ANNEX

Conditions or restrictions with regard to the safe and effective use of the medicinal product to be implemented by the member states

Conditions or restrictions with regard to the safe and effective use of medicinal product to be implemented by the member states

The Member States should ensure that all conditions or restrictions with regard to the safe and effective use of the medicinal product described below are implemented:

The Member States shall ensure that the Marketing Authorisation Holder provides all physicians who are expected to prescribe YERVOY with the following:

- Healthcare Professional FAQ Brochure
- Patient Information Brochures including Alert Cards

Key elements of the Healthcare Professional FAQ Brochure (Q&A format):

- Brief introduction to ipilimumab (indication and the purpose of this tool).
- List of important immune-related adverse reactions (irARs) and their symptoms, as outlined in section 4.4 of the Summary of Product Characteristics (SmPC):
    - Inflammation of the gastrointestinal tract, such as colitis, which can lead to bowel perforation
    - Inflammation of the liver, such as hepatitis, which can lead to liver failure
    - Inflammation of the skin that can lead to severe skin reaction (toxic epidermal necrolysis)
    - Inflammation of the nerves that can lead to neuropathy
    - Inflammation of the endocrine system. including the adrenal, pituitary, or thyroid glands
    - Inflammation of the eyes
    - Other related irARs (e.g. pneumonitis, glomerulonephritis, multi-organ failure…)
    - Severe infusion reaction

- Information that ipilimumab can cause serious side effects in many parts of the body that can lead to death and require early intervention, as outlined in the guidelines for the management of immune-related adverse reactions in section 4.4 of the SmPC.
- Importance of evaluating liver function tests (LFTs), TSH and signs/symptoms of irARs before each treatment.
- Follow-up of patients due to late onset (months after treatment) of irARs
- Reminder to distribute the Patient Information Brochure, and to educate patients/caregivers about symptoms of irARs and of the need to report them immediately to the physician.

Key elements for the Patient Information Brochure and Alert Card:

- Brief introduction to ipilimumab indication and the purpose of this tool.
- Information that ipilimumab can cause serious side effects in many parts of the body that can lead to death and need to be addressed immediately
- Request to inform the physician of all medical conditions before treatment.
- Description of the main symptoms of irARs and the importance of notifying their treating physician immediately if symptoms occur, persist or worsen.
    - Gastrointestinal: diarrhea, bloody stool, abdominal pain, nausea, or vomiting
    - Liver: yellowing of your skin or whites of your eyes
    - Skin: rash, blisters and/or peeling, mouth sores
    - Eye: blurred vision, vision changes, eye pain,
    - General: fever, headache, feeling tired, dizziness or fainting, dark urine, bleeding, weakness, numbness of legs, arms, or faces, changes in behavior, such as less sex drive, being irritable or forgetful
- The importance of not attempting to self-treat any symptoms without consulting their Healthcare professional first.
- Placeholder including the weblink of the Package Leaflet on the EMA website

- The importance of carrying the detachable wallet-sized Patient Alert Card at all times to show it at all medical visits to healthcare professionals other than the prescriber (e.g. emergency healthcare professionals). The Card reminds patients about key symptoms that need to be reported immediately to the physician/nurse. It also contains prompts to enter contact details of the physician and to alert other physicians that the patient is treated with ipilimumab.

The National Competent Authority shall agree the format and content of the above material with the Marketing Authorisation Holder prior to launch of the product in its territory.