

# Recommendations for use of Taxane-containing chemotherapy regimens

for the treatment of early (operable) breast cancer

**JUNE 2008** | Incorporates published evidence to March 2007

## A CLINICAL PRACTICE GUIDELINE DEVELOPED BY NATIONAL BREAST AND OVARIAN CANCER CENTRE (NBOCC)\*

This document supplements systemic *adjuvant* therapy guideline recommendations 12–22 (pp 8–10), specifically those about *chemotherapy* regimens contained in the National Breast Cancer Centre\*\* *Clinical practice guidelines for the management of early breast cancer*, 2nd edition 2001.<sup>1</sup>

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## Purpose

This guideline includes statements and recommendations based on available, high-level evidence about the use of *taxanes* in *adjuvant* and *neoadjuvant chemotherapy* regimens for the treatment of women with early (operable) breast cancer. The guideline aims to provide health professionals with information to assist in making management recommendations for improved patient outcomes. National Breast and Ovarian Cancer Centre (NBOCC)\* also develops information specifically for consumers about *early breast cancer* diagnosis and treatment options.

For information on the *Pharmaceutical Benefits Scheme* (PBS) listing for taxanes, please see PBS section of this guideline.

Endorsed by:



The Royal Australian  
and New Zealand  
College of Radiologists\*

The Faculty of Radiation Oncology



The Royal  
Australasian College  
of Physicians



The Royal Australasian  
College of Surgeons

\*\* In February 2008, National Breast Cancer Centre (NBCC), incorporating the Ovarian Cancer Program, changed its name to National Breast and Ovarian Cancer Centre (NBOCC). In July 2011, NBOCC amalgamated with Cancer Australia to form a single national agency, Cancer Australia, to provide leadership in cancer control and improve outcomes for Australians affected by cancer.

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## Background

Early (operable) breast cancer is defined as tumours not more than five centimetres in diameter, with either impalpable or palpable but not fixed *lymph nodes* and with no evidence of distant metastases.<sup>1</sup>

Taxanes are a class of *chemotherapy* compounds that includes *paclitaxel*, docetaxel and abraxane. As antimicrotubule agents, taxanes inhibit the normal process of reorganisation of the microtubule network essential for cellular function, which leads to a disruption of mitosis (cell division). *Taxanes* can be used as part of *adjuvant* or *neoadjuvant* chemotherapy regimens to treat early (operable) breast cancer. Of the three types of taxanes, only paclitaxel and docetaxel have been investigated in the adjuvant setting.

## Clinical practice recommendations

Recommendations to individuals should be based on their risks without taxane-containing *chemotherapy* regimens, the absolute benefits and harms of treatment, and their preference. These factors should be discussed with the woman. Women receiving a taxane-containing regimen should be reviewed regularly and monitored for adverse effects by clinicians familiar with the drug

RECOMMENDATIONS	LEVEL OF EVIDENCE <sup>24</sup>	REFERENCE
<b>Adjuvant chemotherapy for women with early (operable) breast cancer:</b>		
A taxane-containing regimen should be considered for women at intermediate-to-high risk of breast cancer recurrence	I	Cochrane <sup>2</sup>
The risks and benefits of using a taxane-containing regimen should be discussed with the woman, taking into consideration her individual risk profile and co-morbidities	I	NBCC* & NCCI <sup>25</sup>
<b>Optimal schedule of administration</b>		
The optimal scheduling and dosing of taxanes in adjuvant chemotherapy regimens for survival benefits is unknown		
Decisions on scheduling and dosing of taxane-containing regimens should be based on factors other than survival outcomes, and take into consideration the woman's individual risk profile and co-morbidities— consideration of toxicity effects should guide dosing and scheduling decisions		
<b>Hormone receptor status</b>		
Taxane-containing regimens should be considered as an option regardless of tumour hormone-receptor status	I	Cochrane <sup>2</sup>
<b>Adverse events</b>		
Women should be informed of the increased risk of febrile neutropenia associated with taxane-containing regimens		
For women at significant risk of febrile neutropenia, primary prophylaxis with <i>growth factor</i> support should be considered		
Women should be informed of the potential adverse effects of a taxane-containing regimen and any uncertainties about long-term effects	I	Cochrane <sup>2</sup>
<b>Women unsuitable for anthracycline</b>		



