Aciclovir (Acyclovir) 2024

Newborn use only

Alert	Increased risk of renal impairment if there is concomitant use of other nephrotoxic medications, pre-existing renal disease or dehydration. Turbidity or crystallisation may occur even when mixed with compatible fluids. Discard preparation if this occurs before or during the infusion. Highly alkaline and IV extravasation can cause severe tissue damage.
Indication	Therapeutic or pre-emptive treatment of neonatal herpes simplex virus (HSV) infection Oral suppression therapy following IV aciclovir treatment for neonatal HSV Neonatal varicella-zoster virus (VZV)(Neonatal Chickenpox) infection[1]
Action	Inhibits viral DNA synthesis when activated in infected cells.
Drug type	Guanine analogue antiviral
Trade name	**IV:** Aciclovir Accord Concentrate, Aciclovir Powder for solution for infusion (Wockhardt, UK), Aciclovir Viatris Powder for infusion, DBL Aciclovir Intravenous Infusion (Concentrate for infusion) **Oral:** Aciclovir GH Tablets, Aciclovir Sandoz Tablets, Aciclovir-WGR Tablets, ARX-Aciclovir Tablets, Zovirax Dispersible tablets
Presentation	**IV:** **Solution Vials** Aciclovir Accord 250mg/10mL, 500mg/20mL and 1000mg/40mL DBL Aciclovir Intravenous Infusion 250mg/10mL and 500mg/20mL **Dry Powder Vials** Aciclovir Powder for Solution for infusion (Wockhardt, UK) 250mg Aciclovir Viatris Powder for infusion 250mg and 500mg **Oral:** Aciclovir GH and Aciclovir Sandoz – available as 200mg, 400mg, 800mg Tablets Aciclovir WGR and ARX-Aciclovir – available as 200mg and 800mg Tablets Zovirax Dispersible 200mg Tablets
Dose	**Therapeutic or pre-emptive Treatment of acute HSV** **IV:** 20 mg/kg/dose 8 hourly **Duration of IV therapy (expert recommendation)[1,2]** Pre-emptive therapy for high-risk asymptomatic infant with HSV confirmed on surface swab, but CSF and blood PCR negative and CSF and LFTs normal: 10 days Laboratory or clinically confirmed HSV confined to skin, eye, and mouth: 14 days[2,3] HSV encephalitis or disseminated disease: 21 days **Oral suppression therapy after completion of IV treatment of Neonatal HSV CNS disease +/- disseminated infection – To discuss with paediatric infectious disease specialist** 300 mg/BSA (m^2)/dose, administered 3 times daily for 6 months – This equals to approximately 20 mg/kg/dose 8 hourly for 6 months **Body Surface Area (BSA) calculation:** $$BSA\ (m^2) = \sqrt{\frac{height\ (cm) \times weight\ (kg)}{3600}}$$ **IV treatment of acute neonatal VZV[1]** To discuss with Paediatric Infectious diseases specialist. ASID recommendation: 20 mg/kg/dose IV 8 hourly for infants with active chickenpox in the following circumstances: <28 weeks at birth or birthweight <1000g or clinically significant disease irrespective of gestational age at birth and birthweight, e.g. unwell, disseminated disease, pneumonitis. The duration of therapy is to be discussed with a paediatric infectious diseases specialist.
Dose adjustment	**Therapeutic hypothermia –** No information. Adjust dose if there is associated renal impairment. **ECMO –** No information on dose adjustment. Refer to the evidence section. **Hepatic impairment** – No dose adjustment. **Renal impairment**

<table>
<tr><td></td><td>Renal dysfunction is commonly associated with severe infection. The benefit of treatment of severe HSV or VZV disease outweighs any risk that may be associated with aciclovir. If renal dose adjustment is considered, the following table provides guidance (ANMF consensus).[4]
<table>
<tr><th>Renal dysfunction</th><th>Dosage and Interval adjustment</th></tr>
<tr><td>CrCl 25-50 mL/min/1.73 m^2 OR 70–100 micromol/L</td><td>20 mg/kg 12 hourly</td></tr>
<tr><td>CrCl 10-<25 mL/min/1.73 m^2 OR 101–130 micromol/L</td><td>20 mg/kg 24 hourly</td></tr>
<tr><td>CrCl <10 mL/min/1.73 m^2 OR > 130 micromol/L and/or urine output < 1 mL/kg/hour</td><td>10 mg/kg 24 hourly</td></tr>
</table></td></tr>
<tr><td>Maximum dose</td><td></td></tr>
<tr><td>Total cumulative dose</td><td></td></tr>
<tr><td>Route</td><td>IV or Oral</td></tr>
<tr><td>Preparation</td><td>IV
First dilution:
If using powder for solution vials
Reconstitute 250mg vial with 10 mL or 500mg vial with 20 mL of water for injection to obtain 25mg/mL solution.

