



Ipilimumab (YerVOY)

Drug type

- A targeted T-cell antibody
- Recombinant, human cytotoxic T-lymphocyte antigen 4 (CTLA-4)-blocking monoclonal antibody

Indications

- Treatment of unresectable or metastatic melanoma

Mechanism of action

- CTLA-4 is a negative regulator of T-cell activation
- Ipilimumab binds to CTLA-4 and blocks the interaction of CTLA-4 with its ligands, CD80/CD86.
- Blockade of CTLA-4 has been shown to augment T-cell activation and proliferation
- Proposed mechanism of action is indirect, possibly through T-cell-mediated antitumor immune responses
- IgG1 kappa immunoglobulin with an approximate molecular weight of 148 kd; produced in mammalian (Chinese hamster ovary) cell culture

Dosage and administration

- IV solution
 - 50 mg/10 mL (5 mg/mL)
 - 200 mg/40 mL (5 mg/mL)
- 3 mg/kg IV every 3 weeks for a total of four doses
 - infuse over 90 minutes
- Geriatric dosing
 - No overall differences in safety or efficacy were reported in elderly patients
- Pediatric dosing
 - Safety and efficacy not established

Pregnancy and lactation

- Pregnancy Category: C

- Use only if potential benefit justifies potential risk to fetus
- Human IgG1 is known to cross placental barrier; ipilimumab is an IgG1.
- Potential for drug to be transmitted from mother to developing fetus
- Lactation
 - Unknown whether distributed in breast milk
 - Because of potential for serious adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or to discontinue ipilimumab, taking into account importance of therapy to the mother

Black box warnings

- Severe and fatal immune-mediated adverse reactions due to T-cell activation and proliferation may involve any organ system
- Most common severe immune-mediated adverse reactions: dermatitis (including toxic epidermal necrolysis), endocrinopathy, enterocolitis, hepatitis, and neuropathy
- Reactions typically manifest during treatment but may occur weeks to months after discontinuation
- If severe immune-mediated reactions occur, permanently discontinue ipilimumab and initiate systemic high-dose corticosteroid therapy
- Assess signs and symptoms of dermatitis, endocrinopathy, enterocolitis, neuropathy
 - Evaluate clinical chemistries, including liver function
- Other immune-mediated adverse reactions (<1%):

hemolytic anemia, iritis, meningitis, nephritis, pericarditis, pneumonitis, uveitis

Cautions

- Withhold dose for moderate immune-mediated adverse reactions until return to baseline, improvement to mild severity, or complete resolution, and patient is receiving <7.5 mg/d prednisone or equivalent
- Administer systemic high-dose corticosteroids for severe, persistent, or recurring immune-mediated reactions
- Evaluate liver function before each dose
- Monitor thyroid function and clinical chemistries prior to each dose
- Evaluate at each visit for signs and symptoms of endocrinopathy and institute hormone replacement therapy (HRT) as needed
- Binding antibodies against ipilimumab may develop

Adverse effects

- Most frequent: dermatitis (immune-mediated manifestations), diarrhea, fatigue, pruritus, rash
- Less frequent: colitis, endocrinopathies including adrenal insufficiency, immune-mediated enterocolitis, immune-mediated hepatitis, hypogonadism, hypothyroidism
- Rare: angiopathy, arthritis, autoimmune thyroiditis, conjunctivitis, erythema multiforme, meningitis, myocarditis, pancreatitis, pericarditis, polymyalgia rheumatica, psoriasis, temporal arteritis, vasculitis
 - Nephrotic immune-mediated manifestations: nephritis
 - Neurologic immune-mediated manifestations: Guillain-Barré syndrome, peripheral motor neuropathy
 - Ocular immune-mediated manifestations: iritis, uveitis
 - Pulmonary immune-mediated manifestations: pneumonitis

Drug interactions

- Ipilimumab is a human monoclonal antibody not metabolized by cytochrome P450 enzymes or other drug-metabolizing enzymes; therefore, it is not expected to inhibit or induce CYPs or other drug-metabolizing enzymes.
 - Caution should be used with immunosuppressants such as corticosteroids, tacrolimus, cyclosporine, etc.
 - Use the Nursing Immune-mediated Adverse Reaction checklist from Bristol-Myers Squibb at www.yervoy.com/hcp/pdf/rems-nursing-checklist.pdf before administering this drug.

What to tell your patient

- You have been prescribed ipilimumab, which is a monoclonal antibody. It attaches to cancer cells so your body's immune system can fight them.
- Ipilimumab is given as an infusion through a vein (intravenously or IV).
- Your doctor has prescribed this medication because he or she has judged that the benefit is greater than the risk of side effects.
- Ipilimumab can cause serious side effects in many parts of your body that can lead to death. Call your health care provider immediately if you experience any of the following symptoms.
 - Stomach and bowel: blood in the stool or dark, tarry, sticky stool; diarrhea (loose stools) or more bowel movements than usual; stomach or abdominal pain or tenderness
 - Eyes: blurry vision, double vision, or other vision problems; eye pain or redness
 - Skin: blisters and/or peeling, mouth sores, skin rash with or without itching
 - General: bleeding or bruising more easily than normal; changes in behavior, such as less sex drive, being irritable, or forgetful; dark urine; dizziness or fainting; feeling tired; fever; headache; nausea or vomiting; numbness or tingling in hands or feet; weakness of legs, arms, or face; yellowing of your skin or the whites of your eyes
- Even seemingly mild symptoms can lead to severe conditions if not treated promptly and appropriately.
- You should not treat any of these symptoms with over-the-counter (OTC) medications, dietary supplements, or prescription medications until you discuss the symptoms with your health care provider and he or she approves the use of these products.
- Be sure to tell all health care providers that you are being treated with ipilimumab. ■

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SEE THE ONLINE VERSION OF THIS ARTICLE TO LINK TO:

Nursing immune-mediated adverse reaction checklist
www.yervoy.com/hcp/pdf/rems-nursing-checklist.pdf

Yervoy (ipilimumab) Patient Wallet Card
<http://www.yervoy.com/hcp/pdf/rems-wallet-card.pdf>