



PROTEASE INHIBITORS & ABNORMAL BLEEDING EPISODES

Protease Inhibitors (PIs) are a class of drug that are now central to providing effective control of HIV infection. There are currently four drugs in the class licensed in the UK for the treatment of HIV infection. They are normally given in combination with at least two other drugs from one or more different classes of anti-HIV drug. All Protease Inhibitors (PIs) are known by two names: a generic name (in bold below) and a brand name (in italics). For ease we will refer to the generic names, but give both below as you may encounter them by either.

Currently Licensed Protease Inhibitor Drugs in the UK

- ❑ **Saquinavir** (*Invirase or Fortovase*)
- ❑ **Indinavir** (*Crixivan*)
- ❑ **Ritonavir** (*Norvir*)
- ❑ **Nelfinavir** (*Viracept*)

Since 1996, there has been some concern that people with HIV and haemophilia or von Willebrand's Syndrome being treated with these drugs have been at risk of increased bleeds. This was initially based on anecdotal reports but there are now a number of studies on the subject.^{1,2}

Some points were common from all the papers presented:

- ❑ Increased bleeding occurs in some, but not all people with haemophilia on PIs
- ❑ The side effects seem to be equal for all PIs.³
- ❑ Most people manage to control the bleeding to some extent on increased prophylaxis.
- ❑ About 1 in 10 people have such severe bleeding that they have to stop treatment
- ❑ Increased bleeding seems to occur equally in people with haemophilia A, B or von Willebrand's Syndrome.
- ❑ Bleeds can vary quite widely in type. This could be an increase in bleeds into target joints, bleeds in to muscles, bleeds in to knuckles and toes, nose bleeds, blood in urine and stools, and heavy periods in women.
- ❑ The majority of people seem to recover from this within in a few months of starting treatment.

What is not clear is how many people are affected - studies vary from 51% of people with haemophilia on HIV combination therapy in a UK study, to 12% in a Dublin study. It is also unclear how protease inhibitors cause this kind of bleeding. No other groups on PIs have had this side effect, nor are there any measurable changes in clotting factors, platelets or any other processes to do with blood clotting.

What should I do?

If you are on, or considering going on to a drug regime that includes protease inhibitors, there are some questions to ask your doctor:

- ◆ How have other people at your centre managed on PIs?
- ◆ How often will you be monitoring me to see if there is any change in my bleeding?
- ◆ What alternatives are there if I cannot manage on PIs?

Things to consider before starting treatment

Before starting therapy, or changing combination to a regime containing a PI, there are some factors to be considered.

- Most people with HIV (around 80%) show a marked improvement in health on drug regimes including PIs.
- The problems related to bleeding seem to be managed by most people reasonably well, and are not permanent.
- There are alternative drug regimes that do not require the use of PIs, and which can be just as effective.
- Increased and/or abnormal bleeding is not a reason to be refused treatment with PIs, but should be talked over with your doctor before you start.

Here are some contact details for organisations that can keep you up to date on treatment issues, and help you to make an informed choice (see also HIV and hepatitis resources fact sheet). These include:

- The National Birchgrove Group, PO Box 9755, Solihull, B29 9WA. Email: birchgrove1@hotmail.com
- Terrence Higgins Trust helpline **0207 242 1010** noon to 10.00pm daily

Information on line:

- www.aidsmap.com. The National AIDS Manual & British HIV Association Website.
- www.hivandhepatitis.com. Information on HIV and hepatitis treatment
- www.positivelywomen.org.uk. Information about women and HIV

This fact sheet can only give basic general information drawing on medical opinion and evidence available at the time of writing. Different people may give you different advice on certain points; and there may be some variations in the way care is managed in different hospitals or areas. It is important that you contact your own doctor(s) and nurse(s) for further information and advice on your own individual circumstances.

The Society would like to thank Professor Christine Lee, Royal Free Haemophilia Centre Director, for help with this fact sheet and the Elton John AIDS Foundation and other trust and corporate supporters.

1. Yee TT, Amrolia PJ, Lee CA, et al Protease Inhibitors and unusual bleeding in haemophiliacs, *Haemophilia* 1997; 3:219-221
2. Wilde JT, Lee CA, Collins P, et al Increased bleeding associated with PI therapy in HIV-positive patients with bleeding disorders. *Br J Haematol* 1999;107:556-559
3. Although anecdotal reports suggest that **Nelfinavir** may cause fewer abnormal or increased bleeding problems than any of the other drugs.

July 2002