If using vials of solution
No reconstitution required as is already a 25mg/mL solution

Further dilute
Draw up 4 mL (100mg) of aciclovir and add 16 mL sodium chloride 0.9% to make final volume 20 mL with a final concentration of 5mg/mL.

Risk of phlebitis and extravasation increases at >10mg/mL. If a higher concentration is required, a solution of up to 25mg/mL must be administered via a CENTRAL LINE ONLY.

Oral
Where clinically appropriate round the dose to the nearest quarter tablet. Only round tablets are appropriate to quarter. Disperse part tablet in 2 mL of water for injection for each 50 mg of aciclovir and give immediately.

If not clinically appropriate to round the dose, follow the instructions below:
1. Disperse 200mg tablet in 10mL of water for injection in a syringe to achieve a 20mg/mL concentration
2. Shake syringe to ensure even dispersion
3. Give required dose
4. Discard remaining dispersion.</td></tr>
<tr><td>Administration</td><td>IV: Infuse via syringe driver over at least 60 minutes.
Turbidity or crystallisation may occur even when mixed with compatible fluids. Discard preparation if this occurs before or during the infusion.
Oral: Dose can be given with feed.</td></tr>
<tr><td>Monitoring</td><td>Before commencing treatment: check renal function, full blood count, electrolytes, liver function tests.
During IV treatment:
At least biweekly renal function, full blood count, electrolytes, liver function test.[5]
Strict fluid balance and avoid dehydration
IV site for extravasation: IV solution is extremely alkaline (pH 11). Monitor for signs of extravasation
During oral suppression therapy:
Monthly renal function, full blood count, electrolytes, liver function tests.[5]</td></tr>
<tr><td>Contraindications</td><td>Known hypersensitivity to aciclovir, valaciclovir or any component of the product.</td></tr>
</table>

