**PROFESSIONAL INFORMATION**

**SCHEDULING STATUS** **S4**

**PROPRIETARY NAME AND DOSAGE FORM**

**VIDEX EC capsules 250 mg**

**VIDEX EC capsules 400 mg**

**COMPOSITION**

Capsules containing didanosine (250 and 400 mg).

Excipients:

Inactive ingredients in the beadlets include:

Carboxymethylcellulose sodium 12, diethyl phthalate, methacrylic acid copolymer, sodium hydroxide. Sodium starch glycollate and talc.

Inactive ingredients in the capsule shell include:

colloidal silicon dioxide, gelatine, sodium lauryl sulphate and titanium dioxide. Capsules are imprinted with edible inks.

**PHARMACOLOGICAL CLASSIFICATION**

A 20.2.8 Antiviral agents

**PHARMACOLOGICAL ACTION:**

**Pharmacodynamic properties**

Didanosine (2',3'-dideoxyinosine or ddI) is an inhibitor of the *in vitro* replication of the Human Immunodeficiency Virus (HIV) in human primary cell cultures and in established cell lines. After didanosine enters the cell, it is enzymatically converted to dideoxyadenosine-5'-triphosphate (ddATP), its active metabolite. In viral nucleic acid replication, incorporation of this 2',3'-dideoxynucleoside prevents chain extension and thereby inhibits viral replication. In addition, ddATP inhibits HIV-reverse transcriptase by competing with dATP for binding to the enzyme's active site, preventing proviral DNA synthesis. The relationship between *in vitro* susceptibility of HIV to didanosine and clinical response to therapy has not been established. Likewise, *in vitro* sensitivity results vary greatly and methods to establish virologic responses have not been proven.

**Pharmacokinetic properties**

**Adults:**

Didanosine is rapidly degraded at an acidic pH. The gastro-resistant granules in the VIDEX EC capsules release didanosine into the higher pH of the small intestine.

The administration of VIDEX EC capsules with a high fat meal results in a significant decrease in AUC (19 %) and $C_{max}$ (46 %) of didanosine compared to the fasting condition. Therefore, VIDEX EC should be administered on an empty stomach.
Equivalent values for AUC are observed for the tablet and capsule formulation of

didanosine in healthy volunteers and subjects infected with HIV. The rate of absorption from VIDEX EC capsules is slower compared to the tablet; the value for $C_{max}$ for the gastro-resistant capsule is 60 % of the value for the tablet. The time to reach $C_{max}$ is approximately 2 hours for the VIDEX EC capsule and 0,67 hours for the VIDEX tablet.

The steady state volume of distribution after IV administration of didanosine averages 54 litters. The concentration of didanosine in the cerebrospinal fluid (CSF), one hour after infusion, averages 21 % of that of the simultaneous plasma concentration. Renal clearance in patients with normal renal function which is equivalent to approximately 400 ml/min represents an average of 50 % of total body clearance, indicating that active tubular secretion in addition to glomerular filtration is responsible for the renal elimination of didanosine.

Urinary recovery of didanosine is approximately 20 % of the dose after oral treatment. There is no evidence of didanosine accumulation after the administration of oral doses for 4 weeks.

The average elimination half-life is 1,6 hours.
The metabolism of didanosine in man has not been evaluated. However, based on animal studies, it is presumed that it follows the same pathways responsible for the elimination of endogenous purines. *In vitro* human plasma protein binding is less than 5

% with didanosine, indicating that interactions involving binding site displacement are not anticipated.

*Renal impairment*: The apparent medicine clearance of didanosine decreased as creatinine clearance decreased. Dose adjustment is recommended in patients with impaired renal function (< 60 ml/min/1,73 $m^2$) (see DOSAGE AND DIRECTIONS FOR USE).

