**1.3.1.1 PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE**

**SCHEDULING STATUS**

**S4**

## 1. NAME OF THE MEDICINE

**ASPEN ACYCLOVIR 250 mg** powder for solution for infusion

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial of ASPEN ACYCLOVIR 250 mg contains 250 mg acyclovir as the lyophilised sodium salt.

Sugar free

For full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

ASPEN ACYCLOVIR 250 mg is a white to off-white lyophilised cake.

## 4. CLINICAL PARTICULARS

### 4.1. Therapeutic indications

ASPEN ACYCLOVIR 250 mg is indicated in:

A. *Herpes simplex* infections in immunocompromised patients:

- ASPEN ACYCLOVIR 250 mg is indicated for the treatment of *herpes simplex* infections.
- ASPEN ACYCLOVIR 250 mg is indicated for the prophylaxis of *herpes simplex* infections in patients.

B. ASPEN ACYCLOVIR 250 mg is indicated in the treatment of *varicella zoster* infections in immuno-compromised patients:

- Chickenpox - prophylaxis and therapy of pneumonial complications.
- Shingles - only if the lesions are not older than 72 hours.

C. ASPEN ACYCLOVIR 250 mg is indicated for treatment of *herpes simplex* infections in the neonate.

D. ASPEN ACYCLOVIR 250 mg is indicated for the treatment of *herpes simplex* encephalitis.

E. ASPEN ACYCLOVIR 250 mg is indicated for the prevention of reactivation of cytomegalovirus infection in seropositive patients following bone marrow transplantation.

### 4.2. Posology and method of administration

**Posology**

The required dose of ASPEN ACYCLOVIR 250 mg should be administered by slow intravenous infusion over a one-hour period.

A course of treatment with ASPEN ACYCLOVIR 250 mg usually lasts 5 days, but this may be adjusted according to the patient's condition and response to therapy.

The duration of prophylactic administration of ASPEN ACYCLOVIR 250 mg is determined by the duration of the period at risk.

Treatment for herpes encephalitis usually lasts 10 days. Treatment for neonatal herpes usually lasts 14 to 21 days. The duration of prophylactic administration of ASPEN ACYCLOVIR 250 mg is determined by the duration of the period at risk.

*Adults*

| Indication | Immune status | Dosage |
|---|---|---|

| | | |
|---|---|---|
| *Herpes simplex* infection (except herpes encephalitis) | Immunocompromised | 5 mg/kg body weight every 8 hours |
| *Varicella zoster* infection | Immunocompromised (normal renal function) | 10 mg/kg body weight every 8 hours |
| *Herpes simplex* encephalitis | Normal or immuno-compromised (normal renal function) | 10 mg/kg body weight every 8 hours |

Obese patients should be dosed at the recommended adult dose using ideal body weight, rather than actual body weight.

**Special populations**

*Elderly population*

The possibility of renal impairment in the elderly must be considered and the dosage should be adjusted accordingly (see Dosage in renal impairment below).

Adequate hydration should be maintained.

**Dosage for the prevention of cytomegalovirus reactivation following bone marrow transplantation:**

**Adults**: 500 mg/m$^2$ ASPEN ACYCLOVIR 250 mg should be given intravenously 3 times daily at approximately 8-hour intervals. The duration of treatment recommended in bone marrow transplant recipients is from 5 days before, up to 30 days after transplant.

**Children**: Limited data suggest that for the prevention of cytomegalovirus reactivation in children over 2 years of age, who have undergone bone marrow transplantation, the adult dose may be given.

*Renal impairment*

Caution is advised when administering ASPEN ACYCLOVIR 250 mg to patients with impaired renal function. The following adjustments in dosage are suggested:

***Dosage adjustments in adults and adolescents:***

| **Creatinine Clearance (ml/min/1,73m$^2$)** | **Percentage of recommended dose (5 or 10 mg/kg body weight) (%)** | **Dosing interval (hours)** |
|---|---|---|
| > 50 | 100 % | 8 |
| 25 to 50 | 100 % | 12 |
| 10 to 25 | 100 % | 24 |
| 0 to 10 | 50 % | 24 |
| | *Haemodialysis:*<br>50 % | 24 and after dialysis |

