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FAX request form and IN TOUCH phone list are provided if additional information is needed.

BENEFIT DRUG LIST

The following new program has been funded by the Provincial Systemic Therapy Program effective 22 November 1999:

Palliative therapy for metastatic breast cancer using trastuzumab (Herceptin®) and paclitaxel (Taxol®) as first-line treatment for recurrent breast cancer refractory to anthracycline adjuvant chemotherapy

Trastuzumab is now approved as a Class II drug on the benefit list when used in combination with paclitaxel. A Class II form must be completed and submitted to the Provincial Systemic Therapy Program before the drug will be dispensed at a radiation cancer centre or reimbursed to a community hospital. Use of trastuzumab as a single agent therapy will continue to require approval under "Undesignated Indication".

Susan O'Reilly, MB, FRCPC
Provincial Systemic Program Leader

PROTOCOL UPDATE

Protocol codes for treatments requiring "Undesignated Indication" approval prior to use are prefixed with the letter U.

- INDEX to BCCA Protocol Summaries revised monthly (includes tumour group, protocol code, indication, drugs, last revision date and version)

- BRAVTRAP new (replacing UBRAVTRAP): Palliative therapy for metastatic breast cancer using trastuzumab and paclitaxel as first-line treatment for recurrent breast cancer refractory to anthracycline adjuvant chemotherapy

FOCUS ON TRASTUZUMAB (HERCEPTIN®)

Trastuzumab (Herceptin®) is an antibody against HER2, an oncogene overexpressed in some cancer cells. HER2 overexpression occurs in 20-30% of breast cancer patients.

Trastuzumab in combination with paclitaxel is included on the BCCA Benefit Drug List for patients with metastatic breast cancer who (1) substantially overexpressed HER2 and (2) have relapsed within 12 months of anthracycline-containing adjuvant chemotherapy (see protocol BRAVTRAP). A Class II form must be submitted.

Trastuzumab and Chemotherapy

A randomised multinational controlled Phase III trial studied the addition of trastuzumab to chemotherapy in women with metastatic breast cancer that overexpressed HER2. Four hundred and sixty-nine patients received either (1) doxorubicin-cyclophosphamide (AC) or (2) paclitaxel for those patients that had previously received anthracyclines.¹ As well, half of the patients were randomised to receive weekly trastuzumab.

The addition of trastuzumab to chemotherapy significantly improved response rates and time to disease progression compared to chemotherapy alone. The response rate for paclitaxel plus trastuzumab was 57% (vs. 25% with paclitaxel alone) and time to disease progression was 7.1 months (vs. 4.2 months with paclitaxel alone). Although the same improvement was seen with the

addition of trastuzumab to AC, excessive cardiotoxicity in this group precludes the use of this combination in clinical practice.

Cardiotoxicity

There was a 2-4% incidence of cardiotoxicity using trastuzumab with paclitaxel.^{2,3} The mechanism of the cardiotoxicity is not clear but appears to be related to previous anthracycline exposure. For patients with equivocal cardiac status, a MUGA scan or echocardiogram should be done prior to treatment. Only patients with a normal left ventricular ejection fraction should be treated with trastuzumab.

Administration

Trastuzumab is given intravenously using a loading dose of 4 mg/kg followed by weekly maintenance doses of 2 mg/kg. The first trastuzumab dose is given in 250 mL NS over 90 minutes. If well tolerated, subsequent trastuzumab doses can be given over 30 minutes. The first paclitaxel dose is given the day following the first trastuzumab dose, but if well tolerated both drugs can subsequently be scheduled for the same day.

Trastuzumab is given weekly whereas paclitaxel is given every 3 weeks. If there is no response after 2 cycles of paclitaxel, the treatment should be discontinued. Otherwise the planned treatment duration for paclitaxel is 6 doses in a responding patient. At this time the optimal duration of trastuzumab therapy is unknown so it may be continued until progression or toxicity in a responding patient. Continued use of trastuzumab as single agent therapy beyond 6 cycles would

require an approval for "Undesignated Indication". Because of the risk of cardiotoxicity, the patient must be carefully monitored for both response and toxicity.

Trastuzumab Infusion-Associated Symptoms

Chills and fever occur in 40% of patients during the first trastuzumab infusion but are infrequent with subsequent infusions. Other signs and symptoms may include nausea, vomiting, pain (sometimes at tumour sites), rigors, headache, dizziness, dyspnea, hypotension, rash and asthenia. Symptoms may be treated with acetaminophen, diphenhydramine and meperidine with or without an infusion rate reduction.

R. O'Brien PharmD, BCCA Drug Information Pharmacist
Reviewed by K. Gelmon, MD, BCCA Medical Oncologist

References

1. Slamon D et al. Proc Am Soc Clin Oncol 1998;17:98a.
2. Herceptin® Monograph, Hoffmann-La Roche August 1999.
3. Norton L et al. Proc Am Soc Clin Oncol 1999;18:127a.

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Index of Protocol Summaries	H:\Protocol\Index\Index_NT or Index_W6
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<input type="checkbox"/>	Index: Protocol Summaries (current month)
	Reimbursement
<input type="checkbox"/>	Benefit Drug List (01 Jun 99)
<input type="checkbox"/>	Class 2 Form (01 Nov 99)
<input type="checkbox"/>	Undesignated Drug Request Form (01 Sep 99)