Ipilimumab: Drug information

(For additional information see "Ipilimumab: Patient drug information ")

For abbreviations and symbols that may be used in Lexicomp (show table)

ALERT: US Boxed Warning

Immune-mediated adverse reactions:

Ipilimumab can result in severe and fatal immune-mediated adverse reactions. These immune-mediated reactions may involve any organ system; however, the most common severe immune-mediated adverse reactions are enterocolitis, hepatitis, dermatitis (including toxic epidermal necrolysis), neuropathy, and endocrinopathy. The majority of these immune-mediated reactions initially manifested during treatment; however, a minority occurred weeks to months after discontinuation of ipilimumab.

Permanently discontinue ipilimumab and initiate systemic high-dose corticosteroid therapy for severe immune-mediated reactions.

Assess patients for signs and symptoms of enterocolitis, dermatitis, neuropathy, and endocrinopathy, and evaluate clinical chemistries, including liver function tests, adrenocorticotropic hormone (ACTH) level, and thyroid function tests, at baseline and before each dose.

Brand Names: US Yervoy

Brand Names: Canada Yervoy

Pharmacologic Category Antineoplastic Agent, Monoclonal Antibody

Dosing: Adult

Melanoma, unresectable or metastatic: IV: 3 mg/kg every 3 weeks for a maximum of 4 doses; doses may be delayed due to toxicity, but all doses must be administered within 16 weeks of the initial dose.

Melanoma, adjuvant treatment: IV: 10 mg/kg every 3 weeks for 4 doses, followed by 10 mg/kg every 12 weeks for up to 3 years unless disease progression or unacceptable toxicity occur (Eggermont 2016); if toxicity occurs, doses are omitted (not delayed).

Melanoma, unresectable or metastatic, first-line combination therapy (off-label use): IV: 3 mg/kg every 3 weeks for 4 doses (in combination with nivolumab; with nivolumab continued until disease progression or unacceptable toxicity) (Larkin 2015).

Small cell lung cancer, progressive (off-label use): IV: 3 mg/kg every 3 weeks (in combination with nivolumab) for 4 doses, followed by nivolumab monotherapy (Antonia 2016).

Dosing: Renal Impairment

No dosage adjustment necessary.

Dosing: Hepatic Impairment

Impairment at baseline:

Mild impairment (total bilirubin >1 to 1.5 x ULN **or** AST >ULN): No dosage adjustment necessary.

Moderate or severe impairment (total bilirubin >1.5 x ULN and any AST): There are no dosage adjustments provided in the manufacturer's labeling (has not been studied).

Impairment during treatment:

AST or ALT >2.5 to ≤5 x ULN or bilirubin >1.5 to ≤3 x ULN: Temporarily withhold treatment.

ALT or AST >5 times ULN, or total bilirubin >3 times ULN: Permanently discontinue; also administer systemic corticosteroids (prednisone 1 to 2 mg/kg/day or equivalent). May begin tapering corticosteroid (over 1 month) when LFTs show sustained improvement or return to baseline.

Dosing: Adjustment for Toxicity

Dermatologic toxicity: Treat symptomatically for mild to moderate dermatitis (eg, localized rash and pruritus); topical or systemic corticosteroids should be administered if not resolved within 1 week. Withhold ipilimumab for moderate to severe dermatologic symptoms. Permanently discontinue for Stevens-Johnson syndrome, toxic epidermal necrolysis, or rash complicated by dermal ulceration (full thickness) or necrotic, bullous, or hemorrhagic manifestations; also initiate systemic corticosteroids (prednisone 1 to 2 mg/kg/day or equivalent). When dermatitis is controlled, taper corticosteroid over at least 1 month.

Endocrinopathy: Temporarily withhold ipilimumab for symptomatic endocrinopathy; initiate systemic corticosteroids (prednisone at 1 to 2 mg/kg/day or equivalent), and begin appropriate hormone replacement therapy. Resume treatment in patients with complete or partial resolution of toxicity (≤ grade 1) and who are receiving prednisone <7.5 mg daily (or equivalent). Permanently discontinue ipilimumab for symptomatic endocrinopathy lasting 6 weeks or longer, or if unable to reduce corticosteroid dose to prednisone ≤7.5 mg daily (or equivalent).

