1.3.2 PATIENT INFORMATION LEAFLET

SCHEDULING STATUS **S4**

PROPRIETARY NAME, STRENGTH AND PHARMACEUTICAL FORM

RIATEM (film-coated tablets)

Read all of this leaflet carefully before you start taking RIATEM.

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.

  RIATEM has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

WHAT RIATEM CONTAINS

The active substances are:

- Atazanavir sulphate equivalent to Atazanavir 300 mg
- Ritonavir 100 mg

The other ingredients are:

- Colloidal Silicone Dioxide
- Copovidone
- Crospovidone
- Lactose Monohydrate
- Magnesium Stearate
- Microcrystalline Cellulose
- Polysorbate 80
- Sodium Stearyl Fumarate
- Sorbitan Monolaurate.

The film-coating of **RIATEM** contains:

- Hypromellose
- Titanium dioxide (CI 77891)
- Macrogol/PEG
- Talc
- Iron oxide yellow (CI 77492)
- Polysorbate 80

RIATEM contains sugar: lactose monohydrate 164,36 mg

WHAT IS RIATEM IS USED FOR

RIATEM is used with other anti-HIV medicines (antiretroviral), to treat people that are infected with the human immuno-deficiency virus (**HIV**). HIV is the virus that causes acquired immune deficiency syndrome (**AIDS**).

RIATEM helps to block enzymes that are needed for the HIV virus to multiply.

RIATEM consists of two anti-HIV medicines used in combination (atazanavir and ritonavir) so that it is more effective against the HIV virus.

BEFORE YOU TAKE RIATEM

Do not take RIATEM:

- If you know you are allergic to, or have had an allergic reaction to atazanavir, ritonavir or to any of the ingredients contained in **RIATEM** (see **WHAT RIATEM CONTAINS**).
- If you have moderate to severe liver problems (see **Take Special care with RIATEM and How to take RIATEM**).
- If you are taking products which contain St. John's wort (*Hypericum perforatum) [herb used to treat mental disorders, anxiety etc]* (see **Take special care with RIATEM**)
- If you are old (over 70 years of age) since the safety has not been established.

- If you are pregnant or breastfeeding since the safety has not been established (see **Pregnancy and breast-feeding**).

Potential RIATEM interactions:

- Do **not** take **RIATEM** if you are taking the following medicines:

  Ergot medicines: dihydroergotamine, ergonovine, ergotamine, methylergonovine.

  Triazolam, midazolam, pimozide, or cisapride

  Serious life-threatening side-effects or death may happen
- Do **not** take the following medicines with **RIATEM** because of possible serious side-effects:

  Irinotecan, indinavir, lovastatin, simvastatin and atorvastatin (see **Take special care with RIATEM**), disopyramide, mexiletine, nefadozone or fluoxetine
- Do **not** take the following medicines with **RIATEM** because they may lower the amount of **RIATEM** in your blood:

  Rifampicin, St. John's wort *(Hypericum perforatum),* proton-pump inhibitors such as esomeprazole and tobacco, phenobarbital, carbamazepine, dexamethasone, phenytoin
- Do **not** take the following medicines if you are taking **RIATEM** (due to the ritonavir component):

  Voriconazole, ketoconazole, quinidine, astemizole, terfenadine, cisapride, bepridil.

  There exists a potential for serious and/or life-threatening adverse events.

Also DO NOT take RIATEM if you are taking medicines which contain the following (see **Taking other medicines with RIATEM**)**:**

- **Medicine used to treat tuberculosis** e.g., rifampicin
- **Medicines used to treat abnormal heart rhythms** e.g. digoxin, amiodarone, bepridil, flecainide, encainide, propafenone and quinidine
- **Medicines used to treat allergies or rashes**
- **Medicines used to treat migraine or used during childbirth/abortion to stop excessive bleeding** e.g., dihydroergotamine, ergometrine, ergotamine, ergonovine, methylergonovine
- **Medicines used to treat stomach problems** e.g., cisapride
- **Medicines used to treat mental disorders** e.g., pimozide

- **Medicines used to treat anxiety disorders and induce sleep** e.g. triazolam and midazolam
- **Medicines used to treat fungal infections** e.g. voriconazole
- **Medicines used to lower high cholesterol levels in the blood** e.g. lovastatin and simvastatin (see **Take Special care with RIATEM and Taking other medicines with RIATEM**).

