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What’s New in Treatment Information?

New Formulation of Sustiva Available

There is a new 600mg formulation of efavirenz (Sustiva). The information below is a reprint from the FDA HIV/AIDS email Service.

On February 1, 2002 the FDA approved a new formulation of Sustiva (efavirenz), a non-nucleoside reverse transcriptase inhibitor for the treatment of HIV infection. Sustiva will now be available as a 600mg tablet to be taken once daily, in combination with a protease inhibitor and/or nucleoside analogue reverse transcriptase inhibitors (NRTIs). Sustiva, will continue to also be available in the 50mg, 100, and 200mg capsules.

In addition, the Sustiva label was revised to include new statements in the DOSAGE AND ADMINISTRATION section. The revised statements are shown within > < symbols, below.

"Adults: The recommended dosage of SUSTIVA is 600mg orally, once daily, in combination with a protease inhibitor and/or nucleoside analogue reverse transcriptase inhibitors (NRTIs). It is recommended that SUSTIVA be taken on an empty stomach, preferably at bedtime. The increased efavirenz concentrations observed following administration of SUSTIVA with food may lead to an increase in frequency of adverse events. Dosing at bedtime may improve the tolerability of nervous system symptoms."<

In addition, the CLINICAL PHARMACOLOGY and PRECAUTIONS sections have been updated to include drug interaction information on Sustiva with the following medications: St. John’s wort, lorazepam, methadone, cetirizine and rifabutin. The ADVERSE REACTION section was also revised to update the incidences of adverse events and laboratory abnormalities seen in clinical trials.

The revised label is available in PDF format at www.fda.gov/cder/foi/label/2002/21360lbl.pdf.

Dear Doctor Letter regarding Kava Kava

The FDA communicates information about serious events or problems encountered with medical products using different means, including press releases, articles in professional journals and with industry through what are called “Dear Doctor” and “Dear Health Professional” letters.

Below is a reprint of a “Dear Doctor” letter from the FDA about an herb called Kava Kava (Piper methysticum). Additional information provided by CATIE (Canadian Treatment Information Exchange) is included in italics within the reprinted text. CATIE sent a general alert to the HIV community last week about Kava kava and liver toxicity is included in document in italics.

Please note

- Kava is listed as an herb with reported herb drug interactions in Project Inform’s publication titled Herb, Supplements & HIV. (http://www.projectinform.org/fs/herbs.html).
- The following signs/symptoms may be associated with liver problems: jaundice (yellowing of the skin or whites of the eyes), brown urine, nausea, vomiting, unusual tiredness, weakness, stomach or abdominal pain and/or loss of appetite.
- If a someone suspects she or he may be having medical problems related to the use of Kava Kava, refer him or her to medical care and encourage filing a report of the incident with the FDA MedWatch program by telephone (1-800-332-1088) or through the Internet (http://www.fda.gov/medwatch).

Dear Health Care Professional Colleague:

The Food and Drug Administration (FDA) needs your help. The agency is investigating whether the use of dietary supplements containing kava (also known as kava kava or Piper methysticum) is associated with liver toxicity. To help us determine whether there is a problem in the United States, we are asking that you review your cases of liver toxicity to determine if any may be related to the use of kava-containing dietary supplements.

Products containing herbal extracts of kava have been implicated in cases of serious liver toxicity in Germany and Switzerland. Approximately 25 reports of hepatic toxicity associated with the use of products containing kava extracts have been reported in these countries. Serious hepatic adverse effects
Osteonecrosis, Osteopenia and Osteoporosis

This information is from the Federal Guidelines for the Treatment HIV-Infected Adults and Adolescents. The Federal Guidelines were updated on February 4.

Avascular necrosis and decreased bone density are now recognized as one of the emerging metabolic complications of HIV infection that may be linked to highly active antiretroviral regimens. Both of these bone abnormalities have been reported in adults and children with HIV infection who are now surviving longer with their disease in part because of HAART.

