

YOUR OPDIVO[®] (nivolumab)/YERVOY[®] (ipilimumab) ACTION PLAN

(to be filled out by a member of your oncology team)

For Liver Cancer

Patient Name _____ Date _____
Full Name *Today's Date*

Side effects discussed _____

Key points _____

BMS RESOURCES

Financial Assistance

BMS Access Support
1-800-861-0048
<http://www.bmsaccesssupport.bmscustomerconnect.com/patient>

Patient Resources

For more information about this therapy and support:
Guide to Opdivo/Yervoy Combination Treatment
<https://www.opdivo.com/about-opdivo/how-the-combination-works-combinationtherapy>

TAKING THE MEDICATION

OPDIVO® (nivolumab)/YERVOY® (ipilimumab)

HOW IT'S GIVEN:

- Opdivo is given through your vein via an intravenous (IV) line. The treatment takes 30 minutes
- Yervoy is also given by IV line over 30 minutes
- When the drugs are used in combination, Opdivo and Yervoy are usually given every 3 weeks for a total of 4 doses. After that, Opdivo is given alone every 2 or 4 weeks
- Your oncologist will decide how many treatments you need of each drug
- You will need to have blood tests before, during, and after treatment
- It is important to keep appointments with your oncology team to receive your treatment. If you miss an appointment, call as soon as possible to reschedule and to receive instructions about what to do

Problems you may have while receiving the medications through the IV line: Some people may have a bad reaction to the IV treatment itself. Tell your healthcare team member immediately if you have any of these symptoms during a treatment session:

- Chills or shaking
- Itching or rash
- Flushing (turning red)
- Difficulty breathing
- Dizziness
- Fever or feeling hot
- Feeling like you are going to pass out

Common side effects of this combination

therapy: Even minor side effects could be serious and you should report them all to your oncologist's office. The most common side effects of taking Opdivo/Yervoy are:

- Feeling tired
- Diarrhea
- Fever
- Shortness of breath
- Nausea
- Vomiting
- Rash
- Itching
- Headache
- Weight loss
- Lack of appetite
- Difficulty falling asleep or staying asleep

Report any changes in how you feel to your oncologist's office:

Even small changes in your health or the way you feel that don't seem like a big deal may be a sign of a serious side effect. Don't "tough it out" or try to manage it yourself if you think you are having a side effect—report it immediately! Getting it checked out early may prevent it from becoming a bigger problem.

Avoid pregnancy: Use birth control during therapy and for 3 months after your last treatment if you are of childbearing age. Tell your oncologist's office right away if you or your partner becomes pregnant or think you are pregnant while on these medications as they can cause harm to an unborn baby.

IMPORTANT SIDE EFFECTS

Your oncology team may discuss some side effects of Opdivo/Yervoy that can lead to serious problems if they aren't taken care of right away. These sections give information about possible symptoms, what you should tell your oncology team, when you should get medical help immediately, and any steps you can take to help ease the symptoms.

LUNG AND BREATHING PROBLEMS

OPDIVO® (nivolumab)/YERVOY® (ipilimumab)

Report immediately to your oncologist's office

What are the symptoms?

- Changes in breathing
- Worsening of existing breathing symptoms
- Dry cough
- Shortness of breath when you walk or exercise
- Chest pain
- Shortness of breath when you are resting

What you should tell your oncology team member:

- When you first noticed the changes in your breathing or cough
- If you are feeling very tired, are wheezing (making a whistling sound when you breathe), or have a fever
- If the symptoms are interfering with your daily activities
- If you've ever had breathing problems before and if your existing symptoms are worse
- If you have respiratory allergies to pollen, trees, pets, or other things or food allergies and if you've recently been exposed to these allergens
- If you think you've been exposed to cold or flu viruses
- Interventions you've tried at home (eg, inhaler, cough medicine, etc)

Red flag(s):

- If you are having any trouble breathing, new or worsening cough, and particularly if symptoms come on suddenly
- Any chest pain

Call your oncologist's office immediately. If no one is available, go directly to the emergency room.

