1.3.1.1 Professional Information

SCHEDULING STATUS:

Schedule 4

PROPRIETARY NAME (AND DOSAGE FORM):

KAVIMUN PAED (film-coated tablets)

COMPOSITION:

Each **KAVIMUN PAED** film-coated tablet contains:

Abacavir sulfate equivalent to abacavir 60 mg

Sugar free

List of excipients: cellulose microcrystalline, silica colloidal anhydrous, magnesium stearate, sodium starch glycolate,

Film-coat: hypromellose, titanium dioxide, polyethylene glycol 400, iron oxide yellow, iron oxide red

PHARMACOLOGICAL CLASSIFICATION:

A 20,2,8 Antivirals

WARNING:

LACTIC ACIDOSIS AND SEVERE HEPATOMEGALY WITH STEATOSIS, INCLUDING FATAL CASES, HAVE BEEN REPORTED WITH THE USE OF NUCLEOSIDE ANALOGUES ALONE OR IN COMBINATION WITH OTHER ANTIRETROVIRALS (SEE WARNINGS).

Hypersensitivity Reaction:

Skin patch testing has no utility in the clinical management of patients and therefore should not be used in the clinical setting.

Before initiating treatment with KAVIMUN PAED, screening for carriage of the HLA-B*5701 allele should be performed. KAVIMUN PAED should not be used in patients known to carry the HLA-B*5701 allele.

In clinical studies approximately 5 % of subjects receiving abacavir developed a hypersensitivity reaction. Some of these cases were life-threatening and resulted in a fatal outcome despite taking precautions.

Studies have shown that carriage of the HLA-B*5701 allele is associated with a more than 50 % increased risk of a hypersensitivity reaction to abacavir.

In any patient treated with KAVIMUN PAED, the clinical diagnosis of suspected hypersensitivity reaction must remain the basis of clinical decision-making. Even in the absence of HLA-B*5701 allele, it is important to permanently discontinue KAVIMUN PAED and not rechallenge with KAVIMUN PAED or any product containing abacavir if a hypersensitivity reaction cannot be ruled out on clinical grounds, due to the potential for a severe or even fatal reaction.

• Clinical Description

Hypersensitivity reactions are characterised by the appearance of symptoms indicating multi-organ system involvement.

Almost all hypersensitivity reactions

will have fever and/or rash as part of the syndrome.

Other signs and symptoms may include respiratory signs and symptoms such as dyspnoea, sore throat, cough, and abnormal chest x-ray findings (predominantly infiltrates, which can be localised), gastro-intestinal symptoms, such as nausea, vomiting, diarrhoea, or abdominal pain, and may lead to misdiagnosis of hypersensitivity as respiratory disease (pneumonia, bronchitis, pharyngitis), or gastro-enteritis. Other frequently observed signs or symptoms of the hypersensitivity reaction may include lethargy or malaise and musculoskeletal symptoms (myalgia, rarely myolysis, arthralgia).

• Clinical Management

Hypersensitivity reaction symptoms usually appear within the first six weeks of initiation of treatment with KAVIMUN PAED, although these reactions may occur at any time during therapy. Patients should be monitored closely, especially during the first two months of treatment with KAVIMUN PAED, with consultation every two weeks.

Patients who are diagnosed with a hypersensitivity reaction whilst on therapy MUST discontinue KAVIMUN PAED tablets immediately.

KAVIMUN PAED tablets, or any other medicinal product containing abacavir,

Restarting KAVIMUN PAED or other medicines containing abacavir following a hypersensitivity reaction, results in a prompt return of symptoms within hours. This recurrence is usually more severe than on initial presentation, and may include life-threatening hypotension and death.

To avoid a delay in diagnosis and minimise the risk of a life-threatening hypersensitivity reaction, KAVIMUN PAED tablets must be permanently discontinued if hypersensitivity cannot be ruled out, even when other diagnoses are possible (respiratory diseases, flu-like illness, gastro-enteritis or reactions to other medicinal products).

