Stavudine or zidovudine in three-drug combination therapy for initial treatment of HIV infection in antiretroviral-naïve individuals

NICE has developed the Cochrane Quality and Productivity (QP) topics to help the NHS identify practices which could be significantly reduced or stopped completely, releasing cash and/or resources without negatively affecting the quality of NHS care. Each topic has been derived from a Cochrane systematic review that has concluded that the evidence shows that the practice is harmful or ineffective and should not be used, or that there is insufficient evidence to support widespread use of the practice

Summary

NICE summary of review conclusions

Overall the systematic review showed no critical difference between stavudine and zidovudine as part of first-line therapy for patients with HIV. Other existing literature reports a more significant side-effect profile with stavudine than zidovudine, and thus stavudine is not recommended as first-line treatment. Future studies and recommendations should focus on specific toxicities and tolerability when comparing these drugs.

Patients with HIV should be given zidovudine as a first-line agent rather than stavudine. This is In accordance with WHO guidelines. This will improve the quality of clinical care by using a drug with similar efficacy but a lower side-effect profile.

The 'Implications for practice' section of the Cochrane review stated:

'While stavudine and zidovudine appear to be clinically equivalent in the trial literature, there is a large literature about severe metabolic side effects with stavudine, and for this reason WHO has recently recommended against using stavudine for first-line antiretroviral therapy. Its use may evolve to be restricted to patients with severe anaemia who cannot tolerate zidovudine, or in second-line therapy. Clinical and public health judgment will be needed to weigh the risks and benefits of stavidine compared to zidovudine.'

Details of Cochrane review

Cochrane review title

Stavudine or zidovudine in three-drug combination therapy for initial treatment of HIV infection in antiretroviral-naïve individuals

Citation

Spaulding A, Rutherford GW, Siegfried N. Stavudine or zidovudine in three-drug combination therapy for initial treatment of HIV infection in antiretroviral-naïve individuals. Cochrane Database of Systematic Reviews 2010, Issue 8. Art. No.: CD008651. DOI: 10.1002/14651858.CD008651

When the review content was assessed as up to date

7/8/2009

QIPP category

Long-term conditions

Relevant codes	OPCS	ICD10	HRG
	n/a	B20–B24	n/a

Programme budget

Infectious diseases

Evidence

Relevance to the NHS

The Cochrane review identified nine randomised controlled trials which enrolled 2,159 participants taking nine different drug combinations overall. The quality of evidence for all five critical outcomes (mortality; clinical progression to AIDS; severe adverse events; response of the virus to treatment; and adherence, tolerance, or retention) was low to very low for all key outcomes.

This was due largely to design limitations. Seven of the eight studies were open-label studies, many had small sample sizes, and industry funded four of the larger studies, which accounted for almost half of all patients randomised. Only one study reported on drug resistance, and no studies reported on sexual transmission of HIV. The length of follow-up time and study settings varied greatly.

Overall, these studies showed no critical difference between stavudine and zidovudine and no statistically significant difference between the two drug combinations, including severe adverse events and adherence tolerance or retention. There was a non-significant trend towards stavudine being slightly less tolerated compared with zidovudine.

Although stavudine and zidovudine appear to be clinically equivalent in trials, evidence shows severe metabolic side-effects with stavudine and for this reason WHO has recently recommended against using stavudine for first-line antiretroviral treatment. Its use may evolve to be restricted to patients with severe anaemia who cannot tolerate zidovudine or in second-line therapy.

The authors concluded that given the different factors to be taken into account when prescribing antiretroviral treatment both in the developed and developing world, clinical and public health judgment will be needed to weigh the risks and benefits of stavudine compared with zidovudine.

Relevant NICE guidance

No relevant NICE guidance was available at the time of publication (October 2011).

Other information

World Health Organization. Rapid advice: antiretroviral therapy for HIV infection in adults and adolescents. Geneva, Switzerland: World Health Organization, 2009. Available from www.who.int/hiv/pub/arv/advice/en/index

Potential productivity savings

Estimate of current NHS use

In 2008, an estimated 83,000 people were living with HIV in the UK (approximately 69,000 in England). In 2008–09 approximately 6600 new cases of AIDS were diagnosed in England.

Level of productivity savings anticipated

Stavudine costs £5.38 for an average dose of 80 mg daily. Zidovudine costs £5.23 for an average dose of 500 mg daily. Financial savings may be generated by reducing the costs associated with treating side effects of stavudine.

Type of saving

Cash releasing

Any costs required to achieve the savings

Change can be achieved with minimal costs

Potential impact on quality of NHS care

Impact on clinical quality

Clinical quality will be improved resulting in better outcomes anticipated for patients

Impact on patient safety

Patient safety will be improved by using medications with lower known side effect profiles

Impact on patient and carer experience

Not anticipated to have any impact on patient and carer experience

Likely ease of implementation

Time taken to implement

Can be achieved quickly: 0–3 months

Healthcare sectors affected

Affects one team or department

Stakeholder support

Likely to be supported by most key influencers