YERVOY™
(ipilimumab)
Concentrate for solution for infusion

Healthcare Professional

Frequently Asked Questions Brochure

YERVOY™ is indicated for the treatment of advanced (unresectable or metastatic) melanoma in adults.[1]

ADR forms can be downloaded from www.medicinesauthority/adrportal and sent by post to 203, Level 3 Rue D'Argens Gzira or by email to postlicensing.medicinesauthority@gov.mt.

YERVOY™ is subject to additional monitoring to quickly identify new safety information.
Healthcare Professionals are asked to report any suspected adverse reactions via the national reporting system.

Bristol-Myers Squibb

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What is the purpose of this brochure?

These FAQs are provided by Bristol-Myers Squibb for Nurses* and other Healthcare Professionals (HCPs) who are involved in the treatment of patients on YERVOY™ (ipilimumab).

This educational material is mandatory as a condition of the marketing authorisation in order to further minimise important selected risks.

This document will enable you to:

- understand how YERVOY™ is used
- understand potential adverse reactions and how they should be treated
- present the Patient Information Brochure (including the Patient Alert Card) and its objectives for patients

What is YERVOY™?

YERVOY™ is a medicine designed to help the immune system to fight tumours by increasing the activity of T-cells. It is a recombinant, fully human, monoclonal IgG1 antibody and it works by blocking CTLA-4 (cytotoxic T lymphocyte associated antigen 4), a molecule on T-cells that acts as a natural brake on the immune response.[1]

What is YERVOY™ indicated for?

YERVOY™ is indicated for the treatment of advanced (unresectable or metastatic) melanoma in adults.[1]

Checklist for prescribing YERVOY™

Before prescribing YERVOY™, and before each infusion, check:

- ✓ **liver function tests (LFTs)**
- ✓ **thyroid function tests**
- ✓ **signs or symptoms of immune-related Adverse Reactions, including diarrhoea and colitis**
- ✓ **pregnancy**

Caution

Careful consideration of the potential risk-benefit ratio is warranted in patients with a history of **autoimmune disease**. YERVOY™ should be avoided in patients with severe active **autoimmune disease** where further immune activation is potentially life-threatening.[1]

* Subject to local regulations.

Infusion reactions

Have infusion reactions been reported?

There were isolated reports of severe infusion reactions in clinical trials.[1]

How should infusion reactions be treated?

Severe infusion reactions:

YERVOY™ therapy must be discontinued and appropriate medical therapy administered.[2]

Mild or moderate infusion reactions (mild pruritus, flushing, and rash):

Manage by decreasing the rate of infusion until recovery of symptoms. Symptomatic treatment may be administered at the discretion of the treating physician.

Patients with mild or moderate infusion reactions may receive additional doses with close monitoring.

Premedication before future doses may be considered, as clinically appropriate.[2]

Adverse reactions

What are the potential adverse reactions of YERVOY™ treatment?

YERVOY™ is associated with inflammatory adverse reactions resulting from increased or excessive immune activity (immune-related Adverse Reactions, irARs), likely to be related to its mechanism of action. Immune-related Adverse Reactions, which can be severe or life-threatening, may involve the gastrointestinal, liver, skin, nervous, endocrine, or other organ systems. While most irARs occurred during the induction period, onset months after the last dose of YERVOY™ has also been reported.[1]

Unless an alternate aetiology has been identified, diarrhoea, increased stool frequency, bloody stool, Liver Function Tests (LFTs) elevations, rash and endocrinopathy must be considered inflammatory and YERVOY™-related.[1]

Early diagnosis and appropriate management are essential to minimise life-threatening complications. Systemic high-dose corticosteroid with or without additional immunosuppressive therapy may be required for the management of severe immune-related Adverse Reactions.[1]

YERVOY™-specific management guidelines for irARs are described in the Summary of Product Characteristics.

When could adverse reactions with YERVOY™ occur?

While most immune-related adverse reactions occurred during the induction period (immediately after the first dose or within days), onset months after the last dose of YERVOY™ has also been reported.

Therefore, follow-up of patients after the last dose is warranted.[1]

Adverse reactions (cont'd)

Which irARs may be experienced by patients on YERVOY™ treatment?