Special care is needed for those patients simultaneously starting treatment with KAVIMUN PAED tablets and other medicinal products known to induce skin toxicity (such as nucleotide and non-nucleoside reverse transcriptase inhibitors - NNRTIs). This is because it is currently difficult to differentiate between rashes induced by these products and abacavir related hypersensitivity reactions.

• Management after an interruption of KAVIMUN PAED tablets therapy.

If therapy with KAVIMUN PAED tablets has been discontinued for any reason and restarting therapy is under consideration, the reason for discontinuation must be established to assess whether the patient had any symptoms of a hypersensitivity reaction. If a hypersensitivity reaction cannot be ruled out, the KAVIMUN PAED or any other medicinal product containing abacavir must not be restarted.

Hypersensitivity reactions with rapid onset, including life-threatening reactions have occurred after restarting abacavir in patients who had only one of the key symptoms of hypersensitivity (skin rash, fever, gastro-intestinal, respiratory or constitutional symptoms such as lethargy and malaise) prior to stopping abacavir.

The most common isolated symptom of a hypersensitivity reaction was a skin rash. Moreover, on rare occasions hypersensitivity reactions have been reported in patients who have restarted therapy, and who had no preceding symptoms of a hypersensitivity reaction. In both cases if a decision is made to restart abacavir this must be done in a setting where medical assistance is readily available.

• Essential patient information.

Prescribers must ensure that patients are fully informed regarding the following information on the hypersensitivity reaction:

- **Patients must be made aware of the possibility of a hypersensitivity reaction to abacavir as in KAVIMUN PAED that may result in a life-threatening reaction or death.**
- **Patients developing signs or symptoms possibly linked with a hypersensitivity reaction MUST CONTACT their doctor IMMEDIATELY.**
- **Patients who are hypersensitive to abacavir should be reminded that they must never take KAVIMUN PAED tablets or any other medicinal product containing abacavir again.**

- **In order to avoid restarting abacavir, patients who have experienced a hypersensitivity reaction should dispose of their remaining KAVIMUN PAED tablets in their possession in accordance with the local requirements, and ask their doctor or pharmacist for advice.**
- **Patients who have stopped KAVIMUN PAED tablets for any reason and particularly due to possible adverse reactions or illness must be advised to contact their doctor before restarting.**
- **Patients should be advised of the importance of taking KAVIMUN PAED tablets regularly.**
- **Each patient should be reminded to read the Patient Information Leaflet included in the KAVIMUN PAED tablets package.**
- **They should be reminded of the importance of removing the Alert Card included in the package, and keeping it with them at all times.**

PHARMACOLOGICAL ACTION:

Mechanism of action:

Abacavir is a nucleoside analogue reverse transcriptase inhibitor. It is a potent selective inhibitor of HIV-1 and HIV-2, including HIV-1 isolates with reduced susceptibility to zidovudine, lamivudine, zalcitabine, didanosine or nevirapine. Abacavir is metabolised intracellularly to the active moiety, carbovir 5'-triphosphate (TP). *In vitro* studies have demonstrated that its mechanism of action in relation to HIV is inhibition of the HIV reverse transcriptase enzyme, an event that results in chain termination and interruption

of the viral replication cycle. Abacavir shows synergy *in vitro* in combination with nevirapine and zidovudine. It has been shown to be additive in combination with didanosine, zalcitabine, lamivudine and stavudine.

Abacavir-resistant isolates of HIV-1 have been selected *in vitro* and are associated with specific genotypic changes in the reverse transcriptase (RT) codon region (codons M184V, K65R, L74V and Y115F). Viral resistance to abacavir develops relatively slowly *in vitro* and *in vivo,* requiring multiple mutations to reach an eight-fold increase in ICso over wild-type virus, which may be a clinically relevant level.

Isolates resistant to abacavir may also show reduced sensitivity to lamivudine, zalcitabine and/or didanosine, but remain sensitive to zidovudine and stavudine.

Crossresistance between abacavir and protease inhibitors or non-nucleoside reverse transcriptase inhibitors is unlikely.

Treatment failure following initial therapy with abacavir, lamivudine and zidovudine is mainly associated with the M184V alone, thus maintaining many therapeutic options for a second-line regimen.