Gastrointestinal toxicity:

Moderate enterocolitis: Withhold ipilimumab and administer antidiarrheal treatment; if moderate enterocolitis persists for >1 week, initiate systemic corticosteroids (prednisone at 0.5 mg/kg/day or equivalent). May resume treatment in patients with complete or partial resolution of toxicity (≤ grade 1) and who are receiving prednisone <7.5 mg daily (or equivalent).

Severe enterocolitis: Permanently discontinue. Initiate systemic corticosteroids (prednisone 1 to 2 mg/kg/day or equivalent). Upon improvement to ≤ grade 1, taper corticosteroids slowly over ≥1 month (rapid tapering may cause recurrence or worsen symptoms). May consider adding anti-tumor necrosis factor (TNF) or other immunosuppressive therapy for management of immune-mediated enterocolitis unresponsive to 3 to 5 days of systemic corticosteroids or recurring after symptomatic improvement.

Neuropathy: Withhold therapy for moderate neuropathy (not interfering with daily activities). Permanently discontinue for severe neuropathy which interferes with daily activities, such as Guillain-Barré-like syndromes. Consider initiating systemic corticosteroids (prednisone 1 to 2 mg/kg/day or equivalent) for

severe neuropathies.

Ophthalmologic toxicity: Administer corticosteroid eye drops for uveitis, iritis, or episcleritis. Permanently discontinue for grade 2 through 4 immune-mediated reactions which do not improve to ≤ grade 1 within 2 weeks while receiving topical therapy or which require systemic treatment.

Pancreatitis, immune-mediated: Permanent discontinuation is recommended for grades 3 or 4 amylase or lipase increases (Weber 2012)

Other toxicity: Temporarily withhold ipilimumab for grade 2 adverse reactions. May resume treatment in patients (with grade 2 toxicity) with complete or partial resolution of toxicity (≤ grade 1) and who are receiving prednisone <7.5 mg daily (or equivalent). Initiate systemic corticosteroids (prednisone 1 to 2 mg/kg/day or equivalent) for severe immune-mediated adverse reactions. Permanently discontinue for clinically significant or severe immune-mediated adverse reactions, grade 2 reactions lasting 6 weeks or longer, grade 3 or 4 toxicity, or if unable to reduce corticosteroid dose to prednisone ≤7.5 mg daily (or equivalent).

Dosage Forms

Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Solution, Intravenous [preservative free]:

Yervoy: 50 mg/10 mL (10 mL); 200 mg/40 mL (40 mL) [contains polysorbate 80]

Generic Equivalent Available (US)

No

Medication Guide and/or Vaccine Information Statement (VIS)

An FDA-approved patient medication guide, which is available with the product information and at http://www.fda.gov/downloads/Drugs/DrugSafety/UCM249168.pdf, must be dispensed with this medication.

Administration

IV: Infuse over 90 minutes through a non-pyrogenic, low protein-binding in-line filter. Do not administer with other medications. Flush with NS or D5W at the end of infusion

Use

Melanoma, unresectable or metastatic: Treatment of unresectable or metastatic melanoma

Melanoma, adjuvant treatment: Adjuvant treatment of cutaneous melanoma in patients with pathologic involvement of regional lymph nodes of more than 1 mm who have undergone complete resection, including total lymphadenectomy

Use: Off-Label

Melanoma, unresectable or metastatic, first-line combination therapy; Small cell lung cancer (progressive)

Medication Safety Issues

Sound-alike/look-alike issues:

Ipilimumab may be confused with idaruCIZUmab

High alert medication:

This medication is in a class the Institute for Safe Medication Practices (ISMP) includes among its list of drug classes which have a heightened risk of causing significant patient harm when used in error.