*Hepatic impairment*: The metabolism of didanosine may be altered in patients with more severe or other types of hepatic impairment (see CONTRAINDICATIONS). The pharmacokinetics of didanosine has been studied in 12 non-HIV infected subjects with moderate (n=8) to severe (n=4) hepatic impairment (Child-Pugh Class B or C). Mean AUC and $C_{max}$ values following a single 400 mg dose of didanosine were approximately 13 % and 19 % higher, respectively, in patients with hepatic impairment compared to matched healthy subjects. AUC and $C_{max}$ values in these patients with hepatic impairment were similar to those observed in healthy subjects from other studies and are within the pharmacokinetic variability of didanosine (see DOSAGE AND DIRECTIONS FOR USE).

**Paediatric and Adolescent Patients:**

There are no specific pharmacokinetic data from paediatric and adolescent patients treated with VIDEX EC capsules.

**INDICATIONS:**

VIDEX EC should be used in combination with other antiretroviral agents for the palliative treatment of adults with advanced HIV infection.

This indication is based on increases in CD4 counts observed in patients during therapy with VIDEX EC. Increases in CD4 counts are considered markers of anti-viral activity and have been linked to clinical benefit in previous AIDS therapy trials.

**CONTRAINDICATIONS:**

VIDEX EC is contraindicated in patients with hypersensitivity to didanosine or to any of the components of the formulation.

Safety and efficacy of VIDEX EC in children have not been established.

There are insufficient data to recommend the use of VIDEX EC in patients with impaired hepatic function.

**WARNINGS AND SPECIAL PRECUATIONS:**

**Pancreatitis:**

**Fatal and non-fatal pancreatitis has occurred during therapy with VIDEX EC used alone or in combination regimens in both treatment-naïve and treatment-experienced patients, regardless of degree of immunosuppression. Patients treated with VIDEX EC in combination with stavudine with or without hydroxyurea may be at increased risk for pancreatitis. VIDEX EC should be suspended in**

**patients with signs and symptoms of pancreatitis and discontinued in patients with confirmed pancreatitis**.

Suspension should also be considered when biochemical markers of pancreatitis have increased to clinically significant levels even in the absence of symptoms and in patients with clinical symptoms suggestive of pancreatitis (e.g. abdominal pain, nausea, vomiting) until pancreatitis is excluded by appropriate laboratory and imaging techniques.
In clinical trials, lower rates of pancreatitis were seen in patients with earlier stage HIV infection who were treated with currently recommended doses. The incidence of pancreatitis in clinical trials was dose-related. When treatment is required with other medicines known to cause pancreatic toxicity (e.g. pentamidine) or known to increase exposure or activity of didanosine (e.g. hydroxyurea or allopurinol), suspension of VIDEX EC therapy is recommended. Allopurinol was observed to increase exposure to didanosine in renally impaired patients and healthy volunteers and may increase the risk of dose-related toxicities such as pancreatitis. It is recommended that these two medicines not be administered together (see INTERACTIONS). VIDEX EC should be used with caution in patients with risk factors for pancreatitis. For example, the following patients may be at increased risk for developing pancreatitis and should be followed closely for signs and symptoms of pancreatitis; patients with advanced HIV infection, patients with a history of pancreatitis, elderly patients, patients with

significantly elevated triglycerides and patients with renal impairment if treated with unadjusted doses.

*Lactic acidosis*:

Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases have been reported with the use of nucleoside analogues alone or in combination including didanosine and other antiretrovirals. A majority of these cases have been in women. Obesity and prolonged nucleoside exposure may be risk factors. Treatment with VIDEX EC should be suspended in the setting of rapidly elevating aminotransferase levels, raised blood levels of bilirubin, progressive hepatomegaly, or metabolic/lactic acidosis of unknown aetiology. Caution should be exercised when administering VIDEX EC to any patient, particularly obese women with hepatomegaly, hepatitis, or other known risk factors for liver disease. These patients should be followed carefully while on therapy with VIDEX EC.