***Dosage adjustments in neonates, infants and children:***

| **Creatinine Clearance (ml/min/1,73m$^2$)** | **Dosage recommendation** | **Dosing interval** |
|---|---|---|
| Normal renal function | 20 mg/kg body weight | Three times per day |
| 25 to 50 | 20 mg/kg body weight | Twice a day |
| 10 to 25 | 10 mg/kg body weight | Twice a day |
| 0 to 10 | 5 mg/kg body weight<br><br>*Haemodialysis:*<br>5 mg/kg body weight | Twice a day<br><br>Twice daily after dialysis |

***Dosage recommendation in adults and adolescents with impaired renal function for prophylaxis of CMV infection:***

| Creatinine Clearance | Dosage |
|---|---|
| 25 to 50 mL/min | 500 mg/m² given every 12 hours. |
| 10 to 25 mL/min | 500 mg/m² given every 24 hours. |
| 0 (anuric) to 10 mL/min | 500 mg/m² halved and administered every 24 hours. |
| Patients on haemodialysis | 500 mg/m² halved and administered every 24 hours and after dialysis. |

***Dosage recommendations in infants and children with renal impairment for prophylaxis of CMV infection:***

| Creatinine Clearance (mL/min/1,73m²) | Dosage |
|---|---|
| 25 to 50 mL/min | 20 mg/kg body weight given every 12 hours |
| 10 to 25 mL/min | 20 mg/kg body weight given every 24 hours |
| 0 (anuric) to 10 mL | 20 mg/kg body weight halved and administered every 24 hours |
| Patients on haemodialysis | 20 mg/kg body weight halved and administered every 24 hours after dialysis |

**Paediatric population**

*Children*

The dose of ASPEN ACYCLOVIR 250 mg for children aged between 3 months and 12 years is calculated on the basis of body weight.

| Indication | Immune status | Dosage |
|---|---|---|
| *Herpes simplex* (except herpes encephalitis) | Immunocompromised | 20 mg/kg body weight every 8 hours for 14 days |
| *Varicella zoster* infection | Immunocompromised (normal renal function) | 20 mg/kg body weight four times per day for 5 days |
| *Herpes simplex* encephalitis | Normal (normal renal function) | 20 mg/kg body weight every 8 hours for 21 days |

Children with impaired renal function require an appropriately modified dose and/or dose interval, according to the degree of impairment as indicated under "Dosage in renal impairment".

*Neonates*

The dosage of ASPEN ACYCLOVIR 250 mg in neonates and infants up to 3 months of age is calculated on the basis of bodyweight. Neonates with herpes simplex infections should be given ASPEN ACYCLOVIR 250 mg in doses of 20 mg/kg every 8 hours for 21 days.

**Method of administration**

For intravenous use.

For reconstitution and administration refer to sections 6.2 and 6.6.

## 4.3. Contraindications

ASPEN ACYCLOVIR 250 mg is contraindicated in:

- Patients with hypersensitivity to acyclovir or to any excipients in ASPEN ACYCLOVIR 20 mg (see section 6.1).

## 4.4. Special warnings and precautions for use

Safety of ASPEN ACYCLOVIR 250 mg treatment in pregnancy and lactation has not been established (see section 4.6).

*Use in patients with renal impairment and in elderly patients:*

ASPEN ACYCLOVIR 250 mg should be administered with caution to patients with renal impairment and doses should be adjusted according to creatinine clearance (see section 4.2). Elderly patients are likely to have reduced renal function and therefore the need for dose reduction must be considered in this group of patients. Both elderly patients and patients with renal impairment are at increased risk of developing neurological side effects and should be closely monitored for evidence of these effects. In the reported cases, these reactions may be reversible on discontinuation of treatment (see section 4.8).

Parenteral administration should be by slow infusion over one hour to avoid precipitation of acyclovir in the kidney; rapid or bolus injection should be avoided, and adequate hydration maintained (see section 4.2). Renal impairment usually responds rapidly to rehydration of the patient and/or dosage reduction or withdrawal of ASPEN ACYCLOVIR 250 mg. Progression to acute renal failure, may occur.

