

Antiviral management of genital herpes

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The 'ciclovirs' are extraordinarily effective and safe therapies for genital herpes, and are probably underused.

It has been 23 years since aciclovir was introduced into clinical practice and, despite its low bioavailability necessitating frequent dosing, it has gained a reputation as an effective and safe agent for the management of genital herpes. More recent introductions to the antiviral market for genital herpes are famciclovir (Famvir) and valaciclovir (Valtrex).

How do these ciclovirs work?

Aciclovir's safety and efficacy are derived from the fact that in its native state it has no significant antiviral activity but in a herpes-infected cell it is converted by viral thymidine kinase to an active form – aciclovir triphosphate. (After administration of the drug, levels of aciclovir triphosphate in herpes-infected cells are about 100 times greater than levels in uninfected cells.) Aciclovir triphosphate prevents viral replication by competing with guanosine triphosphate as a substrate for viral DNA polymerase.

Valaciclovir is the L-valine ester of aciclovir, and after absorption is converted to aciclovir (making valaciclovir a prodrug of a prodrug!). Meanwhile, famciclovir is a prodrug of penciclovir which, like aciclovir, is phosphorylated in herpes-infected cells to its active form – penciclovir triphosphate. The active form inhibits viral DNA polymerase but in a slightly different manner to aciclovir.

All three agents are approximately equivalent in efficacy against herpesviruses. Valaciclovir and famciclovir have more convenient dosing regimens than aciclovir.



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Figure. Genital herpes. Recurrent HSV-2 infection.

Clinical uses

First episode genital herpes

Early antiviral therapy is indicated in all cases of first episode genital herpes. Starting treatment as soon as possible reduces the length of time that lesions take to heal, overall pain burden, viral shedding and risk of autoinoculation. There is no evidence that antiviral therapy of primary herpes has any impact on the risk of subsequent recurrences.

Most first presentations of herpes are actually recurrences of previously asymptomatic infection; however, it is not always possible to distinguish recurrent lesions from those of primary infection. Therefore, it is prudent to treat a first presentation promptly rather than risk leaving untreated an early primary (and potentially more prolonged and prone to complication) infection.

A swab should be taken at first presentation to confirm the diagnosis. However, it should be noted that false negative viral cultures are not uncommon and a negative culture does not exclude the diagnosis. Polymerase chain reaction (PCR) testing is much more sensitive than culture and can be performed on swab specimens.

Recurrent herpes

Not all patients with genital herpes require or want treatment. Those who seek treatment for recurrent symptoms should be offered a choice between episodic treatment and suppressive therapy.

Episodic treatment

Early self-initiated therapy shortens the healing time of lesions and may abort the development of lesions if started at the time of onset of prodromal symptoms. This strategy works well for

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Table. Dosage options in treating genital herpes

Indication for PBS Authority	Drug	Dosage options	Pack size (Repeats)
Moderate to severe initial genital herpes*	Aciclovir	200 mg five times daily for 5 to 10 days or, 400 mg three times daily for 5 to 10 days	200 mg x 50
	Valaciclovir	500 mg twice daily for 5 to 10 days	500 mg x 20
	Famciclovir†	–	–
Episodic treatment of moderate to severe recurrent genital herpes ‡	Aciclovir	200 mg five times daily for 5 days or, 400 mg three times daily for 5 days	200 mg x 90 (Rp 5)
	Valaciclovir	500 mg twice daily for 3 days	500 mg x 30 (Rp 5)
	Famciclovir	125 mg twice daily for 5 days	125 mg x 40 (Rp 1)
Suppressive therapy of moderate to severe recurrent genital herpes‡	Aciclovir	200 mg three times daily or, 400 mg twice daily	200 mg x 90 (Rp 5)
	Valaciclovir	500 mg once or twice daily	500 mg x 30 (Rp 5)
	Famciclovir	250 mg twice daily	250 mg x 56 (Rp 5)

* Microbiological confirmation of diagnosis is desirable but need not delay treatment.

† Famciclovir is not available on the PBS for first episode genital herpes.

‡ Microbiological confirmation of diagnosis is required but need not delay treatment. Pathology reports from accredited laboratories must be available for audit by the HIC.

patients with occasional recurrences and clearly recognisable prodromal symptoms. Episodic treatment has little impact on number of recurrences or on the risk of transmission to sexual partners.

Suppressive therapy

Most patients with genital herpes, particularly those with frequent recurrences and where risk to sexual partners is a concern, prefer suppressive rather than episodic therapy. Adequate suppressive therapy will prevent at least 70% of clinical recurrences and reduce the frequency and duration of asymptomatic viral shedding episodes. Once-daily valaciclovir has been shown to reduce the risk of transmission to sexual partners.

There is no recommended upper limit to the duration of suppressive therapy. Most patients take suppressive therapy for six to 18 months, and then switch to episodic treatment. Some patients with persistently troublesome symptoms will need to resume suppressive therapy.

Monitoring and safety

There is no need for biochemical or haematological monitoring before or during therapy. However, care should be exercised in patients with advanced renal failure as accumulation may occur.

Long term use (five years or longer) is considered safe, but

clinical monitoring is important. Persistent genital symptoms despite adequate suppressive therapy should alert the prescriber to the possibility of a cause other than herpes.

Use in pregnancy and in lactating women should be avoided if possible, although there is no evidence of any adverse effect on fetal or neonatal development. No specific paediatric formulations are available.

Prescribing restrictions

In Australia, aciclovir, famciclovir and valaciclovir are all available as authority required pharmaceutical benefits. The Table summarises the indications, doses, pack sizes and repeats.

Conclusion

Antiviral therapy for acute, episodic or suppressive treatment of genital herpes is effective and generally well tolerated. It is not recommended during pregnancy or lactation, and dosing may need adjustment in patients with renal impairment. **MT**

This article is for general information purposes only, and the full product information should be consulted before prescribing the aforementioned medication(s).

DECLARATION OF INTEREST: Dr Denham has acted as a consultant for Novartis Pharmaceuticals and GlaxoSmithKline Australia.