Taking care of your lungs:

- Avoid environments that can irritate your lungs or make it hard to breathe. For instance, if you work outdoors, pollen or chemicals may affect you. If you have a hobby like painting, use of certain chemicals might be a problem
- Wear a pollen mask or a respirator when you are around things that may irritate your lungs
- Adhere to any pre-existing asthma or allergy treatment plans during your cancer therapy
- Check with your HCP before using any steroid-based inhalers

DIARRHEA /STOMACH PROBLEMS

OPDIVO® (nivolumab)/YERVOY® (ipilimumab)

Report immediately to your oncologist's office

What are the symptoms?

- Diarrhea or mushy stools
- Changes in your bowel movements (more or less frequent)
- Pain or cramping in the stomach
- Nausea (upset stomach) and vomiting (throwing up)
- Bloating in the stomach and/or gas
- Lack of interest in food
- Feeling very tired
- Fever

What you should tell your oncology team member:

- When you first noticed the changes in your bowel movements
- What your bowel movements are like—hard, solid, soft, loose, or liquid
- What color your stool is—light or dark—and if there is blood or mucus in it
- If your stool floats
- How often you are having bowel movements
- If you have any of the other symptoms listed in the box above
- If you have been losing or gaining weight without trying
- How much and what you are eating and drinking each day
- If you've ever had digestive/stomach problems before
- If the symptoms are interfering with your daily activities
- A list of medications and supplements you're taking
- Anything else you have tried at home to manage the symptoms

Red flag(s):

- If you have sudden, severe pain or tenderness in the stomach, especially if you also have a fever

Call your oncologist's office immediately. If no one is available, go directly to the emergency room.

Taking care of your digestive system:

- Call your oncologist's office IMMEDIATELY if you have diarrhea
- Take over-the-counter or prescription medications AS INSTRUCTED by your oncology team
- Avoid spicy foods, high-fiber cereals, red meats, fats, dairy products, raw fruits (except bananas), vegetables, caffeine, alcohol, and sugar
- Instead, eat bland foods such as bananas, pudding, rice, toast, oatmeal, or crackers
- Drink water, weak tea, clear broth, watered-down juice, Pedialyte®, or sports drinks (Gatorade®, Powerade®), or suck on popsicles to prevent dehydration
- Do not use laxatives or stool softeners if you have diarrhea

KIDNEY PROBLEMS

OPDIVO® (nivolumab)/YERVOY® (ipilimumab)

Report immediately to your oncologist's office

What are the symptoms?

- Changes in how often you urinate
- Changes in the color of your urine, blood in your urine
- Pain or hesitation when you urinate
- Pain in your upper back or belly and sides (flank pain)

What you should tell your oncology team member:

- When you first noticed the changes in urination and if the changes came on slowly or suddenly
- What the color of your urine is (light, dark) and whether you've noticed blood in it
- If your urine is foamy or bubbly
- How often you are urinating (more or less frequently)
- If you are having any trouble urinating
- How much and what you are drinking each day
- If you have pain in your lower stomach or back:
 - Sharp or dull
 - Constant or it comes and goes
- If you also have nausea or vomiting (throwing up)
- If you have a headache and/or a general feeling of being unwell
- If you have swelling in your ankles
- If you have a fever
- If you have lost your appetite
- If you've ever had urinary tract infections or kidney problems before
- If the symptoms are interfering with your daily activities
- A list of medications and supplements you're taking
- Anything else you have tried at home to manage the symptoms

Red flag(s):

- If symptoms come on suddenly and you are in intense pain, have a high fever, or can't stop vomiting

Call your oncologist's office immediately. If no one is available, go directly to the emergency room.

Taking care of your kidneys:

- Drink lots of fluids every day to flush your system out
- Avoid alcohol and caffeine
- Check with HCP before taking any non-steroidal anti-inflammatory drugs (NSAIDs) such as aspirin, naproxen, and ibuprofen

SKIN CHANGES

OPDIVO® (nivolumab)/YERVOY® (ipilimumab)

Report immediately to your oncologist's office

What are the symptoms?