In patients receiving ASPEN ACYCLOVIR 250 mg at higher doses (e.g. for herpes encephalitis), specific care regarding renal function should be taken, particularly when patients are dehydrated or have any renal impairment.

Reconstituted ASPEN ACYCLOVIR 250 mg has a pH range of 10,7 to 11,7 and should be administered by intravenous infusion only. ASPEN ACYCLOVIR 250 mg should not be administered topically, intramuscularly, orally, subcutaneously or ophthalmically.
Rapid increases in blood urea and creatinine levels are believed to be related to peak plasma levels and the state of hydration of the patient. To avoid this effect, ASPEN ACYCLOVIR 250 mg should not be given as an intravenous bolus injection, but by slow infusion over a one hour period (see section 4.2).

*Risk of Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)*
There is a risk of drug reaction with eosinophilia and systemic symptoms (DRESS) associated with the use of valacyclovir/acyclovir-containing medicines.
• DRESS is classified among the severe cutaneous adverse reactions (SCARs) which are unpredictable and present a serious risk to patients that can be life-threatening or fatal.
• DRESS has been reported in association with valacyclovir/acyclovir treatment. DRESS is a serious skin reaction that may affect one or more organs (commonly liver).
• Valacyclovir is a prodrug of acyclovir. The metabolism of valacyclovir occurs within the gut lumen and in the liver. After uptake of valacyclovir, hydrolysis of the molecule rapidly yields

acyclovir, resulting in significantly greater systemic acyclovir levels with oral valacyclovir compared with oral acyclovir.

At the time of prescription patients should be advised of the signs and symptoms and monitored closely for skin reactions. If signs and symptoms suggestive of DRESS appear, acyclovir as contained in ASPEN ACYCLOVIR 250 mg, should be withdrawn immediately and an alternative treatment considered (as appropriate). If the patient has developed DRESS with the use of ASPEN ACYCLOVIR 250 mg, treatment with ASPEN ACYCLOVIR 250 mg must not be restarted in this patient at any time.

### 4.5. Interaction with other medicines and other forms of interaction

No clinically significant interactions have been identified.

Acyclovir as contained in ASPEN ACYCLOVIR 250 mg is eliminated primarily unchanged in the urine via active renal tubular secretion. Any medicines administered concurrently that compete with this mechanism may increase acyclovir plasma concentrations. Probenecid and cimetidine increase the AUC of acyclovir by this mechanism and reduces acyclovir renal clearance.

In patients receiving intravenous ASPEN ACYCLOVIR 250 mg, caution is required during concurrent administration with medicines which compete with acyclovir for elimination, because of the potential for increased plasma levels of one or both medicines or their metabolites. Increases in plasma AUCs of acyclovir and of the inactive metabolite of mycophenolate mofetil, an immunosuppressant medicine used in transplant patients, have been shown when the medicines are co-administered.

If lithium is administered with high dose acyclovir IV, the lithium serum concentration should be closely monitored because of the risk of lithium toxicity.

Care is also required (with monitoring for changes in renal function) if administering intravenous ASPEN ACYCLOVIR 250 mg with medicines which affect other aspects of renal physiology (e.g. ciclosporin, tacrolimus).

## 4.6. Fertility, pregnancy and lactation

Safety in pregnancy and lactation has not been established (see section 4.4).

**Lactation:**

Following oral administration of 200 mg five times a day, acyclovir has been detected in breast milk at concentrations ranging from 0,6 to 4,1 times the corresponding plasma levels. These levels would potentially expose nursing infants to acyclovir dosages of up to 0,3 mg/kg/day.

Lactating women on ASPEN ACYCLOVIR 250 mg treatment should not breastfeed.

**Fertility**

There is no information on the effect of ASPEN ACYCLOVIR 250 mg on human female fertility. In a study of 20 male patients with normal sperm count, oral acyclovir administered at doses of up to 1 g per day for up to six months has been shown to have no clinically significant effect on sperm count, motility or morphology.

## 4.7. Effects on ability to drive and use machines

ASPEN ACYCLOVIR 250 mg is generally used in an in-patient hospital population and information on ability to drive and operate machinery is not usually relevant.

There have been no studies to investigate the effect of acyclovir on driving performance or the ability to operate machinery.

