

Recommendations and Reasons

Committee to Evaluate Drugs (CED)

Nab-paclitaxel

Product:

Nab-Paclitaxel (Abraxane®) 100mg/vial injection

Class of drugs:

Antineoplastic

Indication:

Treatment of metastatic breast cancer

Manufacturer:

Abraxis Oncology

The manufacturer has acknowledged CED's concerns and has submitted updated information. The resubmission is currently under review.

Highlights of Recommendation:

- ◆ Nab-paclitaxel is licensed for use in the treatment of metastatic breast cancer. It is given intravenously.
- ◆ Nab-paclitaxel is a new formulation of paclitaxel, a drug often used to treat breast cancer. Some patients have allergic or adverse reactions to the other ingredients used in standard preparation of paclitaxel. The new formulation coats paclitaxel in a protein which reduces or prevents the allergic or adverse reactions.
- ◆ Usually, patients taking standard paclitaxel or docetaxel (a different taxane product) have to take other medications to reduce allergic reactions or side effects, before receiving paclitaxel or docetaxel intravenously.
- ◆ The CED reviewed several studies, including one which showed a greater response rate for nab-paclitaxel than for standard paclitaxel.
- ◆ Although the two drugs have not been directly compared, the CED noted that the evidence for docetaxel is stronger than for nab-paclitaxel.
- ◆ Nab-paclitaxel may be useful for some patients who have important contraindications to corticosteroids or other pre-medications given before administration of paclitaxel or docetaxel.
- ◆ **Overall, the CED noted that when compared to standard paclitaxel and docetaxel, there is less risk that nab-paclitaxel will cause adverse reactions in patients. The CED concluded that nab-paclitaxel has a place in the treatment of patients who have had adverse or allergic reactions to taxanes or who cannot take the pre-medications used to lessen the adverse effects with the taxane class of drugs.**

Background:

Breast cancer is the most common cancer among Canadian women. In Ontario, about 8,400 women are diagnosed with breast cancer every year; about 10 percent will develop metastatic disease, advanced breast cancer that has spread beyond the original tumour site. About 3 percent will already have metastatic breast cancer by the time they are diagnosed. Most women in Ontario who develop metastatic breast cancer are treated with either hormone therapy, or a single anti-cancer drug (chemotherapy).

Women whose metastatic breast cancer is progressing rapidly are often offered combination chemotherapy, because a quick response to treatment is necessary to gain control of the disease. Combination chemotherapy generally results in more dangerous side effects than treating the cancer with a single drug.

Paclitaxel and docetaxel are taxane drugs which are effective in the management of metastatic breast cancer, but are associated with significant side effects and can be difficult for patients to tolerate. The method of preparing these medications so they can be administered, in solutions consisting of a type of castor oil (cremophor EL) and polysorbate 80, are believed to be responsible for some of the side effects. Patients often take other drugs before having paclitaxel and docetaxel administered, to help reduce these adverse reactions.

Nab-paclitaxel (nanoparticle albumin-bound paclitaxel) is a formulation of paclitaxel encased in albumin, a non-toxic, water-soluble protein found in human blood, as well as in plants and seeds. Encasing paclitaxel this way is designed to deliver the drug directly to the tumour site, with fewer side-effects than paclitaxel or docetaxel. Nab-paclitaxel, like all taxanes, works by slowing or stopping the growth of cancer cells in the body. This drug is injected into a vein, on its own or in combination with other medications as part of chemotherapy.

continued...

CED Recommendation-

The CED recommended that nab-paclitaxel (Abraxane) be funded under Cancer Care Ontario's New Drug Funding Program for the treatment of metastatic breast cancer, with specific criteria.

Executive Officer Decision

Based on the CED's recommendation, the Executive Officer decided to fund nab-paclitaxel (Abraxane) under Cancer Care Ontario's New Drug Funding Program, according to specific criteria.

Status

Funding available through Cancer Care Ontario's New Drug Funding Program.

