Benefit definition: Locally recurrent or metastatic breast cancer

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Contents

Disclaimer:

The breast cancer benefit definition has been developed for the majority of standard patients. These benefits may not be sufficient for outlier patients. Therefore regulation 15h and 15I may be applied for patients who are inadequately managed by the stated benefits. The procedure codes are just an indication of applicable procedure codes, however some significant procedure codes may not have been included. The benefit definition does not describe specific in-hospital management such as theatre, anaesthetists, anaesthetist drugs, supportive medication nursing care. However, these interventions form part of care and are prescribed minimum benefits.

1. Introduction

1.1 The legislation governing the provision of the prescribed minimum benefits (PMBs) are contained in the regulations enacted under the Medical Schemes Act 131 of 1998. In respect of some of the diagnosis treatment pairs (DTPs), medical scheme beneficiaries find it difficult to know their entitlements in advance. In addition, medical schemes interpret these benefits differently, resulting in a lack of uniformity of benefit entitlements.

1.2 The benefit definition project is coordinated by the Council for Medical Schemes (CMS) and aims to define the PMB package and to guide the interpretation of the PMB provisions by relevant stakeholders. The guidelines are based on the available evidence of clinical and cost effectiveness taking into consideration affordability constraints and financial viability of medical schemes in South Africa.

2. Scope and purpose

2.1 This is a recommendation for the diagnosis, treatment and care of individuals with advanced breast cancer in any clinically appropriate setting as outlined in the Medical Schemes Act.

2.2 The purpose is to improve clarity in respect of funding decisions by medical schemes, taking into considerations evidence based medicine, affordability and in some instances cost-effectiveness

Table 1: Possible ICD10 codes for identifying breast cancer

ICD 10	*WHO description*
Z12.3	Special screening examination for neoplasm of breast
C50.0	Malignant neoplasm, nipple and areola
C50.1	Malignant neoplasm, central portion of breast
C50.2	Malignant neoplasm, upper-inner quadrant of breast
C50.3	Malignant neoplasm, lower-inner quadrant of breast
C50.4	Malignant neoplasm, upper-outer quadrant of breast
C50.5	Malignant neoplasm, lower-outer quadrant of breast
C50.6	Malignant neoplasm, axillary tail of breast
C50.8	Malignant neoplasm, overlapping lesion of breast
C50.9	Malignant neoplasm, breast, unspecified

3. Epidemiology

3.1 Breast cancer is the most common cancer in women both in the developed and less developed world. In 2012, 1.7 million women were diagnosed with breast cancer while the prevalence stood at 6.3 million women. According to WHO Breast cancer was also the most common cause of cancer death among women with 508 000 deaths in 2011 and 522 000 deaths in 2012. Breast cancer was also the most frequently diagnosed cancer among women in 140 of 184 countries worldwide[1].

3.2 Although breast cancer is thought to be a disease of the developed world, almost 50% of breast cancer cases and 58% of deaths occur in less developed countries. Incidence rates of breast cancer vary greatly worldwide from 19.3 per 100,000 women in Eastern Africa to 89.7 per 100,000 women in Western Europe. In contrast to Eastern Africa, breast cancer was the most commonly diagnosed cancer and the leading cause of cancer death among women in Southern Africa (9000 cases, 4500 deaths)[2].

3.3 Breast cancer survival rates vary greatly worldwide, ranging from 80% or more in North America, Sweden and Japan to around 60% in middle-income countries and below 40% in low-income countries[3]. The low survival rates in less developed countries can be explained mainly by the lack of early detection programmes, resulting in a high proportion of women presenting with late-stage disease, as well as by the lack of adequate diagnosis and treatment facilities. Currently in South Africa 10% of patients with breast cancer present with stage 1 diseases and the remainder presents with 30% each for stages two three and four[4]. According to the South African National Cancer Registry, Breast cancer was the most prevalent cancer amongst women with a lifetime risk of 1:35[5].

4. Diagnostic procedures

4.1 Minimal staging workup for women who present with metastatic breast cancer or recurrent disease includes a history and physical examination, haematology and biochemistry tests, and imaging of chest, abdomen, and bone[6-8].

4.2 Consultation and clinical examination is covered as a PMB level of care.

4.3 Complete blood count, liver and renal function tests, alkaline phosphatase, LDL, calcium, tumour marker (Ca 15.3) and menopausal screening (Follicle stimulating hormones, Luteinising hormones, Oestradiol) are PMB level of care where indicated .

4.4 Oestrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2) status are PMB level of care if receptor status was not assessed at initial diagnosis.

4.5 Chest x-ray and abdominal ultrasound is indicated for patients with locally recurrent or metastatic disease [8].

4.6 Bone scan is indicated for patients with locally recurrent or metastatic disease [8, 9]

4.7 Computed tomography (CT scan) is indicated for patients locally recurrent or metastatic disease where other methods are not appropriate [10]

4.8 [18F]-fluorodeoxyglucose Positron emission tomography–computed tomography (FDG-PET/CT) is indicated when conventional methods are not conclusive in determining metastases [11, 12].