Precautions	Increased risk of renal impairment if there is concomitant use of other nephrotoxic medications (e.g. gentamicin, furosemide (frusemide), cephalosporins, pre-existing renal disease or dehydration. Administration interval may be lengthened to minimise renal effects. Refer to the renal adjustment dose in the dose adjustment section.
Drug interactions	Nitisinone, Mycophenolate mofetil, emtricitabine, tenofovir, phenytoin, valproate (valproic acid), zidovudine – Increased risk of adverse reactions.
Adverse reactions	Neutropenia Renal dysfunction and crystalluria – Adequate hydration is required.[5] Phlebitis at IV injection site (highly alkaline solution). The solution can be dilute. Other: Vomiting, diarrhoea, encephalopathy, agitation, oedema, rash, weakness, seizures, anaemia, thrombocytopaenia, hepatitis, Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis, anaphylaxis.
Compatibility	Fluids:[6] dextrose 5% in sodium chloride 0.45%, dextrose 5% in sodium chloride 0.9%, dextrose 5%, sodium chloride 0.9%, dextrose 5% in sodium chloride 0.2%, sodium chloride 0.45%. Note: Turbidity or crystallisation may occur even when mixed with compatible fluids. Discard preparation if this occurs before or during the infusion. TPN (Y site):[7] SMOFlipid emulsion. Y Site:[6] Alemtuzumab, alfentanil hydrochloride, allopurinol sodium, amikacin sulfate, aminophylline, amphotericin B cholesteryle sulfate complex, amphotericin B lipid complex, amphotericin B liposome, ampicillin sodium, anidulafungin, argatroban, arsenic trioxide, asparaginase, atenolol, atracurium besylate, azithromycin, bivalirudin, bleomycin sulfate, bumetanide, buprenorphine hydrochloride, busulfan, butorphanol tartrate, calcium chloride, calcium gluconate, carboplatin, carmustine, caspofungin acetate, cefamandole nafate, cefazolin sodium, cefoperazone, cefotaxime sodium, cefotetan disodium, cefoxitin sodium, ceftarloine fosamil, ceftazidime, ceftizoxime sodium, ceftobiprole medocaril, ceftriaxone sodium, cefuroxime sodium, cephapirin sodium, chlorampheinicol sodium succinate, cimetidine hydrochloride, cisatrcurium besylate, cisplatin, clindamycin phosphate, cloxacillin sodium, cychlphosphamide, cyclosporine, cytarabine, dactinomycin, dantrolene sodium, daunorubicin citrate liposome, defibrotide sodium, dexamethasone sodium phosphate, dexmedetomidine hydrochloride, digoxin, diltiazem hydrochloride, dimnhydrinate, docetaxel, doripenem, doxacurium chloride, doxorubicin hydrchloride liposome, doxycyline hyclate, droperidol, enalaprilate, ephedrine sulfate, ertapenem sodium, erthryomycin lactobionate, etoposide, etoposide phosphate, famotidine, fat emulsion, fentanyl citrate, filgrastim, fluconazole, fluorouracil, fosphenytoin sodium, furosemide (frusemide), gallium nitrate, gatifloxacin, gentamicin sulfate at maximum concentration of 1.6mg/mL, glycopyrrolate, heparin sodium, hydrocortisone sodium succinate, hydromorphone hydrochloride, isofosfamide, imipenem/cilastatin sodium, insulin human regular, isoproterenol hydrochloride, lansoprazole in sodium chloride 0.9%, lepirudin, leucovorin calcium, linezolid, lorazepam, magnesium sulfate, mannitol, mechlorethamine hydrochloride, melphalan hydrochloride, meropenem at maximum concentration 1mg/mL, methohexital sodium, methotrexate sodium, methylprednisolone sodium succinate, metoprolol tartrate, metronidazole, milrinone lactate, mitoxantrone hydrochloride, mivacurium chloride, morphine sulfate at maximum concentration 0.08mg/mL, nafcillin sodium, naloxone hydrochloride, nesiritide, nitroglycerin, octreotide acetate, oxacillin sodium, oxytocin, paclitaxel, pamidronate disodium, pancuronium bromide, pantoprazole sodium a maximum concentration 0.4mg/mL, pemetrexed, penicillin g potassium, pentobarbital sodium, pentoxifylline, perphenazine, phenobarbital sodium, piperacillin sodium, polymyxin b sulfate, potassium acetate, potassium chloride, propofol, propranolol hydrochloride, remifentanil hydrochloride, rituximab, rocuronium bromide, sodium acetate, sodium bicarbonate, succinylcholine chloride, sufentanil citrate, sulfamethoxazole/trimethoprim, teniposide, theophylline, thiopental sodium, thiotepa, ticarcillin disodium, tigecycline, tirofiban hydrochloride, tobramycin sulfate, trastuzumab, vancomycin hydrochloride, vasopressin, vinblastine sulfate, vincristine sulfate, voriconazole, zidovudine and zoledronic acid.
Incompatibility	Fluids:[6] No information. TPN (Y-site):[6] Amino acid solutions. Y Site:[6] Acetaminophen (paracetamol),adrenaline (epinephrine) amifostine, amino acid solution, aminocaproic acid, amiodarone hydrochloride, amphotericin B, ampicillin sodium/sulbactam sodium, amsacrine, aztronam, caffeine citrate, capreomycin, cefepime hydrochloride, chloropromazine