Adverse Reactions

>10%:

Central nervous system: Fatigue (41% to 46%), headache (15% to 33% [Hodi 2010])

Dermatologic: Pruritus (24% to 45% [Hodi 2010]), skin rash (19% to 50% [Hodi 2010]), dermatitis (grade 2: 12% to 21%; grades 3/4: 2% to 4% [includes Stevens-Johnson syndrome, toxic epidermal necrolysis, dermal ulceration, necrotic, bullous or hemorrhagic dermatitis])

Endocrine & metabolic: Weight loss (32%), pituitary insufficiency (4%; grade 2: ≤2% to 16%; grades 3/4: 2% to 7%)

Gastrointestinal: Diarrhea (32% to 49%), nausea (25% to 35% [Hodi 2010]), decreased appetite (14% to 27% [Hodi 2010]), increased serum lipase (26%), vomiting (13% to 24% [Hodi 2010]), constipation (21% [Hodi 2010]), colitis (8% to 16%), enterocolitis (grade 2: 5% to 14%; grades 3 to 5: 7% to 16%), increased serum amylase (17%), abdominal pain (15% [Hodi 2010])

Hematologic & oncologic: Decreased hemoglobin (25%), anemia (12% [Hodi 2010])

Hepatic: Increased serum ALT (≤2% to 46% [Hodi 2010]), increased serum AST (≤38% [Hodi 2010]), increased serum alkaline phosphatase (17%), increased serum bilirubin (11%), hepatitis (grade 2: 5%; grades 3/4: 11%)

Respiratory: Cough (16% [Hodi 2010]), dyspnea (15% [Hodi 2010])

Miscellaneous: Fever (12% to 18% [Hodi 2010])

1% to 10%:

Central nervous system: Insomnia (10%), neuropathy (grade 2: <1%; grades 3 to 5: 2%)

Dermatologic: Urticaria (2%), vitiligo (2% [Hodi 2010])

Endocrine & metabolic: Hypophysitis (2% [Hodi 2010]), adrenal insufficiency (≤2% [Hodi 2010]), hypothyroidism (≤2% [Hodi 2010])

Gastrointestinal: Intestinal perforation (1% to 2%), pancreatitis (1%)

Hematologic & oncologic: Eosinophilia (1% to 2%)

Hepatic: Hepatotoxicity (grade 2: 3%)

Immunologic: Antibody development (1%)

Renal: Increased serum creatinine (10%), nephritis (≤1%)

<1%, postmarketing, and/or case reports: Acute respiratory distress, adrenocortical insufficiency (Hodi 2010), arthritis, blepharitis, bronchiolitis obliterans organizing pneumonia (Barjaktarevic 2013), capillary

leak syndrome (Hodi 2010), conjunctivitis, Cushing syndrome, DRESS syndrome, encephalitis, episcleritis, erythema multiforme, esophagitis, gastrointestinal ulcer, giant-cell arteritis, Graves' ophthalmopathy, Guillain-Barré syndrome, hemolytic anemia, hepatic failure, hepatitis (immune-mediated), hypersensitivity angiitis, hyperthyroidism, hypoacusis (neurosensory), hypogonadism, increased thyroid stimulating hormone level, infusion related reaction, iritis, meningitis, myasthenia gravis, myelofibrosis, myocarditis, myositis, myositis (ocular), pericarditis, peripheral motor neuropathy, peritonitis, pneumonitis, polymyalgia rheumatica, polymyositis, psoriasis, renal failure, sarcoidosis, scleritis, sepsis, thyroiditis (autoimmune), uveitis, vascular disease, vasculitis

Contraindications

There are no contraindications listed in the manufacturer's US labeling.

