

National Pharmaceutical Pricing Authority

3rd Floor, YMCA Cultural Centre

1 Jai Singh Road

New Delhi 110001

File No. 23(01)2014/Div.III (Pt)

Dated 21st November 2014

NPPA Invites Comments of Pharmaceutical Industry & Trade, Consumer Organisations, Public Health Experts and other Stakeholders on the Recommendations of Tata Memorial Centre under Department of Atomic Energy, Government of India on Revision of National List of Essential Medicines (NLEM) with respect to Oncology from Price Control/ Affordability Angle

The National Pharmaceutical Pricing Authority (NPPA) has been assigned with the task of evaluating the impact of NLEM 2011 in making essential and lifesaving drugs both affordable and available to all, and for making necessary recommendations with respect to updating the list of scheduled drugs in order to ensure that all essential and lifesaving drugs of mass consumption are under price control for safeguarding public interest.

2. In pursuance with the above direction of the Government of India the NPPA has undertaken a detailed study of the impact of the NLEM 2011 in meeting the abovementioned objective and also held meetings with civil society/ consumer organisations, public health experts, state drug controllers, and pharmaceutical industry & trade associations.

3. Based on the study carried out and stakeholder interactions held by the NPPA, draft recommendations related to correction of anomalies/ discrepancies in specifications/ description of certain drug formulations in terms of active pharmaceutical ingredient, route of administration, dosage form and strength were published on the NPPA website on 13 November inviting comments from all stakeholders, which are awaited.

4. As part of the ongoing consultative study process, the **NPPA now invites comments/ suggestions from all stakeholders, including pharmaceutical industry and consumer organisations, on the recommendations received from the Tata Memorial Centre (Mumbai) under the Department of Atomic Energy, Government of India regarding addition/ deletion of drugs relating to ONCOLOGY in the NLEM 2011**, which are elaborated below, before making its own recommendations in this regard to the Department of Pharmaceuticals, Ministry of Chemicals & Fertilizers and the Core Committee on Revision of NLEM 2011 set up by the Ministry of Health & Family Welfare.

5. The recommendations are based on a careful review of the list of medications included in the NLEM taking into consideration the following factors:

(i) unequivocal proof of benefit versus previous comparator. Improvement in overall survival (OS) is ranked highest followed by disease-free and progression-free survivals (PFS) in the adjuvant and metastatic settings, respectively;

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- (ii) higher priority to drugs that have the potential to cure a fraction of patients versus those that have been proven to only prolong lives in metastatic setting;
- (iii) the number of patients potentially impacted in India based on data from population based cancer registries of the National Cancer Registry Programme;
- (iv) the non-availability of alternative medications of the same or other pharmacological class that can act as a reasonable 'substitute'; and
- (v) Price of the drug to patients and the differential in price between various brands.

6. Drugs recommended for deletion from NLEM

Cytotoxic medicines:

1. **Busulphan** - restricted use mainly as a part conditioning regimen before autologous stem cell transplant.

Hormonal therapy:

1. **Raloxifene** - Restricted usage in postmenopausal women only for pharmacological prevention of breast cancer. This is rarely, if ever, practiced in India.
2. **Danazol** – Not used commonly in oncology at present.

7. Drugs recommended to be added to the NLEM

Cytotoxic and targeted drugs:

(1) All Trans Retinoic Acid (ATRA):

Justification: The outcome of patients with acute promyelocytic leukemia (APL) has substantially improved since the successful introduction of ATRA, the first molecularly targeted therapy in treatment of human cancer. The combination of ATRA with chemotherapy is curative in approximately 80% of patients with newly diagnosed APL.

Current cost of treatment: for 100 capsules (10 mg each) the cost is Rs 5, 795/-. The approximate total cost of treatment (for this drug) for an average sized adult is Rs. 75,000/-.

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(2) Bendamustine:

Justification: the estimated incidence of Non-Hodgkins lymphoma (NHL) in India is 23,801 new cases per year. Bendamustine is an older drug that has been rediscovered for use in indolent (low grade) lymphomas. The most important trial with this drug has shown that the combination of Bendamustine (B) and Rituximab (R) lead to significant increase in PFS compared to nearest comparator. Moreover the B+R regimen was well tolerated with lower haematological toxicity, infections, peripheral neuropathy, and stomatitis compared to nearest comparator.

Current cost of treatment: One vial of 100 mg strength costs Rs 2, 756/-. Approximate total cost of treatment (for this drug) for an average sized adult is Rs 35, 000/-.

