ANNEX III

LABELLING AND PACKAGE LEAFLET
A. LABELLING
OUTER CARTON

Ziagen 300 mg film coated tablets
Abacavir

Each film-coated tablet contains abacavir 300 mg as abacavir sulfate

60 film-coated tablets

READ ENCLOSED LEAFLET BEFORE USE

For oral use

Keep all medicines out of the reach and sight of children.

Do not store above 30°C

EU/1/99/112/001

Glaxo Group Ltd
Greenford
Middlesex UB6 0NN
United Kingdom

Medicinal product subject to medical prescription.

LOT
EXP

Detach enclosed Alert Card, it contains important safety information

WARNING! In case of any symptoms suggesting hypersensitivity reactions, contact your doctor IMMEDIATELY.

“Pull here” (with Alert card attached)
Patients taking Ziagen may develop a hypersensitivity reaction (serious allergic reaction) which can be life threatening if treatment with Ziagen is continued. If you have symptoms from TWO OR MORE of the following groups:

1) fever
2) skin rash (redness and/or itching)
3) nausea or vomiting or diarrhoea or abdominal pain
4) severe tiredness or achiness or generally ill feeling

CALL YOUR DOCTOR IMMEDIATELY who will advise you whether you should stop taking Ziagen. If you have discontinued Ziagen due to this reaction, YOU MUST NEVER TAKE Ziagen again as within hours you may experience a life-threatening lowering of your blood pressure or death.

(see reverse of card)

SIDE 2

You should immediately contact your Doctor if you think you are having a hypersensitivity reaction to Ziagen. Write your Doctors details below:

Doctor: ................................................................. Tel: ..................................................

If your Doctor is not available, you must urgently seek alternative medical advice (e.g. the emergency unit of the nearest hospital).

For general Ziagen information enquiries, contact Glaxo Wellcome UK Ltd on +44 (0)208 990 9000

BLISTER FOIL

Glaxo Group Ltd
Ziagen 300 mg
Abacavir
LOT
EXP
OUTER CARTON

Ziagen 20 mg/ml oral solution
Abacavir

Bottle contents:
240 ml oral solution containing 20 mg/ml abacavir as abacavir sulfate
This product contains 340 mg/ml of sorbitol, propylene glycol, banana and strawberry
flavour.

READ ENCLOSED LEAFLET BEFORE USE

For oral use

Keep all medicines out of the reach and sight of children.

Do not store above 30°C

Discard two months after first opening

EU/1/99/112/002

Glaxo Group Ltd
Greenford
Middlesex UB6 0NN
United Kingdom

Medicinal product subject to medical prescription.

LOT
EXP

Detach enclosed Alert Card, it contains important safety information

WARNING! In case of any symptoms suggesting hypersensitivity reactions, contact your
doctor IMMEDIATELY.

“Pull here” (with Alert card attached)
ALERT CARD TEXT

SIDE 1

IMPORTANT - ALERT CARD
ZIAGEN (abacavir sulfate) Oral solution
Carry this card with you at all times

Patients taking Ziagen may develop a hypersensitivity reaction (serious allergic reaction) which can be life threatening if treatment with Ziagen is continued. If you have symptoms from TWO OR MORE of the following groups:
1) fever
2) skin rash (redness and/or itching)
3) nausea or vomiting or diarrhoea or abdominal pain
4) severe tiredness or achingness or generally ill feeling

CALL YOUR DOCTOR IMMEDIATELY who will advise you whether you should stop taking Ziagen. If you have discontinued Ziagen due to this reaction, YOU MUST NEVER TAKE Ziagen again as within hours you may experience a life-threatening lowering of your blood pressure or death.

(see reverse of card)

SIDE 2

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Doctor: ...................................................... Tel: ..............................................

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For general Ziagen information enquiries, contact Glaxo Wellcome UK Ltd on +44 (0)208 990 9000

BOTTLE LABEL

Ziagen 20 mg/ml oral solution
Abacavir
Contents: 240 ml oral solution containing 20 mg/ml abacavir as abacavir sulfate

This product contains 340 mg/ml of sorbitol, propylene glycol, banana and strawberry flavour.

For oral use

Keep all medicines out of the reach and sight of children.

Do not store above 30° C

Discard two months after first opening

EU/1/99/112/002

Glaxo Group Ltd
Greenford
Middlesex UB6 0NN
United Kingdom

Medicinal product subject to medical prescription.

LOT
EXP
B. PACKAGE LEAFLET
This leaflet contains important information about your treatment with Ziagen. Please read it carefully before you start to take your medicine. It does not tell you everything about your medicine. If you have any questions or are not sure about something then ask your doctor or pharmacist. You may need to read this leaflet again. Please do not throw it away until you have finished treatment with Ziagen.