Canadian labeling: Hypersensitivity to ipilimumab or any component of the formulation; active life-threatening autoimmune disease, or with organ transplantation graft where further immune activation is potentially imminently life-threatening

Warnings/Precautions

Concerns related to adverse effects:

• Immune-mediated adverse effects: **[US Boxed Warning]: Severe and fatal immune-mediated adverse effects may occur. While any organ system may be involved, common severe effects include dermatitis (including toxic epidermal necrolysis), endocrinopathy, enterocolitis, hepatitis, and neuropathy. Reactions generally occur during treatment, although some reactions have occurred weeks to months after treatment discontinuation. Discontinue treatment (permanently) and initiate high-dose systemic corticosteroid treatment for severe immune-mediated reactions. Evaluate liver function, adrenocorticotropic hormone (ACTH) level, and thyroid function tests at baseline and prior to each dose. Assess for signs and symptoms of enterocolitis, dermatitis, neuropathy, and endocrinopathy at baseline and prior to each dose.** Uncommon immune-mediated adverse effects reported include eosinophilia, hemolytic anemia, iritis, meningitis, myocarditis (fatal), nephritis, pancreatitis, pericarditis, pneumonitis, sarcoidosis, and uveitis. Other rare immune-mediated reactions reported in clinical trials include angiopathy, arthritis, autoimmune central neuropathy (encephalitis), autoimmune thyroiditis, blepharitis, conjunctivitis, episcleritis, erythema multiforme, leukocytoclastic vasculitis, myositis, neurosensory hypoacusis, ocular myositis, polymyalgia rheumatica, polymyositis, psoriasis, scleritis, temporal arteritis, and vasculitis. Initiate systemic corticosteroids (prednisone 1 to 2 mg/kg/day or equivalent) for severe reactions.

• Dermatologic toxicity: Severe, life-threatening, or fatal immune-mediated dermatitis has been reported. The median time to onset for dermatologic toxicity is 2 to 3 weeks. Monitor for signs/symptoms of dermatitis, including rash and pruritus; dermatitis should be considered immune-mediated unless identified otherwise. Mild-to-moderate dermatitis (localized rash and pruritus) should be treated symptomatically; topical or systemic corticosteroids should be administered if not resolved within 1 week. Withhold treatment for moderate to severe dermatologic symptoms. Permanently discontinue ipilimumab and initiate systemic corticosteroids (prednisone 1 to 2 mg/kg/day or equivalent) for Stevens-Johnson syndrome, toxic epidermal necrolysis, or rash complicated by dermal ulceration (full thickness) or necrotic, bullous, or hemorrhagic manifestations; when dermatitis is controlled, taper corticosteroid over at least 1 month

• Endocrinopathy: Severe or life-threatening endocrine disorders (hypophysitis, adrenal insufficiency [including adrenal crisis], hyperthyroidism and hypothyroidism) have been reported; may require hospitalization. Endocrine disorders of moderate severity (including hypothyroidism, adrenal insufficiency, hypopituitarism, and less commonly hyperthyroidism and Cushing's syndrome) which have required hormone replacement therapy or medical intervention have also been reported. The median onset for moderate to severe endocrine disorders was 2.2 to 2.5 months; long-term hormone replacement therapy has been required in many cases. Monitor thyroid function tests, adrenocorticotropic hormone (ACTH) level, and serum chemistries prior to each dose and as clinically necessary; also monitor for signs of hypophysitis, adrenal insufficiency and thyroid disorders (eg, abdominal pain, fatigue, headache, hypotension, mental status changes, unusual bowel habits); rule out other potential causes such as underlying disease or brain metastases. Endocrine disorders should be considered immune-mediated unless identified otherwise; consider endocrinology referral for further evaluation. If symptomatic, withhold ipilimumab treatment and initiate systemic corticosteroids (prednisone 1 to 2 mg/kg/day or equivalent) and appropriate hormone replacement therapy.