(3) Rituximab:

Justification: Rituximab is a monoclonal antibody against CD 20 antigen. For diffuse large B-cell lymphoma (DLBCL), follicular lymphoma and mantle cell lymphoma, inclusion of Rituximab in standard chemotherapy regimens has been shown to significantly improve patient outcome and is standard first-line therapy for CD20-positive lymphomas.

Current cost of treatment: For innovator brand the cost of one vial of 500mg strength is Rs 25, 291/-. Approximate total cost of treatment (for this drug) for an average sized adult is Rs 2, 28, 000/-.

For the generic brands the cost of one vial of 500 mg strength is Rs 19, 695/-. Approximate total cost of treatment (for this drug) for an average sized adult is Rs 1, 32, 000/-.

(4) Lenalidomide:

Justification: It is an immunomodulatory and antiangiogenic drug, which is being used in wide range of cancers like multiple myeloma (in induction as well as maintenance therapy), CLL, mantle cell lymphoma, elderly AML and MDS with 5 q del. The estimated incidence of Multiple myeloma in India is 6, 955 cases per year. There is an improved PFS and overall response (OR) in patients treated with lenalidomide plus dexamethasone versus patients treated with placebo and dexamethasone (nearest comparator).

Lenalidomide reduces transfusion requirements (in 76 % of patients) and reverse cytologic and cytogenetic abnormalities in patients (36 % of cases) who have the myelodysplastic syndrome.

Older patients with acute myeloid leukemia have limited treatment options and a poor prognosis. Thirty percent of elderly patients achieved CR and the median duration of

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CR is 10 months with the use of single agent lenalidomide. The drug is fairly well tolerated by this group of patients in whom conventional chemotherapy is contraindicated.

Current cost of treatment: the cost of 10 capsules (25 mg strength) is Rs 2, 425/-. Approximate total cost of treatment (for this drug) for an average sized adult with myeloma is Rs 60, 000/-.

(5) Trastuzumab:

Justification: Breast cancer is the most common cancer seen in Indian women with an estimated annual incidence of 14, 49, 37 cases. Approximately 20-25% of women with breast cancer have tumors. For women with non-metastatic breast cancer that over-expresses HER2 receptor, the addition of trastuzumab to chemotherapy reduces mortality by more than 30%. The combined hazard ratio for overall survival (OS) and disease-free survival (DFS) significantly favoured the use of trastuzumab. Even in metastatic breast cancer the addition of trastuzumab to standard chemotherapy is associated with increased overall survival as seen in multiple trials.

Current cost of treatment: the cost of one vial of- 440 mg strength is Rs 50,583/-. Approximate total cost of treatment (for this drug) for an average sized adult is Rs 800,000/-.

For the generic brands the cost of one vial of 440 mg strength is Rs 45, 000/-. Approximate total cost of treatment (for this drug) for an average sized adult is Rs 6, 75, 000/-.

(6) Capecitabine

Justification: It is used in the adjuvant setting in many gastrointestinal cancers, including stomach and colorectal. The estimated annual incidence of GI cancer in India is 1,99,926. Capecitabine is also used in other cancers like advanced breast, pancreatic, esophageal, etc. where its use is associated with prolongation in progression-free survival and good symptomatic palliation to patients.

Current cost of treatment: The cost of innovator brand for 10 tablets (500 mg strength each) is Rs 577. Approximate total cost of treatment (for this drug) for an average sized adult is Rs 30, 000/-.

The cost of generic brand for 10 tablets (500 mg strength each) is Rs 277. Approximate total cost of treatment (for this drug) for an average sized adult is Rs 14, 000/-.

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(7) Temozolomide (TMZ):

Justification: This is a novel alkylating agent used in management of malignant gliomas. Positive therapeutic evidence for improvement in overall survival rates in glioblastoma. The estimated annual incidence of Brain tumor in India is 18, 831. It is also used in the palliative treatment of resistant neuroendocrine tumors and malignant melanoma.

Current cost of treatment: The cost of innovator brand for 5 capsules (250 mg strength each) is Rs 24, 000/-. Approximate total cost of treatment (for this drug) for an average sized adult is Rs 2, 16, 000/-.

The cost of generic brand for 5 capsules (250 mg strength each) is Rs 1, 826/-. Approximate total cost of treatment (for this drug) for an average sized adult is Rs 20, 000/-.