You should however, exercise caution until you are aware of the extent to which ASPEN ACYCLOVIR 250 mg may influence your ability to drive or use machinery.

## 4.8. Undesirable effects

*a) Tabulated list of adverse reactions*

| System organ class | Frequent | Less frequent | Frequency unknown (cannot be estimated from the available data) |
|---|---|---|---|
| **Blood and the lymphatic system disorders** | | Decreases in haematological indices (anaemia, thrombocytopenia, leucopenia). | |
| **Vascular disorders** | Phlebitis. | | |
| **Gastrointestinal disorders** | Nausea, vomiting. | | |
| **Hepatobiliary disorders** | Reversible increases in liver-related enzymes. | | |
| **Skin and subcutaneous tissue disorders** | Rashes (including photosensitivity), urticaria, pruritus, fevers. | | Drug Reaction with Eosinophillia and Systemic Symptoms (DRESS) |
| **Renal and urinary disorders** | Increases in blood urea and creatinine levels. | | |

**Adverse Effects Derived from Post-Marketing Data:**

The following events have been identified during post-approval use of ASPEN ACYCLOVIR 250 mg from spontaneous reports. As these are reported from a population of unknown size, precise estimates of frequency cannot be made.

***Immune system disorders:*** Anaphylaxis, angioedema.

***Psychiatric and nervous system disorders:*** Headache, dizziness, agitation, confusion, tremor, ataxia, dysarthria, hallucinations, psychotic symptoms, convulsions, somnolence, encephalopathy, coma.

The above effects may be reversible and usually reported in patients with renal impairment, or with other predisposing factors (see section 4.4).

***Respiratory, thoracic and mediastinal disorders:*** Dyspnoea

***Gastrointestinal disorders:*** Diarrhoea, abdominal pain

***Hepatobiliary disorders:*** Reversible increases in bilirubin, hepatitis jaundice

***Skin and subcutaneous tissue disorders:*** Accelerated diffuse hair loss. The relationship of accelerated diffuse hair loss to ASPEN ACYCLOVIR 250 mg therapy is uncertain.

***Renal and urinary disorders:*** Renal impairment, acute renal failure, renal pain.

Renal pain may be associated with renal failure and crystalluria.

***General disorders and administration site conditions:*** Fatigue, fever, local inflammatory reactions.

Severe local inflammatory reactions sometimes leading to ulceration have occurred when ASPEN ACYCLOVIR 250 mg has been inadvertently infused into extravascular tissues.

*b) Description of selected adverse reactions*

Acyclovir sodium, as contained in ASPEN ACYCLOVIR 250 mg, when administered intravenously, may cause local reactions at the injection site with inflammation and phlebitis; these reactions may be associated with extravasation that may lead to ulceration. Some patients experience transient increases in blood concentrations of urea and creatinine.

Renal impairment may occur in a few patients; it is usually reversible but may progress to acute renal failure. The risk of renal toxicity is increased by conditions favouring deposition of acyclovir crystals in the tubules such as when the patient is poorly hydrated, has existing renal impairment, or when the medicine is given at a high dosage or by rapid or bolus injection.

Renal impairment developing during treatment with ASPEN ACYCLOVIR 250 mg may respond to hydration of the patient and/or dosage reduction or withdrawal of the medicine (see section 4.2).

Progression to acute renal failure, however, may occur.

The dose of ASPEN ACYCLOVIR 250 mg must be adjusted in patients with impaired renal function in order to avoid accumulation of acyclovir in the body.

Occasional adverse effects following intravenous administration include increased values for liver enzymes, haemotological changes, skin rashes, nausea, vomiting and headache.

Encephalopathic changes including lethargy, confusion, tremors and seizures have been reported in a small number of patients, particularly in those who are immunocompromised.

*Reporting of suspected adverse reactions*

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine.

Healthcare providers are asked to report any suspected adverse reactions to **SAHPRA** via the the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

**Aspen Pharmacare:**

**E-mail:** Drugsafety@aspenpharma.com

**Tel:** 0800 118 088

### 4.9. Overdose

**Symptoms**

Overdosage of intravenous ASPEN ACYCLOVIR 250 mg has resulted in elevations in serum creatinine, blood urea nitrogen and subsequent renal failure. Neurological effects including confusion, hallucinations, agitation, seizures and coma have been described in association with overdosage.