Fatal lactic acidosis has been reported in pregnant women who received the combination of didanosine and stavudine with other antiretroviral agents. VIDEX EC and stavudine are contraindicated in pregnancy.

Lactic acidosis should be monitored in accordance with lactate levels, as presented in Table 1 below:

**Table 1**:

| |
|---|
| **Lactate 2 - 5 mmol/l**: Monitor regularly and be alert for clinical signs. |
| **Lactate 5 -10 mmol/l without symptoms:** Monitor closely. |
| **Lactate 5 -10 mmol/l with symptoms**: STOP all therapy. Exclude other causes, (e,g. sepsis, uremia, diabetic ketoacidosis, thyrotoxicosis, lymphoma). |
| **Lactate ≥ 10 mmol**/l: STOP all therapy (80 % mortality in case studies). |

The lactate values in the table may not be relevant for children.

*Peripheral neuropathy*:

Peripheral neuropathy, which was severe in some cases, has been reported in HIV-infected patients receiving hydroxyurea in combination with antiretroviral agents, including VIDEX EC, with or without stavudine (see SIDE EFFECTS).

Patients on VIDEX EC may develop toxic peripheral neuropathy, usually characterised by bilateral symmetrical distal numbness, tingling and pain in feet and hands. Whenever warranted by clinical conditions, VIDEX EC therapy should be suspended until resolution of symptoms. Many patients tolerate a reduced dose after resolution of symptoms.

Liver failure:

Liver failure of unknown aetiology has occurred. Patients should be observed for liver enzyme elevations and VIDEX EC should be suspended if enzymes rise to a clinically significant level above the upper limit of normal. In the event of rapidly elevating aminotransferase levels, consideration should be given to discontinuation of all nucleoside analogue therapy.

Rechallenge should be considered only if the potential benefits clearly outweigh the potential risks.

Fatal hepatic failure, as well as peripheral neuropathy, pancreatitis, and symptomatic hyperlactataemia/lactic acidosis have been reported in patients receiving didanosine and ribavirin with or without stavudine. The administration of VIDEX EC and ribavirin should be avoided.

**Hepatotoxicity and hepatic failure resulting in death were reported during post-marketing surveillance in HIV-infected patients treated with antiretroviral agents**

**in combination with hydroxyurea. Fatal hepatic events were reported most often in patients treated with the combination of hydroxyurea, VIDEX EC and stavudine. This combination should be avoided**.

The safety and efficacy of VIDEX EC have not been established in patients with significant underlying liver disorders. During combination antiretroviral therapy, patients with pre-existing liver dysfunction, including chronic active hepatitis have an increased frequency of liver function abnormalities, including severe and potentially fatal hepatic adverse events and should be monitored according to standard practice. If there is evidence of worsening liver disease in such patients interruption or discontinuation of treatment must be considered (see CONTRAINDICATIONS).

*Non-cirrhotic portal hypertension:*

Post-marketing cases of non-cirrhotic portal hypertension have been reported, including cases leading to liver transplantation or death. Cases of didanosine-associated non-cirrhotic portal hypertension were confirmed by liver biopsy in patients with no evidence of viral hepatitis. Onset of signs and symptoms ranged from months to years after start of VIDEX therapy. Common presenting features included elevated liver enzymes, oesophageal varices, haematemesis, ascites, and splenomegaly.

Patients receiving VIDEX EC should be monitored for early signs of portal hypertension (e,g. thrombocytopenia and splenomegaly) during routine medical visits. Appropriate laboratory testing including liver enzymes, serum bilirubin, albumin, complete blood count, and international normalised ratio (INR) and ultrasonography should be

considered. VIDEX EC should be discontinued in patients with evidence of non-cirrhotic portal hypertension.

*Retinal or optic nerve changes:*

Paediatric patients have demonstrated retinal or optic nerve changes, particularly at doses above those recommended. There have been reports of retinal depigmentation and optical neuritis in adults and paediatric and adolescent patients. Patients should undergo retinal examination every 6 months or if a change in vision occurs. The long-term effects of VIDEX EC are unknown.

