New drugs

Retapamulin

Approved indication: skin infections
Altargo (GlaxoSmithKline)
tubes containing 1% ointment
Australian Medicines Handbook section 8.4.3

Retapamulin is a topical pleuromutilin antibiotic. It is indicated for impetigo and mild secondary skin infections arising from lacerations, abrasions, sutured wounds, psoriasis or dermatitis. These infections are mainly caused by *Staphylococcus aureus*, but can also be due to *Streptococcus pyogenes*.

In vitro, retapamulin is bacteriostatic against *S. aureus* and *S. pyogenes*. It is thought to act by inhibiting protein synthesis through the 50S bacterial ribosomal unit. From in vitro studies, the likelihood of *S. aureus* and *S. pyogenes* becoming resistant to retapamulin is predicted to be low.

The recommended dose is a thin layer of ointment, twice a day for five days. Systemic exposure following application to intact skin is generally very low. However, detectable concentrations were observed in 69% of babies aged 2–9 months. Retapamulin is therefore contraindicated in babies under nine months. As this drug is metabolised by cytochrome P450 (CYP) 3A4, inhibitors of this enzyme (e.g. ketoconazole) may increase retapamulin exposure in children under two years.

The efficacy of retapamulin 1% ointment in patients aged nine months and older has been studied in several phase III trials (see Table).

Impetigo

There have been two comparative trials of retapamulin for impetigo – one with a placebo[1] and the other with sodium fusidate ointment 2% (3 times daily for 7 days).[2] The median age of the participants was 7–9 years and most of them had only one impetigo lesion. Clinical success was defined as drying up (without crusts) or resolution of the lesion, or an improvement such that no further treatment was needed. The efficacy of retapamulin was significantly better than placebo and was non-inferior to sodium fusidate (see Table).

Infected wounds

Retapamulin has also been compared to a 10-day course of oral cephalexin 500 mg (twice a day) in people with secondarily infected wounds caused by trauma.[3] Two identical trials enrolled participants who had wounds less than 10 cm long with no more than 2 cm of surrounding erythema. Response to treatment was scored using a skin infection rating scale which

Table **Efficacy of topical retapamulin 1% for superficial skin infections in phase III trials**

Indication	Trial	Treatment‡	Number of patients	Clinical success rates§
Impetigo	Koning[1]	retapamulin	139	85.6%
		placebo	71	52.1%
	Oranje[2]	retapamulin	345	94.8%
		sodium fusidate	172	90.1%
Secondarily-infected wounds	Free[3]	retapamulin	1268	86.3%
		oral cephalexin	636	85.7%
	Tomayko[4]	retapamulin	246	74.8%
		placebo	113	66.4%
Secondarily-infected dermatoses	Parish[5]	retapamulin	363	82.9%
		oral cephalexin	183	86.3%

‡ retapamulin ointment was applied twice a day for 5 days, sodium fusidate ointment was applied 3 times a day for 7 days, oral cephalexin 500 mg was given twice a day for 10 days

§ clinical success was reported in the intention-to-treat population and defined as resolution or improvement in signs and symptoms such that no further treatment was needed at the end of the study period

Some of the views expressed in the following notes on newly approved products should be regarded as preliminary, as there may be limited published data at the time of publication, and little experience in Australia of their safety or efficacy. However, the Editorial Executive Committee believes that comments made in good faith at an early stage may still be of value. Before new drugs are prescribed, the Committee believes it is important that more detailed information is obtained from the manufacturer's approved product information, a drug information centre or some other appropriate source.

assessed exudates, crusting, inflammation, tissue warmth, oedema, itching and pain. The efficacy of retapamulin appeared to be non-inferior to oral cephalexin, with most patients requiring no further treatment at the end of the study period (see Table).

In another trial, retapamulin did not reach statistically significant superiority over placebo for people with secondarily infected wounds. This was presumably because clinical success rates were quite high in the placebo arm (see Table).[4]

Infected dermatoses

A single trial investigated retapamulin for secondary infections arising from psoriasis or dermatitis (atopic or allergic). The ointment was found to have comparable efficacy to oral cephalexin 500 mg twice a day for 10 days (see Table).[5]

MRSA infections

Evidence that retapamulin is effective against infections caused by methicillin-resistant *S. aureus* (MRSA) is limited. In one of the studies of secondarily infected wounds, clinical success rates were lower for MRSA infections than for methicillin-sensitive *S. aureus* infections – 68.6% (35/51) versus 92.2% (330/358).[3]

In an unpublished study of people with impetigo or secondarily infected wounds caused by MRSA, clinical success rates were significantly lower with retapamulin than with oral linezolid (63.9% vs 90.6%).

Safety and precautions

Application site reactions were the most frequently reported adverse events with retapamulin and included irritation, pruritus, paraesthesia and pain. In most of the trials, these were reported by less than 2% of people.[1-5] In comparative trials with oral cephalexin, diarrhoea was less common with retapamulin than with oral cephalexin (1.6% vs 2.7%).[3,5]

Retapamulin should not be used to treat abscesses or cellulitis and should not be applied to mucosal membranes or eyes. When prescribing antibiotics for skin infections, geographical variations in antibiotic susceptibility should be considered. If a patient is not responding to retapamulin, they may need to be switched to the appropriate systemic therapy.

Conclusion

Retapamulin ointment is better than placebo for impetigo, however, it has not been compared to mupirocin ointment. Retapamulin may be a preferable alternative to oral antibiotic therapy for mild secondary skin infections. Clinical evidence does not support the use of this drug for MRSA infections.

T manufacturer provided the product information

REFERENCES *†A

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The Transparency score (T) is explained in 'New drugs: T-score for transparency', Aust Prescr 2014;37:27.

* At the time the comment was prepared, information about this drug was available on the website of the Food and Drug Administration in the USA (www.fda.gov)

† At the time the comment was prepared, a scientific discussion about this drug was available on the website of the European Medicines Agency (www.ema.europa.eu)

A At the time the comment was prepared, information about this drug was available on the website of the Therapeutic Goods Administration (www.tga.gov.au/industry/pm-auspar.htm)