Avascular necrosis involving the hips was first described in HIV-infected adults and more recently in HIV-infected children (known as Legg Calve Parthese Disease). The diagnosis of osteonecrosis is usually made by CT scan or MRI, when these studies are performed in response to patient’s complaints of pain in an affected hip or spine. However, asymptomatic disease can occur in 5% of patients. It does not appear that avascular necrosis is clearly associated with a specific antiretroviral regimen in HIV-infected adults, but it has been linked to corticosteroids use in some patients. Factors associated with osteonecrosis include alcohol abuse, hemoglobinopathies, corticosteroid treatment, hyperlipidemia, and hypercoagulability states. The occurrence of hyperlipidemia suggests an indirect link between antiretroviral therapy and the occurrence of osteonecrosis in HIV-infected patients. However, prospective clinical studies will be required to establish this association. There is no generally accepted medical therapy for avascular necrosis and surgery sometimes becomes necessary for disabling symptoms.

The decrease in bone mineral density (BMD) — both moderate (osteopenia) and severe (osteoporosis)—is a reflection of the competing effects of bone reabsorption by osteoclasts and bone deposition by osteoblasts and is measured by bone densitometry. Prior to HAART, there were reports of marginal decrease in BMD in HIV-infected individuals. This evidence for decrease bone formation and turnover has been demonstrated with more potent antiretroviral therapy, in particular protease inhibitors. Studies of bone demineralization in a limited number of patients receiving HAART have shown that up to 50% of patients receiving a PI-based regimen developed evidence of osteopenia compared to 20% of patients who are untreated or receiving a non-PI-containing regimen. Other studies have shown that patients with lipodystrophy with extensive prior PI therapy had associated findings of osteopenia (28%) or osteoporosis (9%) respectively. The preliminary observations that there are increased serum and urinary markers of bone turnover in patients on protease-containing HAART who have osteopenia support the possible link of bone abnormalities to other metabolic abnormalities observed in HIV-infected patients. There is no recommendation at the present time for routine measurement of bone density in asymptomatic patients by dual energy X-ray absorptiometry (DEXA) or by newer measurements such as quantitative ultrasound (QUS). Specific prophylaxis or treatment recommendations to prevent more significant osteoporosis have not been developed for HIV-infected patients with osteopenia. Based on experience in the treatment of primary osteoporosis, it would be reasonable to recommend adequate intake of calcium and vitamin D and appropriate weight bearing exercise. When fractures occur and osteoporosis is documented, more specific and aggressive therapies with bisphosphonates, raloxifene or calcitonin may be indicated.

Skin Rash

This information is from the Federal Guidelines for the Treatment HIV-Infected Adults and Adolescents. The Federal Guidelines were updated on February 4. Skin rash occurs most commonly with the NNRTI class of drugs. Most cases are mild to moderate in nature, occurring within the first few weeks of therapy. Some experts suggest managing the skin rash with antihistamine for symptomatic relief without drug discontinuation, although the wisdom of treating through such rashes has been questioned. More serious cutaneous manifestations such as Stevens-Johnson syndrome (SJS) and toxic epidermal necrosis (TEN) should result in the prompt and permanent discontinuation of the NNRTI or other offending agents.

Most cases of skin rash are confined to cutaneous reactions. However, a severe or even life-threatening syndrome of drug rash with eosinophilia and systemic symptoms (DRESS) has also been
described. The systemic symptoms may include fever, hematological abnormalities, and multiple organ involvement.

Among the NNRTIs, skin rash occurs more frequently and in greater severity with nevirapine. Using a two-week lead-in dose escalation schedule when initiating nevirapine therapy may reduce the incidence of rash. In a case-control multi-national study, SJS and/or TEN were reported in 18 HIV-infected patients. Fifteen of the 18 patients were receiving nevirapine. The median time from initiation of nevirapine to onset of cutaneous eruption was 11 days, with two-thirds of the cases occurring during the initial dosing period. Female patients appear to have as much as seven-fold higher risk for developing grade 3 or 4 skin rashes than male patients. The use of systemic corticosteroid or antihistamine therapy at the time of the initiation of nevirapine to prevent development of skin rash has not proven effective. In fact, a higher incidence of skin rash has been reported in the steroid- or antihistamine-treated patients. At present, prophylactic use of corticosteroids should be discouraged.

Skin rash appears to be a "class adverse reaction" of the NNRTIs. The incidence of cross hypersensitivity reactions between these agents is not known. In a small number of reports, patients with prior history of nevirapine-associated skin rash had been able to tolerate efavirenz without increase rate of cutaneous reactions. Most experts would not recommend the use of another NNRTI in those patients who experienced SJS or TEN with one NNRTI. Initiating NNRTI in a patient with history of mild to moderate skin rash with another NNRTI should be done with caution and close follow-up.