Pharmacokinetics:

Abacavir is well absorbed following oral administration. The absolute bioavailability of oral abacavir in adults is about 83 %. Following oral administration, the mean time (t_{max}) to maximal serum concentrations of abacavir is about 1,5 hours for the tablet formulation.

Food delayed absorption and decreased C_{max} but did not affect overall plasma concentrations (AUC). Therefore **KAVIMUN PAED** can be taken with or without food.

Distribution:

Following intravenous administration, the apparent volume of distribution was about 0,8 l/kg, indicating that abacavir penetrates freely into body tissues.

Studies in HIV infected patients have shown good penetration of abacavir into the cerebrospinal fluid (CSF), with a CSF to plasma AUC ratio of between 30 to 44 %.

Plasma protein binding studies *in vitro* indicate that abacavir binds only low to moderately (~ 49 %) to human plasma proteins at therapeutic concentrations. This indicates a low likelihood for interactions through plasma protein binding displacement.

Metabolism:

Abacavir is primarily metabolised by the liver with approximately 2 % of the administered dose being renally excreted, as unchanged compound. The primary pathways of metabolism in man are by alcohol dehydrogenase and by glucuronidation to produce the 5'-carboxylic acid and 5'-glucuronide which account for about 66 % of the dose in the urine.

Elimination:

The mean half-life of abacavir is about 1,5 hours. Elimination of abacavir is via hepatic metabolism with subsequent excretion of metabolites primarily in the urine. The metabolites and unchanged abacavir account for about 83 % of the administered abacavir dose in the urine and the remainder is eliminated in the faeces.

Special populations:

Hepatically impaired:

Abacavir is metabolised primarily by the liver. The pharmacokinetics of abacavir have been studied in patients with mild hepatic impairment (Child-Pugh score 5-6). The results showed that there was a mean increase of 1,89-fold in the abacavir AUC, and 1,58-fold in the half-life of abacavir. The AUCs of the metabolites were not modified by the liver disease. However, the rates of formation and elimination of these were

decreased. The pharmacokinetics have not been studied in patients with moderate or severe hepatic impairment, therefore **KAVIMUN PAED** is contra-indicated in these patient groups.

Renally impaired:

Abacavir is primarily metabolised by the liver with approximately 2 % of abacavir excreted unchanged in the urine. The pharmacokinetics of abacavir in patients with endstage renal disease is similar to patients with normal renal function. Therefore, no dosage reduction is required in patients with renal impairment.

Children:

Abacavir is well absorbed from an oral solution administered to children. The overall pharmacokinetic parameters in children are comparable to adults, with slightly greater variability in plasma concentrations. The recommended dose for children from three months to 12 years is 8 mg/kg twice daily. This will provide slightly higher mean plasma concentrations in children, ensuring that the majority will achieve therapeutic concentrations equivalent to 300 mg twice daily in adults.
There are insufficient safety data to recommend the use of **KAVIMUN PAED** in infants less than three months old.

Elderly:

The pharmacokinetics of abacavir have not been studied in patients over 65 years of age. When treating elderly patients consideration needs to be given to the greater frequency of decreased hepatic, renal and cardiac function, and concomitant disease or other medicinal therapy.

INDICATIONS:

KAVIMUN PAED is indicated in antiretroviral combination therapy for the treatment of Human Immunodeficiency Virus (HIV-1) infected children.

CONTRA-INDICATIONS:

KAVIMUN PAED is contra-indicated in patients:

- with known hypersensitivity to abacavir or to any of the excipients of **KAVIMUN PAED** (for abacavir hypersensitivity, see **WARNINGS** and **SPECIAL PRECAUTIONS** and **SIDE-EFFECTS AND SPECIAL PRECAUTIONS)**
- with severe hepatic impairment

WARNINGS:

Hypersensitivity reaction:

Patients who develop a hypersensitivity reaction must discontinue KAVIMUN PAED and MUST NOT be re-challenged with KAVIMUN PAED (see SIDE-EFFECTS AND SPECIAL PRECAUTIONS).

