(1) Does the application adequately address the issue of the public health need for the medicine?
   Yes ☒  No ☐

Please provide brief details:
All studies have been conducted in North America, Europe and other high countries. Economic analysis has been conducted in some developing countries indicating the current cost of treatment is prohibitive and challenging for the LMICs in the public sector hospitals in LMICs. Checkpoint inhibitors are mainly administered to patients privately with high out of pocket expenditures. Over 80% patients discontinue therapy prematurely due to extremely high out of pocket expenditures.

(2) Have all important studies/evidence of which you are aware been included in the application?
   Yes ☒  No ☐

Please provide brief comments on any relevant studies that have not been included:

(3) Does the application provide adequate evidence of efficacy/effectiveness of the medicine for the proposed use?
   Yes ☒  No ☐

(a) Briefly summarise the reported benefits (e.g. clinical versus surrogate) and comment, where possible, on the actual magnitude of benefit associated with use of the medicine:

Immune checkpoint inhibitors have shown significantly meaningful improvement in PFS & OS for both melanoma and NSCLC. In addition, when combined with chemotherapy there is no significant increase in adverse effects.
A recent metanalysis of 19 randomised Phase III studies of immune checkpoint inhibitors demonstrated improvement in overall survival in several tumour types (30% v 23%) compared to conventional therapy in all patients treated with the same drugs in the same trial.
Durable responses of the magnitude of 25% v 11% were also seen in patients with melanoma and lung cancers compared to conventional therapy in all patients treated with the same drugs in the same trial.
DEFINITIONS
Overall survival (OS): defined as mean proportion of patients who had an OS that exceeded 2 times the median OS.
Progression free survival (PFS): exceeded 3 times the median PFS of the whole population.

ESMO MCBS score 5
(b) Is there evidence of efficacy in diverse settings and/or populations? Please provide brief details:
Yes.

(4) Has the application adequately considered the safety and adverse effects of the medicine? Are there any adverse effects of concern, or that may require special monitoring?
Yes ☒ No ☐

Please provide brief details:

(5) Yes. Education of health care personnel involved in cancer care of patients receiving check point inhibitors in managing the adverse side effect profile.
ADDITIONAL CONSIDERATIONS:

(6) Are there special requirements or training needed for the safe, effective and/or appropriate use of the medicine?

Yes ☒ No ☐

Please provide brief details:

Pathologists need to be trained in identification of biomarkers required before administering the checkpoint inhibitors. The cost of kits for these biomarkers are also expensive.

Education of all health care providers and general care physicians looking after cancer patients receiving immunotherapies on timely recognition and management of side effects related to the drugs.

(7) Are there any issues regarding the registration of the medicine by regulatory authorities? (e.g., recent registration, new indications, off-label use)

Yes ☐ No ☒

Please provide brief details:

(8) Is the medicine recommended for use in a current WHO GRC-approved Guideline (i.e., post 2008)?

Yes ☒ No ☐

Please provide brief details:

(9) Please comment briefly on issues regarding cost and affordability of this medicine.

Checkpoint inhibitors are highly effective but extremely expensive. Without availability of generic drugs, pragmatic drug pricing and significant subsidies, the current cost of these drugs are prohibitive and not sustainable in majority of LMICs in the public sector. These drugs should not be used indiscriminately, and all stakeholders need to identify and implement strategies where these drugs will provide maximum benefit with rational use of the limited health care resources. drug

(10) Any additional comments?
Individual countries among the LMICs have already registered checkpoint inhibitors. Patients use them on individual basis.

(11) Please frame the decisions and recommendations that the Expert Committee could make.

NOT APPROVED

(12) References (if required)

Comparative analysis of durable responses on immune checkpoint inhibitors versus other systemic therapies: A pooled analysis of Phase III Trials. EP Tostivint: JCO Precision Oncology 2018 Feb 6


Economic impact of immune checkpoint inhibitor therapy in Brazil and startegies to improve access. PN Aguilar Abst: 6612. JCO May 2017.