Patients receiving VIDEX EC may continue to develop opportunistic infections and other complications of HIV infection.

*Geriatric use:*

Elderly patients had a higher frequency of pancreatitis (10 %) than younger patients (5 %) in an Expanded Access Program that enrolled patients with advanced HIV infection (see WARNINGS AND SPECIAL PRECAUTIONS, Pancreatitis).

Because elderly patients are more likely to have decreased renal function care should be taken in dose selection, renal function should be monitored and dosage adjustments made accordingly (see DOSAGE AND DIRECTIONS FOR USE).

*Immune Reconstitution Inflammatory Syndrome*

Immune reconstitution inflammatory syndrome (IRIS) is an immunopathological response resulting from the rapid restoration of pathogen-specific immune responses to pre-existing antigens combined with immune dysregulation, which occurs shortly after starting

combination Anti-Retroviral Therapy (cART).

Typically, such reaction presents by paradoxical deterioration of opportunistic infections being treated or with unmasking of an asymptomatic opportunistic disease, often with an atypical inflammatory presentation. IRIS usually develops within the first three months of initiation of ART and occurs more commonly in patients with low CD4 counts. Common examples of IRIS reactions to opportunistic diseases are tuberculosis, cytomegalovirus retinitis, and cryptococcal meningitis.

Appropriate treatment of the opportunistic disease should be instituted or continued and ART continued. Inflammatory manifestations generally subside after a few weeks. Severe cases may respond to glucocorticoids, but there is only limited evidence for this in patients with tuberculosis IRIS.

Autoimmune disorders (such as Graves' disease) have also been reported as IRIS reactions; however, the reported time to onset is more variable and these events can occur many months after initiation of treatment.

*Fat Redistribution:*

Redistribution/accumulation of body fat (lipodystrophy/lipoatrophy) including central obesity, dorsocervical fat enlargement (buffalo hump), peripheral wasting facial wasting, breast enlargement, and "cushingoid appearance" have been observed in patients receiving antiretroviral therapy.

*Patients on a sodium restricted diet:*

Each VIDEX EC capsule contains 1,06mg for the 250 mg capsule and 1.70 mg for the 400 mg formulation.

**INTERACTIONS**

Co-administration of VIDEX EC with medicines that are known to cause peripheral neuropathy or pancreatitis may increase the risk of these toxicities (see WARNINGS AND SPECIAL PRECAUTIONS).

Specific interaction studies have been conducted with VIDEX chewable/dispersible tablets and loperamide, metoclopramide, ranitidine, zidovudine, stavudine, rifabutin, foscamet, trimethoprim, sulfamethoxazole and dapsone without evidence of interaction. Specific interaction studies with ciprofloxacin, ketoconazole and indinavir, showed no evidence of significant interaction. Therefore, VIDEX EC capsules can be prescribed concomitantly with these medicines.

**Methadone**: When didanosine was administered to opiate-dependant patients (n = 16) chronically treated with methadone, didanosine exposure as measured by AUC, was decreased by 57 %, compared to untreated controls (n=10). No studies have been conducted with VIDEX EC capsules.

**Allopurinol:** When VIDEX tablets were co-administered with allopurinol in 2 patients with renal impairment (creatinine clearance of 15 to18 ml/min), the AUC of didanosine increased approximately 4-fold. In 14 healthy volunteers, the mean AUC of didanosine increased approximately 2-fold when VIDEX tablets were given with allopurinol. Thus the risk of dose-related toxicities, such as pancreatitis (see WARNINGS AND SPECIAL PRECAUTIONS, Pancreatitis), may be increased if VIDEX EC and allopurinol are administered together. It is recommended that these two medicines not be administered together.

Administration of didanosine 2 hours prior to, or concurrent with ganciclovir was associated with a mean increase of 111 % in the steady state AUC for didanosine. A minor decrease (21 %) in the steady state AUC of ganciclovir was seen when didanosine was given 2 hours prior to ganciclovir, but not when both medicines were given simultaneously.

