

KOATE - October 1975 (UK)

Draft Koate package insert and draft labelling for the UK

The package insert begins by drawing attention to the hepatitis risk :

"SEE SECTIONS ENTITLED "INDICATIONS" AND "WARNING" FOR DESCRIPTION OF HEPATITIS RISK."

and a further warning appears, again in capital letters at point 7 of the paragraph headed "Description" :

"THIS PRODUCT IS PREPARED FROM UNITS OF HUMAN PLASMA WHICH HAVE BEEN TESTED AND FOUND NON-REACTIVE FOR HEPATITIS ASSOCIATED (AUSTRALIA) ANTIGEN. UNFORTUNATELY THIS TEST DOES NOT WITH CERTAINTY PRECLUDE THE PRESENCE OF HEPATITIS VIRUS. SEE WARNING."

And under "Indications" there is the caution :

"CAUTION: BECAUSE OF THE POSSIBILITY THAT ANY LOTS OF KOATE™ MIGHT CONTAIN THE CAUSATIVE AGENTS OF VIRAL HEPATITIS, ITS USE MUST BE CONSIDERED IN LIGHT OF THIS HAZARD, PARTICULARLY IN PERSONS WITH FEW PREVIOUS TRANSFUSIONS OF BLOOD AND PLASMA PRODUCTS.

Kasper and Kipnis⁽⁴⁾ have concluded that those who had little exposure to blood products had a high risk of developing hepatitis after introduction of clotting factor concentrates, such as this product. For those patients, especially those with mild hemophilia, they recommend single donor products. However, for patients with moderate or severe hemophilia who have received numerous infusions of blood and plasma products, they feel that the risk of hepatitis is small. They believe that the clotting factor concentrates have so greatly improved the management of severe hemophilia that these products should not be denied to appropriate patients."

followed in the same paragraph by a boxed WARNING :

"Koate™ concentrate is a purified dried fraction of pooled plasma obtained from many donors. *SINCE THE PRESENCE OR ABSENCE OF HEPATITIS VITUS IN KOATE™ CONCENTRATE CANNOT BE PROVEN WITH ABSOLUTE CERTAINTY, THE PRESENCE OF SUCH A VIRUS SHOULD BE ASSUMED.* and the hazard of administering Koate™ concentrate should be weighed against the medical consequences of withholding it."

The subsequent paragraph offers the following advice :

"Since there is this definite risk of hepatitis, we suggest that the physician give consideration to explaining to the patient (or the patient's family) the relative

risks of giving or withholding this product. Then, should the patient develop hepatitis, as a result of the injection, it will not come as a surprise, and there is not nearly the likelihood of resentment, which will most surely follow and unexplained and unexpected infection."

and under the paragraph headed "Warranty" is a further reminder of the risk of hepatitis :

" and that the risk of transmitting viral hepatitis [be] carefully weighed before the product is prescribed. The foregoing statement is made in lieu of any other warranty express or implied, including any warranty of merchantability or fitness....."

The proposed carton label repeats the warning, on one of the top flaps :

"HEPATITIS DANGER SEE DIRECTION SHEET."

and on the side panel repeats a (portion of) the boxed warning from the package insert :

"Since the presence or absence of hepatitis virus in Koate™ concentrate cannot be proven with absolute certainty, the presence of such a virus should be assumed and the hazard of administering Koate™ concentrate should be weighed against the medical consequences of withholding Koate™."

the proposed container label states :

"HEPATITIS DANGER. SEE DIRECTION SHEET."