

Safety of Antiviral Therapy of Chronic Hepatitis B During Pregnancy

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The worldwide magnitude of hepatitis B infection is difficult to overstate. Of the two billion people with HBV, approximately 350 million are thought to be chronically infected.¹ Although the source of infection varies with the demographics of the patient, perinatal infection via vertical transmission is a leading cause of chronic hepatitis B. In 1985, it was estimated that the frequency of chronic hepatitis B infection in pregnancy was 5-15/1,000.² In addition to protecting the health of the mother, treatment during pregnancy may reduce the risk of vertical transmission and consequently reduce the prevalence of chronic disease.³ Unfortunately, very little has been published about the safety of anti-hepatitis B medications in pregnancy. Consequently, the available information is limited to that from pregnancy registries, case reports, and inadvertent exposures reported to the manufacturer. There are five FDA-approved medications for treatment of chronic hepatitis B.

Adefovir Dipivoxil—FDA category C

In a communication from the manufacturer dated February 1, 2006, there have been 14 pregnancies among study patients taking ADV. There were three spontaneous abortions and five elective abortions. Of the remaining six pregnancies, four patients delivered apparently unaffected infants, one patient was undelivered at last report, and the final patient delivered a preterm infant at 24-26 weeks' gestation. That infant, though apparently not dysmorphic, died 4 days after birth from cerebral hemorrhage and hyaline membrane disease, frequent complications of severe prematurity.

The Antiretroviral Pregnancy Registry Interim report issued in December 2005 documents five live births following exposure to ADV. There were no malformations reported.⁴

Entecavir—FDA category C

No published studies or reports of outcomes following accidental exposure during pregnancy were found.

Lamivudine—FDA category C

Lamivudine readily crosses the placenta and accumulates in human amniotic fluid.⁵ Clinical experience has demonstrated no increased incidence of congenital anomalies among infants following intrauterine exposure to lamivudine.^{4,6,7}

Interferon alfa—FDA category unknown

Based on pharmacokinetic studies in two human pregnancies, interferon alfa is not thought to cross the placenta in significant amounts.⁸ Information from the manufacturer has documented that, in rhesus monkeys, exposure to very high doses (20 to 500 times the human dose) of interferons alpha-2a and alpha-2b may result in an increased incidence of spontaneous abortions.

There are several case reports of successful pregnancies following treatment with interferon alfa for a variety of indications, including chronic myeloid leukemia, essential

thrombocytopenia, mycosis fungoides, chronic hepatitis C, and chronic inflammatory demyelinating polyneuropathy.⁶ Although no evidence of an increased risk of congenital malformations has been seen, there are case reports suggesting an increased risk of intrauterine growth restriction and perhaps neonatal lupus.⁹

Peginterferon alfa-2a— FDA category C

No published studies or reports of outcomes following accidental exposure during pregnancy were found.

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