Table 2: Diagnostic work-up for metastatic breast cancer

	Procedure	**Indication**
Blood tests	Full blood count	
Liver function tests	Total Bilirubin	Baseline tests to assess possible liver involvement
	Albumin	
	Alanine transminase (ALT)	
	Aspartate transminase (AST)	
	Alkaline Phosphatase (ALP)	
Renal function tests	Urea	Assessment of possible obstructive renal symptoms
	Creatinine	
	Electrolytes	
	Calcium	
	Phosphates	
Histology	ER, PR and HER2 determination (by IHC and FISH/SISH)	Indicated if receptor status was not assessed at initial diagnosis

Imaging	Chest X-ray	To determine the presence of pulmonary metastases.
	Bone Scan	To determine the presence of metastases to bone
	CT Scan	To determine metastatic regions

5. Management

5.1 Patients with metastatic disease are those with stage IV disease.

5.2 Advanced breast cancer is treatable but still generally incurable. Standard therapies provide palliation or prolonged symptom free survival. Locally recurrent disease is to be treated with curative intent as cure is possible.

5.3 Management of metastatic breast cancer is a prescribed minimum benefit and care aims at improving survival, quality of life and minimising the acute effects/symptoms of cancer. In the explanatory notes of the Act, solid organ tumour(s) are regarded as treatable where:

a. They involve only the organ of origin and have not spread to adjacent organs;

b. There is no evidence of distant metastatic spread;

c. They have not, by means of compression, infarction, or other means brought about irreversible and irreparable damage to the organ from which they originated or another vital organ; or

d. If points (a-c) do not apply, there is a well demonstrated five years survival rate of greater than 10% for the given therapy for the condition concerned.

5.4 The treatment of advanced breast cancer includes a combination of systemic chemotherapy, hormonal therapy, radiotherapy and psychosocial support to optimise the outcomes of treatment.

5.5 Endocrine therapy

5.5.1 Endocrine therapy is PMB level of care in patients with ER-positive advanced breast cancer.

5.5.2 Tamoxifen is indicated in premenopausal, perimenopausal or women with ER-positive advanced breast cancer not previously treated with Tamoxifen.

5.5.3 Aromatase Inhibitors are indicated in postmenopausal or pre-menopausal patients together with LHRH agonists with ER-positive breast cancer.

5.5.4 Luteinizing hormone-releasing hormone (LHRH) agonists are indicated in premenopausal ER+ patients requiring aromatase inhibitors.

5.6 Chemotherapy

5.6.1 Systemic sequential chemotherapy is indicated in patients with advanced breast cancer.

5.6.2 Combination chemotherapy is indicated in patients with advanced disease with life threatening visceral disease, rapid progression and when rapid symptom control is necessary[13] [6].

5.6.3 The following regimens are PMB level of care:

Single agents:

- Doxorubicin
- Capecitabine
- Paclitaxel
- Vinorelbine
- Docetaxel
- Gemcitabine
- Cisplatin
- Mitoxantrone
- Methotrexate
- Mitomycin C
- 5FU

Combination therapy:

- FAC
- AC
- MMM
- CMF
- Vinorelbine/capecitabine
- Cisplatin/gemcitabine
- Doxorubicin/docetaxel
- Metronomic cyclophosphamide/ methotrexate

C = cyclophosphamide, M = methotrexate, F = 5-Fluoruracil, D = docetaxel, A = Adriamycin, E = epirubicin

5.8 Managing complications

5.8.1 Bisphosphonates are indicated in patients with bone metastases to prevent skeletal-related events and to reduce pain [14-16].

5.8.2 Radiological assessment is indicated in patients with persistent and localized bone pain to determine impending or actual pathological fractures [15, 17].

5.8.3 MRI is indicated to assess neurological symptoms and signs which suggest the possibility of spinal cord compression and brain metastases [8]. MRI is not routinely recommended in asymptomatic patients with previous diagnosis of malignancy.

5.8.4 External beam radiotherapy is indicated in patients with bone metastases, brain metastases, spinal cord compression and pain.

5.8.5 Surgery or radiosurgery is indicated in patients with single or small number of potentially resectable brain metastases[18].

5.8.6 Management of lymphoedema is PMB level of care[19]. Physiotherapy and lymphoedema compression stocking are PMB level of care.

Table 4: Management of side effects of treatment for breast cancer

Local symptoms	***Treatment modality***
Local pain	External beam radiotherapy analgesia (Opiods plus adjuvant antidepressant; anti-seizure and NSAIDS)
Spinal cord compression	This is an emergency condition and patients must have an MRI , steroidal treatment and surgery and/or radiotherapy
Diffuse pain	Hormonal therapy/chemotherapy
Inflammatory syndrome	Steroids and NSAIDS
Bone metastasis	Bisphosphonates to reduce pain

Brain metastasis	Surgery, whole brain radiation therapy (WBRT)
Lymphoedema	Physiotherapy, Lymphoedema compression stocking

5.9 Follow-up and palliative care

5.9.1 Follow-up for patients with metastatic breast cancer is indicated to provide best possible palliation of symptoms and to maintain quality of life.

5.9.2 Follow-up every 2-4 months is indicated for patients on endocrine therapy [6].

5.9.3 Patient's assessment for treatment related toxicity and response at every chemotherapy cycle is PMB level of care.

5.9.4 Response evaluation is indicated if progression is suspected due to aggravation or appearance of new symptoms and/or significant increase in tumour marker levels [6].

5.9.5 Serum tumour makers (ca 15.3) may be useful in monitoring response particularly in absence of easily measurable disease. Full blood count, tumour marker, liver and renal function tests and calcium tests are PMB level of care for monitoring response.

5.9.6 Palliative care is PMB level of care for uncontrolled local disease to control pain and relieve other symptoms [15].

5.9.7 Pain treatment is indicated for patients in need of pain relief [15, 18].

5.9.8 Terminal care and the subsequent admission to a hospice is PMB level of care.

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