• Gastrointestinal toxicity: Immune-mediated enterocolitis (including fatal cases) may occur. The median time to onset of grade 3 to 5 enterocolitis was 1.1 to 1.7 months. Monitor for signs and symptoms of enterocolitis (abdominal pain, blood in stool, diarrhea, or mucous in stool; with or without fever) and intestinal perforation (peritoneal signs, ileus). If enterocolitis develops, infectious causes should be ruled out; consider endoscopy for persistent or severe symptoms. Withhold ipilimumab treatment and administer antidiarrheals for moderate enterocolitis (diarrhea with ≤6 stools over baseline abdominal pain, mucous or blood in stool); if persists for >1 week, initiate systemic corticosteroids (prednisone at 0.5 mg/kg/day or equivalent). If severe enterocolitis (diarrhea ≥7 stools above baseline, fever, ileus, peritoneal signs) develops, permanently discontinue ipilimumab and initiate systemic corticosteroids (prednisone 1 to 2 mg/kg/day or equivalent); when resolved to ≤grade 1, taper corticosteroids slowly over ≥1 month (rapid tapering may cause recurrence or worsen symptoms). May consider adding anti-tumor necrosis factor (TNF) or other immunosuppressive therapy for management of immune-mediated enterocolitis unresponsive to 3 to 5 days of systemic corticosteroids or recurring after symptomatic improvement.

• Hepatotoxicity: Severe, life-threatening or fatal hepatotoxicity and immune-mediated hepatitis have been observed. The median time to onset for grade 3 or 4 immune-mediated hepatitis in patients receiving ipilimumab for adjuvant treatment of melanoma was 2 months. Monitor liver function tests (LFTs) and evaluate for signs of hepatotoxicity prior to each dose; if hepatotoxicity develops, infectious or malignant causes should be ruled out and liver function should be monitored more frequently until resolves. Withhold treatment for grade 2 hepatotoxicity (ALT or AST 2.5 to 5 times ULN or total bilirubin 1.5 to 3 times ULN). If severe or grade 3 or 4 hepatotoxicity develops (ALT or AST >5 times ULN or total bilirubin >3 times ULN), permanently discontinue ipilimumab and initiate systemic corticosteroids (prednisone 1 to 2 mg/kg/day or equivalent). If transaminases do not decrease within 48 hours of steroid initiation, consider adding mycophenolate mofetil (Weber 2012). May begin tapering corticosteroid (over 1 month) when LFTs show sustained improvement or return to baseline.

• Neuropathy: Immune-mediated neuropathies (some fatal) may occur. Severe peripheral motor neuropathy and fatal Guillain-Barré syndrome have been reported (rare). The median time to onset of grade 2 to 5 immune-mediated neuropathy in patients receiving ipilimumab for adjuvant treatment of melanoma was 1.4 to 27.4 months. Monitor for signs of motor or sensory neuropathy (unilateral or bilateral weakness, sensory changes or paresthesia). Withhold treatment in patients with

neuropathy that does not interfere with daily activities (moderate neuropathy). Permanently discontinue for severe neuropathy (interferes with daily activities, including symptoms similar to Guillain-Barré syndrome) and treat accordingly. Consider initiating systemic corticosteroids (prednisone 1 to 2 mg/kg/day or equivalent) for severe neuropathies.

• Ophthalmic toxicity: Administer corticosteroid ophthalmic drops in patients who develop episcleritis, iritis, or uveitis; permanently discontinue ipilimumab if unresponsive to topical ophthalmic immunosuppressive treatments. For severe immune-mediated episcleritis or uveitis, initiate systemic corticosteroids (prednisone 1 to 2 mg/kg/day or equivalent); taper over at least 1 month (Weber 2012).

Metabolism/Transport Effects

None known.

Drug Interactions

(For additional information: Launch drug interactions program) Lexicomp®

Vemurafenib: Ipilimumab may enhance the hepatotoxic effect of Vemurafenib. Management: Consider alternatives to this combination when possible. Use of this combination should only be undertaken with extra close monitoring of liver function (hepatic transaminases and bilirubin) and signs/symptoms of hepatotoxicity. *Risk D: Consider therapy modification*

Pregnancy Implications

Adverse effects were observed in animal reproduction studies. Ipilimumab is an IgG1 immunoglobulin and human IgG1 is known to cross the placenta, therefore, ipilimumab may be expected to reach the fetus. Ipilimumab may cause fetal harm if administered during pregnancy (based on the mechanism of action). Women of reproductive potential should use effective contraception during treatment and for 3 months following the last ipilimumab dose.