The concomitant administration of **RIATEM** with the above medicines may produce large increases in your blood concentration of these medicines, and may cause severe or life-threatening diseases (e.g. abnormal heart rhythms, blood abnormalities, fits, circulation problems, increased sleepiness and abnormally slow and/or shallow breathing).
Always inform your doctor first if you are currently taking any of these medicines so that he can prescribe an alternative or more suitable medicine.

Take special care with RIATEM:

RIATEM:

- May be prescribed in combination with other antiretroviral medicines
- Is not a cure for HIV or AIDS
- You may still develop infections or other illnesses associated with HIV or AIDS so always tell your doctor if you are not feeling well
- It does not lower your risk of passing HIV to others
- Appropriate precautions should therefore be taken to prevent passing the disease through sexual contact (e.g. use of a condom) or blood contamination (you should not give blood or share needles)
- Your doctor should carry out blood tests and cholesterol tests before initiation of therapy or if he suspects any abnormality during therapy.

Tell your healthcare provider:

- If you have liver problems or are infected with the hepatitis B or C virus (see **Do not take RIATEM** and **HOW TO TAKE RIATEM**)
- If you have diabetes

- If you are feeling sick with nausea, vomiting or stomach pain as you may have an inflammation of the pancreas
- If you have any heart condition or abnormality in heart rhythms
- If you have haemophilia (clotting disorder)
- If you are lactose intolerant
- If you have or have had kidney stones (nephrolithiasis) or any renal disease
- If you have diarrhoea or vomiting which is not improving as it may reduce how well your medicine works
- If you experience joint aches and pain, joint stiffness or difficulty in movement. These are the signs for development of necrosis of the bones
- If your body fat increases or your fat accumulates on certain parts of your body, inform you healthcare provider
- If you develop blurred vision or blindness, painful swallowing, diarrhoea, numbness of the legs and general pain (cytomegalovirus infection)
- If you develop any other inflammatory conditions or infections with persistent cough, chest infections or muscle weakness
- If you develop any signs of jaundice (yellowing of the skin)
- If a rash develops or if you have difficulty breathing
- If you are taking any nasal sprays or inhalers with cortisone (medicine used to reduce inflammation of the airways as it may cause Cushing's syndrome (development of a rounded face)
- If you have erectile dysfunction and taking any medicine to improve libido (e.g. sildenafil, tadalafil or vardenafil as it may cause low blood pressure, visual changes and prolonged penile erection (see **Taking other medicines with RIATEM**)
- If you are taking any medicine containing St. John's Wort (may reduce plasma concentration of **RIATEM**) [see **Do not take RIATEM**]
- If you are taking medicines to lower high cholesterol levels in your blood e.g. simvastatin and lovastatin (see **Do not take RIATEM and Taking other medicines with RIATEM**).

Taking RIATEM with food and drink:

RIATEM should be taken with food (a meal or a substantial snack) as this helps the body absorb the medicine (see **How to take RIATEM**).

Pregnancy and Breast-feeding:

RIATEM:

- Should not be taken if you are pregnant or breast-feeding since the safety during pregnancy and breast-feeding has not been established (see **Do not take RIATEM**)
- It is not known if **RIATEM** can harm your unborn baby
- Therefore, if you think that you are pregnant or if you are planning a pregnancy, it is very important that you inform your doctor
- It is not known if **RIATEM** is secreted in breast-milk
- Therefore, you should not breast-feed your baby if you are HIV-positive because of the risk of passing the HIV virus to your baby and because your baby can experience serious side-effects with the use of this medicine

If you are pregnant or breast-feeding your baby please consult your healthcare provider for advice before taking this medicine.