RECOMMENDATIONS	LEVEL OF EVIDENCE <sup>24</sup>	REFERENCE
If a woman is not suitable to receive an anthracycline-containing regimen, a taxane-containing non-anthracycline regimen can be considered	II	Jones <sup>5</sup>

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## Statements of evidence

STATEMENTS	LEVEL OF EVIDENCE <sup>24</sup>	REFERENCE
<b>Adjuvant chemotherapy in women with early(operable)breast cancer:</b>		
<b>Overall and disease free survival benefit</b>		
Inclusion of a taxane in adjuvant chemotherapy regimens improves disease-free and overall survival compared to non-taxane containing regimens	I	Cochrane <sup>2</sup>
<b>Type of taxane</b>		
There are similar benefits for disease-free and overall survival for taxane regimens containing either <i>paclitaxel</i> or docetaxel	I	Cochrane <sup>2</sup>
<b>Schedule and duration of administration</b>		
There are similar benefits for <i>disease-free survival</i> and overall survival for women treated with a taxane-containing regimen regardless of whether the <i>anthracycline</i> is administered sequentially or concurrently with the taxane	I	Cochrane <sup>2</sup>
There are similar benefits for disease-free and overall survival for women treated with a taxane-containing regimen when adding or substituting a taxane as part of a chemotherapy regimen	I	Cochrane <sup>2</sup>
There are similar benefits for disease-free and overall survival for women treated with a taxane-containing regimen: <ul style="list-style-type: none"> <li>• which is of the same duration as the non-taxane containing regimen, or</li> <li>• which is of longer duration than the non-taxane containing regimen</li> </ul>		
<b>Lymph node status</b>		
There are similar benefits for disease-free survival and overall survival between studies that include women with node positive disease only and studies that include women with node positive or node negative disease	I	Cochrane <sup>2</sup>
No studies have reported results on the use of taxane-containing regimens in women with node negative disease only		
<b>Hormone receptor status</b>		
There was no level I evidence reporting efficacy of taxanes according to hormone receptor status		



STATEMENTS	LEVEL OF EVIDENCE <sup>24</sup>	REFERENCE
Results from individual randomised controlled phase III studies are conflicting and no recommendation can be made according to hormone receptor status		
<b>Adverse events</b>		
Taxane-containing regimens are associated with an increased incidence of febrile neutropenia compared with non-taxane-containing chemotherapy regimens  The increase in febrile neutropenia is most pronounced in concurrent anthracycline and taxane regimens	I	Cochrane <sup>2</sup>
Taxane-containing chemotherapy regimens are associated with decreased incidence of nausea and vomiting compared with a non-taxane containing chemotherapy regimens  The decrease in nausea and vomiting is most pronounced where the inclusion of a taxane has resulted in lower doses of anthracycline	I	Cochrane <sup>2</sup>
Taxane-containing regimens may be associated with a reduction in cardiac toxicity compared with non taxane-containing chemotherapy regimens, where the inclusion of a taxane has resulted in lower cumulative anthracycline exposure	I	Cochrane <sup>2</sup>
<b>Neoadjuvant chemotherapy in women with early(operable)breast cancer:</b>		
One study reported that the inclusion of a taxane in a neoadjuvant chemotherapy regimen significantly increased pathological and clinical complete response rates compared to a non-taxane-containing chemotherapy regimen  There is currently insufficient evidence to determine the optimal role of taxane-containing regimens in neoadjuvant chemotherapy treatment	II	NSABP B27 <sup>16</sup>

## Summary of evidence

This guideline is based on one meta-analysis<sup>2</sup> about the use of taxane-containing regimens for *adjuvant* treatment of *early breast cancer* and a NBOCC\* systematic review<sup>3</sup> about taxane-containing regimens for *neoadjuvant* treatment of early breast cancer.