Immune-related Adverse Reactions (irARs) can include:

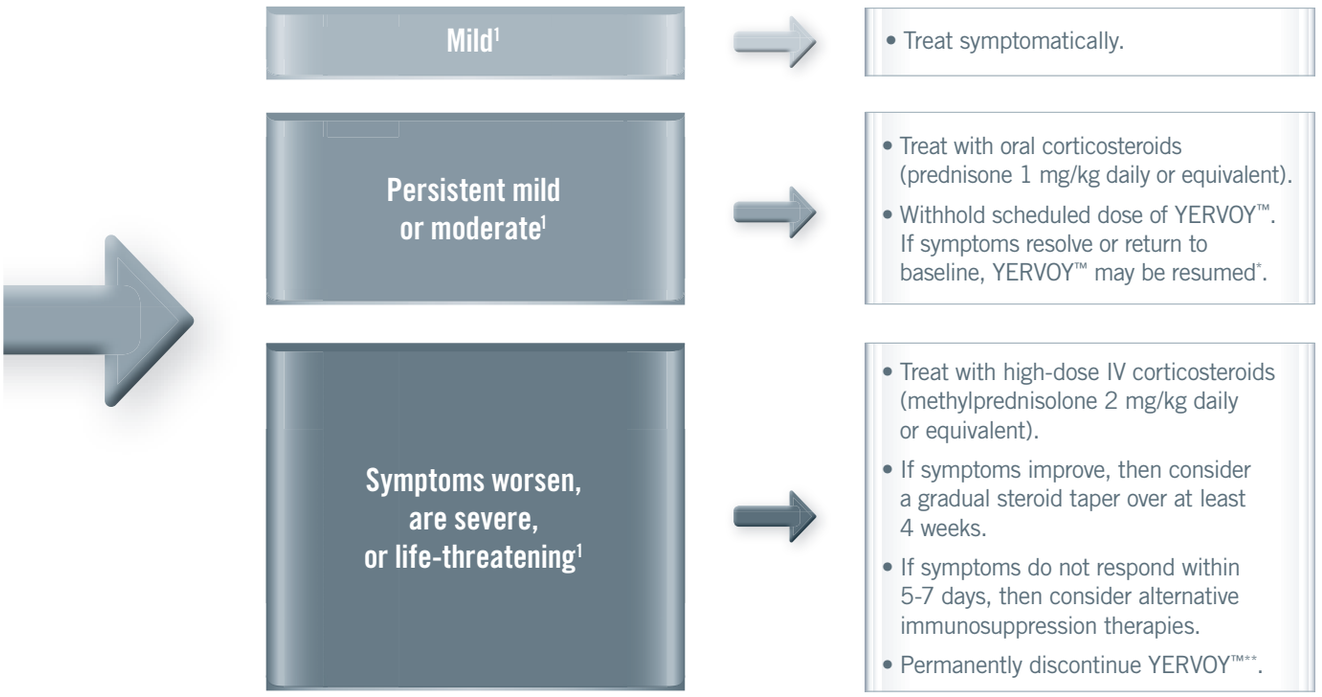
- **inflammation of the intestines (colitis)** which can worsen to bleedings or bowel perforation. Signs and symptoms of colitis may include diarrhoea (watery, loose or soft stools), increased number of bowel movements than usual, bloody stools or darker-coloured stools, abdominal pain, vomiting and nausea.[3]
- **inflammation of the liver (hepatitis)** that can lead to liver failure. Signs and symptoms of hepatitis may include abnormal hepatic function, jaundice, tiredness.[3]
- **inflammation of the skin** that can lead to severe skin reaction (toxic epidermal necrolysis). Signs and symptoms of severe skin reaction may include skin rash with or without itching, peeling of the skin, dry skin.[3]
- **inflammation of the nerves** that can lead to neuropathy. Symptoms may include muscle weakness, numbness or tingling in hands or feet, loss of consciousness or difficulty waking up.[3]
- **inflammation of hormone-producing glands** (including the pituitary, adrenal or thyroid glands) that may affect how these glands work. Signs and symptoms that glands are not working properly may include headaches, blurred or double vision, tiredness, decreased sexual drive, behavioural changes.[3]
- **inflammation of the eyes.** Signs and symptoms may include redness/pain in the eye, vision problems or blurred vision.[3]

The following additional adverse reactions suspected to be immune-related have been reported in patients treated with YERVOY™ in study MDX010-20: uveitis, eosinophilia, lipase elevation, and glomerulonephritis. In addition, iritis, haemolytic anaemia, amylase elevations, multi organ failure, and pneumonitis have been reported in patients treated with YERVOY™ 3 mg/kg + gp100 peptide vaccine.[1]

How should irARs be managed?