**Treatment**

Since there is no specific antidote, treatment of adverse effects and/or overdose should be symptomatic and supportive with possible utilisation of the following:

Adequate hydration to prevent precipitation of acyclovir in the renal tubules. Haemodialysis to aid in the removal of acyclovir from the blood, especially in patients with acute renal failure and anuria (see section 4.2).

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1. Pharmacodynamic properties

Category and Class: A 20.2.8 Antiviral agents

Pharmacotherapeutic group: Direct acting antivirals, Nucleosides and nucleotides excl. reverse transcriptase inhibitors

ATC code: J05AB01.

*Mechanism of action*

Acyclovir is a synthetic purine nucleoside analogue with *in vitro* and *in vivo* inhibitory activity against human herpes viruses, including *herpes simplex* virus (HSV) types 1 and 2 and *varicella zoster* virus (VZV). In cell culture, acyclovir has the greatest anti-viral activity against HSV-1, followed (in decreasing order of potency) by HSV-2 and VZV. The inhibitory activity of acyclovir for HSV-1, HSV-2 and VZV is highly selective. The enzyme thymidine kinase (TK) of normal, uninfected cells does not use acyclovir effectively as a substrate, hence toxicity to mammalian host cells is low; however, TK encoded by HSV, VZV converts acyclovir to acyclovir monophosphate, a nucleoside analogue, which is further converted to the diphosphate and finally to the triphosphate by cellular enzymes. Acyclovir triphosphate interferes with the viral DNA polymerase and inhibits viral DNA replication with resultant chain termination following its incorporation into the viral DNA.

### 5.2. Pharmacokinetic properties

**Absorption**

In adults, mean steady state peak plasma concentrations ($C_{ssmax}$) following a one-hour infusion of 2,5 mg/kg, 5 mg/kg, 10 mg/kg and 15 mg/kg were 22,7 micromoles (5,1 micrograms/mL), 43,6 micromoles (9,8 micrograms/mL), 92 micromoles (20,7 micrograms/mL) and 105 micromoles (23,6 micrograms/mL), respectively. The corresponding trough levels ($C_{ssmin}$) 7 h

later were 2,2 micromoles (0,5 micrograms/mL), 3,1 micromoles (0,7 micrograms/mL), 10,2 micromoles (2,3 micrograms/mL) and 8,8 micromoles (2,0 micrograms/mL), respectively. In children over 1 year of age similar mean peak ($C_{ssmax}$) and trough ($C_{ssmin}$) levels were observed when a dose of 250 mg/m$^2$ was substituted for 5 mg/kg and a dose of 500 mg/m$^2$ was substituted for 10 mg/kg. In neonates (0 to 3 months of age) treated with doses of 10 mg/kg administered by infusion over a one-hour period every 8 h the $C_{ssmax}$ was found to be 61,2 micromoles (13,8 micrograms/mL) and the $C_{ssmin}$ to be 10,1 micromoles (2,3 micrograms/mL).

**Distribution**

Cerebrospinal fluid levels are approximately 50 % of corresponding plasma levels. Plasma protein binding is relatively low (9 to 33 %) and drug interactions involving binding site displacement are not anticipated.

**Biotransformation**

Acyclovir is predominantly excreted unchanged by the kidney. The only significant urinary metabolite is 9-carboxymethoxy-methylguanine, and accounts for 10 to 15 % of the dose excreted in the urine.

**Elimination**

In adults the terminal plasma half-life of acyclovir after administration of acyclovir IV for infusion is about 2,9 h. Most of the drug is excreted unchanged by the kidney. Renal clearance of acyclovir is substantially greater than creatinine clearance indicating that tubular secretion in addition to glomerular filtration contributes to the renal elimination of the drug. 9-carboxymethoxy-methylguanine is the only significant metabolite of acyclovir and accounts for approximately 10 to 15 % of the dose excreted in the urine. When acyclovir is given one hour after 1 gram of probenecid the terminal half-life and the area under the plasma concentration time curve is extended by 18 % and 40 % respectively.

In neonates (0 to 3 months of age) treated with doses of 10 mg/kg administered by infusion over a one-hour period every 8 h the terminal plasma half-life was 3,8 h.

