

	at the lower dosages tested (600 mg/kg/day or less)	
Treatment with zidovudine has been associated with loss of subcutaneous fat which is most evident in the face, limbs and buttocks. Patients receiving Retrovir should be frequently examined and questioned for signs of lipoatrophy. When such development is found, treatment with Retrovir should not be continued (see section 4.4). Weight and levels of blood lipids and glucose may increase during antiretroviral therapy (see section 4.4).	**[…]** --- **[…]** **[…]**	**Undesirable effects**
Reproductive Toxicity: Studies in pregnant rats and rabbits given zidovudine orally at dosage levels up to 450 and 500 mg/kg/day respectively during the major period of organogenesis have revealed no evidence of teratogenicity. There was, however, a statistically significant increase in foetal resorptions in rats given 150 to 450 mg/kg/day and in rabbits given 500 mg/kg/day. A separate study, reported subsequently, found that rats given a dosage of 3000 mg/kg/day, which is very near the oral median lethal dose (3683 mg/kg), caused marked maternal toxicity and an increase in the incidence of foetal malformations. No evidence of teratogenicity was observed in this study at the lower dosages tested (600 mg/kg/day or less).	**[…]** --- **[…]** **[…]**	**Preclinical safety data**

מצ"ב העלון, שבו מסומנות ההחמרות המבוקשות על רקע צהוב.
שינויים שאינם בגדר החמרות סומנו (בעלון) בצבע שונה. יש לסמן רק תוכן מהותי ולא שינויים במיקום הטקסט.