(8) Irinotecan:

Justification: This is a camptothecin derivative, used in various cancers such as colorectal, gliomas, glioblastomas, esophageal, stomach, cervical, ovarian, lung and mesothelioma. This drug is mainly used in recurrent and second line setting in many of these cancers where its use leads to PFS benefit and useful symptomatic palliation.

Current cost of treatment: The cost of innovator brand for one vial of 100 mg strength is Rs 7, 780/-. Approximate total cost of treatment (for this drug) for an average sized adult is Rs 1, 87, 000/-.

The cost of generic brand for one vial of 100 mg strength is Rs 918/-. Approximate total cost of treatment (for this drug) for an average sized adult is Rs 25, 000/-.

(9) Erlotinib:

Justification: Lung cancer is the leading cause of death among Indian men and women. The estimated annual incidence of lung cancer in India is 70, 275. Use of Erlotinib either in first- or second line setting is associated with a response rate of rate of 71. When Erlotinib is used upfront in patients with EGFR mutation positive, it is significantly superior to chemotherapy in terms of PFS and response rate. Moreover Erlotinib proved to be better tolerated than chemotherapy.

Current cost of treatment: The cost of innovator brand for 10 tablets (150 mg strength each) is Rs 16, 358/-. Approximate total cost of treatment (for this drug) for an average sized adult is Rs 3, 00, 000/-.

The cost of generic brand for 30 tablets (150 mg strength each) is Rs 2, 730/-. Approximate total cost of treatment (for this drug) for an average sized adult is Rs. 18, 000/-.

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Palliative and supportive medicines:

(10) Zoledronic acid:

Justification: This drug of the bisphosphonate class is an osteoclast inhibitor that has been found to reduce the incidence of skeletal related events (severe pain, fracture, etc.) in patients with multiple myeloma and a variety of solid tumors (breast, lung, kidney, prostate, etc.) that are metastatic to the bone. It has also shown better result in terms of OS and PFS compared to clodronic acid.

Current cost of treatment: The cost of innovator brand for one vial of 4 mg strength is Rs 10000. Approximate total cost of treatment (for this drug) for an average sized adult is Rs 120,000.

The cost of generic brand for one vial of 100 mg strength is Rs 265/-. Approximate total cost of treatment (for this drug) for an average sized adult is Rs 3, 180/-.

Hormonal therapy:

(11) Megestrol acetate:

Justification: This is a progestogenic drug that is used in metastatic hormone receptor positive breast cancer, endometrial stromal sarcoma and endometrial cancer. The estimated number of hormone receptor positive metastatic breast cancer in India is 72, 468. Megestrol use in metastatic breast cancer is associated with response rate (CR, PR, or stable disease) of 65%. Toxicity was minimal, and side effects consisted primarily of weight gain, which was seen in 14.5% cases. Megestrol acetate can provide effective palliation in patients with advanced breast cancer.

Current cost of treatment: The cost of 10 tablets (40 mg strength each) is Rs 189. Approximate total cost of treatment (for this drug) for an average sized adult assuming 6 months of treatment is Rs 12, 000/-.

(12) Letrozole:

Justification: This drug belongs to a class of drugs that reduce estrogen to very low levels in postmenopausal women due to inhibition of the enzyme aromatase. The principal use of this drug is as an adjuvant therapy in postmenopausal women with estrogen receptor (ER) positive breast cancer where it has been shown to result in PFS and OS benefit compared to tamoxifen. The estimated annual incidence of ER positive non-metastatic breast cancer in postmenopausal women in India is 25, 000. In the early Breast Cancer Trialists Collaborative Group metaanalysis the use of aromatase inhibitors (versus tamoxifen) has been shown to reduce the risk of recurrence by 38%,

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risk of death by 30% and risk of contralateral breast cancer by 40%. Letrozole is also used in treatment of metastatic endometrial cancer and endometrial stromal sarcoma.

Current cost of treatment: The cost of innovator brand for 10 tablets (2.5 mg strength each) is Rs 1, 568/-. Approximate total cost of treatment (for this drug) for an average sized adult is Rs 2, 82, 000/-.

The cost of generic brand for 10 tablets (2.5 mg strength each) is Rs 46. Approximate total cost of treatment (for this drug) for an average sized adult is Rs 8, 280/-.

8. Comments, if any, on the above draft recommendations for addition/ deletion from NLEM 2011 may be submitted to NPPA within a period of 2 weeks from the date of the notice.



**(Injeti Srinivas)
Chairman NPPA
21.11.2014**