A pregnancy registry has been established to collect information about women exposed to ipilimumab during pregnancy.Advise pregnant women to enroll in the Pregnancy Safety Surveillance Study by calling 1-844-593-7869.

Breast-Feeding Considerations

It is not known if ipilimumab is present in breast milk. The manufacturer recommends to discontinue breastfeeding during treatment and for 3 months following the final dose.

Monitoring Parameters

Monitor liver function and evaluate for signs of hepatotoxicity prior to each dose; if hepatotoxicity develops, liver function should be monitored more frequently until resolves. If liver functions tests are >8 times ULN, monitor every other day until begin to fall, then weekly until normal (Weber 2012). Monitor serum chemistries and adrenocorticotropic hormone (ACTH) prior to each dose. Monitor for signs of hypophysitis, adrenal insufficiency and thyroid disorders (eg, abdominal pain, fatigue, headache, hypotension, mental status changes, unusual bowel habits). Monitor TSH, free T_4 and cortisol levels (morning) at baseline, prior to dose, and as clinically indicated. Monitor for signs and symptoms of enterocolitis (abdominal pain, blood or mucus in stool or diarrhea, and intestinal perforation (peritoneal signs, ileus). Monitor for rash, pruritus, and other signs of dermatologic toxicity. Monitor for signs of motor or sensory neuropathy (unilateral or bilateral weakness, sensory changes or paresthesia). Monitor for ocular toxicity at baseline, then at 4 to 8 weeks with further evaluations as clinically indicated (Renouf 2012).

Mechanism of Action

Ipilimumab is a recombinant human IgG1 immunoglobulin monoclonal antibody which binds to the cytotoxic T-lymphocyte associated antigen 4 (CTLA-4). CTLA-4 is a down-regulator of T-cell activation pathways. Blocking CTLA-4 allows for enhanced T-cell activation and proliferation. In melanoma, ipilimumab may indirectly mediate T-cell immune responses against tumors.

Pharmacodynamics/Kinetics

Half-life elimination: Terminal: 15.4 days

Pricing: US

Solution (Yervoy Intravenous)

50 mg/10 mL (10 mL): $8355.90

200 mg/40 mL (40 mL): $33423.58

Disclaimer: The pricing data provide a representative AWP and/or AAWP price from a single manufacturer of the brand and/or generic product, respectively. The pricing data should be used for benchmarking purposes only, and as such should not be used to set or adjudicate any prices for reimbursement or purchasing functions. Pricing data is updated monthly.

International Brand Names

Winglore (AU); Yervoy (AR, AT, AU, BE, BR, CH, CL, CY, CZ, DE, DK, EE, ES, FI, FR, GB, HK, HR, HU, IE, IL, IS, JP, KR, LT, LU, LV, MT, NL, NO, NZ, PE, PL, PT, QA, RO, SA, SE, SI, SK, TH, TR)