Hypersensitivity to abacavir:

In clinical studies, approximately 5 % of subjects receiving abacavir developed a hypersensitive reaction, which in some cases has proven fatal. Hypersensitivity is characterised by the appearance of symptoms indicating multi-organ/body-system involvement. **Patients who develop a hypersensitivity reaction must discontinue KAVIMUN PAED and MUST NOT be rechallenged with KAVIMUN PAED, or any other product containing abacavir (see SIDE-EFFECTS AND SPECIAL PRECAUTIONS).**

Lactic acidosis/severe hepatomegaly with steatosis:

Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of a nucleoside analogue alone or in combination, in the treatment of HIV infection.

Use of **KAVIMUN PAED** can result in potentially fatal lactic acidosis.

Clinical features are non-specific, and include nausea, vomiting, abdominal pain, dyspnoea, fatigue and weight loss. Suspicious biochemical features include raised transaminases, raised lactate dehydrogenase (LDH) and/or creatine kinase. In patients with suspicious symptoms of biochemistry, measure the venous lactate level (normal < 2 mmol/1) and respond as follows:

- Lactate 2-5 mmol/1: monitor regularly and be alert for clinical signs
- Lactate 5-10 mmol/1 without symptoms, monitor closely
- Lactate 5-1 0 mmol/1 with symptoms: STOP all therapy. Exclude other causes e.g. sepsis, uraemia, diabetic ketoacidosis, thyrotoxicosis, lymphoma
- Lactate> 10 mmol/1: STOP all therapy (80 % mortality in case studies)
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The above lactate values may not be applicable to paediatric patients.

Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of **KAVIMUN PAED** alone on in combination.

Caution should be exercised when administering **KAVIMUN PAED** to any patient (particularly obese women) with hepatomegaly, hepatitis or other known risk factors of liver disease and hepatic steatosis (including certain medicinal products and alcohol).

Treatment with **KAVIMUN PAED** should be suspended in any patient who develops clinical or laboratory findings of lactic acidosis or hepatomegaly.

Patients co-infected with hepatitis C and treated with alpha interferon and ribavirin may constitute a special risk.

Patients at increased risk should be followed closely.

Lipodystrophy:

Combination antiretroviral therapy has been associated with the redistribution of body fat (lipodystrophy) in HIV patients. The long-term consequences of these events are currently unknown. Knowledge about the mechanism is incomplete. A connection between visceral lipomatosis and protease inhibitors (PIs) and lipoatrophy and nucleoside reverse transcriptase inhibitors (NRTIs) has been hypothesised. A higher risk of lipodystrophy has been associated with individual factors such as older age, and with medicine related factors such as longer duration of antiretroviral treatment and associated metabolic disturbances. Clinical examination should include evaluation for physical signs of fat redistribution. Consideration should be given to the measurement of fasting serum lipids and blood glucose. Lipid disorders should be managed as clinically appropriate.

Pancreatitis:

Pancreatitis has been reported, but a causal relationship to abacavir is uncertain.

Risk of virological failure:

Triple nucleoside therapy:

There have been reports of a high rate of virological failure, and of emergence of

resistance at an early stage when abacavir and lamivudine were combined with tenofovir disoproxil fumarate as a once daily regimen.

Liver disease:

The safety and efficacy of **KAVIMUN PAED** has not been established in patients with significant underlying liver disorders. **KAVIMUN PAED** is contra-indicated in patients with severe hepatic impairment.

Patients with chronic hepatitis B or C and treated with combination antiretroviral therapy are at an increased risk of severe and potentially fatal hepatic adverse reactions. In case of concomitant antiviral therapy for hepatitis B or C, please refer also to the relevant product information for these medicinal products.

Patients with pre-existing liver dysfunction, including chronic active hepatitis have an increased frequency of liver function abnormalities during combination antiretroviral therapy, 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.

