

Release of di(2-ethylhexyl)phthalate from polyvinylchloride bags during docetaxel infusions

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Docetaxel (Taxotere[®]), a cytotoxic anticancer drug belonging to the taxane family, is administered by intravenous infusion after dilution of an injection concentrate in a solvent supplied by the manufacturer followed by further dilution in 5% glucose or 0.9% NaCl. Although Taxotere[®] contains an excipient, polysorbate 80, which has been shown to be responsible for the release of the plasticizer di(2-ethylhexyl) phthalate (DEHP) from medical devices made of PVC, the supplier does not indicate that the docetaxel solutions should be made up in PVC-free containers. We tested for the presence of DEHP in docetaxel solutions stored in PVC and in low-density polyethylene (LPDE) bags according to various conditions of storage.

MATERIALS AND METHODS

- Docetaxel
TAXOTERE 80 mg/8 ml
Sanofi-Aventis



- LDPE bags
ECOFLAC 50 ml,
B B. Braun medical

- PVC bags
PERFUFLEX 50 ml
Fresenius



DEHP concentrations determined by HPLC.
Samples analysed at T0, 1h, 2h, 4h, 24h, 48 h and 192 h.
Docetaxel solutions stored in PVC and in low-density polyethylene (LPDE) bags at 0.74 mg/ml in 0.9% NaCl.

Interactions
drug/container PVC
and LPDE

Ambient
temperature
and light

Refrigerator
at 4°C

RESULTS



Chromatographic assay of solutions of docetaxel in containers showed no DEHP after 8 days storage irrespective of conditions of temperature and light.



Table 1: DEHP ($\mu\text{g/ml}$) in solutions containing 0.74 mg/ml docetaxel in 0.9% NaCl contained in PVC bags.

PVC bags conservation	After reconstitution T0	T1h	T2h	T4h	T24h	T48h	T192h
Ambient temperature and light	24.55	40.46	53.56	85.94	321.13	487.87	787.41
Refrigerator	25.41	31.71	37.23	46.28	127.00	184.78	301.91

The release was less marked when the bags were stored in the refrigerator but the values still largely exceeded the acceptable limit value of 5 $\mu\text{g/ml}$.

CONCLUSION



PVC containers are to be avoided for the preparation of docetaxel solutions since release of DEHP into such solutions began as soon as they came into contact with the container, and increased thereafter with storage time.