There were no changes in renal clearance for either medicine. It is not known whether these changes are associated with alterations in either the safety of VIDEX EC or the efficacy of ganciclovir.

There is no evidence available that VIDEX EC potentiates the myelosuppressive effects of ganciclovir.

Ribavirin increases the intracellular triphosphate levels of didanosine. Fatal hepatic failure, as well as peripheral neuropathy, pancreatitis, and symptomatic hyperlactataemia/lactic acidosis have been reported in patients receiving didanosine and ribavirin with or without stavudine. The administration of VIDEX EC and ribavirin should be avoided.

**Tenofovir disoproxil fumarate**: Exposure to didanosine is increased when coadministered with tenofovir. Therefore, a dose reduction is recommended when coadministered with tenofovir. All patients receiving tenofovir disoproxil fumarate and

VIDEX EC concomitantly should be monitored for didanosine-associated adverse events and clinical response.

As experience of medicine interaction with VIDEX EC is still limited care should be taken in combining other medicine regimens with VIDEX EC.

In the presence of food the AUC for VIDEX EC was reduced by 19 % compared to the fasting state.

Failure of dapsone to prevent *P.carinii (P. jiroveci)* pneumonia in HIV patients has been reported with the concurrent administration of dapsone and didanosine.

**PREGNANCY AND LACTATION**

Safe use in pregnancy has not been established. Fatal lactic acidosis has been reported in pregnant women who received the combination of VIDEX EC and stavudine with other antiretroviral agents. It is not known whether VIDEX EC is excreted in human milk. It is recommended that women taking VIDEX EC do not breastfeed because of the potential for serious adverse reactions from VIDEX EC in breastfeeding infants.

**DOSAGE AND DIRECTIONS FOR USE**

DUE TO THE REDUCED ABSORPTION IN THE PRESENCE OF FOOD, VIDEX EC SHOULD BE TAKEN ON AN EMPTY STOMACH at least one hour before or two hours after a meal.

**Recommended dosage:**

The recommended total daily dose is based on body weight (kg) and is administered as one capsule given on a once daily schedule as outlined in the table below.
VIDEX EC capsules should be swallowed intact (not chewed or opened).

**TABLE 2: Recommended VIDEX EC Dosage**

| **Patient Baseline Weight** | **Dosage** |
|---|---|
| Weight (kg) | Total daily dose |
| at least 60 kg | 400 mg |
| Less than 60 kg | 250 mg |

***Dose adjustment in patients with renal impairment***

*Adults*: In adult patients with impaired renal function, the dose of VIDEX EC should be adjusted to compensate for the lower rate of elimination. The recommended reductions in dose and/or dosage interval are as follows, based on creatinine clearance:

**TABLE 3:**

| **Creatinine clearance (ml/min/1,73 $m^2$)** | **Patient Weight ≥ 60 kg** | **Patient Weight < 60 kg** |
|---|---|---|
| ≥ 60 (normal dose) | 400 mg once daily | 250 mg once daily |

VIDEX EC is not suitable for patient with creatinine clearance <60 ml/min.

For patients undergoing dialysis, the daily dose of VIDEX EC should be administered after dialysis. It is not necessary to administer a supplemental dose of VIDEX EC following dialysis.

***Geriatric patients**:* Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection. In addition, renal function should be monitored and dosage adjustments should be made accordingly.

***Patients with symptoms of peripheral neuropathy**:* If symptoms of peripheral neuropathy occur, VIDEX EC therapy should be suspended until resolution of symptoms. After resolution of these symptoms, patients may tolerate a reduced dose of VIDEX EC.

**Hepatic impairment:**

During treatment with VIDEX EC, patients should be observed for liver enzyme elevations and VIDEX EC suspended if enzymes rise to a clinically significant level. In the event of rapidly elevating aminotransferase levels, consideration should be given to discontinuation of all nucleoside analogue therapy (see WARNINGS AND SPECIAL PRECAUTIONS).