INTERACTIONS:

Based on the results of *in vitro* experiments and the known major metabolic pathways of abacavir, the potential for interactions with other medicinal products involving abacavir is low. Abacavir shows no potential to inhibit metabolism mediated by the cytochrome P450 3A4 enzyme. It has also been shown *in vitro* not to interact with substances that are metabolised by CYP 3A4, CYP2C9 or CYP2D6 enzymes.

Potent enzymatic inducers such as rifampicin, phenobarbital and phenytoin may via their action on UDP-glucuronyltransferases slightly decrease the plasma concentrations of

abacavir.

Ethanol:

The metabolism of abacavir is altered by concomitant ethanol resulting in an increase in AUC of abacavir of about 41 %. No dose reduction of abacavir is necessary. Abacavir has no effect on the metabolism of ethanol.

Methadone:

In a pharmacokinetic study, co-administration of 600 mg abacavir twice daily with methadone showed a 35 % reduction in abacavir C_{max} and a one hour delay in t_{max} but the AUC was unchanged. The changes in abacavir pharmacokinetics are not considered clinically relevant. In this study abacavir increased the mean methadone systemic clearance by 22 %. This change is not considered clinically relevant for the majority of patients, however occasionally methadone re-titration may be required.

Retinoids:

Retinoid compounds such as isotretinoin are eliminated via alcohol dehydrogenase. Interaction with **KAVIMUN PAED** is possible, but has not been studied.

PREGNANCY AND LACTATION:

Pregnancy:

KAVIMUN PAED is not recommended during pregnancy. The safety of abacavir in human pregnancy has not been established. Studies with abacavir in animals have shown reproductive toxicity.

It is recommended that HIV-infected women do not breast-feed their infants under any circumstances in order to avoid transmission of HIV. It is expected that abacavir will be

secreted into human milk, although this has not been confirmed. It is therefore recommended that mothers do not breast-feed their babies while receiving treatment with **KAVIMUN PAED.**

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. The main adverse reactions reported are haematological disorders (anaemia, neutropenia), metabolic disorders (hyperlactataemia, hyperlipidaemia). These reactions are often transitory. Some late-onset neurological disorders have been reported (hypertonia, convulsion, abnormal behaviour). Whether the neurological disorders are transient or permanent is currently unknown. Any child exposed *in utero* to nucleoside and nucleotide analogues, even HIV-negative children, should have clinical and laboratory follow-up and should be fully investigated for possible mitochondrial dysfunction in case of relevant signs or symptoms.

DOSAGE AND DIRECTIONS FOR USE:

KAVIMUN PAED should be prescribed by medical practitioners experienced in the management of HIV infection.

KAVIMUN PAED can be taken with or without food (see Pharmacokinetics).

KAVIMUN PAED tablets may be crushed and mixed with a small amount of water or food and ingested immediately.

Children from 3 months to 12 years: The recommended dose is 8 mg/kg twice daily

up to a maximum of 600 mg daily.

KAVIMUN PAED DOSAGE:

The recommended dose of **KAVIMUN PAED** tablets 60 mg based on body weight is as follows:

Child's weight	**Number of tablets**	
	60 mg	
	Morning	**Evening**
3 - 5,9kg	1	1
6 - 9,9kg	1,5*	1,5*
10 -13,9 kg	2	2
14 - 19,9kg	2,5**	2,5**
20 - 24,9 kg	3	3

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http://www.who.int/hiv/paediatric/Sum_ WHO ARV Ped_ARV dosing.pdf

Children less than three months: There are no data available on the use of **KAVIMUN PAED** in this age group.

Renal impairment: No dosage adjustment of **KAVIMUN PAED** is necessary in patients with mild to moderate renal dysfunction (see Pharmacokinetics).

Hepatic impairment: Abacavir is metabolised primarily by the liver. There are insufficient data to recommend the use of abacavir in patients with impairment of hepatic function.