	hydrochloride, ciprofloxacine, codeine phosphate, dacarbazine, daptomycin, daunorubicine hydrochloride, dexrazoxane, diazepam, dobutamine hydrochloride, dolasetron meylate, dopamine hydrochloride, doxorubicin hydrochloride, epinephrine (adrenaline), epirubicin hydrochloride, eptifibatide, esomolol hydrochloride, denoldopam mesylate, fludarabine phosphate, foscarnet sodium, garenoxacin mesylate, gemcitabine hydrochloride, gemtuzumab oxogamicin, haloperidol lactate, hydralazine hydrochloride, hydroxyzine hydrochloride, idarubicin hydrochloride, irinotecan hydrochloride, ketamine hydrochloride, ketorolac tromethamine, labetaolol hydrochloride, lansoprazole in glucose 5%, levofloxacin, lidocaine hydrochloride, meropenem at concentrations >1mg/mL, mesna, methadone hydrochloride, methyldopate hydrochloride, midazolam hydrochloride, mitomycin, morphine sulfate at concentrations > 0.08mg/mL, mycophenolate mofetil hydrochloride, nicardipine hydrochloride, ondansetron hydrochloride, palonosetron hydrochloride, pantoprazole sodium at concentrations > 0.4mg/mL, paracetamol, pentamidine isethionate, phenylephrine hydrochloride, phenytoin sodium, piperacillin sodium/tazobactam sodium, potassium phosphate, procainamide hydrochloride, prochloperazine edisylate, promethazine hydrochloride, quinidine gluconate, quinuprisitn/dalfopristin, sargramostim, sodium nitroprusside, sodium phosphate, streptozocin, tacrolimus, ticarcillin disodium/clavulanate potassium, topotecan hydrochloride, vecuronium bromide, verapamil hydrochloride, and vinorelbine tartrate.
Stability	**IV:** Reconstituted solution to be used immediately and discard remaining. **Oral:** Dispersed tablet suspension use immediately and discard remaining.
Storage	Store below 25°C. Do NOT refrigerate (may result in precipitation).
Excipients	**IV Solution:** Sodium hydroxide, hydrochloric acid, water for injections. Aciclovir Powder for solution for infusion - Sodium hydroxide DBL Aciclovir Intravenous Infusion - Sodium hydroxide, water for injections. Viatris Powder for infusion – no excipients. **Tablets:** GH Tablets - magnesium stearate, microcrystalline cellulose, sodium starch glycollate, pregelatinised maise starch, colloidal anhydrous silica. Sandoz Tablets - lactose, microcrystalline cellulose, sodium starch glycollate (type A), copovidone, magnesium stearate. WGR Tablets - colloidal anhydrous silica magnesium stearate microcrystalline cellulose pregelatinised maise starch sodium starch glycollate ARX Tablets - Magnesium stearate, microcrystalline cellulose, sodium starch glycollate, pregelatinised maise starch, colloidal anhydrous silica. Zovirax Dispersible Tablets (200 mg, 400 mg and 800 mg). Microcrystalline cellulose, aluminium magnesium silicate, sodium starch glycollate, povidone, magnesium stearate, Opadry Complete film coating system White Y-1-7000 and macrogol 8000. Zovirax 200 mg Tablets. Microcrystalline cellulose, lactose monohydrate, magnesium stearate, povidone and sodium starch glycollate. Zovirax 400 mg and 800 mg Tablets. Microcrystalline cellulose, magnesium stearate, povidone and sodium starch glycollate.
Special comments	Slower administration rate can minimise the risk of renal impairment. Solution can be prepared more dilute to reduce the risk of extravasation injury. Do not give the IV solution orally as it is very alkaline with a pH of 11 and can cause irritation. Discard the solution if visible turbidity or crystallisation appears.
Evidence	**Overview** Herpes simplex virus type 1 (HSV-1) and HSV type 2 (HSV-2) are the two types of HSVs that may cause neonatal disease.[5] In Australia, the reported incidence of neonatal HSV disease is very low (approx. 3 per 100,000 live births). The majority (>65%) of neonatal HSV infections are due to HSV1 and are acquired during delivery through an infected birth canal.(1) True intrauterine infection accounts for <5% of reported cases. Postnatal infection occurs in approximately 10% of cases from an infected care giver. Breast milk transmission has not been reported. Most genital HSV infections in women (primary, non-primary or recurrent HSV1 or HSV2) are asymptomatic and mothers are unaware of lesions. Risk of neonatal infection is determined by the type of maternal infection (primary versus recurrent), the presence of maternal type specific IgG, the use of devices that break skin integrity e.g. fetal scalp

electrodes, fetal scalp blood sampling, or instrument delivery, and the type of delivery (vaginal >caesarean section). Caesarean section reduces risk of neonatal HSV transmission in women shedding HSV at the time of birth but does not provide complete protection against neonatal HSV disease. The low risk of mother to child transmission of HSV after vaginal delivery in women with recurrent genital herpes lesions need to be balanced against the risks of caesarean section.[1]