- A skin rash with or without itching
- Skin burning or tightness
- Itching without a rash
- Skin blisters
- Peeling skin
- Sores in your mouth or rectum

What you should tell your oncology team member:

- When you first noticed the rash or itchiness
- What the rash looks like (eg, flat, bumpy, red, acne-like, hives)
- Where the rash is and how much of the body it is covering
- If the skin change is making it difficult for you to get dressed, perform daily activities, or sleep
- If you have had any skin problems in the past
- If you have started any new medications recently
- If you have been using a new soap or been around new chemicals or animals recently
- What you have tried at home to manage the symptoms

Red flag(s):

- If you have a rash that covers a large part of your body or that is quickly getting worse
- Blisters in your mouth or on your rectum
- Skin that is peeling and/or intense or widespread itching

Call your oncologist's office immediately. If no one is available, go directly to the emergency room.

Taking care of your skin:

- Avoid soap. Instead, use gentle, nonsoap cleansers such as Cetaphil®
- Avoid hot showers or baths (short, lukewarm showers are OK)
- Apply a cool cloth to the area
- Apply a cooling cream with menthol or camphor to the area (refrigerate the cream first for even greater relief)
- Keep your fingernails short to protect your skin from damage if you scratch
- Apply a moisturizer that contains the ingredients urea or glycerin daily
- Don't use lotions that have perfumes or dyes
- Protect your skin from the sun by wearing sunscreen, a hat, and UV-protective clothing and sunglasses. Don't forget your hands and face
- Your oncology team may tell you to take an antihistamine by mouth or apply a corticosteroid cream to reduce the itching

MOUTH PROBLEMS

OPDIVO[®] (nivolumab)/YERVOY[®] (ipilimumab)

Report immediately to your oncologist's office

What are the symptoms?

- Sensitivity or burning when you eat/drink
- Mouth sores
- Mouth pain affecting your tongue, gums, and the inner lining of the cheeks and lips
- Dry mouth, dry or thick saliva

What you should tell your oncology team member:

- When you first noticed the changes in your mouth
- If the changes are making it difficult for you to eat, drink, or swallow
- If you have been losing or gaining weight without trying
- If you are waking up at night to sip water
- If your symptoms are worsening
- Any mouth or dental problems you have had in the past and how severe they were
- How much and what you are drinking each day
- A list of medications and supplements you're taking
- If you are using any lozenges for dry mouth
- Anything else you have tried at home to manage the symptoms

Red flag(s):

- If you feel weak, dizzy, confused, or have intense pain

Call your oncologist's office immediately. If no one is available, go directly to the emergency room.

Taking care of your mouth:

- Drink lots of fluids every day
- Avoid hot, spicy, or acidic foods (such as tomatoes)
- Brush your teeth at least twice a day using a soft toothbrush. Avoid toothpaste with whitening agents
- Floss once a day
- Use mouth rinses, mints, or other products recommended by your oncology team to relieve your mouth symptoms
- Avoid commercial mouthwashes or those that have alcohol in them as they can dry your mouth out more
- Have regular dental checkups

LIVER PROBLEMS

OPDIVO® (nivolumab)/YERVOY® (ipilimumab)

Report immediately to your oncologist's office

What are the symptoms?

- Changes in your energy level (more tired)
- Yellowing of your skin or the whites of your eyes
- Change in the color of your stool (paler)
- Change in the color of your urine (darker, tea-colored)
- Abdominal pain, particularly on the upper right side of the stomach
- Bruising more easily
- Bleeding more easily
- Fever
- Confusion, drowsiness, feeling "foggy"
- Increased sweating
- Abdominal bloating

What you should tell your oncology team member:

- When you first noticed the symptoms above
- How severe the symptoms are
- If you have been losing or gaining weight without trying
- If the symptoms are interfering with your daily activities
- A list of medications and supplements you're taking (especially any product containing acetaminophen [example, Tylenol®])
- If you drink alcohol and how much per day
- If you've ever had liver problems before
- Anything else you have tried at home to manage the symptoms

Red flag(s):

- If you have severe pain and/or swelling in your stomach
- You're very drowsy all day
- Your skin or the whites of your eyes have turned yellow
- You feel confused or foggy

Call your oncologist's office immediately. If no one is available, go directly to the emergency room.