Early intervention and treatment are key to the management of irARs. The irARs management guidelines are detailed in section 4.4 of the Summary of Product Characteristics.[1]

Immune-related Adverse Reactions (irARs) resolve on average within 6 weeks following treatment or withdrawal of therapy.[1]



* Refer to revised recommendation in the SmPC.
** In skin irARs: Severe grade 3: Withhold scheduled dose. Severe grade 4 Rash or Severe grade 3 Pruritus: Discontinue YERVOY™.

Suspected irARs should be evaluated to rule out alternate (non-immune-related) causes prior to starting corticosteroid therapy.[1]

Please refer to the YERVOY™ Summary of Product Characteristics for more information.

Patients must not try to treat their own symptoms.
Patients should be advised to contact their specialist (and/or nurse†) immediately, as some adverse reactions can worsen rapidly if not treated.[3]

Early diagnosis and appropriate management are essential to minimise life-threatening complications.

Patients should contact their specialist: he/she has the expertise in managing the adverse reactions and will know precisely how to treat them.

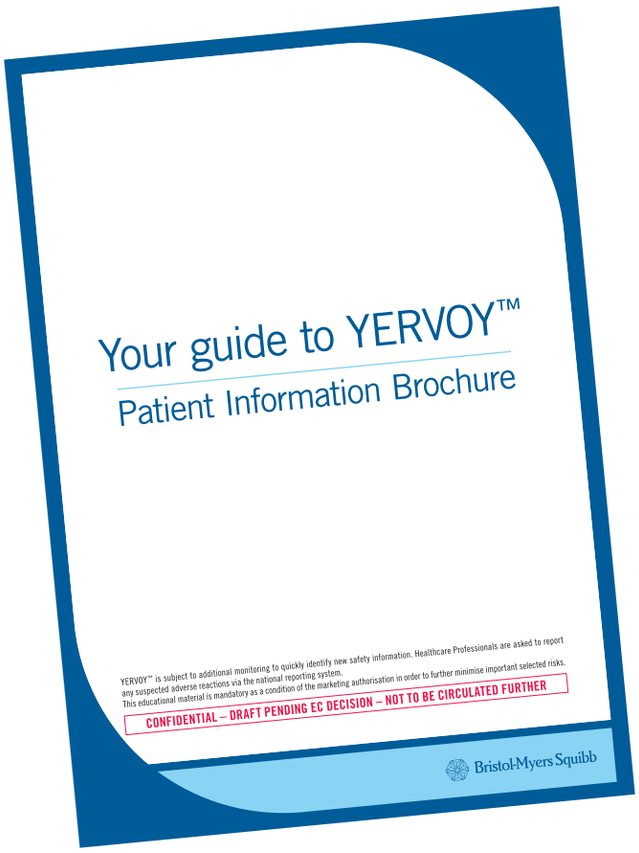
† Subject to local regulations.

What is the Patient Information Brochure?

You are encouraged to distribute a Patient Information Brochure to all patients receiving YERVOY™ treatment for the first time or patients that ask for a new copy. You can use the Patient Information Brochure to discuss YERVOY™ treatment.

The Patient Information Brochure will help patients understand their treatment and most importantly how to act should they experience adverse reactions (e.g. irARs).

The Patient Information Brochure also includes a Patient Alert Card, with contact details, for patients to carry at all times.



Where can I obtain further information?

To learn more about YERVOY™, please refer to YERVOY™ Summary of Product Characteristics, visit www.medicinesauthority.gov.mt or call +356 23976333 pv@ammangion.com.mt for Medical Information.

NOTES

1. YERVOY™ Summary of Product Characteristics.
2. Protocol for: Hodi FS, O'Day SJ, McDermott DF, *et al.* Improved survival with ipilimumab in patients with metastatic melanoma. *N Engl J Med.* 2010;363:711-723. DOI: 10.1056/NEJMoa1003466. Accessible at: http://www.nejm.org/doi/suppl/10.1056/NEJMoa1003466/suppl_file/nejmoa1003466_protocol.pdf
3. YERVOY™ Package Leaflet.

YERVOY™
for adults
with advanced melanoma

To learn more about YERVOY™, please visit www.medicinesauthority.gov.mt
or call +356 23976333 pv@ammangion.com.mt for Medical Information

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