Aciclovir is recommended in neonates (1) as an empiric therapy from birth in asymptomatic neonates but at high risk for neonatal HSV disease due to exposure, (2) treatment of neonatal HSV disease and (3) ongoing suppressive oral therapy after completion of IV therapy to prevent CNS sequelae.[1,8,9]

Efficacy

There are no RCTs comparing aciclovir versus placebo in neonatal HSV disease.[10]

High-dose versus low-dose for HSV treatment

An open-label evaluation of IV aciclovir prospectively compared 16 patients receiving 45 mg/kg/day and 72 patients receiving 60 mg/kg/day in divided doses to historical controls from a previously reported trial which used 30 mg/kg/day. Survival rate for the high-dose aciclovir was found to be significantly greater than for low-dose aciclovir. Recipients of high dose aciclovir also had a borderline significant decrease in morbidity. Neutropenia, renal dysfunction, abnormal platelet count, low haemoglobin and elevated AST were noted but the possible adverse drug reactions of high-dose aciclovir couldn't be separated from the effects of viral infection and underlying medical conditions.[11] Sampson et al suggested a higher dose for 36-41 weeks gestation post menstrual age (20 mg/kg 6 hourly).[12] AAP and ASID recommend 20 mg/kg/dose 8 hourly irrespective of gestational age at birth and postmenstrual age.[1,2]

Duration of therapy

The recommended duration of therapy by AAP and ASID are similar, except for skin, eye and mouth disease – AAP recommends 14-day therapy and ASID recommends 10-14 days.[1,2]

Oral HSV suppression therapy following neonatal HSV treatment to prevent CNS sequelae

Neonates were enrolled in two parallel, identical, double-blind, placebo-controlled studies. Neonates with central nervous system (CNS) involvement were enrolled in one study, and neonates with skin, eye, and mouth involvement only were enrolled in the other. After completing a regimen of 14 to 21 days of parenteral aciclovir, the infants were randomly assigned to immediate aciclovir suppression (300 mg per square meter of body-surface area per dose orally, three times daily for 6 months) or placebo. The Mental Development Index of the Bayley Scales of Infant Development was assessed at 12 months of age in 28 of 45 infants enrolled with HSV CNS involvement. After adjustment for covariates, infants assigned to aciclovir suppression had significantly higher mean scores than infants assigned to placebo. There was a trend toward more neutropenia in the aciclovir group.[9]

Aciclovir and preterm infants

Although the standard of care is 20 mg/kg per dose every 8 hours, there have been reports of practitioners reducing frequency to every 12 hours for preterm infants <30 weeks postmenstrual age because of decreased renal function in lower gestational ages.[5,12] A 1991 study by Englund et al determined pharmacokinetic profile in preterm neonates and recommended increasing dose interval similar to renal dose adjustment frequency for preterm infants <33 weeks.[4] However gestational age wise dose adjustment has not been adopted by American Academy of Pediatrics (AAP) or Australasian Society for Infectious Diseases (ASID).[1,2]

Aciclovir and ECMO

Cies et al suggested dose escalation (e.g., 30 mg/kg per dose every 8 hours) in the setting of continuous renal replacement therapy and/or extracorporeal membranous oxygenation.[13]

Aciclovir and renal dysfunction

Aciclovir is mainly eliminated via kidneys. Neonates at highest risk for potential aciclovir related toxicity are critically ill and have compromised organ function. Renal, hepatic, and neurologic dysfunction are commonly associated with progressive disseminated HSV infection, and often difficult to determine if the deterioration was the result of progressions of disease or drug toxicity from aciclovir. Englund et al, 1991 determined the pharmacokinetic parameters of aciclovir in neonates with renal dysfunction.[4] In the study, majority of neonates received 10 mg/kg/dose, half of the currently recommended dose of 20 mg/kg. They suggested increasing the dose interval to avoid accumulation of aciclovir in infants with worsening serum creatinine or creatinine clearance or urine output. ANMF consensus was to adopt the dose interval adjustment as described in the study.[4]