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## Taxanes for neoadjuvant treatment of early (operable) breast cancer

The statements and recommendations about *taxanes* for *adjuvant* treatment of *early breast cancer* are based on a Cochrane review and meta-analysis,<sup>2</sup> which includes available evidence from twelve randomised trials<sup>4-15</sup> assessing the adjuvant use of taxanes in early (operable) breast cancer. The trials compared taxane-containing adjuvant



chemotherapy regimens with adjuvant regimens not containing a taxane in the management of women with early (operable) breast cancer. Both pre-menopausal and post-menopausal women were eligible in all trials. Five of the twelve trials used *paclitaxel*.<sup>4,8-11</sup> The remaining seven trials used docetaxel.<sup>5-7,12-15</sup>

**(see table 1 for trial details)**

## Taxanes for adjuvant treatment of early (operable) breast cancer

The statements about *taxanes* for *neoadjuvant* treatment of *early breast cancer* are based on evidence from a NBOCC\* systematic review<sup>3</sup> of eight randomised trials<sup>16-23</sup> assessing the neoadjuvant use of taxanes for early (operable) breast cancer.

**(see table 3 for trial details)**

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## Details of trials or studies

TRIAL	PATIENT NUMBERS	INTERVENTION	COMPARATOR
CALGB 9344 <sup>4</sup>	3121	AC x 4 → P x 4	AC x 4
Jones <sup>5</sup>	1016	DC x 4	AC x 4
BCIRG 001 <sup>6</sup>	1491	DAC x 6	FAC x 6
E2197 <sup>7</sup>	2889	AD x 4	AC x 4
ECTO <sup>8</sup>	904	AP x 4 → CMF x 4	A x 4 → CMF x 4
GEICAM 9906 <sup>9</sup>	1248	FEC90 x 4 → P x 8	FEC90 x 6
HECOG <sup>10</sup>	595	E x 4 → P x 3 → CMF x 4	E x 4 → CMF x 4
NSABP B-28 <sup>11</sup>	3059	AC x 4 → P x 4	AC x 4
FinHer <sup>12</sup>	1010	D x 3 (+/- T) → FEC60 x 3	Vin x 3 (+/- T) → FEC60 x 3
PACS 01 <sup>13</sup>	1999	FEC100 x 3 #D x 3	FEC100 x 6
Taxit 216 <sup>14</sup>	972	E x 4 → D x 4 → CMF x 4	E x 4 → CMF x 3
BIG 2-98 <sup>15</sup>	2887	A x 3 → D x 3 → CMF x 3 AD x 4 → CMF x 4	A x 4 → CMF x 3 AC x 4 → CMF x 3

Notes: A=doxorubicin; C=cyclophosphamide; D=docetaxel; E=epirubicin; F=flourouracil; M=methotrexate; P=paclitaxel; T=trastuzumab; Vin=vinorelbine



<b>SUB-GROUP ANALYSIS**</b>	<b>OVERALL SURVIVAL OR (95% CI)</b>	<b>DISEASE-FREE SURVIVAL OR (95% CI)</b>
Overall effect of taxanes	0.81 (0.75-0.88), p<0.00001	0.81 (0.77-0.86), p<0.00001
<b>Type of taxane</b>		
Docetaxel	0.76 (0.67-0.86), p<0.0001	0.80 (0.74-0.87), p<0.00001
Paclitaxel	0.85 (0.76-0.94), p=0.001	0.82 (0.76-0.89), p<0.00001
<b>Taxane given sequentially or concurrently with anthracycline</b>		
Concurrent	0.79 (0.66-0.94), p=0.007	0.79 (0.70-0.90), p=0.0003
Sequential	0.82 (0.75-0.90), p<0.0001	0.81 (0.76-0.88), p<0.00001
<b>Addition or substitution of taxane</b>		
Addition	0.84 (0.76-0.93), p=0.0008	0.82 (0.76-0.89), p<0.00001
Substitution	0.76 (0.67-0.87), p<0.0001	0.78 (0.71-0.86), p<0.00001
<b>Lymph node status</b>		
Node positive only	0.81 (0.74-0.89), p<0.00001	0.81 (0.76-0.87), p<0.00001
Node positive & negative	0.81 (0.69-0.95), p=0.01	0.80 (0.71-0.91), p=0.0004
<b>Duration of chemotherapy</b>		
Longer duration	0.85 (0.77-0.94), p=0.002	0.83 (0.77-0.90), p<0.00001
Same duration	0.76 (0.67-0.86), p<0.0001	0.77 (0.70-0.85), p<0.00001