**Special Patient Populations:**

In patients with chronic renal failure the mean terminal half-life was found to be 19,5 h. The mean acyclovir half-life during haemodialysis was 5,7 h. Plasma acyclovir levels dropped approximately 60 % during dialysis.

In the elderly total body clearance falls with increasing age, associated with decreases in creatinine clearance, although there is little change in the terminal plasma half-life.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1. List of excipients

Sodium hydroxide (for pH-adjustment)

### 6.2. Incompatibilities

Sterile acyclovir sodium is incompatible with biological or colloidal solutions (e.g. blood products, protein-containing solutions).

Parabens are incompatible with sterile acyclovir sodium and may cause precipitation.

This medicine must not be mixed with other medicine except those mentioned in section 6.6.

### 6.3. Shelf life

24 months.

### 6.4. Special precautions for storage

Store at or below 25 °C.

Keep in original packaging until required for use.

The reconstituted solution is stable at 15 °C to 25 °C for up to 12 hours.

The reconstituted and diluted solution is stable at 15 °C to 25 °C for up to 24 hours.

**The reconstituted or diluted solution should not be refrigerated (refer to section 6.6).**

## 6.5. Nature and contents of container

1 x 20 ml clear, colourless, glass vial with an aluminium seal, dark grey bromobutyl rubber stopper and a light blue polypropylene flip-top cover. 5 vials are packed in an outer cardboard carton.

## 6.6. Special precautions for disposal and other handling

**Reconstitution**

Each vial of ASPEN ACYCLOVIR 250 mg should be reconstituted by the addition of 10 ml of Water for Injection BP.

This provides a solution containing 25 mg acyclovir per ml.

When reconstituted as directed the solution will have a pH range of 10,7 to 11,7.

After reconstitution with sterile Water for Injection, solutions retain their potency for 12 hours at controlled room temperature (15 °C to 25 °C).
After further dilution with standard electrolyte- and dextrose-containing solutions for intravenous infusion, solutions retain their potency for up to 24 hours at controlled room temperature (15 °C to 25 °C).

**Administration**

ASPEN ACYCLOVIR 250 mg after reconstitution may be injected directly into a vein over one hour by a controlled-rate infusion pump or be further diluted for administration by infusion.

For intravenous injection by a controlled-rate infusion pump, a solution containing 25 mg acyclovir per ml is used.

For intravenous infusion each vial of ASPEN ACYCLOVIR 250 mg should be reconstituted and then wholly or in part according to the dosage required added to and mixed with at least 50 ml infusion solution. The contents of two vials (500 mg of acyclovir) may therefore be added to 100 ml of infusion solution.

ASPEN ACYCLOVIR 250 mg is known to be compatible with the following infusion fluids when diluted to a concentration not greater than 0,5 % *m/v* acyclovir:

- Sodium Chloride Intravenous Infusion BP (0,45 % and 0,9 % *m/v*).
- Sodium Chloride (0,18 % *m/v*) and Dextrose (4 % *m/v*) Intravenous Infusion BP.
- Sodium Chloride (0,45 % *m/v*) and Dextrose (2,5 % *m/v*) Intravenous Infusion BP.
- Compound Sodium Lactate Intravenous Infusion BP (Hartmann's Solution).

ASPEN ACYCLOVIR 250 mg, when diluted in accordance with the above schedule, will give an acyclovir concentration not greater than 0,5 % *m/v*.

**Since no antimicrobial preservative is included, reconstitution and dilution must be carried out under full aseptic conditions, preferably immediately before use, and any unused solution discarded.**

Should visible turbidity or crystallisation appear in the solution before or during infusion, the preparation should be discarded.

## 7. HOLDER OF CERTIFICATE OF REGISTRATION

PHARMACARE LIMITED

Healthcare Park

Woodlands Drive

Woodmead 2191

## 8. REGISTRATION NUMBER

32/20.2.8/0257

## 9. DATE OF FIRST AUTHORISATION

16 August 2001

## 10. DATE OF REVISION OF TEXT

18 February 2025

Die Afrikaanse Professionele Inligting is op versoek beskikbaar. Mediese Blitslyn: 0800 118 088.

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