**Method of administration**:

The VIDEX EC capsules should be swallowed intact (not chewed). To optimise absorption, the capsule should be taken with at least 100 ml of water. Do not open the capsule to facilitate administration as the stability of the gastro-resistant granules out of the capsule shell has not been studied.

**Concomitant therapy**

Tenofovir disoproxil fumarate: A dose reduction of VIDEX EC is recommended when coadministered with tenofovir.

VIDEX EC: 250 mg (≥ 60 kg) or 200 mg (< 60 kg) once daily together with tenofovir and a light meal (≤ 400 kcalories, ≤ 20 % fat) or in the fasted state.

When VIDEX EC is used in combination with other antiretroviral agents, the respective package inserts should be referred to.

## SIDE EFFECTS

### Adults

**Pancreatitis**

**Fatal and nonfatal pancreatitis has occurred during therapy with VIDEX EC used alone or in combination regimens in both treatment-naïve and treatment-experienced patients, regardless of degree of immunosuppression. VIDEX EC should be suspended in patients with signs or symptoms of pancreatitis and discontinued in patients with confirmed pancreatitis.**

**Patients treated with VIDEX EC in combination with stavudine, with or without hydroxyurea, may be at increased risk for pancreatitis.**

Other important toxicities include lactic acidosis and severe hepatomegaly with steatosis, retinal changes and optical neuritis (see WARNINGS AND SPECIAL PRECUTIONS) and peripheral neuropathy (see WARNING AND SPECIAL PRECAUTIONS, DOSAGE AND DIRECTIONS FOR USE).

When VIDEX EC is used in combination with other agents with similar toxicities, the incidences of these toxicities may be higher than when VIDEX EC is used alone. Thus patients treated with combination regimens including stavudine may be at increased risk for liver function abnormalities and peripheral neuropathy (see WARNINGS AND SPECIAL PRECAUTIONS).

Patients receiving VIDEX EC may develop peripheral neuropathy, usually characterised by bilateral symmetrical distal numbness, tingling and pain in feet, and, less frequently, hands. In clinical trials, the frequency appeared to be related to dose and/or stage of disease. Lower rates were seen in patients with less advanced disease. In controlled clinical trials, neuropathy has occurred more frequently in patients with a history of neuropathy or concomitant use of neurotoxic medicine therapy. Peripheral neuropathy, which was severe in some cases, has been reported in HIV-infected patients receiving hydroxyurea in combination with antiretroviral agents, including VIDEX EC with or without stavudine. Most of the serious adverse events observed have generally reflected the recognised clinical course of AIDS and AIDS-related complex (ARC).

Concurrent dosing with a variety of medicines was allowed in the studies. Therefore, it is difficult to distinguish which events are related to VIDEX EC administration, to the disease itself, or to other therapy-related events.

**Adverse events**

The following undesirable effects which occurred at a frequency of ≥ 2 %, were reported. Frequency is defined as very common (≥ 1/10 or ≥ 10 %); common (≥ 1/100, < 1/10 or ≥ 1 % and < 10 %); uncommon (≥ 1/1000, < 1/100 or ≥ 0,1 % and < 1 %), rare (≥ 1/10000, < 1/1000 or ≥ 0,01 % and < 0,1 %) or very rare (< 1/10000 or < 0,01 %).

***Nervous system disorders***

*Common*: peripheral neurologic symptoms (including neuropathy), headache.

***Gastrointestinal***

*Very common*: diarrhoea.

*Common*: nausea, vomiting, abdominal pain.

***Skin and subcutaneous tissue disorder***

*Common*: rash/pruritus.

***General disorders***

*Common*: fatigue.

