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SERVICE PROVIDER NEWSLETTER
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Voluntary counselling and testing

The estimated HIV prevalence among beneficiaries of medical schemes is thought to be around 6%. Research carried out by the Centre for Actuarial Research (CARE) in 2002 showed that on average only 0.42% of all beneficiaries with access to HIV disease management programmes (DMP) actually registered with the programmes. AfA was somewhat more successful at enrolling HIV+ beneficiaries, with enrolment of 0.73% as compared to 0.16% for other DMPs. Following a concerted education and awareness programme, AfA has now increased this to 1.3% of total covered lives.

While it is possible that some HIV+ beneficiaries are aware of their status but choose not to join their DMP, it is likely that most are simply unaware of their HIV status.

Data obtained from hospital records suggest that many beneficiaries may now be moving from the asymptomatic HIV+ stage to the symptomatic AIDS stage. Accessing antiretroviral therapy at a late stage in the disease is less effective and is associated with a less favourable outcome.

For these reasons, we would like to appeal to all doctors to provide as many of their patients as possible with the opportunity to undergo voluntary counselling and testing (VCT).

High risk groups include any sexually active individuals who practise unprotected sexual intercourse, injecting drug users, as well as their sexual partners and children. In South Africa, in common with the rest of Africa, any sexually active person is at risk. It is particularly important to offer VCT to pregnant women because of the proven effectiveness of mother-to-child transmission prophylaxis.

It should be remembered that the purpose of HIV testing is not simply to identify infected individuals, but also to educate both sero-positive and sero-negative people about prevention of further transmission of the virus. In addition, HIV positive people should be made aware of the availability of effective treatment through Aid for AIDS.

All medical schemes make provision for VCT within their benefit structures.

A full description of HIV testing, as well as pre- and post-test counselling can be found on pages 1-2 of the current AfA Clinical Guidelines. These are available in hardcopy from AfA on request, or on our website.

Visit our Website
www.aidforaids.co.za
for updated clinical guidelines and latest information.

Drug interaction OF THE MONTH

Rifampicin and antiretroviral agents

In view of the epidemic nature of TB in this country, and the increasing numbers of patients co-infected with HIV and TB, it is important to review the interactions between rifampicin and antiretroviral agents.
Rifampicin is a potent inducer of the cytochrome P450 enzyme system, enhancing the metabolism of many concomitantly administered drugs. As the antiretroviral agents belonging to the non-nucleoside RTI and protease inhibitor classes are hepatically metabolized, co-administration with rifampicin may potentially lead to sub-therapeutic levels of these agents, while not significantly affecting rifampicin levels.

Concommitant administration of rifampicin and ARVs:

- **Nucleoside reverse transcriptase inhibitors** are unaffected
- **Non-nucleoside reverse transcriptase inhibitors** (nevirapine and efavirenz) have reduced levels but may still be used with rifampicin (some experts favour an increased dose of efavirenz to 800mg od)
- **Protease inhibitor** levels are markedly reduced and may not be used with rifampicin (with the exception of ritonavir 600mg bid and the dual combination of saquinavir 400mg and ritonavir 400mg bid)

Death knell for structured treatment interruptions

In our March 2003 newsletter we discussed structured treatment interruptions of HAART as a strategy. At that time trials of structured treatment interruptions in patients with established infection were shown to increase resistance without conferring any benefit. In the newsletter we referred to two small studies that had tried a single treatment interruption prior to instituting salvage therapy - both showed better virological results in the patients who underwent treatment interruption. Subsequently a larger randomized controlled trial has been published which shows that a treatment interruption prior to salvage was actually associated with a worse outcome, with more patients in this group experiencing new AIDS illnesses, and no long term virological benefit. Thus there is no place for structured treatment interruptions in routine clinical care - these should only be considered in the context of research.

Reference: Hirschel B. Beware of Drug Holidays before HIV Salvage Therapy. N Engl J Med 2003;349:827-8

Non-nucleoside reverse transcriptase inhibitor in the initial regimen

AfA recommends using a non-nucleoside reverse transcriptase inhibitor (NNRTI) rather than a protease inhibitor (PI) in the initial regimen. The reason for this is that PIs have significant long-term metabolic complications and are associated with the distressing cosmetic features of lipodystrophy. NNRTIs have very few long-term complications and are associated with a favourable alteration in the lipid profile. In randomized trials NNRTI regimens are at least as effective as PI regimens, including patients with high viral loads and low CD4 counts. The preference for NNRTIs rather than PIs in the initial regimen is consistent with current guidelines from the Southern African HIV Clinicians Society, the British HIV Association and the World Health Organisation. In special circumstances (e.g. an infant who received single dose nevirapine in the public sector) we would endorse starting with a PI regimen.

