

# 1592U89 (abacavir) Expanded Access Program Announced

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Glaxo Wellcome announced that the 1592U89 (abacavir) expanded access program will start March 23, 1998. Separate programs for pediatrics and AIDS dementia will be announced. Individuals currently enrolled in the compassionate use program which started last Fall will continue to receive drug through their site and will have an opportunity to switch over to the new program. Glaxo said the submission of their NDA (new drug application) to the FDA for approval was on track for June/July '98.

If a patient or a physician is interested in the program you can call:

1 800 501-4672

## Inclusion Criteria

Over the age of 13; patients who are failing or intolerant to standard therapy and, in the judgement of the physician, unable to construct a viable treatment regimen without abacavir. There are no CD4 or viral load restrictions.

## Guidelines Recommended by Glaxo Wellcome

It is suggested that patients meeting any of the following criteria not enroll in the program:

- patients with current alcohol or illicit drug use which, in the investigator's opinion, may interfere with the patients ability to comply with the requirements of the study (see the discussion below about alcohol)
- patients with renal failure requiring dialysis. Physicians may consult Glaxo to discuss pharmacokinetic monitoring of patients on renal dialysis who wish to obtain abacavir
- patients with hepatic (liver) dysfunction evident by Grade 3 or 4 hyperbilirubinemia (elevated bilirubin) and AST>5 times upper limit of normal
- patients suffering from serious medical conditions such as diabetes, congestive heart failure, cardiomyopathy, or other cardiac dysfunction, which, in the opinion of the investigator would compromise the safety of the patient

## International

Expanded access programs in foreign countries will be handled by the local company officials in that country. You should contact your local Glaxo Wellcome officials for information about their programs – Canada, Europe, Australia, etc.

## Efficacy and Resistance

1592 has been shown to be potent in studies of individuals who have never before taken HIV treatment; that is, treatment naive. In a 12 week monotherapy study of 1592, viral load reductions of -1.7 to 2.1 log have been seen in treatment naive individuals. From a small study, individuals who were NRTI (AZT, 3TC, d4T, etc) experienced and added 1592 onto current NRTI therapy experienced variable responses to 1592. Viral load reductions ranged from about 2 log or more to no reductions at all. Preliminary research suggests the variability depends upon several factors including: prior NRTI experience, the number of NRTI drugs previously used, the amount of resistance to the each NRTI drug used, and possibly phenotypic resistance to 1592 prior to using the drug. Individuals in that research who did not respond to 1592 had high level phenotypic resistance to 1592 and resistance to multiple other NRTIs.

Individuals with none or low phenotypic 1592 resistance, and low resistance to other NRTIs responded to 1592. In the [What's New](#) section on this web site is a [report on 1592](#) discussing in depth this research and what is so far known about this issue. Please read it to get a better understanding of the use of 1592.

### **Side Effect to 1592U89**

A hypersensitivity reaction has been reported due to taking 1592 at an incidence rate of about 3% (reported range 2-5%). If a person has the hypersensitivity reaction to 1592 they are to stop taking the drug, and they cannot take it again. Restarting 1592 after experiencing the hypersensitivity reaction can result in serious effects. As a result of restarting therapy after experiencing hypersensitivity, some individuals have been hospitalized and there is one reported death. It is very important to clearly understand this reaction and to be able to recognize it. It is not dose dependent and is characterized by - a fever first accompanied by one or more of the following- nausea (and/or vomiting), malaise (fatigue or tiredness), rash. Additional effects that can be experienced are swollen lymph glands, diarrhea, and muscle aches. If you think you may be experiencing this reaction please consult with your doctor immediately.

### **IRB Approval**

If a doctor wants to participate in this program they have to get permission from an IRB (Institutional Review Board) who reviews the protocol. Glaxo Wellcome has a central IRB available for any doctors from which the doctor can receive permission. The quicker this process is started the quicker the doctor can start dispensing 1592.

### **Alcohol and 1592**

Alcohol intake can increase 1592 blood levels. Caution should be exercised by individuals who drink heavily. The majority of 1592 is metabolized by one of two pathways- either alcohol dehydrogenase or by UDP-gluuronyl transferase. Alcohol and any agents that inhibit these enzymes may effect the metabolism of 1592. Caution should be exercised when co-administering drugs (i.e., disulfiram, chlorzoxazone, chlorpromazine, isoniazid, chloral hydrate), or substances (i.e., ethanol) which share this metabolic pathway for their metabolism. The metabolism of 1592 is NOT dependent upon the P450 system that is used by protease inhibitors and NNRTIs. To date, no specific contra indications (drugs not to be taken with 1592) to abacavir have been identified, but caution should be exercised with the use of drugs known to cause liver toxicity. Since the hypersensitivity reaction to 1592 is not dose dependent, increased 1592 blood levels from alcohol should not increase the risk of developing the hypersensitivity reaction.

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