Taking care of your liver:

- Drink lots of fluids every day
- Don't drink a lot of alcohol (no more than one drink per day for women and two drinks per day for men) or avoid alcohol all together
- Eat a well-balanced diet without too much fat and stay active to maintain a healthy weight
- Do not take more acetaminophen (example, Tylenol®) or prescription pain medication than recommended

PITUITARY GLAND PROBLEMS

OPDIVO® (nivolumab)/YERVOY® (ipilimumab)

Report immediately to your oncologist's office

What are the symptoms?

- Changes in your energy level (more tired)
- Nausea/vomiting
- Headache
- Dizziness
- Confusion, drowsiness, feeling "foggy"
- Problems with your vision
- Changes in sexual function
- Fever

What you should tell your oncology team member:

- When you first noticed the symptoms above
- How severe the symptoms are
- If the symptoms are interfering with your daily activities
- A list of medications and supplements you're taking
- If you've ever had pituitary problems before
- Anything else you have tried at home to manage the symptoms
- Note: Remind healthcare providers outside the oncology team that you are receiving immunotherapy for your cancer and it can affect your pituitary gland. This is particularly important if they are planning any scans of your head/brain

Red flag(s):

- If you have severe head pain with vision changes, fever, nausea and vomiting, feeling "foggy," and/or very tired

Call your oncologist's office immediately. If no one is available, go directly to the emergency room.

Taking care of your pituitary gland:

- Eat a healthy diet and exercise regularly
- Continue taking any thyroid supplements you were prescribed prior to starting cancer therapy

THYROID PROBLEMS

OPDIVO® (nivolumab)/YERVOY® (ipilimumab)

Report immediately to your oncologist's office

What are the symptoms?

- Changes in your energy level (eg, more tired)
- Changes in your appetite (either you're more hungry or less hungry)
- If you have been losing or gaining weight without trying
- You are not able to tolerate hot or cold temperatures
- Changes in your mood, energy level, or behavior such as decreased sex drive, irritability, or forgetfulness
- Your heart races, seems to skip a beat, or flutters
- You have constipation or diarrhea
- Your skin is either drier or more oily than before
- Your hair is thinning

What you should tell your oncology team member:

- When you first noticed the symptoms above
- How severe the symptoms are
- If the symptoms are interfering with your daily activities
- A list of medications and supplements you're taking
- If you've ever had thyroid problems before
- Anything else you have tried at home to manage the symptoms

Red flag(s):

- If your thyroid gland (located in front of your windpipe) swells up

Call your oncologist's office immediately. If no one is available, go directly to the emergency room.

Taking care of your thyroid gland:

- Eat a healthy diet and exercise regularly
- Continue taking any thyroid supplements you were prescribed prior to starting cancer therapy

DIABETES (HIGH BLOOD GLUCOSE, HYPERGLYCEMIA)

OPDIVO® (nivolumab)/YERVOY® (ipilimumab)

Report immediately to your oncologist's office

What are the symptoms?

- More frequent urination
- Greater thirst
- Increased hunger
- You feel very tired
- Your breath smells sweet or fruity

What you should tell your oncology team member:

- When you first noticed the symptoms above
 - How severe the symptoms are
 - If the symptoms are interfering with your daily activities
 - A list of medications and supplements you're taking
 - If you've been told you have diabetes before
 - Anything else you have tried at home to manage the symptoms
-

Red flag(s):

- If you cannot do your daily living activities because of fatigue
- You faint

Call your oncologist's office immediately. If no one is available, go directly to the emergency room.

Taking care of your pancreas:

- Eat a healthy diet and exercise regularly

NERVE PROBLEMS

OPDIVO® (nivolumab)/YERVOY® (ipilimumab)

Report immediately to your oncologist's office

What are the symptoms?

- Weakness on one or both sides of the body (legs, arms, or face)
- New or worsened pain, numbness, or tingling in the hands or feet
- Trouble walking
- Difficulty writing
- Tremors (shakes)
- Trouble holding items (dropping things)
- Having a hard time getting dressed (eg, buttoning buttons)

What you should tell your oncology team member:

- When you first noticed the symptoms above
- How severe the symptoms are
- If the symptoms are interfering with your daily activities
- A list of medications and supplements you're taking
- If you've ever had similar symptoms before, walking problems, or diabetes
- Anything else you have tried at home to manage the symptoms

Red flag(s):

- If you have trouble breathing along with these symptoms

Call your oncologist's office immediately. If no one is available, go directly to the emergency room.

