U.S. FOOD & DRUG ADMINISTRATION

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FDA HIV Email Updates provide information about FDA HIV product approval, safety warnings, medical product labeling changes, notices of upcoming meetings, and notices about proposed regulatory guidances.

The FDA approved changes to the Sustiva (efavirenz) package insert to:

- Update information on hepatotoxicity in DOSAGE and ADMINISTRATION, WARNINGS AND PRECAUTIONS, ADVERSE REACTIONS and Patient Information sections.
- Update CONTRAINDICATIONS and Patient Information sections with drug-drug interaction information on elbasvir and grazoprevir.
- Update DRUG INTERACTIONS, Table 5 with information about hepatitis C antiviral agents

The specific changes are as follows:

In section **2 DOSAGE AND ADMINISTRATION**, a new sub-section was added.

- 2.1 Hepatic Function - Monitor hepatic function prior to and during treatment with SUSTIVA.

SUSTIVA is not recommended in patients with moderate or severe hepatic impairment (Child Pugh B or C)

In Section **4 CONTRAINDCATIONS**, the following contraindication was added:

- Coadministration of efavirenz with elbasvir and grazoprevir is contraindicated

In Section **5 WARNINGS AND PRECAUTIONS,** we revised the following sub-section:

- 5.5 Psychiatric Symptoms
- 5.9 Hepatotoxicity

5.5 Psychiatric Symptoms

There have also been occasional post-marketing reports of death by suicide, delusions, and psychosis-like behavior although a causal relationship to the use of SUSTIVA cannot be determined from these reports. Post-marketing cases of catatonia have also been reported and may be associated with increased efavirenz exposure.

5.9 Hepatotoxicity

Post-marketing cases of hepatitis, including fulminant hepatitis progressing to liver failure requiring transplantation or resulting in death, have been reported in patients treated with SUSTIVA. Reports have included patients with underlying hepatic disease, including co-infection with hepatitis B or C, and patients without pre-existing hepatic

disease or other identifiable risk factors.

SUSTIVA is not recommended for patients with moderate or severe hepatic impairment. Careful monitoring is recommended for patients with mild hepatic impairment receiving SUSTIVA.

Monitoring of liver enzymes before and during treatment is recommended for all patients. Consider discontinuing SUSTIVA in patients with persistent elevations of serum transaminases to greater than five times the upper limit of the normal range.

Discontinue SUSTIVA if elevation of serum transaminases is accompanied by clinical signs or symptoms of hepatitis or hepatic decompensation.

In section **7 DRUG INTERACTIONS**, we updated Table 5 is updated with information about hepatitis C antiviral agents as follows:

Table 5: Established and Other Potentially Significant Drug Interactions: Alteration in Dose or Regimen May Be Recommended Based on Drug Interaction Studies or Predicted Interaction

Concomitant Drug Class: Drug Name	**Effect**	**Clinical Comment**
Hepatitis C antiviral agents		
Elbasvir/Grazoprevir	↓ elbasvir ↓ grazoprevir	Coadministration of SUSTIVA with elbasvir/grazoprevir is contraindicated [see Contraindications (4)] because it may lead to loss of virologic response to elbasvir/grazoprevir.
Pibrentasvir/Glecaprevir	↓pibrentasvir ↓glecaprevir	Coadministration of SUSTIVA is not recommended because it may lead to reduced therapeutic effect of pibrentasvir/glecaprevir.
Simeprevir	↓ simeprevir ↔ efavirenz	Concomitant administration of simeprevir with SUSTIVA is not recommended because it may result in loss of therapeutic effect of simeprevir
Velpatasvir/ Sofosbuvir	↓ velpatasvir	Coadministration of SUSTIVA and sofosbuvir/velpatasvir is not recommended because it may result in loss of therapeutic effect of sofosbuvir/velpatasvir.
Velpatasvir/Sofosbuvir/Voxilaprevir	↓ velpatasvir ↓ voxilaprevir	Coadministration of SUSTIVA and sofosbuvir/velpatasvir/voxilaprevir is not recommended because it may result in loss of therapeutic effect of sofosbuvir/velpatasvir/voxilaprevir.

The updated label will soon be available at drugs@fda or DailyMed

Steve Morin Office of Health and Constituent Affairs Food and Drug Administration	**Kimberly Struble** Division of Antiviral Products Food and Drug Administration

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