Driving and using Machinery:

- **RIATEM** may make you feel drowsy/sleepy
- Do not drive because **RIATEM** could interfere with your ability to drive safely
- Do not operate any tools or machines

Important Information about some of the ingredients of RIATEM:

RIATEM contains lactose (milk sugar). Patients with the rare hereditary conditions of lactose/fructose or galactose intolerance should not take **RIATEM**. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking **RIATEM**.

RIATEM may have an effect on the control of your blood sugar if you have diabetes mellitus.

Taking other medicines with RIATEM:

Always tell your healthcare provider if you are taking any other medicine.

(This includes complementary or traditional medicines)

When other medicines are taken concomitantly with **RIATEM** (atazanavir in combination with ritonavir)**:**

- **RIATEM** may increase the blood concentration of the other medicine, which could increase or prolong both its therapeutic effects and adverse effects
- The other medicine may increase or decrease the blood concentration of **RIATEM**, thus prolonging or reducing its effect
- Always inform your doctor of any other medicine that you are taking so that he can monitor or adjust your dosage, or recommend alternative therapy
- **RIATEM** may increase the chance of serious side-effects when taken with:
  tadalafil, vardenafil, sildenafil (see **Take special care with RIATEM**), atorvastatin, amiodarone, digoxin, lidocaine, quinidine, bepridil, warfarin, amitriptyline, trimipramine, imipramine, cyclosporin, sirolimus, tacrolimus, trazadone and fluticasone propionate.
  Your healthcare provider will need to monitor your therapy more closely
- The following medicines may require a change in dose of either **RIATEM** or other medicines:
  Saquinavir, nelfinavir, efavirenz, zidovudine, didanosine, nevirapine, tenofovir, rifabutin, methadone, antacids or buffered medicines, fusidic acid, desipramine, delavirdine, buspirone, amprenavir, alprazolam, diltiazem, verapamil, felodipine, nifedipine, nicardipine, clarithromycin, nizatidine, cimetidine, ranitidine, and theophylline

- If you are taking an oral contraceptive ("the Pill") with **RIATEM**, be sure to take it exactly as instructed by your doctor and not miss any doses. However, when taking **RIATEM**, your doctor will prefer alternate methods of non-hormonal contraception
- If you are taking the following medicine concurrently, it does not need alteration of the dose: sulfamethoxazole/trimethoprim.

HOW TO TAKE RIATEM

Do not share medicines prescribed for you with any other person.

Always take RIATEM exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure.

The usual dose is:

RIATEM:

- Should be taken with food (with a meal or a snack) [see **Taking RIATEM with food and drink**]
- May be prescribed for adults who have never taken anti-HIV medicines before or for adult patients that may have responded poorly to prior anti-HIV medicines
- If you have not taken any previous anti-HIV medicine, it is recommended that **RIATEM** (300 mg atazanavir and 100 mg ritonavir) be taken with efavirenz 600 mg or tenofovir 300 mg
- This should be taken all once daily (see **Taking other medicines with RIATEM**)
- If you are taking antacids or didanosine chewable/dispersable buffered tablets, take **RIATEM** 2 hours before or 1 hour after these medicines.
- If you are taking medicines for indigestion or heartburn, take **RIATEM** 2 hours before or 1 hour after these medicines.
- If you are taking medicines for ulcers, talk to your healthcare provider.
- When your supply of **RIATEM** starts to run low, get more from your pharmacy. It is important not to run out of **RIATEM** as the amount of HIV in your blood may increase if the medicine is stopped for even a short time.

Dosage adjustments of RIATEM in Special Populations:

Kidney impairment:

No dosage adjustment of **RIATEM** is recommended if you have with kidney problems.