Notes: CI=confidence interval; OR=odds ratio; \*\*All sub-group analyses were statistically significant

<b>TRIAL</b>	<b>PATIENT NUMBERS</b>	<b>INTERVENTION</b>	<b>COMPARATOR</b>
NSABP B-27 <sup>16</sup>	1605	AC x 4 → D x 4	AC x 4
MDACC <sup>17</sup>	174	P x 4 → FAC x 4	FAC x 4
Dieras <sup>18</sup>	200	AP x 4 #T	AC x 4 #T
Learn <sup>19</sup>	144	AC x 4 → T → D x 4	AC x 4 #T
Malamos <sup>20</sup>	35	PE x 3	FEC x 3
Lee <sup>21</sup>	78	DC x 4	AC x 4
ACCOG <sup>22</sup>	363	AD x 6	AC x 6
Aberdeen <sup>23</sup>	162	CVAPr x 4 → D x 4	CVAPr x 4 #CVAPr x 4

Notes: A=doxorubicin; C=cyclophosphamide; D=docetaxel; E=epirubicin; F=flourouracil; M=methotrexate; P=paclitaxel; T=trastuzumab; V=vinorelbine

## Summary of trial or study results

### Adjuvant chemotherapy



## Overall survival

Overall survival data were available for eleven trials. Pooled analyses of the trial results indicated that taxane-containing regimens improved overall survival, with a *relative risk* reduction of 19% compared to non-taxane-containing *control groups* ( $p < 0.00001$ ).<sup>2</sup> The *absolute risk* reduction for taxane-containing regimens was ~2.6% compared to non-taxane containing regimens.<sup>2</sup>

## Disease-free survival

Disease-free survival data were available for eleven trials. Pooled analyses of the trial results indicated that taxane-containing regimens improved disease-free survival, with a *relative risk* reduction of 19% compared to non-taxane-containing *control groups* ( $p < 0.00001$ ).<sup>2</sup> The *absolute risk* reduction for taxane-containing regimens was ~4.1% compared to non-taxane containing regimens.<sup>2</sup>

## Sub-group analysis

Post-hoc analysis of the data by various sub-groups of trials did not alter the overall or *disease-free survival* estimates,<sup>2</sup> see Table 2 (all remained statistically significant).

## Scheduling of taxane administration

The Cochrane meta-analysis<sup>2</sup> found statistically significant overall survival and *disease-free survival* benefits in side-by-side post-hoc analyses that were not altered by scheduling or duration of *chemotherapy*. *Taxane* treatment was given either concurrently with *anthracycline* or sequentially in the trials. Meta-analysis<sup>2</sup> results investigated trial data where there was an 'addition' of a taxane to the control chemotherapy regimen and where the taxane was 'substituted' for part of the control chemotherapy regimen. **Optimal** scheduling of *adjuvant* taxane-containing chemotherapy regimens is unclear from the available trial results. The recommendation on scheduling reflects that regardless of how a taxane is used in a chemotherapy regimen, there are overall survival and disease-free survival benefits for women. Results of ongoing trials may provide further evidence for optimal scheduling.

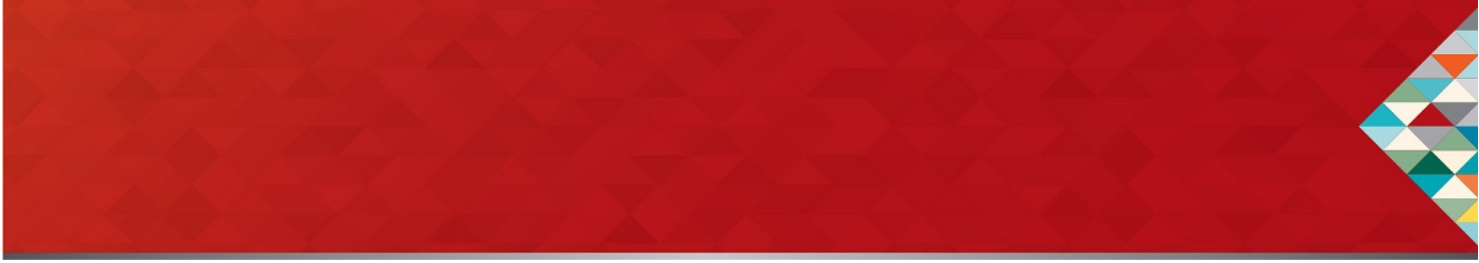
### *Dose density*

Questions regarding dose density were outside the scope of the Cochrane meta-analysis.

