ANNEX

ANNEX III
LABELLING AND PACKAGE LEAFLET
B. PACKAGE LEAFLET
This leaflet contains important information about VISTIDE. If you want to know more information about your illness or your medication, ask your doctor or pharmacist.

The name of your medication is:
VISTIDE, cidofovir, equivalent to 75 mg/mL anhydrous cidofovir, concentrate for solution for intravenous infusion.

What does VISTIDE contain?
VISTIDE is supplied as a sterile solution in clear, glass vials containing 375 mg of the active ingredient, anhydrous cidofovir, in 5 mL formulated in Water for Injection at a concentration of 75 mg/mL. The formulation is pH-adjusted with sodium hydroxide (and hydrochloric acid, if needed) and contains no preservatives.

How does VISTIDE work?
VISTIDE is an antiviral medication which blocks the replication of cytomegalovirus (CMV) by interfering with viral DNA production.

Who is the marketing authorisation holder?
The product marketing authorisation is held by:

Gilead Sciences Limited, UK
Springfield House, Hyde Street, Leeds
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The Manufacturer responsible for batch release in the European Economic Area is:
Pharmacia & Upjohn N.V./S.A.
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What is this medicine used for?
VISTIDE is indicated in the treatment of CMV retinitis in patients with Acquired Immunodeficiency Syndrome (AIDS). VISTIDE will not cure your CMV retinitis but may improve your condition by delaying progression of the disease.

VISTIDE is for intravenous (into a vein) infusion and is not for intraocular injection (direct injection into the eye).

What is CMV retinitis?
CMV retinitis is an eye infection caused by a virus named cytomegalovirus (CMV). CMV attacks the retina of the eye and may cause loss of vision, and eventually lead to blindness. Patients with acquired immunodeficiency syndrome (AIDS) are at high risk of developing CMV retinitis or other forms of CMV disease such as colitis. Treatment for CMV retinitis is necessary to reduce the potential for blindness.

Things to consider prior to using VISTIDE
Your doctor will discuss with you the possible benefits and risks of VISTIDE therapy. However, you should note the following:

Reasons for not giving VISTIDE:

• VISTIDE should not be given to you if you have pre-existing kidney disease.

• VISTIDE should not be given to you if you are allergic to this drug, or if you cannot take the medication probenecid because of a serious allergy to probenecid or other sulfa-containing medications (e.g., sulfamethoxazole).

• You should not be given VISTIDE if you are pregnant. If you become pregnant while taking this medication, you must inform your doctor immediately. VISTIDE has been shown to cause damage in unborn animals and should not be used during pregnancy unless the potential benefits justify the risks to the foetus. Women of childbearing potential should use birth control methods during and for 1 month following treatment with VISTIDE.

• You should not be given VISTIDE if you are breast feeding. It is not known whether VISTIDE is excreted in human milk. Because many drugs are excreted in human milk, nursing mothers should discontinue VISTIDE or stop nursing if they continue to receive VISTIDE.

What you should know prior to using VISTIDE:

• Kidney damage is the major side effect of VISTIDE treatment. To minimise the potential for damage to the kidneys, you will receive intravenous fluids (normal saline) and probenecid tablets with each dose of VISTIDE. Your doctor may also instruct you to drink plenty of fluids. Your doctor will monitor your kidney function prior to each dose of VISTIDE. Your treatment with VISTIDE may be discontinued by your doctor if changes in kidney function occur.

A list of the most common side effects is provided below in section “What are the possible side effects of therapy?”

• Tell your doctor if you have diabetes mellitus. VISTIDE should be used with caution in diabetic patients due to the potential increased risk of developing ocular hypotony (low pressure in the eye).

• VISTIDE may cause transient side effects such as fatigue or weakness. If you drive or operate machinery, discuss this with your doctor to get their recommendation about discontinuing these activities based upon the condition of your disease and your tolerance of the medication.

• VISTIDE caused reduced testes weight and hypospermia (low sperm count) in animals. Although not observed in human studies of VISTIDE, such changes may occur in humans and cause infertility. Men should practice barrier birth control methods during and for 3 months after treatment with VISTIDE.

What to do if you are taking other medications
• Tell your doctor about all medications you currently take. Probenecid may interact with other drugs commonly used in the treatment of AIDS and AIDS-related illnesses, such as zidovudine (AZT). If you are taking zidovudine, you should discuss with your doctor the option to either temporarily discontinue zidovudine or decrease the dose of zidovudine by 50% on days when VISTIDE and probenecid are administered.

• You may continue taking antiretrovirals (anti-HIV medications) and medication to prevent AIDS-related opportunistic infections. However, because the side effects of VISTIDE include kidney damage, it will be necessary to stop taking all other medications that may also cause kidney damage. You should tell your doctor if you are receiving other medications which are known to potentially damage the kidney, such as aminoglycosides, amphotericin B, foscarnet, intravenous pentamidine, and vancomycin.

• The potential for interactions between VISTIDE and anti-HIVprotease inhibitors has not been studied.

How is VISTIDE given?
VISTIDE is administered by intravenous infusion and must not be administered by intraocular injection. VISTIDE must be administered by a health care professional.

To minimise the potential for kidney damage, probenecid tablets and intravenous saline solution must be administered with each VISTIDE infusion.