SIDE-EFFECTS AND SPECIAL PRECAUTIONS:

Side-effects:

In clinical studies approximately 5 % of subjects receiving abacavir developed hypersensitivity reactions (see boxed **WARNING).**

Signs and symptoms of this hypersensitivity reaction:

The signs and symptoms of this hypersensitivity reaction are listed below. Those reported **in at least 10 % of patients** with a hypersensitivity reaction are in bold text.	
Skin	**Rash** (usually maculopapular or urticaria!)
Gastrointestinal tract	**Nausea, vomiting, diarrhoea, abdominal pain,** mouth ulceration
Respiratory tract	**Dyspnoea, cough**, sore throat, adult respiratory distress syndrome, respiratory failure
Miscellaneous	**Fever, lethargy, malaise,** oedema, lymphadenopathy, hypotension, conjunctivitis, anaphylaxis
Neurological/Psychiatry	**Headache,** paraesthesia
Haematological	Lymphopaenia
Liver/pancreas	**Elevated liver function tests,** hepatic failure
Musculoskeletal	**Myalgia,** rarely myolysis, arthralgia, elevated creatine phosphokinase
Urology	Elevated creatinine, renal failure

Each patient must be warned about this hypersensitivity reaction to abacavir.

The adverse reactions considered at least possibly related to **KAVIMUN PAED** are listed by body system, organ class and absolute frequency:

Body system	**KAVIMUN PAED**

Immune system disorders	*Frequent:* hypersensitivity
Metabolism and nutrition disorders	*Frequent:* anorexia, hyperlactataemia *Less frequent:* lactic acidosis, redistribution/accumulation of body fat
Nervous system disorders	*Frequent:* headache
Gastrointestinal disorders	*Frequent:* nausea, vomiting, diarrhoea *Less frequent:* pancreatitis (but a causal relationship to abacavir is uncertain)
Skin and subcutaneous tissue disorders	*Frequent:* rash (without systemic symptoms) *Less frequent:* erythema multiforme, Stevens-Johnson syndrome and toxic epidermal necrolysis
General disorders and administration site conditions	*Frequent:* fever, lethargy, fatigue

Special Precautions:

Before initiating treatment with **KAVIMUN PAED** screening for carriage of the HLAB* 5701 allele should be performed in any HIV-infected patient, irrespective of racial origin.

Screening is also recommended prior to re-initiation of **KAVIMUN PAED** in patients of unknown HLA-B*5701 status who have previously tolerated abacavir.

KAVIMUN PAED should not be used in patients known to carry the HLA-B*5701 allele, unless no other therapeutic option is available in these patients, based on the treatment history and resistance testing (see boxed **WARNING).**

Many of the adverse reactions listed under side-effects occur commonly (nausea, vomiting, diarrhoea, fever, lethargy, rash) in patients with abacavir hypersensitivity. Therefore, patients with any of these symptoms should be carefully evaluated for the presence of this hypersensitivity reaction. If **KAVIMUN PAED** has been discontinued in patients due to experiencing any one of these symptoms and a decision is made to restart a medicinal product containing abacavir, this must be done in a setting where medical assistance is readily available. Cases of erythema multiforme, Stevens-Johnson syndrome or toxic epidermal necrolysis have been reported where abacavir hypersensitivity could not be ruled out. In such cases medicinal products containing abacavir, as in **KAVIMUN PAED,** should be permanently discontinued.

Severe hepatomegaly with steatosis:

Particular caution should *be* exercised when administering **KAVIMUN PAED** to any patient with known risk factors for liver disease; however, cases have also been reported in patients with no known risk factors. Treatment with **KAVIMUN PAED** should be suspended in any patient who develops clinical or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity (which may include hepatomegaly and steatosis even in the absence of marked transaminase elevations).

Cases of lactic acidosis, sometimes fatal, usually associated with severe hepatomegaly and hepatic steatosis, have been reported with the use of nucleoside analogues, such as **KAVIMUN PAED.**

Immune Reactivation Syndrome:

In HIV-infected patients with severe immune deficiency at the time of institution of combination antiretroviral therapy (CART), an inflammatory reaction to asymptomatic or

residual opportunistic pathogens may arise and cause serious clinical conditions, or aggravation of symptoms. Typically, such reactions have been observed within the first few weeks or months of initiation of CART. Relevant examples are cytomegalovirus retinitis, generalised and/or focal mycobacterial infections, and *Pneumocystis jerovicii* pneumonia. Any inflammatory symptoms should be evaluated and treatment instituted when necessary.