## HER2 status

There were no available trial data about *taxanes* and HER2 status at the time of the Cochrane review and meta-analysis<sup>2</sup> (May 2007). Early and retrospective analysis of tissue from the CALGB<sup>26</sup> study (published after March 2007) indicates that the addition of *paclitaxel* to an *adjuvant chemotherapy* regimen improved outcomes in HER2 positive women. Further trial results are required to determine definitive recommendations regarding taxanes and HER2 positive *early breast cancer* patients. This guideline relates specifically to taxanes in adjuvant chemotherapy regimens. It is acknowledged that taxanes have a key role in adjuvant trastuzumab (Herceptin®) trials.

## Adverse events



The twelve trials included in the Cochrane review used a variety of control chemotherapies and different dosing and scheduling of the *taxane* drug. Toxicities need to be considered on a trial-by-trial basis to interpret tolerability of each taxane-containing regimen.

### *Cardiac toxicity*

Pooled analysis of six trials reporting data on cardiotoxicity showed no difference in the risk of cardiotoxicity between taxane-containing and non-taxane-containing regimens. However, for trials in which the use of a taxane resulted in a reduction<sup>8,13</sup> or omission of anthracycline<sup>5</sup>, the risk of cardiotoxicity was reduced in the taxane-containing arm (OR 0.38, 95% CI 0.15-0.98,  $p=0.05$ ).<sup>2</sup>

### *Febrile neutropenia*

Pooled analysis from seven trials demonstrated a significant increase in febrile neutropenia associated with the taxane-containing regimens ( $p<0.0001$ )<sup>2</sup> The risk was particularly high in the trials that administered the taxane concurrently with an *anthracycline*, rather than in those that administered sequential taxane and anthracycline treatment.<sup>2</sup>

### *Other adverse events*

Grade III/IV nausea and/or vomiting were less common in the taxane-containing regimens (OR 0.55, 95% CI 0.39-0.77,  $p=0.0006$ ).<sup>2</sup> There was no difference shown between treatment arms for both grade III/IV fatigue or grade III/IV stomatitis. There was no difference between treatment groups in the number of cases of secondary leukaemia or myelodysplasia reported (25 from taxane-containing regimens, 23 from control regimens). Treatment-related deaths were uncommon and there was no difference between taxane-containing and non-taxane-containing groups (seven treatment-related deaths in each treatment group). There were insufficient and inconsistently reported data for meta-analysis of neurotoxicity or nail changes; however, both toxicities were reported with greater frequency in the taxane-containing arm where reported, with the exception of one study<sup>12</sup> that contained vinorelbine in the control arm and reported greater neurotoxicity in this arm.

## **Quality of life**

Formal analyses of quality of life for patients receiving *taxanes* are limited, with only two trials reporting on quality of life data. One trial<sup>6</sup> reported that both treatment arms experienced a transient reduction in the quality of life score, with a greater reduction in the taxane-containing regimen. However, at first follow-up, both treatment arms had returned to base-line. The other trial<sup>10</sup> did not demonstrate any difference in quality of life scores between the two treatment arms, either at the beginning or at the end of *chemotherapy*. Further research is required to determine the short and long-term effects of taxanes on quality of life.