	VZV (Varicella zoster virus) treatment 20 mg/kg/dose 8 hourly is recommended by ASID guidelines for infants with active chickenpox in the following circumstances: <28 weeks at birth or Birthweight<1000g or clinically significant disease e.g. unwell, disseminated disease, pneumonitis.[1] **Safety** Aciclovir is generally well tolerated.[5] Neutropenia, renal dysfunction and crystalluria, abnormal platelet function, and elevated transaminases have been reported but these are also commonly seen in neonatal HSV disease.[5,11,14] It has been suggested to monitor for potential neutropenia, the absolute neutrophil count should be assessed twice weekly during the initial parenteral therapy.[5] Absolute neutrophil counts should be monitored at weeks 2 and 4 ,and then monthly, for infants receiving oral acyclovir for suppression therapy. Aciclovir dose reduction or granulocyte colony–stimulating factor administration may be considered if the absolute neutrophil count remains under 500/m3 for a prolonged period.[5] **Pharmacokinetics** A study of 28 infants evaluated the pharmacokinetics of aciclovir in neonates with postmenstrual age (PMA) 25–41 weeks and 1–30 postnatal days. Aciclovir pharmacokinetics was described by a 1-compartment model and the study proposed dosing: 20 mg/kg 12 hourly in PMA < 30 weeks; 20 mg/kg 8 hourly in PMA 30 to < 36 weeks and 20 mg/kg 6 hourly in PMA 36–41 weeks.[12] However, this dosage consideration is not adopted by American Academy of Pediatrics or Australasian Infectious Diseases Society.
Practice points	
References	1. Palasanthiran P, Starr M, Jones C, Giles M. Australasian Society for Infectious Diseases 2022. Management of perinatal infections. Australasian Society for Infectious Diseases. Third edition. 2022. 2. American Academy of Pediatrics. [Herpes simplex] In: Kimberlin DW, Barnett ED, Lynfield R, Sawyer MH, eds. Red Book: 2021 Report of the Committee on Infectious Diseases. Itasca, IL: American Academy of Pediatrics: 2021[407-417]. 3. Kimberlin DW. Neonatal herpes simplex infection. Clinical microbiology reviews. 2004;17(1):1-13. 4. Englund JA, Fletcher CV, Balfour Jr HH. Acyclovir therapy in neonates. The Journal of pediatrics. 1991;119(1):129-35. 5. Harris JB, Holmes AP. Neonatal herpes simplex viral infections and acyclovir: an update. The journal of pediatric pharmacology and therapeutics. 2017;22(2):88-93. 6. MerativeTM Micromedex® Complete IV Compatibility (electronic version). Merative, Ann Arbor, Michigan, USA. Available at: https://www.micromedexsolutions.com/ (cited: Dec/5/2024). 7. Senarathna SG, Strunk T, Petrovski M, Woodland S, Martinez J, Chuang VT, et al. Physical compatibility of lipid emulsions and intravenous medications used in neonatal intensive care settings. European Journal of Hospital Pharmacy. 2023. 8. Shah SS, Aronson PL, Mohamad Z, Lorch SA. Delayed acyclovir therapy and death among neonates with herpes simplex virus infection. Pediatrics. 2011;128(6):1153-60. 9. Kimberlin DW, Whitley RJ, Wan W, Powell DA, Storch G, Ahmed A, et al. Oral acyclovir suppression and neurodevelopment after neonatal herpes. New England Journal of Medicine. 2011;365(14):1284-92. 10. Jones CA, Walker KS, Badawi N. Antiviral agents for treatment of herpes simplex virus infection in neonates. Cochrane Database of Systematic Reviews. 2009(3). 11. Kimberlin DW, Lin C-Y, Jacobs RF, Powell DA, Corey L, Gruber WC, et al. Safety and efficacy of high-dose intravenous acyclovir in the management of neonatal herpes simplex virus infections. Pediatrics. 2001;108(2):230-8. 12. Sampson MR, Bloom BT, Lenfestey RW, Harper B, Kashuba AD, Anand R, et al. Population pharmacokinetics of intravenous acyclovir in preterm and term infants. The Pediatric infectious disease journal. 2014;33(1):42-9. 13. Cies JJ, Moore WS, Miller K, Small C, Carella D, Conley S, et al. Therapeutic drug monitoring of continuous-infusion acylovir for disseminated herpes simplex virus infection in a neonate receiving concurrent extracorporeal life support and continuous renal replacement therapy. Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy. 2015;35(2):229-33. 14. Kimberlin DW. When should you initiate acyclovir therapy in a neonate? The Journal of pediatrics.

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