Osteonecrosis:

Although the etiology is considered to be multifactorial (including corticosteroid use, alcohol consumption, severe immunosuppression, higher body mass index), cases of osteonecrosis have been reported particularly in patients with advanced HIV-disease and/or long-term exposure to combination antiretroviral therapy (CART). Patients should be advised to seek medical advice if they experience joint aches and pain, joint stiffness or difficulty in movement.

Lipodystrophy:

Combination antiretroviral therapy has been associated with redistribution of body fat (lipodystrophy) in HIV patients including the loss of peripheral and facial subcutaneous fat, increased intra-abdominal and visceral fat, breast hypertrophy and dorsocervical fat accumulation (buffalo hump).

Opportunistic infections:

Patients should be advised that **KAVIMUN PAED** or any other antiretroviral therapy does not cure HIV infection and that they may still develop opportunistic infections and other complications of HIV infection. Therefore patients should remain under close clinical observation by medical practitioners experienced in the treatment of these associated HIV diseases.

In HIV-infected patients with severe immune deficiency at the time of initiation of combination antiretroviral therapy, an inflammatory reaction to asymptomatic or residual opportunistic infections may arise.

Transmission of HIV:

Patients should be advised that current antiretroviral therapy, including **KAVIMUN PAED,** has not been proven to prevent the risk of transmission of HIV to others through sexual contact or blood contamination. Appropriate precautions should continue to be taken.

Myocardial infarction:

Observational studies have shown an association between myocardial infarction and the use of abacavir, such as in **KAVIMUN PAED.** Those studied were mainly antiretroviral experienced patients. Data from clinical trials showed limited numbers of myocardial infarction and could not exclude a small increase in risk. Overall the available data from observational cohorts and from randomised trials show some inconsistency so can neither confirm nor refute a causal relationship between abacavir treatment and the risk of myocardial infarction. To date, there is no established biological mechanism to explain a potential increase in risk. When prescribing **KAVIMUN PAED,** action should be taken to fry to minimise all modifiable risk factors (e.g. smoking, hypertension, and hyperlipidaemia).

Ability to drive and use machinery:

No studies on the effects on ability to drive and use machines have been performed. Nevertheless, the clinical status of the patient and the adverse reaction profile of should be borne in mind when considering the patient's ability to drive or operate machinery.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

No specific symptoms or signs have been identified following acute overdose with abacavir apart from those listed as side-effects.

If overdose occurs the patient should be monitored for evidence of toxicity, and standard supportive treatment applied as necessary. It is not known whether abacavir can be removed by peritoneal dialysis or haemodialysis.

IDENTIFICATION:

Peach coloured, round biconvex film-coated tablet, debossed with "M20" on one side and break line on the other side

PRESENTATION:

KAVIMUN PAED film-coated tablets are supplied as follows:

High Density Polyethylene (HDPE) bottle Pack (marketable pack) comprising of a white coloured HDPE bottle with white opaque polypropylene (PP) screw cap with induction sealing liner, packed in a carton with a package insert in a pack size of 60.

PVC/PVdC blister pack (marketable pack) comprises of clear, transparent, PVC film coated with PVdC on one side (i.e., PVC/PVdC) and hard tempered aluminium foil coated with VMCH heat seal lacquer on other side packed in a carton with a package insert in a pack size of 60.

STORAGE INSTRUCTIONS:

Store at or below 30 °C. Store in the original container. Protect from light.

Do not use if seal over bottle opening is broken or missing. Do not remove from carton until required for use. Keep the container tightly closed.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER:

46/20.2.8/0006

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

Viatris Healthcare (Pty) Ltd.

4 Brewery Street, Isando,

Gauteng, 1601

DATE OF PUBLICATION OF THE PACKAGE INSERT:

14 September 2012

Signature: Ansie Savrda-M535563 Digitally signed by Ansie Savrda-M535563 Date: 2022.08.31 18:16:41 +02'00'