JOINT PAIN, SWELLING, OR STIFFNESS

OPDIVO® (nivolumab)/YERVOY® (ipilimumab)

Report immediately to your oncologist's office

What are the symptoms?

- Joint pain
- Joint swelling
- Joint stiffness
- Redness around the joint
- Difficulty with walking or performing your daily activities

What you should tell your oncology team member:

- When these symptoms started, what brings them on, and how long they last
- Which joints are affected
- If the symptoms are affecting your ability to do your daily activities
- If you have ever had any joint problems in the past and are those symptoms worsening
- If you also feel very tired
- If you have any associated skin changes
- Anything else you have tried at home to manage the symptoms

Red flag(s):

- If you have sudden or severe onset of joint pain, swelling, or stiffness
- You fall and the joint looks deformed or you can't place weight on the joint (such as your ankle) or use it at all

Call your oncologist's office immediately. If no one is available, go directly to the emergency room.

Managing your side effects:

- With the approval of your oncologist's office, take over-the-counter anti-inflammatories/pain relievers such as ibuprofen (Advil®, Motrin®) or naproxen (Aleve®) to relieve pain and stiffness. Your oncology team member may give you stronger prescription drugs to ease joint problems
- Apply an ice pack to swollen joints for 15 minutes several times a day
- Keep the joint above your heart whenever you can to reduce swelling
- Use elastic wrap or tape on the joint to support it
- Try to stay as active as possible. Do 30 minutes of low-to-moderate-intensity physical activity most days of the week. Also try to do resistance training (calisthenics or with weights), yoga, tai chi, QiGong, Pilates, aquatic exercise, or a focused dance program
- Avoid activities that cause pain

MUSCLE PAIN OR STIFFNESS

OPDIVO® (nivolumab)/YERVOY® (ipilimumab)

Report immediately to your oncologist's office

What are the symptoms?

- Muscle pain
- Muscle stiffness
- Easily tired from activity

What you should tell your oncology team member:

- When the symptom started and how it developed (slowly vs suddenly)
- Whether you did any activity that might have caused it
- Whether you have had an injury
- Whether you have had any changes to your medications
- Which muscles are affected
- If the symptoms are affecting your ability to perform your daily activities
- If you have had muscular problems previously and those existing symptoms are getting worse
- If, in addition to muscle symptoms, you also feel very tired or short of breath
- Anything else you have tried at home to manage the symptoms

Red flag(s):

- If you have sudden, severe, or continuous muscle pain or weakness
- Shortness of breath
- Feeling foggy or confused
- Vomiting
- Tea-colored urine
- Any chest pain

Call your oncologist's office immediately. If no one is available, go directly to the emergency room.

Managing your side effects:

- With the approval of your oncologist's office, take over-the-counter anti-inflammatories/pain relievers such as ibuprofen (Advil®, Motrin®) or naproxen (Aleve®) to relieve pain and stiffness. Your oncology team member may give you stronger prescription drugs to ease joint problems
- Apply heat or take a warm bath to relax the muscle
- Avoid activities that cause pain but do try to stretch and keep active

ADRENAL GLAND PROBLEMS

OPDIVO® (nivolumab)/YERVOY® (ipilimumab)

Report immediately to your oncologist's office

What are the symptoms?

- Fatigue/low energy
- Muscle weakness
- Muscle pain
- Feeling dizzy/light headed
- Feeling confused/foggy
- Feeling faint or actually fainting
- Nausea/vomiting
- Darkening/bronzing of skin
- Craving salty foods/drinks
- Feeling irritable or depressed
- Loss of appetite
- Weight loss

What you should tell your oncology team member:

- When you first noticed the symptoms above and if they developed slowly vs suddenly
- How severe the symptoms are
- If the symptoms are interfering with your daily activities
- If you have recently been stressed or ill
- A list of medications and supplements you're taking (including any steroids and recent dose changes)
- If you've ever had adrenal problems before
- Anything you have tried at home to manage the symptoms

Red flag(s):

- If you faint (pass out)
- Are extremely confused or don't make sense to other people
- Are extremely weak
- Have severe vomiting/diarrhea
- Have sudden, severe pain in your lower back, belly, or legs

Call your oncologist's office immediately. If no one is available, go directly to the emergency room.