### HYPERSENSITIVITY REACTION

Patients taking Ziagen may develop a hypersensitivity reaction (serious allergic reaction) which can be life threatening if treatment with Ziagen is continued. It is essential you read the information on this reaction in the Special Warnings section of this leaflet. There is also an alert card included in the Ziagen pack, to remind you and medical staff about Ziagen hypersensitivity. This card should be removed and kept with you at all times.

If you have symptoms from two or more of the following groups: 1) fever, 2) skin rash (redness and/or itching), 3) nausea or vomiting or diarrhoea or abdominal pain, 4) severe tiredness or achiness or generally ill feeling call your doctor IMMEDIATELY WHO WILL ADVISE YOU WHETHER YOU SHOULD STOP TAKING ZIAGEN.

If you have had this reaction to Ziagen, NEVER take Ziagen again as WITHIN HOURS you may experience a life-threatening lowering of your blood pressure or death.

### Name of the medicinal product

Ziagen 300 mg film-coated tablets

### Composition

Each Ziagen film-coated tablet contains 300 mg of the active ingredient abacavir (as abacavir sulfate).

The tablet core contains microcrystalline cellulose, sodium starch glycollate, magnesium stearate, colloidal anhydrous silica. The tablet coating contains triacetin, methylhydroxypropylcellulose, titanium dioxide, polysorbate 80, iron oxide yellow

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Marketing authorisation holder</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glaxo Wellcome Operations</td>
<td>Glaxo Group Ltd</td>
</tr>
<tr>
<td>Priory Street</td>
<td>Greenford</td>
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<td>Ware</td>
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Pharmaceutical form and contents

The film-coated, capsule shaped tablets are yellow and engraved with ‘GX 623’ on one side. They are provided in blister packs containing 60 tablets.

Pharmaco-therapeutic group

Ziagen belongs to a group of antiviral medicines, also known as antiretrovirals, called nucleoside analogue reverse transcriptase inhibitors (NRTIs). These are used to treat Human Immunodeficiency Virus (HIV) infection.
Therapeutic indications

Ziagen is used in combination with other antiretroviral medicines for the treatment of HIV infection in adults.

What Ziagen does

Ziagen in combination with other antiretrovirals reduces HIV viral load, and keeps it at a low level. It also increases CD4 cell counts. CD4 cells play an important role in maintaining a healthy immune system to help fight infection. Response to treatment with Ziagen varies between patients. Your doctor will be monitoring the effectiveness of your treatment.

Important information you should know before taking Ziagen

When should Ziagen NOT be taken (contraindications)?

This medicine must not be taken if you are allergic to the active substance abacavir or any of the other ingredients found in Ziagen, or if you have serious liver disease. If you are not sure please consult your doctor.

Special warnings and precautions for use

Hypersensitivity reaction (serious allergic reaction): About 3 in every 100 patients, who are treated with Ziagen, develop a hypersensitivity reaction to the active ingredient abacavir. Frequently observed signs or symptoms include high temperature, skin rash, nausea, vomiting, diarrhoea, abdominal pain and severe tiredness. Other symptoms may include joint or muscle pain, swelling of the neck, shortness of breath, headache. Occasionally inflammation of the eye (conjunctivitis), ulcers in the mouth or low blood pressure may occur. The symptoms of this allergic reaction usually occur in the first six weeks of treatment with Ziagen, and get worse with continued treatment.

If you have symptoms from two or more of the following groups: 1) fever, 2) skin rash (redness and/or itching), 3) nausea or vomiting or diarrhoea or abdominal pain, 4) severe tiredness or achiness or generally ill feeling call your doctor IMMEDIATELY WHO WILL ADVISE YOU WHETHER YOU SHOULD STOP TAKING ZIAGEN.

If you have had this serious reaction to Ziagen, NEVER take Ziagen again as within hours you may experience a life-threatening lowering of your blood pressure or death.

If you are hypersensitive to Ziagen you should return all of your unused Ziagen to your doctor or pharmacist for proper disposal.

The class of medicines to which Ziagen belongs (NRTIs) can cause a condition called lactic acidosis, together with an enlarged liver. This rare but serious side effect occurs more often in women, particularly if very overweight.

You should not take Ziagen if you have moderate liver disease. Discuss this with your doctor if you are unsure.

Ziagen helps to control your condition but is not a cure for HIV infection. You will need to take it every day. Do not interrupt your medication without first talking to your doctor. If,
however, a hypersensitivity reaction occurs (see above) call your doctor immediately who will advise you whether you should stop taking Ziagen.