## **Neoadjuvant therapy**

Evidence is available from eight randomised trials<sup>16-23</sup> assessing the *neoadjuvant* use of *taxanes* for *early breast cancer*. Only one of the trials<sup>16</sup> was large enough to detect survival differences (N=1605), the remaining trials were small, enrolling between 35 and 365 participants. The trials show no significant difference between taxane-containing and non-taxane-containing neoadjuvant *chemotherapy* regimens for overall, disease-free or relapse-free survival.<sup>16-18,22</sup> There was a trend that taxane-containing regimens achieved higher clinical and pathological response rates compared to non-taxane-containing regimens,<sup>17-23</sup> however, only one trial reported a statistically significant increase.<sup>16</sup> Breast conserving therapy is performed at least as often after taxane-containing neoadjuvant chemotherapy compared to non-taxane-containing neoadjuvant chemotherapy.<sup>16,18,21,22</sup> Toxicity outcomes are not





consistently reported in all trials and often the number of events are small, therefore it is difficult to determine whether the toxicity profiles differ significantly between taxane and non-taxane-containing neoadjuvant regimens. The most commonly, and consistently, reported outcome was febrile neutropenia, with four trials reporting higher rates in the taxane-containing arms compared to the control arms.<sup>16-18,22</sup> Further information is needed to determine the optimal role of neoadjuvant taxanes for treatment of early breast cancer.

## Strengths and weaknesses of the evidence

The trials for *adjuvant* use of *taxanes* are large, well designed, and well conducted. Some clinical heterogeneity existed between trials, with variation in choice of control *chemotherapy*, doses and scheduling of chemotherapy. Post-hoc analyses in a side-by-side comparison of pooled data were performed for a number of subgroups. Information about optimal taxane regimens and efficacy in certain subgroups is not yet available.

Only one trial for *neoadjuvant* use of taxanes was large enough to detect survival benefits. Future trials and reviews are needed to answer important unanswered questions on neoadjuvant use of taxanes in *early breast cancer*.

Clinical practice recommendations developed by NBOCC\* will be reviewed and revised as required as additional significant evidence becomes available.

\* In July 2011, National Breast and Ovarian Cancer Centre (NBOCC) amalgamated with Cancer Australia to form a single national agency, Cancer Australia, to provide leadership in cancer control and improve outcomes for Australians affected by cancer.

## Unanswered questions

Important unanswered questions about the use of *taxanes* in *early breast cancer* are outlined below; some of these should be addressed in ongoing trials and with longer follow-up of reported trials:

- optimal sequence/timing/duration of *adjuvant* taxanes with chemotherapy
- optimal use/sequence/timing/duration of *neoadjuvant* taxanes with chemotherapy
- the relative benefits and harms of different taxanes
- potential long term/late toxicity associated with taxanes
- use of taxanes in patients with node-negative tumours
- use of taxanes in patients with >4 involved axillary *lymph* nodes
- efficacy of taxanes with regards to hormone receptor status
- efficacy of taxanes with regards to HER2 receptor status
- relative benefits and harms of neoadjuvant use of taxanes compared to adjuvant use
- the short and long-term effects of taxanes on quality of life.

## Ongoing and additional trials or studies

A number of additional phase III trials investigating the *adjuvant* and *neoadjuvant* use of *taxanes* for *early breast cancer* are ongoing and/or awaiting results:

- eight ongoing trials investigating the use of taxanes for adjuvant treatment of early breast cancer (Brain,<sup>27</sup> GEICAM 9805,<sup>28</sup> Goim 9902,<sup>29</sup> GONO-MIG 5,<sup>30</sup> NCI-H99-0038,<sup>31</sup> NCIC CTG MA.21,<sup>32</sup> PACS 04,<sup>33</sup> ICR TACT<sup>34</sup>)