The recommended dosage, frequency of use, or rate of infusion must not be exceeded. VISTIDE must be diluted in 100 milliliters 0.9% (normal) saline prior to administration.
Dosage in Adults

Induction Treatment. The recommended dose of VISTIDE in patients with normal kidney function is 5 mg/kg body weight (given as an intravenous infusion at a constant rate over 1 hour) administered once weekly for two consecutive weeks.

Maintenance Treatment. Beginning two weeks after completion of induction treatment, the recommended maintenance dose of VISTIDE in patients with normal kidney function is 5 mg/kg body weight (given as an intravenous infusion at a constant rate over 1 hr) administered once every two weeks.

Dose Adjustment. If you have decreased kidney function, VISTIDE may not be appropriate therapy for you. Samples of your urine and/or blood will be obtained prior to each infusion of VISTIDE and used for testing kidney function. For patients with evidence of decreased kidney function, your VISTIDE dose may be interrupted or discontinued depending on your individual case.

If you have accidentally taken a dose of VISTIDE greater than prescribed for you, tell your doctor immediately.

Why is the medication probenecid given with VISTIDE?
Probenecid tablets are given to minimise the potential for kidney damage. You must receive a course of probenecid tablets administered orally with each VISTIDE dose. Two grams must be administered 3 hours prior to the VISTIDE dose and one gram administered at 2 hours and again at 8 hours after completion of the 1 hour VISTIDE infusion (for a total of 4 grams). Probenecid is only taken on the same day that VISTIDE is administered.

What are the possible side effects of probenecid?
Potential side effects of probenecid include headache, nausea, vomiting, and allergic reactions. To decrease the potential for nausea and/or vomiting associated with taking probenecid, you should eat food prior to each dose of probenecid. Other measures, such as antihistamines and/or paracetamol, are available to your doctor to decrease or prevent allergic reactions.

Why is normal saline solution given with VISTIDE?
Normal saline is given to minimise the potential for kidney damage. You should receive a total of one liter of 0.9 % (normal) saline solution intravenously with each infusion of VISTIDE. The saline solution should be infused over a 1 hour period immediately before the VISTIDE infusion. If you can tolerate the additional fluid load, your doctor may administer a second liter of fluid. If administered, the second liter of saline should be initiated either at the start of the VISTIDE infusion or immediately afterwards, and infused over a 1 to 3 hour period. Your doctor may also instruct you to drink plenty of fluids.

Use in children
Vistide has not been studied in children. Therefore, this medication should not be used in children.
Can VISTIDE be mixed with other medications prior to use?
The chemical stability of VISTIDE mixed in saline solution has been demonstrated in glass bottles, in infusion bags composed of either polyvinyl chloride (PVC) composition or ethylene/propylene copolymer, and in PVC based vented I.V. administration sets. Other types of I.V. set tubing and infusion bags have not been studied. No other medications or supplements should be added to the VISTIDE infusion bag.

Compatibility of VISTIDE with Ringer’s Solution, Lactated Ringer’s Solution or bacteriostatic infusion fluids has not been evaluated.

How will VISTIDE be prepared and given?
VISTIDE vials should be inspected visually prior to use. If visible particles or discoloration are observed, the vial should not be used.

The health care professional (e.g., physician/nurse) will transfer the appropriate dose of VISTIDE from the vial to an infusion bag containing 100 mL 0.9% (normal) saline solution. The entire volume of the bag will be infused intravenously into you at a constant rate over a period of 1 hour by use of a standard infusion pump.

If not intended for use immediately after preparation, VISTIDE infusion bags may be stored temporarily for up to 24 hours in a refrigerator (2-8°C) when reconstitution is performed under aseptic conditions. Storage beyond 24 hours or freezing is not recommended. Refrigerated bags should be allowed to warm to room temperature prior to use.

VISTIDE is supplied in single-use vials. Partially used vials must be discarded.

VISTIDE should be administered by health care professionals adequately experienced in the care of AIDS patients. Adequate precautions including the use of appropriate safety equipment are recommended for the preparation, administration and disposal of VISTIDE. The preparation of VISTIDE should be done in a laminar flow biological safety cabinet. Personnel preparing the drug should wear surgical gloves, safety glasses and a closed front surgical-type gown with knit cuffs. If VISTIDE contacts the skin, wash membranes and flush thoroughly with water.

What are the possible side effects of therapy?
The major side effect observed with VISTIDE has been damage to the kidneys. Side effects which occurred in at least 10% of patients and were possibly or probably related to VISTIDE were: protein in the urine, low white blood cell counts, weakness/fatigue, increase in serum creatinine, fever, hair loss, and nausea without vomiting.

Side effects of probenecid which occurred in at least 10% of patients were: fever, rash, nausea with vomiting, and nausea without vomiting.

If you experience any of these or any other undesirable effect not mentioned in this leaflet, inform your doctor or pharmacist immediately. These side effects usually disappear when treatment with VISTIDE is stopped. Your Doctor might instruct you to take other medications (e.g., antihistamines or antiemetics) to decrease the side effects of probenecid.
How should VISTIDE vials be stored?
VISTIDE vials should be stored at a temperature between 15° and 30°C. Store out of the reach of children.

Review the expiration date on the label prior to use. Do not use after this date.
If you need further information please contact the local representative of the Marketing Authorisation holder at the following address, telephone and fax number:

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