Treatment with Ziagen has not been shown to reduce the risk of passing HIV infection on to others by sexual contact or by blood transfer. You should continue to use appropriate precautions to prevent this.

You may continue to develop other infections and other illnesses associated with HIV disease. You should therefore keep in regular contact with your doctor while taking Ziagen.

**Pregnancy and breast feeding:**

If you are pregnant, or planning to become pregnant soon, or if you are breast feeding, you must inform your doctor before taking any medicines. The safe use of Ziagen in human pregnancy has not been established. Therefore, Ziagen should not be taken, if you are pregnant.

The active substance abacavir in this medicine is likely to be found in human breast milk. There are no safety data available following treatment with Ziagen in babies under three months of age. You are therefore recommended not to breast feed your baby while taking Ziagen. Additionally, it is recommend that HIV infected women do not breast-feed their infants under any circumstances in order to avoid transmission of HIV.

**Interaction with other medicinal products and other forms of interaction**

Ziagen is unlikely to significantly interact with other medicines you are being treated with, however, it is important that you tell your doctor about all the medicines you are taking or have recently taken, including those you have bought yourself. Alcohol does increase the amount of abacavir in your blood. However this is not considered to be of a safety concern. If you are taking oral vitamin A related medicines, e.g. isotretinoin, you should inform your doctor, since these may also increase the amount of abacavir in your blood.

**Driving and using machines:**

No studies on the effects of Ziagen on the ability to drive and use machines have been performed.

**Dosage and instructions for proper use**

Take Ziagen as your doctor has advised you. If you are unsure about how to take it, ask your doctor or pharmacist.

The usual dose in adults is 300 mg (one tablet) twice a day.

Ziagen is not recommended for use in children.

An oral solution (20 mg abacavir/ml) is available for the treatment of patients unable to take tablets.

Ziagen can be taken with or without food.

**Action to be taken in case of missed dose**
If you forget to take your medicine, take it as soon as you remember, and then continue as before. Do not take a double dose to make up for forgotten individual doses. It is important to take Ziagen regularly because irregular intake increases the risk of hypersensitivity reactions.

**Action to be taken in case of overdose**

Accidentally taking too much of your medicine is unlikely to cause any serious problems. However, you should tell your doctor or your pharmacist, or contact your nearest hospital emergency department for further advice.
**Undesirable effects**

All medicines may cause some side effects. When treating HIV infection it is not always possible to tell whether any undesirable effects that occur are caused by Ziagen, by other medicines you are taking at the same time or by the HIV disease.

The following side effects are thought to be related to treatment with Ziagen: nausea, vomiting, lethargy and fatigue. Other side effects that have been seen are loss of appetite, fever, headache and diarrhoea. In general, most of these have only lasted a short time, been mild or moderate in severity and got better without stopping treatment with Ziagen.

*A hypersensitivity reaction (serious allergic reaction) has been reported in about three in every hundred patients who have been treated with Ziagen. This is described in section “Special warnings” of this leaflet. It is important that you read and understand the information about this serious reaction.*

Always tell your doctor or pharmacist about any new symptoms, even those not mentioned in this leaflet. If you feel ill in any other way that you do not understand, tell your doctor or pharmacist.

**How to store Ziagen**

Do not store above 30°C

Do not take the medicine after the expiry date shown on the tablet pack.

As with all medicines, keep Ziagen out of the reach and sight of children.

**DATE OF LEAFLET REVISION**

**Remember**

This medicine is for you. Never give it to someone else, it may harm them even if their symptoms are the same as yours.
For any information about this product, please contact the local representative of the Marketing Authorisation Holder:
Belgique/België/Belgien
Glaxo Wellcome S.A./N.V
B-1160 Bruxelles/Brussel
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Tlf: + 45 36 35 91 00

Deutschland
Glaxo Wellcome GmbH & Co.
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D-23843 Bad Oldesloe
Tel: + 49 (0)40 415 230

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United Kingdom
Glaxo Wellcome UK Ltd
Stockley Park West
Uxbridge
Middlesex UB11 1BT-UK
Tel: +44 (0)208 990 9000
This leaflet contains important information about your treatment with Ziagen. Please read it carefully before you start to take your medicine. It does not tell you everything about your medicine. If you have any questions or are not sure about something then ask your doctor or pharmacist. You may need to read this leaflet again. Please do not throw it away until you have finished treatment with Ziagen.