REFERENCES

1. *Antonia SJ, López-Martin JA, Bendell J, et al. Nivolumab alone and nivolumab plus ipilimumab in recurrent small-cell lung cancer (CheckMate 032): a multicentre, open-label, phase 1/2 trial. Lancet Oncol. 2016 Jul;17(7):883-895. [PubMed 27269741]*
2. *Barjaktarevic IZ, Qadir N, Suri A, Santamauro JT, Stover D. Organizing pneumonia as a side effect of ipilimumab treatment of melanoma. Chest. 2013;143(3):858-861. [PubMed 23460165]*
3. *Eggermont AM, Chiarion-Sileni V, Grob JJ, et al. Prolonged survival in stage III melanoma with ipilimumab adjuvant therapy. N Engl J Med. 2016;375(19):1845-1855. [PubMed 27717298]*
4. *Hamnvik OP, Larsen PR, Marqusee E. Thyroid dysfunction from antineoplastic agents. J Natl Cancer Inst. 2011;103(21):1572-1587. [PubMed 22010182]*
5. *Hodi FS, O'Day SJ, McDermott DF, et al. Improved survival with ipilimumab in patients with metastatic melanoma. N Engl J Med. 2010;363(8):711-723. [PubMed 20525992]*
6. *Horvat TZ, Adel NG, Dang TO, et al. Immune-Related Adverse Events, Need for Systemic Immunosuppression, and Effects on Survival and Time to Treatment Failure in Patients With Melanoma Treated With Ipilimumab at Memorial Sloan Kettering Cancer Center. J Clin Oncol. 2015;33(28):3193-3198. [PubMed 26282644]*
7. *Larkin J, Chiarion-Sileni V, Gonzalez R, et al. Combined Nivolumab and Ipilimumab or Monotherapy in Untreated Melanoma. N Engl J Med. 2015;373(1):23-34. [PubMed 26027431]*
8. *Lynch TJ, Bondarenko IN, Luft A, et al. Phase II trial of ipilimumab (IPI) and paclitaxel/carboplatin (P/C) in first-line stage IIIb/IV non-small cell lung cancer. J Clin Oncol. 2010;28(15s):7531 [abstract 7531 from 2010 ASCO Annual Meeting].*
9. *Margolin K, Ernstoff MS, Hamid O, et al. Ipilimumab in patients with melanoma and brain metastases: an open-label, phase 2 trial. Lancet Oncol. 2012;13(5):459-465. [PubMed 22456429]*
10. *O'Day S, Hodi FS, McDermott DF, et al. A phase III, randomized, double-blind, multicenter study comparing monotherapy*

with ipilimumab or GP100 peptide vaccine and the combination in patients with previously treated, unresectable stage III or IV melanoma. J Clin Oncol. 2010;28(15s):4 [abstract 4 from 2010 ASCO Annual Meeting].

11. *Prieto PA, Yang JC, Sherry RM, et al. CTLA-4 blockade with ipilimumab: long-term follow-up of 177 patients with metastatic melanoma. Clin Cancer Res. 2012;18(7):2039-2047. [PubMed 22271879]*
12. *Renouf D, Velazquez-Martin JP, Simpson R, et al. Ocular toxicity of targeted therapies. J Clinl Oncol. 2012;30(26):3277-3286. [PubMed 22649132]*
13. *Roila F, Molassiotis A, Herrstedt J, et al. 2016 MASCC and ESMO guideline update for the prevention of chemotherapy- and radiotherapy-induced nausea and vomiting and of nausea and vomiting in advanced cancer patients. Ann Oncol. 2016;27(suppl 5):v119-v133. [PubMed 27664248]*
14. *Vogel WV, Guislain A, Kvistborg P, et al. Ipilimumab-induced sarcoidosis in a patient with metastatic melanoma undergoing complete remission. J Clin Oncol. 2012;30(2):e7-e10. [PubMed 22124094]*
15. *Weber JS, Kähler KC, Hauschild A. Management of immune-related adverse events and kinetics of response with ipilimumab. J Clin Oncol. 2012;30(21):2691-2697. [PubMed 22614989]*
16. *Wolchok JD, Neyns B, Linette G, et al. Ipilimumab monotherapy in patients with pretreated advanced melanoma: a randomised, double-blind, multicentre, phase 2, dose-ranging study. Lancet Oncol. 2010;11(2):155-164. [PubMed 20004617]*
17. *Wolchok JD, Weber JS, Hamid O, et al. Ipilimumab efficacy and safety in patients with advanced melanoma: a retrospective analysis of HLA subtype from four trials. Cancer Immun. 2010;10:9. [PubMed 20957980]*
18. *Yervoy (ipilimumab) [prescribing information]. Princeton, NJ: Bristol-Myers Squibb; March 2017.*
19. *Yervoy (ipilimumab) [product monograph]. Montreal, Canada: Bristol-Myers Squibb Canada; April 2017.*

Topic 16084 Version 114.0