Among the NRTIs, skin rash occurs most frequently with abacavir. Skin rash may be one of the presenting symptoms of abacavir-associated systemic hypersensitivity reaction, in which case, therapy should be discontinued without rechallenge.

Of all the PIs, skin rash occurs most frequently with amprenavir, with incidence of up to 27% in clinical trials. Amprenavir is a sulfonamide, the potential of cross reactivity between amprenavir and other sulfa drugs is not known. As a result, amprenavir should be used with caution in patients with history of sulfa allergies.

What’s New in Public Policy?

President Bush Releases Inadequate HIV/AIDS Budget for Second Year in a Row

In early February, President Bush released his proposed budget for Fiscal Year 2003, which begins on October 1 of this year. Included in this proposal are his suggested funding levels for domestic and international HIV/AIDS programs.

This budget proposal is extremely troubling and demonstrates that the Bush Administration does not consider HIV/AIDS to be a priority. For the second year in a row, the President is calling for no increase for HIV/AIDS care and treatment programs funded through Ryan White CARE Act and the AIDS Drug Assistance Program (ADAP). With the growing number of people living with HIV and increased cost of healthcare and treatment, this budget request is really a cut in funding. In addition, care and treatment services received very inadequate increases in the final budget for the current fiscal year. Many ADAPs across the country are already experiencing financial difficulties and one more year of inadequate funding will likely cause major limitations in treatment access.

The President’s proposed budget also calls for no increase in spending for HIV prevention programs and the Minority HIV/AIDS Initiative, which funds prevention, care, and treatment services targeted to communities of color. It asks for a modest (but not sufficient) increase for housing services funded through the Housing Opportunities for People With AIDS (HOPWA) program and a significant increase in funding for AIDS research programs at the National Institutes of Health (NIH).

On the international front, President Bush is asking for a $200 million contribution to the Global Fund to Fight AIDS, Tuberculosis, and Malaria. This is the same amount pledged by the U.S. last year and falls far short of the $7-10 billion identified as needed each year to fight the global pandemic.

Fortunately, President Bush’s proposed budget is just that—a proposal. Focus now shifts to Congress, which will determine its own spending levels for these programs. In the next few months, subcommittees in the House of Representatives and the Senate will hear public testimony about the importance of adequate funding for HIV/AIDS programs. They will then create their own budget proposal which will be reviewed and voted on by the full House and Senate. If there are differences between the House and Senate versions, a joint House/Senate conference committee will convene to negotiate a final budget.

It will take a strong grassroots campaign to ensure that these funding levels are increased by Congress. We must let our members of Congress know that President Bush’s budget for HIV/AIDS programs is unacceptable. Everyone living with or affected by HIV/AIDS should plan to be a part of this effort. If all of us took a few minutes in the next few months to write a short note to our federal representatives urging them to take a leadership role in the fight for adequate funding, it would make a huge difference.

Project Inform will be sending alerts and updates to Treatment Action Network members as the budget process gets underway. If you would like to be part of this effort, you can join TAN by sending an e-mail to tan@projectinform.org or through on the web at http://projinf.fauldhouse.com/tanlist/tanlist.php4.

AIDSWATCH Dates Announced

The dates for AIDSWATCH, the national constituent HIV/AIDS lobby days in Washington, D.C. were recently announced. The event will be held from June 9-11, 2002.

This lobbying event is organized by the National Association
of People With AIDS (NAPWA), with help from national and local partners, including Project Inform. The purpose of AIDSWATCH is to provide an opportunity for those most affected by HIV/AIDS to speak directly with their elected representatives about the need for adequate funding. Since the President’s proposed budget for HIV/AIDS programs is so troubling, this year’s AIDSWATCH is perhaps more important than ever. Members of Congress need to be reminded by their constituents that AIDS must continue to be a top priority.

AIDSWATCH is a three-day event. The first day consists of a briefing on key HIV/AIDS issues and training on how to have an effective legislative visit. The next two days are spent meeting with members of Congress and/or their staff. You do not need to be an expert on lobbying or the issues to attend AIDSWATCH. You bring your personal stories so that our representatives can understand better how their efforts in securing adequate funding will help those they represent.

For more information about AIDSWATCH, go to NAPWA’s website at www.napwa.org or call Antigone Hodgins at 202-898-0414.

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