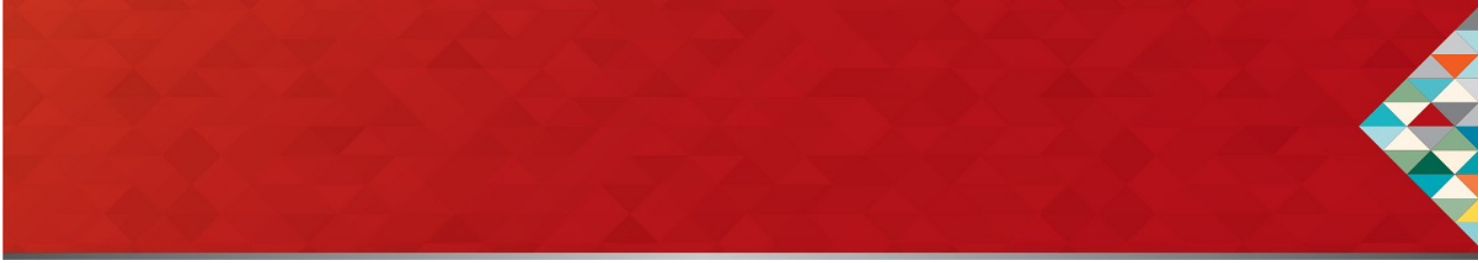


- two ongoing trials investigating the use of taxanes for neoadjuvant treatment of large operable breast cancer (EORTC-10994,<sup>35</sup> INTENS: IKO 2005-01<sup>36</sup>)
- one ongoing trial comparing adjuvant treatment to neoadjuvant treatment of taxanes for early breast cancer (ECTO<sup>8</sup>).

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\*\*\*This article was considered by the NBOCC's Taxanes Subgroup but published after March 2007

## Acknowledgements

### Membership of NBOCC\* taxanes subgroup

This guideline was developed by a multidisciplinary working group convened by NBOCC\*

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\* In July 2011, National Breast and Ovarian Cancer Centre (NBOCC) amalgamated with Cancer Australia to form a single national agency, Cancer Australia, to provide leadership in cancer control and improve outcomes for Australians affected by cancer.

### **Membership of NBOCC\* Early Breast Cancer Working Group**

The development of this guideline was overseen by a multidisciplinary working group convened by NBOCC\*: Dr Karen Luxford (Facilitator), Associate Professor Michael Bilous, Ms Elizabeth Kochman, Mr James Kollias, Dr Craig Lewis, Dr Jonathon Osborne, Dr Sue Pendlebury, Ms Leanne Pentland, Associate Professor Kelly-Anne Phillips, Ms Sue Rovelli, Dr Jane Turner

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### **External review**

NBOCC\* acknowledges those who gave their time to provide comment on the draft guideline recommendations as part of the external review process

Full details of *adjuvant* trial results are provided in the Cochrane review *Taxanes for adjuvant treatment of early breast cancer*<sup>2</sup>, which can be accessed via the Cochrane Library website: [www.cochrane.org](http://www.cochrane.org)

Full details of neoadjuvant trial results are provided in the document *Taxanes for neoadjuvant treatment of early breast cancer: a systematic review*<sup>3</sup>, which can be accessed via the NBOCC\* website: [www.nbocc.org.au](http://www.nbocc.org.au)

\* In July 2011, National Breast and Ovarian Cancer Centre (NBOCC) amalgamated with Cancer Australia to form a single national agency, Cancer Australia, to provide leadership in cancer control and improve outcomes for Australians affected by cancer.

### **Pharmaceutical Benefits Scheme listing for taxanes; paclitaxel and docetaxel**

As of September 2007. For updates after this date go to <http://www.pbs.gov.au>

Paclitaxel and docetaxel are currently subsidised for the following indications in the treatment of early breast cancer:

- Paclitaxel – *adjuvant* treatment of node-positive breast cancer administered sequentially to an *anthracycline* and cyclophosphamide
- Docetaxel – adjuvant treatment of node-positive breast cancer in combination with an anthracycline and cyclophosphamide
- Paclitaxel and docetaxel – treatment of HER2 positive *early breast cancer* in combination with trastuzumab

## Development process

Priority topic areas for NBOCC\* guideline development are determined in consultation with key stakeholders including experts in relevant disciplines and consumer representatives. A specific multidisciplinary Working Group, including consumers, is established for each topic identified and is involved in all aspects of guideline development. A systematic evidence review is undertaken for each guideline. All members are asked to declare any conflicts of interest and these declarations are recorded. The content of the guideline is not influenced by any external funding body. The guideline is reviewed externally by key stakeholders and the wider community and endorsement is sought from relevant professional colleges and groups in Australia.

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Recommendations for use of taxane-containing *chemotherapy* regimens for the treatment of early (operable) breast cancer was prepared and produced by:

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