Pharmacotherapeutic report, summary

Albumin-bound paclitaxal (Abraxane®) for the indication 'metastatic breast cancer'

Approved on 27-08-2012 by the Medicinal Products Reimbursement Committee (CFH)

Medicine. Albumin-bound paclitaxel (5 mg/ml powder for suspension for infusion)

Registered indication. "Treatment of metastatic breast cancer in adult patients who have failed first-line treatment for metastatic disease and for whom standard, anthracycline containing therapy is not indicated."

Posology. 260 mg/m^2, once per 3 weeks, i.v. during 30 minutes.

Mechanism of action. Antimicrotubulair agent that promotes the assembly of microtubules from tubulin dimers and stabilises the microtubules by preventing depolymerisation. This stability results in the inhibition of the normal dynamic reorganisation of the microtubule network that is essential for the vital interphase and mitotic cellular functions. In addition, paclitaxel induces abnormal arrays or "bundles" of microtubules throughout the cell cycle and multiple asters of microtubules during mitosis. Contains human serum albumin-paclitaxel nano-particles, where the paclitaxel is present in a non-crystalline, amorphous state. Albumin is known to mediate endothelial caveolar transcytosis of plasma constituents and the presence of albumin improves the *in vitro* endothelial cell transport of paclitaxel.

Specific details. Unlike conventionally formulated paclitaxel (SB-paclitaxel), Abraxane® (NAB-paclitaxel) uses albumin as a carrier of paclitaxel, which means that premedication is superfluous.

Summary of the therapeutic value

Intended effects. A sub-group analysis involving patients in second and third line settings shows a favourable effect of NAB-paclitaxel in terms of overall survival, TTP and ORR in comparison to SB-paclitaxel. Interpreting these data is hampered by the fact that the analyses were carried out post hoc; furthermore, analysis of the ORR was not blinded in this setting. No data on HER2-status are available and patients with HER2-positive tumours were not treated with trastuzumab. In addition SB-paclitaxel was used over a three-week regime in the control arm, while a weekly regime would probably have been more effective. The effect observed in the control arm may therefore have been underestimated.

Unintended effects. The use of NAB-paclitaxel is associated with reduced myelosuppression, but with increased sensory neuropathy at a 49% higher dose in comparison to SB-paclitaxel. Reversibility of sensory neuropathy occurs more rapidly when NAB-paclitaxel is used, than with SB-paclitaxel. There was no difference between the two paclitaxel formulations with regard to the number of patients who terminated the study or who needed dose adjustments due to unfavourable effects.

Experience. Experience with NAB-paclitaxel is limited, while ample experience has been gained with SB-paclitaxel.

Applicability. The applicability of NAB-paclitaxel is not as broad as that of SB-paclitaxel.

Ease of use. The shorter infusion time and lack of a need to administer premedication means that ease of use is better with NAB-paclitaxel.

Final conclusion on therapeutic value. General survival, TTP and tumour response of patients treated with NAB-paclitaxel in second-line or third-line seems greater in comparison with SB-paclitaxel. However, the probative value of these results is limited because this was a post hoc sub-group analysis, no distinction was drawn between patients with HER2-positive and HER2-negative tumours, and the frequency of administration in the control arm was not the most effective. Both treatments have similar adverse effects, with a smaller incidence of severe neutropenia, but more serious sensory neuropathy with NAB-paclitaxel in comparison with SB-paclitaxel. The administration of premedication is required for SB-paclitaxel but not for NAB-paclitaxel. The conclusion is that the therapeutic value of NAB-paclitaxel is comparable to that of SB-paclitaxel in the second-line or third-line treatment of metastatic breast cancer.