Patient contact details

Complete and accurate patient details are essential for the success of the AfA programme.

When registering a patient with AfA please ensure that a contact telephone number is included on the application form so that our adherence co-ordinators are able to contact the patient to assist you in managing the patient.

AfA and generic antiretroviral agents

Recent years have seen a significant decrease in the price of most branded antiretroviral agents. Further price reductions are anticipated with the availability of generics. The recent announcement in the press of generic HAART for R81 / month negotiated by the Clinton Foundation for South African public sector use illustrates how dramatic the price reduction can be. There is extensive international and limited local experience with generic antiretroviral agents (e.g. the use of generics by the Brazilian state-funded programme and generic agents utilised in the Medecins Sans Frontieres project in Khayelitsha, Cape Town), with good outcomes being reported. Generic stavudine has recently become available and several other generics are awaiting Medicines Control Council (MCC) registration. There are several generic combination tablets that provide three agents in one tablet taken twice daily (e.g. combination stavudine, lamivudine and nevirapine) - this should improve adherence to medication.

AfA has taken the following stance with regards to generic antiretroviral agents:

- Agents utilized in the program will require MCC registration in South Africa to ensure that only good quality agents are used. AfA South Africa will not approve or pay for the use of generic agents in South Africa if not registered for use in this country.
- Generic substitution of antiretroviral agents for patients who are stable on therapy will be required - if patients or clinicians do not want to substitute then the patient would have to pay the difference between the generic and the ethical agent (this is in keeping with the current AfA and broader Medscheme approach to generic substitution).

The Medscheme price list (MPL)

This is applicable to South African medical schemes only.

With the launch of the first registered generic antiretroviral in SA, AfA has been finalising the process to implement MPL in respect of these drugs. We envisage that the inclusion of generic ART into the MPL will begin in earnest in 2004. At the moment the generic price differential is so small as to outweigh the expense of enforcing its use.

However, indications are that by early 2004 several generics will be available and these will have a significant impact on the reduction of the cost of ART. AfA would like to add these drugs to the MPL for all schemes who currently have MPL in place and has begun discussions with these schemes. Communication will be sent out to providers towards the end of 2003 and the beginning of 2004 to inform them of these changes. All registered patients will be informed, in writing, of the policy and the implications of this.

Practice point

OF THE MONTH

Splitting the "D" drugs - choice of nucleoside reverse transcripatse inhibitor combination.

Conventional highly active antiretroviral therapy (HAART) consists of two nucleoside reverse transcriptase inhibitors (NRTIs) plus either a protease inhibitor or a non-nucleoside reverse transcriptase inhibitor. There are six NRTIs available in SA. However, abacavir is currently unaffordable and zalcitabine is toxic and seldom used. Thus for practical purposes clinicians have 4 NRTIs from which to choose: zidovudine (AZT), stavudine (D4T), lamivudine (3TC) and didanosine (ddI). Because D4T and AZT are antagonistic, these two must never be used together. Thus there are four possible dual NRTI combinations: AZT or D4T plus DDI or 3TC. These four combinations are equipotent. However, the combination of D4T plus DDI is associated with an increased risk of the metabolic complication of hyperlactataemia. The risk of severe hyperlactataemia is thought to be higher in pregnancy and the combination of D4T plus DDI should be avoided in pregnant women. Many experienced clinicians are now avoiding this combination in all patients. The current (2003) US guidelines also caution against using the combination of D4T and DDI.

The combination of AZT and 3TC is available in a single combination tablet (Combivir®), which improves adherence. However, it should be borne in mind that most patients will eventually fail their initial regimen. Thus if Combivir® is used first line then the second regimen will have the combination of D4T plus DDI together with a protease inhibitor. The convenience of combination tablets for adherence should be weighed against the toxicity of the combination of the two "D" drugs. Starting with, say D4T and 3TC and then using AZT and DDI in the second line regimen is one option. We expect several other combination antiretroviral preparations soon - many other sub-Saharan African countries are successfully using a combination of D4T and 3TC and nevirapine in one tablet taken twice daily. We also anticipate price reductions that would allow greater access to abacavir. Finally new drugs such as tenofovir should be available soon. These developments would make it easier to split the "D" drugs.