Taking care of your adrenal gland:

- If you have been diagnosed with an adrenal insufficiency, your healthcare team will educate you about wearing a medical alert bracelet and being prepared with stress doses of corticosteroids for surgery, severe illness, injury, etc.

OTHER SYMPTOMS TO LOOK OUT FOR

Below are other symptoms that you can have when you take Opdivo® (nivolumab)/Yervoy® (ipilimumab). We are very concerned about symptoms we have marked with a check mark. Please call the office if you develop any of these symptoms, and consider going directly to the Emergency Room if you have any of the red-flag symptoms.

✓	Symptoms	Red flags (Signs that something serious is going on that needs immediate attention)
	Appetite changes (not feeling hungry or wanting to eat)	<ul style="list-style-type: none"> • If you have no appetite plus you feel faint, pass out, and/or have trouble thinking (cloudy thinking, confusion)
	Chest pain	<ul style="list-style-type: none"> • Any chest pain should be evaluated immediately
	Fatigue (feeling weak or tired)	<ul style="list-style-type: none"> • If you faint or have shortness of breath or chest pain
	Fever	<ul style="list-style-type: none"> • If you have a fever over 104.0°F • If you also have breathing problems
	Headaches	<ul style="list-style-type: none"> • If you have a very painful headache (the “worst headache of your life”), head pain that doesn’t go away after a few hours, or head pain with fever, neck pain or stiffness, and/or rash • If you have head pain and changes in vision
	Nausea	<ul style="list-style-type: none"> • If you have uncontrolled nausea and it is limiting your ability to eat or drink
	Shortness of breath (difficulty catching your breath or getting enough air in your lungs)	<ul style="list-style-type: none"> • If you have any trouble breathing or worsening of your existing symptoms • If you have shortness of breath plus chest pain and/or fainting • If you have shortness of breath and swelling of the legs or leg pain

OTHER SYMPTOMS TO LOOK OUT FOR

(Continued)

✓	Symptoms	Red flags (Signs that something serious is going on that needs immediate attention)
	Sleep changes (difficulty falling or staying asleep)	<ul style="list-style-type: none"> • Fatigue that is affecting your ability to function
	Vision and eye changes (blurry vision, double vision, or other vision problems; eye pain or redness)	<ul style="list-style-type: none"> • Sudden and severe symptoms, such as sudden vision changes, eye pain, or redness
	Vomiting (throwing up)	<ul style="list-style-type: none"> • If you go more than 24 hours without being able to hold down foods or liquids, and/or you vomit blood, your vomit looks like coffee grounds, or you have severe stomach pain
	Weight loss	<ul style="list-style-type: none"> • If you have no appetite plus you feel faint, pass out, and/or have trouble thinking (cloudy thinking, confusion)
	Weakness (general or in your muscles)	<ul style="list-style-type: none"> • If you also have headaches and dizziness • If weakness is on the face or one side of your body plus you have numbness, slurred speech, confusion, drooping in the face • If weakness is all over the body and you feel very tired and even faint, have a fever, and your heart is racing

RESOURCES

BMS RESOURCES

Financial Assistance

BMS Access Support

1-800-861-0048

www.bmsaccesssupport.bmscustomerconnect.com/cms__Main?name=patient

Patient Resources

For more information about this therapy and support:

Guide to Opdivo/Yervoy Combination Treatment

www.opdivo.com/about-opdivo/how-the-combination-works-combinationtherapy

Additional Information Resources

American Cancer Society Resource Section

www.cancer.org/cancer/liver-cancer/treating/immunotherapy.html

American Liver Foundation

www.liverfoundation.org

Blue Faery: The Adrienne Wilson Liver Cancer Association

www.bluefaery.org