***Pancreatitis***: Pancreatitis resulting in death was observed in one patient who received didanosine plus stavudine and nelfinavir, one patient who received didanosine plus stavudine and indinavir and in 2 of 68 patients who received didanosine plus stavudine plus indinavir plus hydroxyurea (see WARNINGS AND SPECIAL PRECAUTIONS, Pancreatitis and SIDE EFFECTS).

**Laboratory abnormalities**

Selected laboratory abnormalities in patients receiving didanosine monotherapy and combination therapy in clinical trials are changes in bilirubin, alkaline phosphatase, [SGOT] ALT, [SGPT] AST, GGT, uric acid, lipase and amylase. The relationship to therapy of these observations has not been established.

**Laboratory abnormalities (grade 3-4) reported in patients receiving VIDEX EC in study AI454-152 (VIDEX EC capsules) included:**

**Table 4:**

| Parameter | AI454-152 |
|---|---|
| Lipase increased | 5 % |
| ALT increased | 6 % |
| AST increased | 5 % |
| Uric acid increase | 2 % |
| Hyperbilirubinemia | <1 % |

**Post-marketing**:

The following events have been identified during post approval use of didanosine. Because they are reported voluntarily from a population of unknown size, estimates of frequency cannot be made. The events have been chosen for inclusion due to their seriousness, frequency of reporting or causal connection to VIDEX EC or a combination of these factors:

*Body as a whole* - alopecia, anaphylactoid reaction, asthenia, chills/fever and pain.

*Digestive disorders* - anorexia, dyspepsia and flatulence.

*Exocrine Gland disorders* - pancreatitis (including fatal cases) (see WARNINGS AND SPECIAL PRECAUTIONS), sialoadenitis, parotid gland enlargement, dry mouth and dry eyes.

*Hematologic Disorders* - anaemia, granulocytopenia, leukopenia and thrombocytopenia.

*Liver* - lactic acidosis and hepatic steatosis, hepatitis and liver failure, non-cirrhotic portal hypertension (see WARNINGS AND SPECIAL PRECAUTIONS).

*Metabolic Disorders* - diabetes mellitus, elevated serum alkaline phosphatase level, hypoglycaemia and hyperglycaemia.

*Musculoskeletal Disorders* - myalgia (with or without increases in creatine kinase), rhabdomyolysis including acute renal failure and haemodialysis, arthralgia and myopathy.

*Ophthalmologic Disorders* - retinal depigmentation and optic neuritis (see WARNINGS AND SPECIAL PRECAUTIONS).

**KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT**

There is no known antidote for VIDEX EC overdosage. Early studies in which didanosine was initially administered at doses ten times the recommended doses indicate that the anticipated complications of chronic overdosage would be hyperuricaemia, pancreatitis, peripheral neuropathy and hepatic dysfunction. Didanosine is not dialysable by peritoneal dialysis, although there is some clearance by

haemodialysis. The fractional removal of didanosine during an average haemodialysis session of 3 to 4 hours is approximately 20 to 35 % of the amount present in the body at the start of dialysis.

**IDENTIFICATION**

VIDEX EC capsule 250 mg: White, opaque, Size#1, two-piece hard gelatine capsule printed in blue with BMS, 250 mg and 6673. Contents of capsules: white to off-white, film coated beadlets.

VIDEX EC capsule 400 mg: White, opaque, Size#0, two-piece hard gelatine capsule printed in red with BMS, 400 mg and 6674. Contents of capsules: white to off-white, film coated beadlets.

**PRESENTATION**

**VIDEX EC capsules**

Colourless ACLAR® and aluminium foil blister packs with 30 capsules.

**STORAGE INSTRUCTIONS**

Store at room temperature not exceeding 25 °C.

**REGISTRATION NUMBERS**

VIDEX EC capsules 250 mg: 36/20.2.8/0065

VIDEX EC capsules 400 mg: 36/20.2.8/0066

**NAME AND BUSINESS ADDRESS OF APPLICANT**

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*Authorised user of the trademark ™VIDEX.