Detailed Discussion:

- ◆ The Committee reviewed several trials, concentrating on Grandishar WJ et al. Phase III trial of nanoparticle albumin-bound paclitaxel compared with polyethylated castor oil-based paclitaxel in women with breast cancer. *J Clin Oncol.* 2005;23:7794-7803.
- ◆ The Committee questioned the statistical power of the study, because its non-inferiority design assumed nab-paclitaxel was at least 75 percent as effective as standard paclitaxel. Non-inferiority is usually predefined at a threshold of 90 percent to be considered as effective as the comparator standard therapy.
- ◆ There is no phase III, randomized controlled trial directly comparing the efficacy of nab-paclitaxel to docetaxel. This was relevant to the review as the most common taxane used to treat metastatic breast cancer is docetaxel rather than paclitaxel.
- ◆ Nab-paclitaxel appears to be less toxic in terms of treatment-related Grade 4 neutropenia, when compared to paclitaxel, but is associated with more frequent sensory neuropathy (damage to the sensory nerves of the peripheral nervous system).
- ◆ The most frequent adverse effects reported in the Grandishar trial included hair loss, numbing, burning and tingling sensations in the arms and legs, tiredness, decreased white blood cells, joint pain, muscle pain, nausea, infection, and diarrhea.
- ◆ Patients who receive paclitaxel or docetaxel also may suffer hypersensitivity (allergic) reactions. They routinely require treatment with histamine blockers and corticosteroids before receiving paclitaxel or docetaxel.
- ◆ Nab-paclitaxel may be advantageous for some patients, such as diabetics, for whom corticosteroids are contraindicated, because treating with nab-paclitaxel does not require pre-medication.
- ◆ The cost-effectiveness analysis submitted by the manufacturer (using life years as the outcome) assumed a mortality benefit by using differential life years but the direct comparison trial showed no difference in survival rate between nab-paclitaxel and paclitaxel.
- ◆ Treating patients with nab-paclitaxel costs almost the same as treating with docetaxel, using the dosage recommended in the Practice in Evidence-based Care guidelines.

- ◆ **Overall, the Committee noted that stronger survival data exist for docetaxel in the treatment of metastatic breast cancer. It also noted that when compared to standard paclitaxel and docetaxel, there is less risk of nab-paclitaxel causing hypersensitivity reactions in patients.**
- ◆ The Committee noted that nab-paclitaxel appears to have a place for patients who have had hypersensitivity/anaphylactic reactions to taxanes or have contraindications to the pre-medications (i.e., steroids) for taxanes.
- ◆ Therefore, the Committee recommended that nab-paclitaxel be reimbursed under Cancer Care Ontario's New Drug Funding Program for the treatment of metastatic breast cancer under the following criteria in patients who:
 - *have had acute infusion reactions with paclitaxel or docetaxel, considered by treating physicians to be due to the vehicle of the taxanes (cremophor and polysorbate 80); or*
 - *have experienced severe toxicity from previous administration of other taxanes. (Severe toxicity could be due to pre-medications for the administration of the taxane or due to the taxane itself.)*
- ◆ The CED worked jointly with a subcommittee involving cancer experts to review this cancer drug, as it does for all cancer drug treatments.

Cancer Care Ontario (CCO):

Information on CCO chemotherapy regimens for breast cancer is available at <http://www.cancercare.on.ca/toolbox/drugs/drugformulary/drugregimens/breastreg/>

The Breast Disease Site Group (DSG) Program in Evidence-based Care (PEBC) guidelines for the treatment of metastatic breast cancer is available at:

http://www.cancercare.on.ca/index_breastCancerGuidelines.htm

CEDAC Recommendation:

(<http://www.cadth.ca/index.php/en/cdr/recommendations>)

The Canadian Expert Drug Advisory Committee (CEDAC) did not review nab-paclitaxel (Abraxane).



Ministry of
Health and Long-Term Care
Ontario Public Drug Programs

For more information, please contact:

Ministry of Health and Long-Term Care
Ontario Public Drug Programs
Hepburn Block, 9th Floor
80 Grosvenor Street, Queen's Park
Toronto, Ontario M7A 1R3
or click: http://www.health.gov.on.ca/english/providers/program/drugs/ced_rec_table.html