Liver impairment:

You should not use **RIATEM** if you have severe liver problems or moderate liver problems and you should use **RIATEM** with caution if you have mild liver problems (see **Do not take RIATEM and Take Special care with RIATEM**).

Your doctor will tell you how long your treatment with RIATEM will last. Do not stop treatment early because the amount of HIV in your blood may increase.

If you have the impression that the effect of RIATEM is too strong or too weak, talk to your doctor or pharmacist.

If you take more RIATEM than you should:

Signs and symptoms of overdose include:

- Yellowing of the skin and eyes
- Changes in heart rhythm
- Changes in kidney function
- Numbness, tingling or a “pins and needles” sensation.

Treatment of overdose with RIATEM:

- Your symptoms will be treated
- Your vital signs will be monitored and you will be medically supported if necessary (e.g. oxygen)
- You may be given activated charcoal to get rid of any unabsorbed medicine.

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison control centre.

If you forget to take RIATEM or missed a dose of RIATEM:

- If you miss a dose of **RIATEM**, take it as soon as possible and then take your next scheduled dose at its regular time
- If however, it is within 6 hours of your next dose, do not take the missed dose
- Wait and take the next dose at the regular time.
- Do **not** take a double dose to make up for a forgotten dose.
- It is important that you do not miss any dose of **RIATEM** or any of your other anti-HIV medicines.

Effects when treatment with RIATEM is stopped:

Even if you feel better, do not stop taking **RIATEM** without talking to your doctor first, as the amount of HIV in your blood may increase.

Taking **RIATEM** as recommended should give you the best chance of delaying resistance to the medicine.

POSSIBLE SIDE EFFECTS

RIATEM can have side-effects.

Not all side-effects reported for RIATEM are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking RIATEM, please consult your healthcare provider for advice.

RIATEM may cause the following side-effects:

If any of the following happens, stop taking RIATEM and tell your doctor immediately or go to the casualty department at your nearest hospital:

Frequent:

- Yellowing of the skin or eyes. These may occur due to increases in bilirubin levels in the blood. Please inform your healthcare provider if your skin or the white part of your eyes turn yellow.

Less Frequent:

- Any allergic reaction which causes swelling of the hands, feet, face, skin or other tissues and which may cause difficulty in swallowing or breathing
- A change in the way your heart beats. If you experience dizziness, light-headedness, or fainting spells, these could be symptoms of a heart problem.
- Difficulty with breathing
- If you think you may have any liver problems (e.g. enlargement of liver and spleen).
- If you have liver disease including hepatitis B or C, as your liver disease may worsen when you take anti-HIV medicines like **RIATEM**.
- Some patients with haemophilia (inability of the blood to clot) have increased bleeding problems when taking protease inhibitors like **RIATEM**.

Frequency unknown:

- Heart attack

These are very serious side-effects of RIATEM. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately if you notice any of the following or go to the nearest casualty department:

Less Frequent:

- Increase in blood pressure, swelling of the body
- Painful muscles, breakdown of muscle tissue, painful joints, severe weakness and wasting of body
- Kidney problems like blood and or proteins in the urine, kidney pain, kidney stones, increase in frequency of urination or excess sugar in the urine, infection
- High blood sugar levels
- Bleeding or bruising of the skin

These are all serious side-effects of RIATEM. You may need urgent medical attention.

Tell your doctor if you notice any of the following:

Frequent:

- Unusual tiredness or weakness
- Changes in body fat or redistribution of body fat. This may result in an increased amount of fat in the upper back and neck, breast and around the trunk. Loss of fat from the legs, arms and face may occur. The cause and long-term health effects of these conditions are not known.
- Other common side-effects of **RIATEM** taken with other anti-HIV medicines include nausea, headache, abdominal pain, vomiting, bloatedness or heartburn, diarrhoea (running stomach), excess stomach winds or any stomach problems, problems with taste and mouth ulcers, dizziness, inability to sleep, numbness, tingling, pins and needles or burning of hands or feet, muscle pain, skin rashes, sore throat, runny nose, lack of appetite and weight loss, increased cough, hiccup or nose bleeds, increased cholesterol levels, anxiety, lack of energy, pain or fever, low blood pressure.