**HYPERSENSITIVITY REACTION**

Patients taking Ziagen may develop a hypersensitivity reaction (serious allergic reaction) which can be life threatening if treatment with Ziagen is continued. It is essential you read the information on this reaction in the Special Warnings section of this leaflet. There is also an alert card included in the Ziagen pack, to remind you and medical staff about Ziagen hypersensitivity. This card should be removed and kept with you at all times.

If you have symptoms from two or more of the following groups: 1) fever, 2) skin rash (redness and/or itching), 3) nausea or vomiting or diarrhoea or abdominal pain, 4) severe tiredness or achiness or generally ill feeling call your doctor IMMEDIATELY WHO WILL ADVISE YOU WHETHER YOU SHOULD STOP TAKING ZIAGEN.

If you have had this reaction to Ziagen, NEVER take Ziagen again as WITHIN HOURS you may experience a life-threatening lowering of your blood pressure or death.

**Name of the medicinal product**

Ziagen 20 mg/ml oral solution

**Composition**

The solution is clear to yellowish in colour with strawberry/banana flavouring. It contains 20 mg of the active ingredient abacavir (as abacavir sulfate) in each ml of the solution. Other ingredients: Sorbitol 70%, saccharin sodium, sodium citrate, citric acid anhydrous, methyl parahydroxybenzoate (E218), propyl parahydroxybenzoate (E216), propylene glycol, maltodextrin, lactic acid, glyceryl triacetate, natural and artificial strawberry and banana flavour, purified water.

**Manufacturer**

Glaxo Wellcome Operations, Speke Boulevard, Speke, Liverpool L24 9JD, United Kingdom

**Marketing authorisation holder**

Glaxo Group Ltd, Greenford, Middlesex UB6 0NN, United Kingdom
**Pharmaceutical form and contents**

Ziagen Oral Solution is supplied in cartons containing a white polyethylene bottle, with a child resistant cap. The bottle contains 240 ml (20 mg abacavir/ml) of solution. A 10 ml oral dosing syringe and a plastic adapter for the bottle is included in the pack.
Pharmaco-therapeutic group

Ziagen belongs to a group of antiviral medicines, also known as antiretrovirals, called nucleoside analogue reverse transcriptase inhibitors (NRTIs). These are used to treat Human Immunodeficiency Virus (HIV) infection.

Therapeutic indications

Ziagen is used in combination with other antiretroviral medicines for the treatment of HIV infection in adults.

What Ziagen does

Ziagen in combination with other antiretrovirals reduces HIV viral load, and keeps it at a low level. It also increases CD4 cell counts. CD4 cells play an important role in maintaining a healthy immune system to help fight infection. Response to treatment with Ziagen varies between patients. Your doctor will be monitoring the effectiveness of your treatment.

Important information you should know before taking Ziagen

When should Ziagen NOT be taken (contraindications)?

This medicine must not be taken if you are allergic to the active substance abacavir or any of the other ingredients found in Ziagen, or if you have serious liver disease. If you are not sure please consult your doctor.

Special warnings and precautions for use

This medicine contains the sweetener sorbitol (approximately 5 g in each 15 ml dose), which occasionally may cause stomach pain and diarrhoea. Medicines containing sorbitol should not be taken if you have hereditary fructose intolerance.

Hypersensitivity reaction (serious allergic reaction): About 3 in every 100 patients, who are treated with Ziagen, develop a hypersensitivity reaction to the active ingredient abacavir. Frequently observed signs or symptoms include high temperature, skin rash, nausea, vomiting, diarrhoea, abdominal pain and severe tiredness. Other symptoms may include joint or muscle pain, swelling of the neck, shortness of breath, headache. Occasionally inflammation of the eye (conjunctivitis), ulcers in the mouth or low blood pressure may occur. The symptoms of this allergic reaction usually occur in the first six weeks of treatment with Ziagen, and get worse with continued treatment.

If you have symptoms from two or more of the following groups: 1) fever, 2) skin rash (redness and/or itching), 3) nausea or vomiting or diarrhoea or abdominal pain, 4) severe tiredness or achiness or generally ill feeling call your doctor IMMEDIATELY WHO WILL ADVISE YOU WHETHER YOU SHOULD STOP TAKING ZIAGEN.

If you have had this serious reaction to Ziagen, NEVER take Ziagen again as within hours you may experience a life-threatening lowering of your blood pressure or death.

If you are hypersensitive to Ziagen you should return all of your unused Ziagen to your doctor or pharmacist for proper disposal.
The class of medicines to which Ziagen belongs (NRTIs) can cause a condition called lactic acidosis, together with an enlarged liver. This rare but serious side effect occurs more often in women, particularly if very overweight.

