נובמבר 2018

Valcyte
ואלציט
valganciclovir
Film-coated tablets

רופא/ה יקר/ה, רוקח/ת יקר/ה,

חברת רוש פרמצבטיקה (ישראל) בע"מ מבקשת להודיעכם על עדכון בעלון לרופא של התכשיר ואלציט.
בהודעה זו מצוינים רק עדכונים מהותיים ועדכונים אשר מהווים החמרה.

ההתוויות הרשומות לתכשיר בישראל:

Valcyte is indicated for the induction and maintenance treatment of cytomegalovirus (CMV) retinitis in patients with acquired immunodeficiency syndrome (AIDS).

Valcyte is indicated for the prevention of CMV disease in CMV-negative patients who have received a solid organ transplant from a CMV-positive donor.

הסבר:

טקסט עם קו תחתי מציין טקסט שהוסף לעלון.
~~טקסט עם קו חוצה~~ מציין טקסט שהוסר מן העלון.

למידע נוסף יש לעיין בעלון לצרכן ובעלון לרופא כפי שאושרו ע"י משרד הבריאות.

העלונים המעודכנים נשלחו לפרסום במאגר התרופות שבאתר משרד הבריאות, וניתן לקבלם מודפסים על-ידי פנייה לבעל הרישום: רוש פרמצבטיקה (ישראל) בע"מ, ת.ד 6391 , הוד השרון 4524079 טלפון 09-9737777. כתובתנו באינטרנט: www.roche.co.il.

ב ב ר כ ה,

בתאור צפרי-חגג
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עדכונים מהותיים בעלון לרופא

בסעיף 4.6Fertility, pregnancy and lactation , עודכן המידע הבא:

Fertility
A small clinical study with renal transplant patients receiving Valcyte for CMV prophylaxis for up to 200 days demonstrated an impact of valganciclovir on spermatogenesis, with decreased sperm density and motility measured after treatment completion. This effect appears to be reversible and approximately six months after Valcyte discontinuation, mean sperm density and motility recovered to levels comparable to those observed in the untreated controls.
In animal studies, ganciclovir impaired fertility in male and female mice and has shown to inhibit spermatogenesis and induce testicular atrophy in mice, rats and dogs at doses considered clinically relevant.
Based on clinical and nonclinical studies, it is considered likely that ganciclovir (and valganciclovir) may cause temporary or permanent inhibition of human spermatogenesis (see sections 4.4 and 5.3).
~~No human data on the effect of valganciclovir on fertility are available. Fertility studies have not been repeated with valganciclovir because of the rapid and extensive conversion of valganciclovir to ganciclovir in the body. Ganciclovir is associated with impaired fertility in animal studies (see section 5.3).~~

בסעיף4.8 Undesirable effects , עודכן המידע באופן הבא:

Description of selected adverse reactions

c *Paediatric population*
Valcyte has been studied in 179 paediatric solid organ transplant patients who were at risk of developing CMV disease (aged 3 weeks to 16 years) and in 133 neonates with symptomatic congenital CMV disease (aged 2 to 31 days), with duration of ganciclovir exposure ranging from 2 to 200 days.

The most frequently reported adverse reactions on treatment in paediatric clinical trials were diarrhoea, nausea, neutropenia, leukopenia and anaemia.
In solid organ transplant patients, the overall safety profile was similar in paediatric patients as compared to adults. Neutropenia was reported with slightly higher incidence in the two studies conducted in paediatric solid organ transplant patients as compared to adults, but there was no correlation between neutropenia and infectious adverse events in the paediatric population. A higher risk of cytopenias in neonates and infants warrants careful monitoring of blood counts in these age groups (see section 4.4).

בסעיף5.3 Preclinical safety data , עודכן המידע באופן הבא:

Valganciclovir is a pro-drug of ganciclovir and therefore effects observed with ganciclovir apply equally to valganciclovir. Toxicity of valganciclovir in pre-clinical safety studies was the same as that seen with ganciclovir and was induced at ganciclovir exposure levels comparable to, or lower than, those in humans given the induction dose.

These findings were gonadotoxicity (testicular cell loss) and nephrotoxicity (uraemia, cell degeneration), which were irreversible; myelotoxicity (anaemia, neutropenia, lymphocytopenia) and gastrointestinal toxicity (mucosal cell necrosis), which were reversible.
Ganciclovir was mutagenic in mouse lymphoma cells and clastogenic in mammalian cells. Such results are consistent with the positive mouse carcinogenicity study with ganciclovir. Ganciclovir is a potential carcinogen.
~~Ganciclovir causes impaired fertility and teratogenicity in animals. Based upon animal studies where aspermatogenesis was induced at ganciclovir systemic exposures below therapeutic levels, it is considered likely that ganciclovir causes inhibition of human spermatogenesis.~~
Further studies have shown ganciclovir to be teratogenic, embryotoxic, to inhibit spermatogenesis (i.e. impair male fertility) and to suppress female fertility.