Less Frequent:

- Rashes (redness and itching) sometimes occur in patients taking **RIATEM**. This occurs most often in the first few weeks after starting the medicine. Rashes usually go away within 2 weeks with no change in treatment. Tell your healthcare provider if the rash occurs.
- Abnormal dreams, loss of memory, confusion, unable to walk normally
- Dry mouth, stomach inflammation, excess wind, inflammation of the pancreas, swelling of the stomach, impairment of the sense of taste and recurrent mouth ulcers
- Hair loss, itching and rash of the skin
- Chest pain, fever and lack of feeling well
- Lack of appetite, increase in appetite, decrease or increase in weight
- Mood disorders (e.g. depression, anxiety etc.) and sleep disorders (e.g. trouble sleeping or sleeping too much
- Breast enlargement.

- If you think you may be anaemic (decreased iron in the blood stream) or have a deficiency of vitamins
- If you persistently get sick (as you may have decreased white blood cells in the body to fight infection or other blood problems)
- If you have swollen glands, flu-like symptoms, chest pain etc
- If you are swollen or think you may be dehydrated
- If your blood sugar is high or if your diabetes is not being controlled
- If you experience any stomach problems, constipation, bloody diarrhoea etc.
- If you get inflammation in the mouth or gums and difficulty swallowing
- If you get symptoms of gout (inflammation and painful joints)
- If you experience fits, nerve pain or tremors
- If you experience any eye problems
- If you experience any ear problems (e.g. ringing in the ears, loss of balance etc.)
- If you get low blood pressure when you stand up
- If your skin becomes sensitive to the sun, or you get eczema and any other skin disorders
- If you get cramps in the muscles, breakdown of muscle tissue, painful joints
- If you experience decreased libido or problems with the penis
- If you are troubled by an abnormally low body temperature

Frequency unknown:

- Dehydration leading to low blood pressure, fainting or kidney problems
- Abnormally heavy bleeding at menstruation.

So that he may treat your symptoms accordingly.

If you notice any side-effects of **RIATEM** not mentioned in this leaflet, please inform your doctor or pharmacist.

STORING AND DISPOSING OF RIATEM

- Store at or below 30 °C
- Protect from moisture
- Do **not** store this medicine in a damp place such as a bathroom medicine cabinet or near the kitchen sink
- Keep your medicine in a tightly closed container
- KEEP OUT OF REACH OF CHILDREN.
- Return all unused medicine to your pharmacist
- Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

PRESENTATION OF RIATEM

RIATEM:

Pack size 28's and 30's: Tablets are packed in a 120-cc white opaque HDPE container sealed with a 38 mm white opaque child-resistant closure with an induction seal and two silica gel pouches inside the container. The HDPE container is packed in an outer carton.

Pack size 84's and 90's: Tablets are packed in a 250-cc white opaque HDPE container sealed with 53 mm white opaque closure with an induction seal and two silica gel pouches inside the container. The HDPE container is packed in an outer carton.

Pack size 168's and 180's: Tablets are packed in a 500-cc white opaque HDPE container sealed with 53 mm white opaque closure with an induction seal and two silica gel pouches inside the container. The HDPE container is packed in an outer carton.

Not all pack sizes may be marketed.

IDENTIFICATION OF RIATEM

RIATEM:

Creamish yellow coloured, modified film-coated tablet debossed with “EM” on one side and “149” on the other side.

REGISTRATION NUMBER/REFERENCE NUMBER

48/20.2.8/1248

NAME, BUSINESS ADDRESS AND TELEPHONE NUMBER OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

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