You should not take Ziagen if you have moderate liver disease. Discuss this with your doctor if you are unsure. Ziagen helps to control your condition but is not a cure for HIV infection. You will need to take it every day. Do not interrupt your medication without first talking to your doctor. If, however, a hypersensitivity reaction occurs (see above) call your doctor immediately who will advise you whether you should stop taking Ziagen.

Treatment with Ziagen has not been shown to reduce the risk of passing HIV infection on to others by sexual contact or by blood transfer. You should continue to use appropriate precautions to prevent this.

You may continue to develop other infections and other illnesses associated with HIV disease. You should therefore keep in regular contact with your doctor while taking Ziagen.

**Pregnancy and breast feeding:**

If you are pregnant, or planning to become pregnant soon, or if you are breast feeding, you must inform your doctor before taking any medicines. The safe use of Ziagen in human pregnancy has not been established. Therefore, Ziagen should not be taken, if you are pregnant.

The active substance abacavir in this medicine is likely to be found in human breast milk. There are no safety data available following treatment with Ziagen in babies under three months of age. You are therefore recommended not to breast feed your baby while taking Ziagen. Additionally, it is recommend that HIV infected women do not breast-feed their infants under any circumstances in order to avoid transmission of HIV.

**Interaction with other medicinal products and other forms of interaction**

Ziagen is unlikely to significantly interact with other medicines you are being treated with, however, it is important that you tell your doctor about all the medicines you are taking or have recently taken, including those you have bought yourself. Alcohol does increase the amount of abacavir in your blood. However this is not considered to be of a safety concern. If you are taking oral vitamin A related medicines, e.g. isotretinoin, you should inform your doctor, since these may also increase the amount of abacavir in your blood.

**Driving and using machines:**

No studies on the effects of Ziagen on the ability to drive and use machines have been performed.

**Dosage and instructions for proper use**

Take Ziagen as your doctor has advised you. If you are unsure about how to take it, ask your doctor or pharmacist.

The usual dose in adults is 15 ml (300 mg abacavir) twice a day.
Ziagen is not recommended for use in children.

Use the oral dosing syringe supplied with the pack to measure your dose accurately.

1. Remove the bottle cap.
2. Push the plastic adapter into the neck of the bottle, while holding the bottle firmly.
3. Insert the syringe firmly into the adapter.
4. Turn bottle upside down
5. Pull out syringe plunger until the correct amount is withdrawn.
6. Turn the bottle the correct way up and remove the syringe from the adapter.
7. Replace and tighten the bottle cap.
8. Administer the dose into the mouth by placing the tip of the syringe against the inside of the cheek. Slowly depress the plunger, allowing time to swallow. Forceful squirting to the back of the throat may cause choking.

After use the syringe must not be left in the bottle and should be washed thoroughly in clean water.

Ziagen can be taken with or without food.

**Action to be taken in case of missed dose**

If you forget to take your medicine, take it as soon as you remember, and then continue as before. Do not take a double dose to make up for forgotten individual doses. It is important to take Ziagen regularly because irregular intake increases the risk of hypersensitivity reactions.

**Action to be taken in case of overdose**

Accidentally taking too much of your medicine is unlikely to cause any serious problems. However, you should tell your doctor or your pharmacist, or contact your nearest hospital emergency department for further advice.

**Undesirable effects**

All medicines may cause some side effects. When treating HIV infection it is not always possible to tell whether any undesirable effects that occur are caused by Ziagen, by other medicines you are taking at the same time or by the HIV disease.

The following side effects are thought to be related to treatment with Ziagen: nausea, vomiting, lethargy and fatigue. Other side effects that have been seen are loss of appetite, fever, headache and diarrhoea. In general, most of these have only lasted a short time, been mild or moderate in severity and got better without stopping treatment with Ziagen.

A hypersensitivity reaction (serious allergic reaction) has been reported in about three in every hundred patients who have been treated with Ziagen. This is described in section “Special warnings” of this leaflet. It is important that you read and understand the information about this serious reaction.

Always tell your doctor or pharmacist about any new symptoms, even those not mentioned in this leaflet. If you feel ill in any other way that you do not understand, tell your doctor or pharmacist.

**How to store Ziagen**
Do not store above 30°C

Discard oral solution two months after first opening.

Do not take the medicine after the expiry date shown on the bottle.

As with all medicines, keep Ziagen out of the reach and sight of children.

DATE OF LEAFLET REVISION

Remember

This medicine is for you. Never give it to someone else, it may harm them even if their symptoms are the same as yours.
For any information about this product, please contact the local representative of the Marketing Authorisation Holder: