ABRAXANE is a prescription medicine used to treat advanced breast cancer in people who have already received certain other medicines for their cancer.

Please see Important Safety Information on pages 6-9, and accompanying Patient Information and full Prescribing Information, including Boxed WARNING.

People shown are not actual patients unless noted.
Face the challenge with ABRAXANE

If you have metastatic (meh-tuh-tik) breast cancer, or MBC, you are not alone. More than 150,000 people in the United States are living with cancer that has spread from the breast to other parts of the body. This type of cancer is also known as advanced or stage 4 cancer.

ABRAXANE (ah-BRAKS-ane) is a prescription medicine used to treat advanced breast cancer in people who have already received certain other medicines for their cancer.

What you will learn from reading this brochure

This brochure explains how ABRAXANE can help treat MBC. You and your caregivers will learn:

- Important Safety Information for ABRAXANE
- How ABRAXANE works
- How to prepare for treatment with ABRAXANE
- Why it is important to take an active role in your care
- Steps you can take to help with your journey
- How to get the support you need as you go through treatment

Dealing with MBC can be overwhelming. To live as well as you can, it is important to work closely with your healthcare team. It is also important to let your caregivers know what you need from them. It is not always easy to speak up for yourself or to ask for help. But this is the time to put your needs first.

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The information in this brochure does not take the place of talking with your doctor about your medical condition or your treatment. Be sure to talk with your healthcare team about any concerns or questions you may have.
Important Safety Information

Please see Important Safety Information on pages 6-9, and accompanying Patient Information and full Prescribing Information, including Boxed WARNING.
ABRAXANE is a prescription medicine used to treat advanced breast cancer in people who have already received certain other medicines for their cancer.

Important Safety Information About ABRAXANE

**WARNING - LOW WHITE BLOOD CELL COUNT (NEUTROPENIA)**

- Do not take ABRAXANE if your white blood cell count is below 1500 cells/mm³ (neutropenia), since you may be more likely to get a serious infection. While taking ABRAXANE, you must get regular blood tests to check for any problems that could develop.

- ABRAXANE contains albumin, a substance found in human blood. Do not substitute for or with other paclitaxel formulations.

**Who should not receive ABRAXANE?**

- Do not receive ABRAXANE if:
  - your white blood cell count is below 1500 cells/mm³
  - you have had a severe allergic reaction to ABRAXANE

**Serious side effects**

- ABRAXANE may cause serious side effects, including:
  - decreased blood counts. ABRAXANE can cause a severe decrease in neutrophils (a type of white blood cell important in fighting against bacterial infections) and platelets (important for clotting and to control bleeding). Your doctor will check your blood cell count during your treatment with ABRAXANE and after you have stopped your treatment.
  - numbness, tingling, pain, or weakness in the hands or feet (neuropathy).
  - allergic (hypersensitivity) reactions, which could be severe and sometimes fatal, have been reported with ABRAXANE.

**Other risks**

- Treatment with ABRAXANE can make liver problems worse. If you have liver problems, your starting dose of ABRAXANE should be lowered or withheld.

- ABRAXANE contains albumin (human), a product of human blood.

**Risks to pregnancy**

- If you are pregnant or become pregnant, ABRAXANE can harm your unborn baby. You should not become pregnant while taking ABRAXANE. Women who may become pregnant should use effective birth control (contraception). Talk to your doctor about the best way to prevent pregnancy while receiving ABRAXANE.

- If you are a man, you should not father a child during your treatment with ABRAXANE. ABRAXANE can harm the unborn baby of your partner.

Please see Important Safety Information on pages 6-9, and accompanying Patient Information and full Prescribing Information, including Boxed WARNING.
Other possible side effects

- The most common side effects of ABRAXANE include:
  - hair loss
  - numbness, tingling, pain, or weakness in the hands or feet
  - abnormal heart beat
  - tiredness
  - joint and muscle pain
  - changes in your liver function tests
  - rash
  - low red blood cell count (anemia). Red blood cells carry oxygen to your body tissues. Tell your doctor if you feel weak, tired, or short of breath
  - nausea and vomiting
  - infections. If you have a fever (temperature of greater than 100.4°F) or other signs of infection, tell your doctor right away
  - diarrhea
  - loss of body fluid (dehydration)
  - swelling in the hands or feet

- Other side effects include vision problems, decreased appetite, kidney problems, constipation, and difficulty breathing

- In some patients receiving ABRAXANE, severe heart and blood vessel side effects have occurred. These included chest pain, heart attack, fluid under the skin, blood clots in the veins or lungs, high blood pressure, stroke, and heart failure

Other important safety information about ABRAXANE

- You should contact your doctor if you have signs or symptoms of vomiting, diarrhea, dehydration, cough, or breathing difficulties that do not go away, or signs of an allergic reaction. Tell your doctor if you have any other medical conditions

- Treatment with ABRAXANE can cause irritation where the medicine is injected (injection site reactions). You should be monitored by your doctor or nurse during and after you receive ABRAXANE to make sure no problems occur at the injection site. In some cases, these problems occurred 7 to 10 days after the medicine was injected

- It is not known whether ABRAXANE interacts with other drugs, so be sure to tell your doctor about any medicines, including prescription and over-the-counter medicines, vitamins, and herbal supplements you are taking

- Since it is not known if ABRAXANE passes into human milk, you should discuss with your doctor if you should receive ABRAXANE or breastfeed

- It is not known if ABRAXANE is safe or effective in children

- ABRAXANE has not been adequately studied in people with severe kidney problems

These are not all the possible side effects of ABRAXANE. For more information, ask your doctor or pharmacist. You may report side effects to FDA at 1-800-FDA-1088.
What is ABRAXANE?

ABRAXANE is a prescription medicine used to treat advanced breast cancer in people who have already received certain other medicines for their cancer.

ABRAXANE is a chemotherapy (KEE-moh-THAYR-uh-pee). Chemotherapy is a type of medicine that is used to keep cancer cells from growing or to kill cancer cells.

Treatment with ABRAXANE may help control or slow the spread of cancer cells.

Your doctor may recommend treatment with ABRAXANE based on the stage of your cancer, your response to prior therapy, and your overall health. Only your doctor can help you decide if ABRAXANE is right for you.

What is some important safety information I need to know about ABRAXANE?

WARNING - LOW WHITE BLOOD CELL COUNT (NEUTROPENIA)

- Do not take ABRAXANE if your white blood cell count is below 1500 cells/mm³ (neutropenia), since you may be more likely to get a serious infection. While taking ABRAXANE, you must get regular blood tests to check for any problems that could develop

- ABRAXANE contains albumin, a substance found in human blood. Do not substitute for or with other paclitaxel formulations

You should not get ABRAXANE if:

- Your white blood cell count is below 1500 cells/mm³
- You have had a severe allergic reaction to ABRAXANE

ABRAXANE is a different formulation of the cancer-fighting medicine paclitaxel (PAK-li-TAK-sel). ABRAXANE is made by binding paclitaxel to albumin (al-BYOO-min). Albumin is a protein found in the blood.

ABRAXANE is free of solvents

Because ABRAXANE is bound to albumin, no solvents are needed to dissolve it.

Solvents are chemicals that help dissolve some medicines so that they can be given by infusion (in-FYOO-zhun). Some solvents can cause allergic reactions. Since ABRAXANE does not contain solvents, it is not usually necessary to take medicines to prevent allergic reactions before ABRAXANE is given. These medicines are also called premedication.

Allergic reactions can occur with ABRAXANE. Premedication may be needed if you have had an allergic reaction. Allergic reactions may be severe and can lead to death. In case of severe allergic reaction, ABRAXANE should not be used again.
How does ABRAXANE work?

ABRAXANE is a type of prescription medicine that may help stop cancer cells from dividing and making new cells. ABRAXANE works by blocking the action of proteins called microtubules (MY-kroh-TOO-byools). These proteins help cells divide.

*Systemic* (sis-TEH-mik) treatments like ABRAXANE are used to treat metastatic cancer. They travel through the bloodstream. This makes it possible to reach cells in many parts of the body, including cancer cells.

By stopping cells from dividing, ABRAXANE may help slow or prevent the growth of cancer cells.

ABRAXANE may also affect normal cells. This may cause side effects.

What are the most common side effects?

The most common side effects of ABRAXANE include:

- hair loss
- numbness, tingling, pain, or weakness in the hands or feet *(neuropathy [noor-AH-puh-thee]*)
- abnormal heart beat
- tiredness
- joint and muscle pain
- changes in your liver function tests
- rash
- low red blood cell count *(anemia [uh-NEE-mee-uh]*) Red blood cells carry oxygen to your body tissues. Tell your doctor if you feel weak, tired, or short of breath
- nausea and vomiting
- infections. If you have a fever (temperature of greater than 100.4°F) or other signs of infection, tell your doctor right away
- diarrhea
- loss of body fluid *(dehydration [dee-hy-DRAY-shun]*)
- swelling in the hands or feet

Please see pages 26-28 to learn more about the possible side effects of ABRAXANE.
What should I know before I start treatment?

It is important to know what to expect from treatment with ABRAXANE. Getting information from your doctor before you start on ABRAXANE can help you cope with the physical and emotional changes you may experience. Learning about your treatment can prepare you to make decisions and help the doctor better understand your needs and concerns.

What to learn from your doctor before you start treatment

- Why your doctor feels ABRAXANE is the right choice for you
- What you can do to prepare for your treatments
- How your treatments will be given
- Where you will be treated
- How often you will have treatments
- How you will know if ABRAXANE is working
- What side effects you may have during treatment
- How your healthcare team can help you cope with any side effects that occur
- What side effects you should report to the doctor right away
- How long you will need to stay on treatment
- If your health insurance will cover the cost of your treatment

Get more from your doctor visits

Follow these tips to make sure you understand the answers to your questions:

- Bring a friend or family member with you
- Take notes or ask if you can record the doctor’s advice
- Ask the doctor to say something again if you didn’t get it the first time
- Repeat back what you thought you heard and ask if you got it right
- Ask for a visual aid, like a brochure or fact sheet, that you can read at home

Please see Important Safety Information on pages 6-9, and accompanying Patient Information and full Prescribing Information, including Boxed WARNING.
Your doctor also needs to get some information from you before treatment begins. Talking with your doctor about health issues that may affect your treatment can help your healthcare team do a better job of guiding your care.

What to tell your doctor before starting on ABRAXANE

- If you have liver or kidney problems. Treatment with ABRAXANE can make liver problems worse. If you have liver problems, your starting dose of ABRAXANE should be lowered or withheld.

- If you have other medical problems.

- If you are pregnant or intend to become pregnant. ABRAXANE can harm your unborn baby. You should not become pregnant while taking ABRAXANE. Women who may become pregnant should use effective birth control (contraception). Talk to your doctor about the best way to prevent pregnancy while receiving ABRAXANE.

- If you are breastfeeding or planning to breastfeed. It is not known if ABRAXANE passes into breast milk. You and your doctor should decide if you will receive ABRAXANE or breastfeed.

- If you are planning to father a child. You should not father a child during your treatment with ABRAXANE. ABRAXANE can harm your partner’s unborn baby.

- If you take other medicines. Give your doctor a list of all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.
How is ABRAXANE given?

ABRAXANE is given by intravenous (IN-truh-VEE-nus), or IV, infusion.

To begin the infusion

- A nurse inserts a thin, soft tube into your vein to give the medicine. This is often called an IV. If you have a central line in place, the nurse will use that to give you the medicine
- A central line is a long tube that is put into a vein in your chest or arm and threaded to a larger vein in your chest. The other end is secured in place outside your body or attached to a port. A port is a tiny device inserted under the skin
- ABRAXANE flows through the IV into your bloodstream

After each infusion, the nurse removes the IV or the device that delivered the medicine through your central line. Your central line or port stays in place.

Possible site reactions

Treatment with ABRAXANE can cause irritation where the medicine is injected (injection site reactions). You should be monitored by your doctor or nurse during and after you receive ABRAXANE to make sure no problems occur at the injection site. In some cases, these problems occurred 7 to 10 days after the medicine was injected.

Where will I have my treatments?

Your treatment with ABRAXANE will be given in your doctor’s office, at a hospital, or at an infusion center.

How long do infusions take?

Each infusion of ABRAXANE takes 30 minutes. Tests, checkups, or waiting time may affect the length of treatment sessions.

How often is ABRAXANE given?

ABRAXANE is given once every 3 weeks. If you have questions about your treatment schedule, ask your doctor.

Please see Important Safety Information on pages 6-9, and accompanying Patient Information and full Prescribing Information, including Boxed WARNING.
What should I expect when I come in for treatment?

Knowing what to expect on the days you get treatment can help make the process go more smoothly.

Before treatment

- The healthcare team may take blood, check your blood pressure, and monitor your heart rate
  - If your white blood cell count is below 1500 cells/mm³, you should not receive ABRAXANE at that time
- You may be given medicine to help prevent nausea

During treatment

- The healthcare team will continue to check how you are feeling
- Let the doctor or nurse know if you have any signs of an allergic reaction. Signs of an allergic reaction may include:
  - Trouble breathing
  - Skin irritations, such as itching or hives
  - Stuffy or runny nose
  - Sneezing
  - Swelling of the neck, lips, tongue, or throat

After treatment

- Pay attention to how you feel after you get home
- Call the doctor right away if you notice any of the symptoms or side effects on page 27
What are the possible side effects of ABRAXANE?

When starting on ABRAXANE, it is important to pay attention to how you feel. Tell your doctor or nurse about any side effects you may have as soon as you notice them. Ask for advice on how to cope with these side effects. Let your healthcare team know right away if you have pain, changes in your health, or any new or troubling symptoms.

ABRAXANE may cause serious side effects.

These include:

- **Decreased blood cell counts.** ABRAXANE can cause a severe drop in neutrophils (NOO-troh-fils), white blood cells that help fight infection, and platelets (PLAYT-lets) that help control bleeding. Your doctor will check your blood cell count during your treatment with ABRAXANE and after you have stopped your treatment.

- **Numbness, tingling, pain, or weakness in your hands or feet (neuropathy)**

- **Allergic reactions.** Allergic reactions to ABRAXANE can be severe and sometimes fatal.

These are not all the possible side effects of ABRAXANE. For more information, ask your doctor or nurse.

When to call the doctor

Tell your doctor right away if you have:

- A fever of greater than 100.4°F or other signs of infection, such as chills, sore throat, cough, redness, or swelling

- Signs of an allergic reaction, such as trouble breathing, itching, hives, or swelling of the neck, lips, tongue, or throat

- Weakness, tiredness, or shortness of breath, especially if it is new or worse than before

- Nausea that makes it hard to eat or drink or lasts for more than 24 hours and doesn’t go away with the medicines you’ve been given

- Diarrhea that lasts for more than 24 hours and doesn’t go away with the medicines you’ve been given

Other side effects to share with your doctor:

- Numbness, tingling, pain, or weakness in your hands or feet

- Vomiting

- Signs of dehydration, such as dry mouth, thirst, dizziness, or having less urine than usual

Your healthcare team is the best source for medical advice. Always tell your healthcare team about any side effects you may have. This will help them better manage your treatment.

Do not wait for office visits or checkups to report symptoms and side effects like the ones noted above. Be sure to ask how to reach your doctor or nurse outside of normal office hours.
The most common side effects of ABRAXANE include:

- Hair loss
- Numbness, tingling, pain, or weakness in the hands or feet (neuropathy)
- Abnormal heart beat
- Tiredness
- Joint and muscle pain
- Changes in your liver function tests
- Rash
- Low red blood cell count (anemia)
- Nausea and vomiting
- Infections
- Diarrhea
- Loss of too much water and needed fluids from the body (dehydration) that may be caused by vomiting, diarrhea, or fever
- Swelling in the hands or feet

These are not all of the possible side effects of ABRAXANE. Ask your doctor for advice about side effects. You may also report side effects to the FDA at 1-800-332-1088.
What are some tips that may help with side effects?

Side effects of treatment may be different for each person. Your healthcare team is the best source for medical advice on your side effects. It is important to report all side effects to your doctor or nurse right away. Here are some tips to discuss with your healthcare team.

**Hair loss**

**What you may notice**
- Your hair may start to fall out after you start treatment
- You may lose hair on your head (scalp, eyebrows, eyelashes) and body

**Tips your doctor may suggest**

**Before your hair falls out:**
- Consider cutting your hair short
- Wash your hair gently with mild shampoo
- Avoid using hair dyes or styling tools that may hurt your scalp or weaken your hair
- Shop for a wig if you plan to buy one that matches the color of your hair

**After your hair falls out:**
- Wear a hat, turban, or scarf, or use sunscreen to protect your scalp from the sun
- Avoid places that are very hot or cold
- Use a satin pillowcase or wear a soft cap when you sleep
- Think about joining a support group if you are upset about losing your hair

**Neuropathy** (numbness, tingling, pain, or weakness in the hands or feet)

**What you may notice**
- You may have numbness, tingling, pain, or weakness in your hands or feet
- You may feel clumsy or have trouble buttoning your clothes

**Tips your doctor may suggest**

**Protect yourself from injury if you have numbness in your hands or feet:**
- Wear shoes inside and outdoors
- Use no-slip bath mats and clear away clutter to avoid falling
- Handle sharp objects with care
- Wear gloves when cooking, cleaning, or washing dishes
- Test bath water with a thermometer to make sure it’s not too hot
- Walk slowly and use a cane if you feel unsteady
**Tiredness**

**What you may notice**
- You may feel very weary or worn out, even after you rest

**Tips your doctor may suggest**
Find ways to balance activity with rest, cope with stress, and get the nutrients you need for energy:
- Take short naps during the day
- Stick to a routine
- Conserve your energy by pacing yourself and asking others to help with chores or errands
- Try relaxing activities such as massage, meditation, or yoga
- Do some light exercise if approved by your doctor, but start slowly
- Eat a balanced diet
- Drink plenty of fluids, unless you have been advised by your doctor to limit fluids

**Joint and muscle pain**

**What you may notice**
- Your joints or muscles may feel weak or achy

**Tips your doctor may suggest**
Follow your doctor’s advice to stretch, strengthen, and soothe sore muscles and painful joints:
- Ask your doctor if medicines, massage, or acupuncture may help ease your pain
- Apply hot or cold packs, and take warm baths to soothe sore areas
- Try strengthening and flexibility exercises like yoga, but stop if muscle pain gets worse
- Try to maintain a healthy weight to ease strain on your joints
Rash

What you may notice

- You may notice small or large spots on your skin that are flat or raised
- Your skin may burn or be itchy, red, peeling, or hot

Tips your doctor may suggest

Pay attention to skin changes and let your doctor know right away if a rash appears:

- Be sure to tell the doctor when the rash started and what it looks like
- Ask about medicines that may help treat the rash or keep it from getting worse

To help ease or reduce itching, dryness, redness, or peeling:

- Take quick showers or sponge baths with warm or cool water instead of long, hot baths
- Wash with a mild, moisturizing soap
- Take a bath with colloidal (kuh-LOY-dul) oatmeal, a soothing powder that helps relieve itching
- Pat yourself dry after bathing
- Apply moisturizing cream while your skin is still damp
- Avoid using perfume or aftershave made with alcohol
- Wear loose-fitting cotton clothing
- Use sunscreen or protective clothing when outdoors, even on cloudy days

Anemia (low red blood cell counts)

What you may notice

- You may feel short of breath, weak, dizzy, or very tired
- You may look pale

Tips your doctor may suggest

Conserve your energy, get plenty of rest, and eat iron-rich foods:

- Do only the things that are most important to you
- Accept help with daily chores and errands
- Try to get 8 hours of sleep each night
- Take 1 or 2 short naps during the day
- Stand up slowly to avoid getting dizzy
- Eat a well-balanced diet including iron-rich foods such as nuts, eggs, and lean beef (unless you are allergic to any of these foods). Your body needs iron to make new red blood cells
**Nausea and vomiting**

**What you may notice**
- You may feel sick to your stomach or have the urge to throw up
- You may have no appetite or have trouble keeping food down

**Tips your doctor may suggest**

Eat small, bland meals, try to relax, and ask your doctor for advice:
- Eat 5 or 6 small meals through the day instead of 3 big meals
- Choose foods that are easy on your stomach, such as:
  - Clear broth or ginger ale
  - Peppermint or ginger tea
  - Dry toast or crackers
  - White rice or pasta
  - Oatmeal or rice cereal
  - Chicken without skin
  - Bananas or canned fruit
  - Ice pops, sherbet, or gelatin
- Check with your doctor before changing your diet if you have diabetes or other dietary restrictions
- Eat foods at room temperature
- Avoid foods or drinks with strong smells
- Try meditation, deep breathing exercises, or picturing peaceful scenes to help you relax
- Ask your doctor about taking medicines before, after, and between chemotherapy treatments to help prevent nausea

**Decreased appetite**

**What you may notice**
- You may feel like you don’t want to or can’t eat
- Food may not taste like it usually does

**Tips your doctor may suggest**

To increase your appetite:
- Exercise lightly before meals, if approved by your doctor
- Drink 6-12 cups of clear liquids throughout the day, unless your doctor has told you to limit fluids
- Keep healthy snacks handy to eat between meals
- Have someone help you prepare meals in advance
- Perk up the taste and smell of food with lemon juice, mint, basil, and other seasonings
Diarrhea

What you may notice

- You may have loose, watery stools, cramps, bloating, or a sudden urge to have a bowel movement

Tips your doctor may suggest

Replace lost nutrients your body needs:

- Choose foods high in sodium, potassium, pectin, and protein (unless your doctor has told you to avoid certain foods), such as:
  - Soups, broths, sport drinks, apple juice
  - Crackers and pretzels
  - Applesauce and bananas
  - Baked potatoes without skin
  - Lean meat and cooked eggs

Drink plenty of fluids, and know what foods to avoid:

- Drink 8-12 cups of clear liquid every day
- Avoid foods that can make diarrhea worse, such as:
  - Coffee, tea, and alcohol
  - Fried, greasy, spicy, or high-fat foods
  - Milk or milk products
  - Nuts, whole-grain breads, and bran

Infections

What you may notice

- If ABRAXANE causes a drop in your white blood cell count (neutropenia), you are at greater risk of getting an infection
- You may run a fever, your skin may feel hot, and your body may ache
- You may have other signs of infection, such as chills, sore throat, cough, redness, or swelling

Tips your doctor may suggest

Take steps to protect yourself from infections:

- Avoid crowds and people with colds
- Wash your hands often
- Use moisture cream to heal dry, cracked skin
- Wear gloves when washing dishes or gardening
- Brush your teeth after meals with a soft toothbrush and alcohol-free mouthwash
- Clean cuts, scrapes, or burns right away
- Cook food thoroughly
- Check with your doctor before getting a flu shot or vaccines

If you have a fever:

- Take your temperature every 2-3 hours and keep a record
- Call your doctor right away if your fever is over 100.4°F
- Check with your doctor before you take any medicine
- Drink plenty of liquids, unless your doctor has told you to limit your liquids
- Use a cold compress if you feel hot
**Dehydration**

**What you may notice**
- Vomiting, diarrhea, or fever may make it hard for you to keep enough fluid in your body
- Your mouth may feel dry or sticky
- You may feel thirsty, dizzy, or very weak
- Your skin may “tent,” or stay up, when lightly pinched
- You may have less urine than usual or it may look dark

**Tips your doctor may suggest**
Try to control vomiting, diarrhea, and fever, and take in as much fluid as you can:
- Fill a small cooler with juice boxes, bottled water, or other drinks, and keep it nearby. Take small sips throughout the day
- Eat bland, moist foods such as clear soups, canned fruit, gelatin, or popsicles
- Apply moisturizing cream often to soften dry skin
- Use lip balm to avoid painful cracking
- Suck ice chips to relieve dry mouth if you can’t drink enough liquid
- If your doctor has advised you to limit fluids, ask your healthcare team for tips on replacing the fluid in your body

**Swelling** (usually in the legs or feet)

**What you may notice**
- Your hands, arms, legs, or feet may feel puffy, swollen, or tender

**Tips your doctor may suggest**
Find ways to prop up swollen legs or feet and prevent fluid buildup that may cause swelling:
- Ask your doctor about wearing special stockings
- Wear clothing and shoes that are not too tight
- When sitting or lying in bed, raise your feet using a footstool, recliner, or pillows
- Avoid standing on your feet for too long

**Limit salt in your diet:**
- Avoid adding salt at the table and during cooking
- Eat less canned soup, bacon, chips, and other salty foods
- Check sodium content on food labels
- Ask your doctor what your daily limit for sodium should be
Della’s Story

As a single parent and family caregiver, Della was always the one everyone relied on for support.

She worked full time; cheered on her son at baseball and football games; helped care for her live-in parents; and somehow managed to stay on top of the cleaning, laundry, and yard work. But after she was diagnosed with metastatic breast cancer, Della’s family stepped up to support her.

After initially being treated for her metastatic disease and finding that her condition progressed, Della moved closer to home. Her sisters helped Della find a new oncologist with whom she felt comfortable. After she started treatment with ABRAXANE, they went with her to the doctor and kept her company during infusions.

Della needed help paying for ABRAXANE. She qualified for assistance from Celgene Patient Support®. Della knows how hard it is to ask for help, and she hopes that others can learn from her experience.

Della’s advice? Don’t let your pride or fears keep you from asking for the help you need.

Della is a real patient who had been treated with ABRAXANE.
“If you need help, ask for it”

Making sure your questions get answered
“My doctor had her nurse go over a lot of stuff about what to expect. I remember them saying, you know that everybody is different, but I can’t be clear of everything they said. I was in too big of a whirlwind. I know that a few times I would forget to tell the doctor certain things, and so my sister started going with me, and she would remember to ask certain questions.”

Finding support to pay for your care
“When I first started seeing my doctor, I was on what they call charity care and the hospital took all of my bills and paid them, and Celgene Patient Support® gave me my ABRAXANE. I had no insurance. I had no money to pay for it, and, you know, to me that help says a lot.”

Coping with the side effects of treatment
“My hair fell out between my first and second treatment. In the beginning after starting ABRAXANE, my red blood cell counts were low. I could hardly get up and do anything. I would try to go to the mailbox just at the end of the driveway, and that was difficult. I would have to stop and get a good breath and then come back. I talked with my doctor about my side effects and got advice on things that helped me.”

Della always knew her family would be willing to help, but she has been overwhelmed by all the ways they have come through for her.

Learning to accept help
“One night my son saw that I was in a lot of pain, and it scared him. So he called my sister and asked her to come. She dropped everything. And then she ended up not even working that next day, and she helped me do grocery shopping and getting all of that stuff put away, and, you know, how much better support can you get? If you need help, ask for it. I think that is the biggest thing that I am trying to learn. That is what I would say because that is what I told my sister, ‘I hate that you came, but I am so glad that you are here.’”

“Today I ate lunch with some friends. Just being able to get out and enjoy their company, that is a good day to me.”
—Della

This is the story of one patient who was treated with ABRAXANE. Each patient’s results and experiences on ABRAXANE may vary. Your doctor is your best source of medical advice. It is important to discuss questions about your health and treatment with your doctor.
How can I get the support I need?

Family members, friends, neighbors, coworkers, and other people close to you are among your most important care partners. These caregivers play a key role in providing practical help, friendship, comfort, and support.

Keep in mind that your cancer diagnosis affects everyone who cares about you. Many of the people in your personal circle want to help but don’t know how. That is why you may have to tell them what kind of support you need.

There are many ways to let the people in your life step up to help you out.

You may call on your caregivers to:

- Gather information and help you make decisions
- Go with you to doctor visits and checkups
- Make a list of your medical and emergency contacts
- Help with financial, legal, or health insurance matters
- Organize volunteers to bring you meals, take you to treatments, or run errands for you
- Help keep up your appetite, weight, and strength by cooking tempting foods and creating pleasant settings for meals
- Listen when you need to vent your feelings or frustrations
- Entertain you or keep you company when you want to relax or have fun
- Help with household chores like laundry, cleaning, grocery shopping, or dog walking
- Go for walks with you to help you stay active

Sharing information about your cancer

Letting family and friends know what you are going through can bring you comfort. But it can also be stressful. People do not always react the way you hope they will. These tips may help make it easier to talk with others about your cancer.

Give some thought to what you might say. Think about what you want other people to know and write it down.

Decide who to tell and when. You may want to start with a close friend who has “been there for you” in the past. Choose a time to talk that feels right to you.

Find the best way to share the information. You may want to tell some people face-to-face, some on the phone, and others by sending a letter or e-mail.

Seek expert advice. If you are unsure of what to say, it might help to talk with an oncology social worker or other people who are living with metastatic breast cancer (see the resources on pages 54–59).

Keep talking. If friends or loved ones react poorly or cannot handle your news, let them know how that makes you feel. Give them a little time to face their own fears about your cancer.
Celgene is here to help you

Learn about the many services Celgene offers to support people with metastatic breast cancer and their caregivers.

Available resources to:

- Learn more about ABRAXANE
- Get help paying for ABRAXANE

Learn more about ABRAXANE

Visit www.abraxane.com

Find information for you and your doctor about treatment with ABRAXANE, including tips and tools to help you work closely with your healthcare team throughout your cancer journey.

Get help paying for ABRAXANE

Celgene Patient Support® can assist with various financial needs. Turn the page to learn more.

Use the resources on pages 54-59 to get answers, advice, and help from advocacy groups and peers who understand the needs and concerns of people with metastatic breast cancer.
Celgene Patient Support®

A free, personal, and confidential service to help you get access to ABRAXANE

At Celgene, we know how hard it can be to understand insurance plans. It can also be hard to find information and resources to help pay for your medicine. We can help.

How Celgene Patient Support® can help you

Celgene Patient Support® provides you with a single point of contact who will work closely with you and your doctor’s office. Your dedicated Celgene Patient Support® Specialist can help you:

- Explore options to help pay for your ABRAXANE
- Get insurance related services for ABRAXANE
- Identify coverage options for ABRAXANE if you have no insurance

Help is just a phone call away.

TO GET STARTED:
Call: 1-800-931-8691
Visit: www.CelgenePatientSupport.com
E-mail: patientsupport@celgene.com
Fax: 1-800-822-2496

Do you need help with the costs of getting to and from your doctor’s office? Celgene Patient Support® can help locate transportation assistance options to assist with the costs of traveling to and from your doctor visits.

These programs are not insurance and Celgene does not provide insurance advice or decisions.

Please see Important Safety Information on pages 6-9, and accompanying Patient Information and full Prescribing Information, including Boxed WARNING.
Resources for you and your caregivers

Your need for information, services, and support may change as you go through treatment for metastatic breast cancer (MBC). Knowing where to find the resources you need to help manage these challenges can help you feel more in control.

Celgene resources

<table>
<thead>
<tr>
<th>Your concern or need</th>
<th>Where to turn for help</th>
<th>Services provided</th>
</tr>
</thead>
<tbody>
<tr>
<td>Learning more about ABRAXANE® (paclitaxel protein-bound particles for injectable suspension) (albumin-bound)</td>
<td>ABRAXANE patient information <a href="http://www.abraxane.com">www.abraxane.com</a></td>
<td>Information for you and your doctor about treatment with ABRAXANE, including tips and tools to help you work closely with your healthcare team throughout your cancer journey</td>
</tr>
<tr>
<td>Getting help paying for ABRAXANE</td>
<td>Celgene Patient Support® <a href="http://www.CelgenePatientSupport.com">www.CelgenePatientSupport.com</a> 1-800-931-8691</td>
<td>A free program to help you get access to Celgene medicines (see pages 52-53 for more information)</td>
</tr>
</tbody>
</table>

Other sources of support

This is a list of additional resources that can help you find more information about MBC. Some organizations may have eligibility criteria for their services. Ask your healthcare team about other resources that they recommend. Celgene Corporation does not endorse any of the organizations on this list or their communications.

<table>
<thead>
<tr>
<th>Your concern or need</th>
<th>Where to turn for help</th>
<th>Services provided</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wondering what to do first?</td>
<td>Living Beyond Breast Cancer (LBBC) <a href="http://www.lbbc.org">www.lbbc.org</a> 1-855-807-6386</td>
<td>Connection to a dedicated community of support and information for people with MBC offering:</td>
</tr>
<tr>
<td></td>
<td>Metastatic Breast Cancer Network (MBCN) <a href="http://www.mbcn.org">www.mbcn.org</a> 1-888-500-0370</td>
<td>• Advice from experts</td>
</tr>
<tr>
<td></td>
<td>AdvancedBC.org <a href="http://advancedbc.org">http://advancedbc.org</a></td>
<td>• Telephone support</td>
</tr>
<tr>
<td></td>
<td>Living Beyond Breast Cancer (LBBC) Helpline 1-800-977-4121</td>
<td>• Patient stories</td>
</tr>
<tr>
<td></td>
<td>SHARE Breast Cancer Helpline 1-866-891-2392</td>
<td>• Booklets and newsletters</td>
</tr>
<tr>
<td>To get one-on-one support by phone</td>
<td>ABCD Helpline 1-800-977-4121</td>
<td>• Referrals to resources</td>
</tr>
<tr>
<td></td>
<td>Living Beyond Breast Cancer (LBBC) Helpline 1-888-753-5222</td>
<td>• Conferences and webinars</td>
</tr>
<tr>
<td></td>
<td>SHARE Breast Cancer Helpline 1-866-891-2392</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Young Survival Coalition Survivor Link 1-877-972-1011</td>
<td>One-on-one peer support for women aged 40 and under with breast cancer</td>
</tr>
<tr>
<td></td>
<td>E-mail: <a href="mailto:resourcelink@younsurvival.org">resourcelink@younsurvival.org</a></td>
<td></td>
</tr>
<tr>
<td>Your concern or need</td>
<td>Where to turn for help</td>
<td>Services provided</td>
</tr>
<tr>
<td>----------------------</td>
<td>------------------------</td>
<td>--------------------</td>
</tr>
</tbody>
</table>
| Connecting with other patients and support groups on the Internet, by phone, or in person (continued) | **To find a support group in your area**  
MetaVIVOR  
www.metavivor.org/support/finding-a-support-program/  
www.facebook.com/metavivor | Information to help you find—or set up—a support group, or connect with the metastatic breast cancer (MBC) community through Facebook and social media |
| | CancerCare®  
www.cancercare.org  
1-800-813-4673 | Free counseling and support groups led by oncology social workers to help you manage the emotional and practical challenges of cancer |
| | Cancer Support Community  
www.cancersupportcommunity.org  
1-888-793-9355 | Referrals to local chapters that run support groups |
| | **To connect online with other survivors and caregivers**  
BCMets.org  
www bcmets.org  
Breastcancer.org discussion boards  
http://community.breastcancer.org  
Triple Negative Breast Cancer (TNBC) Foundation  
http://forum.tnbcfoundation.org | Online discussion forums for people with MBC |
<table>
<thead>
<tr>
<th>Your concern or need</th>
<th>Where to turn for help</th>
<th>Services provided</th>
</tr>
</thead>
</table>
| Seeking help for anxiety or depression due to cancer-related health issues | **American Society of Psychosocial Oncology (APOS) Helpline**  
1-866-276-7444 | Referrals to professional counselors who are skilled at helping people manage cancer-related distress |
| | **Getting advice on how to talk with your healthcare team**  
Open to Options™  
www.cancersupportcommunity.org/open2options  
1-888-793-9355 | A free professional counseling program that helps prepare you to make informed treatment decisions |
| | **Understanding your type of cancer and treatment options**  
National Cancer Institute (NCI) Cancer Information Service  
1-800-422-6237  
American Cancer Society  
www.cancer.org  
1-800-227-2345  
National Institutes of Health Senior Health  
http://nihseniorhealth.gov/category/cancer.html | Easy-to-understand information and treatment guidelines for different types and stages of cancer |
| | **Choosing an insurance plan or paying for coverage**  
Health Insurance Marketplace  
www.healthcare.gov  
1-800-318-2596  
Centers for Medicare & Medicaid Services (CMS)  
www.cms.gov  
1-800-633-4227 | Information to help you access healthcare coverage through Medicare, Medicaid, or the Affordable Care Act |
### Your concern or need

| Choosing an insurance plan or paying for coverage (continued) | Patient Advocate Foundation (PAF)  
  www.patientadvocate.org  
  1-800-532-5274 | Free web chats, webinars, search tools, and guides to help uninsured and underinsured patients find resources to help ease the burden of paying for treatment |
|---|---|---|
| Seeking information about financial or legal issues related to cancer | Patient Advocate Foundation (PAF)  
  www.patientadvocate.org  
  1-800-532-5274 | Free professional information about health insurance, medical debt, disability, or job-related issues |
| Cancer Legal Resource Center  
  www.disabilityrightslegalcenter.org/cancer-legal-resource-center  
  1-866-843-2572 | Offers short-term aid for basic living expenses to breast cancer patients who have lost income during active treatment |
| The Pink Fund  
  www.thepinkfund.org  
  1-877-234-7465 | Grants to patients with metastatic breast cancer (MBC) to cover the cost of transportation to and from treatment |
| American Cancer Society  
  www.cancer.org  
  1-800-227-2345 | Referrals to local and national groups that provide funding for travel and other out-of-pocket expenses related to treatment |

### Where to turn for help

| Getting information on pain or side effects of treatment to discuss with your healthcare team | Breastcancer.org  
  www.breastcancer.org  
  1-800-813-4673 | Practical information about pain and/or side effects of cancer treatment |
| Learning how to cope with hair loss and skin changes | Look Good Feel Better  
  www.lookgoodfeelbetter.org  
  1-800-395-5665 | Free workshops offering makeup, beauty, and skin care tips to women in treatment for cancer |
| Lining up home care or help for older adults | Eldercare Locator  
  www.eldercare.gov  
  1-800-677-1116 | Free referrals to community services for older adults and their families |
| Organizing help from friends and family | MyLifeLine.org  
  www.mylifeline.org | Web sites and mobile apps that allow you to set up a free private online network for giving and receiving help |
| Getting support for caregivers | Cancer Support Community  
  www.cancersupportcommunity.org  
  1-888-793-9355  
  CancerCare  
  www.cancercare.org  
  1-800-813-4673  
  Family Caregiver Alliance  
  www.caregiver.org  
  1-800-445-8106 | Support groups, information, advice, and referrals to resources for local and long-distance caregiving |
ABRAXANE® for Injectable Suspension (paclitaxel protein-bound particles for injectable suspension) 
(albumin-bound) 
Initial U.S. Approval: 2005

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**HIGHLIGHTS OF PRESCRIBING INFORMATION**
These highlights do not include all the information needed to use ABRAXANE safely and effectively. See full prescribing information for ABRAXANE.

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**WARNING: NEUTROPENIA**
See full prescribing information for complete boxed warning.

- Do not administer ABRAXANE therapy to patients with baseline neutrophil counts of less than 1,500 cells/mm³. (4)
- It is recommended that frequent peripheral blood cell counts be performed to monitor the occurrence of bone marrow suppression. (4, 5.1, 6.1, 6.2, 6.3)

DO NOT SUBSTITUTE FOR OR WITH OTHER PACLITAXEL FORMULATIONS.

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**RECENT MAJOR CHANGES**
- Dosage and Administration (2.4, 2.8) 12/2014
- Dosage and Administration (2.7) 07/2015
- Warnings and Precautions, Hepatic Impairment (5.6) 12/2014

**INDICATIONS AND USAGE**
ABRAXANE is a microtubule inhibitor indicated for the treatment of:
- Metastatic breast cancer, after failure of combination chemotherapy for metastatic disease or relapse within 6 months of adjuvant chemotherapy. Prior therapy should have included an anthracycline unless clinically contraindicated. (1.1)
- Locally advanced or metastatic non-small cell lung cancer (NSCLC), as first-line treatment in combination with carboplatin, in patients who are not candidates for curative surgery or radiation therapy. (1.2)
- Metastatic adenocarcinoma of the pancreas as first-line treatment, in combination with gemcitabine. (1.3)

**DOSE AND ADMINISTRATION**
- Metastatic Breast Cancer: Recommended dosage of ABRAXANE is 260 mg/m² intravenously over 30 minutes every 3 weeks. (2.1)
- Non-Small Cell Lung Cancer: Recommended dosage of ABRAXANE is 100 mg/m² intravenously over 30 minutes on Days 1, 8, and 15 of each 21-day cycle; administer carboplatin on Day 1 of each 21-day cycle immediately after ABRAXANE. (2.2)
- Adenocarcinoma of the Pancreas: Recommended dosage of ABRAXANE is 125 mg/m² intravenously over 30-40 minutes on Days 1, 8 and 15 of each 28-day cycle; administer gemcitabine on Days 1, 8 and 15 of each 28-day cycle immediately after ABRAXANE. (2.3)
- Do not administer ABRAXANE to any patient with AST > 10 x ULN or bilirubin > 5 x ULN. Do not administer ABRAXANE to patients with metastatic adenocarcinoma of the pancreas who have moderate to severe hepatic impairment. For diseases other than metastatic adenocarcinoma of the pancreas, reduce starting dose in patients with moderate to severe hepatic impairment. (2.4)
- Dose Reductions: Dose reductions or discontinuation may be needed based on severe hematologic, neurologic, cutaneous, or gastrointestinal toxicities. (2.5)
- Use caution when handling cytotoxic drugs. Closely monitor the infusion site for extravasation and infiltration. No premedication is required prior to administration. (2.6)

**ADVERSE REACTIONS**
The most common adverse reactions (≥ 20%) in metastatic breast cancer are alopecia, neutropenia, sensory neuropathy, abnormal ECG, fatigue/asthenia, myalgia/arthritis, AST elevation, alkaline phosphatase elevation, anemia, nausea, infections, and diarrhea. (6.1)

The most common adverse reactions (≥ 20%) in NSCLC are anemia, neutropenia, thrombocytopenia, alopecia, peripheral neuropathy, nausea, and fatigue. (6.2)

The most common (≥ 20%) adverse reactions of ABRAXANE in adenocarcinoma of the pancreas are neutropenia, fatigue, peripheral neuropathy, nausea, alopecia, peripheral edema, diarrhea, pyrexia, vomiting, decreased appetite, rash, and dehydration. (6.3)

To report SUSPECTED ADVERSE REACTIONS, contact Celgene Corporation at 1-888-423-5436 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

**DRUG INTERACTIONS**
- Use caution when concomitantly administering ABRAXANE with inhibitors or inducers of either CYP2C8 or CYP3A4. (7)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 07/2015
FULL PRESCRIBING INFORMATION
ABRAXANE® for Injectable Suspension (paclitaxel protein-bound particles for injectable suspension) (albumin-bound)

WARNING: NEUTROPENIA

- Do not administer ABRAXANE therapy to patients who have baseline neutrophil counts of less than 1,500 cells/mm³. In order to monitor the occurrence of bone marrow suppression, primarily neutropenia, which may be severe and result in infection, it is recommended that frequent peripheral blood cell counts be performed on all patients receiving ABRAXANE [see Contraindications (4), Warnings and Precautions (5.1) and Adverse Reactions (6.1, 6.2, 6.3)].

- Note: An albumin form of paclitaxel may substantially affect a drug’s functional properties relative to those of drug in solution. DO NOT SUBSTITUTE FOR OR WITH OTHER PACLITAXEL FORMULATIONS.

1 INDICATIONS AND USAGE

1.1 Metastatic Breast Cancer
ABRAXANE is indicated for the treatment of breast cancer after failure of combination chemotherapy for metastatic disease or relapse within 6 months of adjuvant chemotherapy. Prior therapy should have included an anthracycline unless clinically contraindicated.

1.2 Non-Small Cell Lung Cancer
ABRAXANE is indicated for the first-line treatment of locally advanced or metastatic non-small cell lung cancer, in combination with carboplatin, in patients who are not candidates for curative surgery or radiation therapy.

1.3 Adenocarcinoma of the Pancreas
ABRAXANE is indicated for the first-line treatment of patients with metastatic adenocarcinoma of the pancreas, in combination with gemcitabine.

2 DOSAGE AND ADMINISTRATION

2.1 Metastatic Breast Cancer
After failure of combination chemotherapy for metastatic breast cancer or relapse within 6 months of adjuvant chemotherapy, the recommended regimen for ABRAXANE is 260 mg/m² administered intravenously over 30 minutes every 3 weeks.

2.2 Non-Small Cell Lung Cancer
The recommended dose of ABRAXANE is 100 mg/m² administered as an intravenous infusion over 30 minutes on Days 1, 8, and 15 of each 21-day cycle. Administer carboplatin on Day 1 of each 21 day cycle immediately after ABRAXANE [see Clinical Studies (14.2)].

2.3 Adenocarcinoma of the Pancreas
The recommended dose of ABRAXANE is 125 mg/m² administered as an intravenous infusion over 30-40 minutes on Days 1, 8 and 15 of each 28-day cycle. Administer gemcitabine immediately after ABRAXANE on Days 1, 8 and 15 of each 28-day cycle [see Clinical Studies (14.3)].

2.4 Dosage in Patients with Hepatic Impairment
For patients with mild hepatic impairment (total bilirubin greater than ULN and less than or equal to 1.5 x ULN and aspartate aminotransferase [AST] less than or equal to 10 x ULN), no dose adjustments are required, regardless of indication.

Do not administer ABRAXANE to patients with metastatic adenocarcinoma of the pancreas who have moderate to severe hepatic impairment.

Do not administer ABRAXANE to patients with total bilirubin greater than 5 x ULN or AST greater than 10 x ULN regardless of indication as these patients have not been studied.

Recommendations for dosage adjustment for the first course of therapy are shown in Table 1.
Table 1: Recommendations for Starting Dose in Patients with Hepatic Impairment

<table>
<thead>
<tr>
<th>SGOT (AST) Levels</th>
<th>Bilirubin Levels</th>
<th>ABRAXANE Dosea</th>
<th>MBC</th>
<th>NSCLC c</th>
<th>Pancreatic c Adenocarcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>&lt; 10 x ULN AND</td>
<td>&gt; ULN to ≤ 1.5 x ULN</td>
<td>260 mg/m²</td>
<td>100 mg/m²</td>
<td>125 mg/m²</td>
</tr>
<tr>
<td>Moderate</td>
<td>&lt; 10 x ULN AND</td>
<td>&gt; 1.5 to ≤ 3 x ULN</td>
<td>200 mg/m²b</td>
<td>80 mg/m²b</td>
<td>not recommended</td>
</tr>
<tr>
<td>Severe</td>
<td>&lt; 10 x ULN AND</td>
<td>&gt; 3 to ≤ 5 x ULN</td>
<td>200 mg/m²b</td>
<td>80 mg/m²b</td>
<td>not recommended</td>
</tr>
<tr>
<td></td>
<td>&gt; 10 x ULN OR</td>
<td>&gt; 5 x ULN</td>
<td>not recommended</td>
<td>not recommended</td>
<td>not recommended</td>
</tr>
</tbody>
</table>

MBC = Metastatic Breast Cancer; NSCLC = Non-Small Cell Lung Cancer.

a Dosage recommendations are for the first course of therapy. The need for further dose adjustments in subsequent courses should be based on individual tolerance.

b A dose increase to 260 mg/m² for patients with metastatic breast cancer or 100 mg/m² for patients with non-small cell lung cancer in subsequent courses should be considered if the patient tolerates the reduced dose for two cycles.

c Patients with bilirubin levels above the upper limit of normal were excluded from clinical trials for pancreatic or lung cancer.

2.5 Dose Reduction/Discontinuation Recommendations

Metastatic Breast Cancer
Patients who experience severe neutropenia (neutrophils less than 500 cells/mm³ for a week or longer) or severe sensory neuropathy during ABRAXANE therapy should have dosage reduced to 220 mg/m² for subsequent courses of ABRAXANE. For recurrence of severe neutropenia or severe sensory neuropathy, additional dose reduction should be made to 180 mg/m². For Grade 3 sensory neuropathy hold treatment until resolution to Grade 1 or 2, followed by a dose reduction for all subsequent courses of ABRAXANE [see Contraindications (4), Warnings and Precautions (5.1, 5.2) and Adverse Reactions (6.1)].

Non-Small Cell Lung Cancer
• Do not administer ABRAXANE on Day 1 of a cycle until absolute neutrophil count (ANC) is at least 1500 cells/mm³ and platelet count is at least 100,000 cells/mm³ [see Contraindications (4), Warnings and Precautions (5.1) and Adverse Reactions (6.2)].

• In patients who develop severe neutropenia or thrombocytopenia withhold treatment until counts recover to an absolute neutrophil count of at least 1500 cells/mm³ and platelet count of at least 100,000 cells/mm³ on Day 1 or to an absolute neutrophil count of at least 500 cells/mm³ and platelet count of at least 50,000 cells/mm³ on Days 8 or 15 of the cycle. Upon resumption of dosing, permanently reduce ABRAXANE and carboplatin doses as outlined in Table 2.

• Withhold ABRAXANE for Grade 3-4 peripheral neuropathy. Resume ABRAXANE and carboplatin at reduced doses (see Table 2) when peripheral neuropathy improves to Grade 1 or completely resolves [see Warnings and Precautions (5.2) and Adverse Reactions (6.2)].

Table 2: Permanent Dose Reductions for Hematologic and Neurologic Adverse Drug Reactions in NSCLC

<table>
<thead>
<tr>
<th>Adverse Drug Reaction</th>
<th>Occurrence</th>
<th>Weekly ABRAXANE Dose (mg/m²)</th>
<th>Every 3-Week Carboplatin Dose (AUC mg•min/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutropenic Fever</td>
<td>First</td>
<td>75</td>
<td>4.5</td>
</tr>
<tr>
<td>ANC less than 500/mm³</td>
<td>OR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Delay of next cycle</td>
<td>Second</td>
<td>50</td>
<td>3</td>
</tr>
<tr>
<td>by more than 7 days</td>
<td>OR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ANC less than 500/mm³</td>
<td>for more than 7 days</td>
<td>Third</td>
<td>Discontinue Treatment</td>
</tr>
<tr>
<td>Platelet count less than 50,000/mm³</td>
<td>First</td>
<td>75</td>
<td>4.5</td>
</tr>
<tr>
<td></td>
<td>Second</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>Severe sensory</td>
<td>First</td>
<td>75</td>
<td>4.5</td>
</tr>
<tr>
<td>Neuropathy – Grade 3</td>
<td>Second</td>
<td>50</td>
<td>3</td>
</tr>
<tr>
<td>or 4</td>
<td>Third</td>
<td></td>
<td>Discontinue Treatment</td>
</tr>
</tbody>
</table>

Reference ID: 3793488
Adenocarcinoma of the Pancreas

Dose level reductions for patients with adenocarcinoma of the pancreas, as referenced in Tables 4 and 5, are provided in Table 3.

Table 3: Dose Level Reductions for Patients with Adenocarcinoma of the Pancreas

<table>
<thead>
<tr>
<th>Dose Level</th>
<th>ABRAXANE (mg/m²)</th>
<th>Gemcitabine (mg/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full dose</td>
<td>125</td>
<td>1000</td>
</tr>
<tr>
<td>1st dose reduction</td>
<td>100</td>
<td>800</td>
</tr>
<tr>
<td>2nd dose reduction</td>
<td>75</td>
<td>600</td>
</tr>
<tr>
<td>If additional dose reduction required</td>
<td>Discontinue</td>
<td>Discontinue</td>
</tr>
</tbody>
</table>

Recommended dose modifications for neutropenia and thrombocytopenia for patients with adenocarcinoma of the pancreas are provided in Table 4.

Table 4: Dose Recommendation and Modifications for Neutropenia and/or Thrombocytopenia at the Start of a Cycle or within a Cycle for Patients with Adenocarcinoma of the Pancreas

<table>
<thead>
<tr>
<th>Cycle Day</th>
<th>ANC (cells/mm³)</th>
<th>Platelet count (cells/mm³)</th>
<th>ABRAXANE / Gemcitabine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>&lt; 1500 OR &lt; 100,000</td>
<td>&lt; 100,000</td>
<td>Delay doses until recovery</td>
</tr>
<tr>
<td>Day 8</td>
<td>500 to &lt; 1000 OR 50,000 to &lt; 75,000</td>
<td>&lt; 50,000</td>
<td>Reduce 1 dose level</td>
</tr>
<tr>
<td></td>
<td>&lt; 500 OR &lt; 50,000</td>
<td>&lt; 50,000</td>
<td>Withhold doses</td>
</tr>
<tr>
<td>Day 15: If Day 8 doses were reduced or given without modification:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>500 to &lt; 1000 OR 50,000 to &lt; 75,000</td>
<td>&lt; 50,000</td>
<td>Reduce 1 dose level from Day 8</td>
</tr>
<tr>
<td></td>
<td>&lt; 500 OR &lt; 50,000</td>
<td>&lt; 50,000</td>
<td>Withhold doses</td>
</tr>
<tr>
<td>Day 15: If Day 8 doses were withheld:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>≥ 1000 OR ≥ 75,000</td>
<td>&lt; 100,000</td>
<td>Reduce 1 dose level from Day 1</td>
</tr>
<tr>
<td></td>
<td>500 to &lt; 1000 OR 50,000 to &lt; 75,000</td>
<td>&lt; 50,000</td>
<td>Reduce 2 dose levels from Day 1</td>
</tr>
<tr>
<td></td>
<td>&lt; 500 OR &lt; 50,000</td>
<td>&lt; 50,000</td>
<td>Withhold doses</td>
</tr>
</tbody>
</table>

ANC = Absolute Neutrophil Count

Recommended dose modifications for other adverse drug reactions in patients with adenocarcinoma of the pancreas are provided in Table 5.

Table 5: Dose Modifications for Other Adverse Drug Reactions in Patients with Adenocarcinoma of the Pancreas

<table>
<thead>
<tr>
<th>Adverse Drug Reaction</th>
<th>ABRAXANE</th>
<th>Gemcitabine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Febrile Neutropenia:</td>
<td>Withhold until fever resolves and ANC ≥ 1500; resume at next lower dose level</td>
<td></td>
</tr>
<tr>
<td>Grade 3 or 4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peripheral Neuropathy:</td>
<td>Withhold until improves to ≤ Grade 1; resume at next lower dose level</td>
<td>No dose reduction</td>
</tr>
<tr>
<td>Grade 3 or 4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cutaneous Toxicity:</td>
<td>Reduce to next lower dose level; discontinue treatment if toxicity persists</td>
<td></td>
</tr>
<tr>
<td>Grade 2 or 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal Toxicity:</td>
<td>Withhold until improves to ≤ Grade 1; resume at next lower dose level</td>
<td></td>
</tr>
<tr>
<td>Grade 3 mucositis or diarrhea</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2.6 Preparation and Administration Precautions

ABRAXANE is a cytotoxic drug and, as with other potentially toxic paclitaxel compounds, caution should be exercised in handling ABRAXANE. The use of gloves is recommended. If ABRAXANE (lyophilized cake or reconstituted suspension) contacts the skin, wash the skin immediately and thoroughly with soap and water. Following topical exposure to paclitaxel, events may include tingling, burning and redness. If ABRAXANE contacts mucous membranes, the membranes should be flushed thoroughly with water.
Given the possibility of extravasation, it is advisable to closely monitor the infusion site for possible infiltration during drug administration. Limiting the infusion of ABRAXANE to 30 minutes, as directed, reduces the likelihood of infusion-related reactions [see Adverse Reactions (6.4)].

Premedication to prevent hypersensitivity reactions is generally not needed prior to the administration of ABRAXANE. Premedication may be needed in patients who have had prior hypersensitivity reactions to ABRAXANE. Patients who experience a severe hypersensitivity reaction to ABRAXANE should not be re-challenged with this drug [see Warnings and Precautions (5.5)].

2.7 Preparation for Intravenous Administration
ABRAXANE is supplied as a sterile lyophilized powder for reconstitution before use. AVOID ERRORS, READ ENTIRE PREPARATION INSTRUCTIONS PRIOR TO RECONSTITUTION.

1. Aseptically, reconstitute each vial by injecting 20 mL of 0.9% Sodium Chloride Injection, USP.
2. Slowly inject the 20 mL of 0.9% Sodium Chloride Injection, USP, over a minimum of 1 minute, using the sterile syringe to direct the solution flow onto the INSIDE WALL OF THE VIAL.
3. DO NOT INJECT the 0.9% Sodium Chloride Injection, USP, directly onto the lyophilized cake as this will result in foaming.
4. Once the injection is complete, allow the vial to sit for a minimum of 5 minutes to ensure proper wetting of the lyophilized cake/powder.
5. Gently swirl and/or invert the vial slowly for at least 2 minutes until complete dissolution of any cake/powder occurs. Avoid generation of foam.
6. If foaming or clumping occurs, stand solution for at least 15 minutes until foam subsides.

Each mL of the reconstituted formulation will contain 5 mg/mL paclitaxel.

The reconstituted suspension should be milky and homogenous without visible particulates. If particulates or settling are visible, the vial should be gently inverted again to ensure complete resuspension prior to use. Discard the reconstituted suspension if precipitates are observed. Discard any unused portion.

Calculate the exact total dosing volume of 5 mg/mL suspension required for the patient and slowly withdraw the dosing volume of the reconstituted suspension from the vial(s) into a syringe: Dosing volume (mL) = Total dose (mg)/5 (mg/mL).

Inject the appropriate amount of reconstituted ABRAXANE into an empty, sterile intravenous bag [plasticized polyvinyl chloride (PVC) containers, PVC or non-PVC type intravenous bag]. The use of specialized DEHP-free solution containers or administration sets is not necessary to prepare or administer ABRAXANE infusions. The use of medical devices containing silicone oil as a lubricant (ie, syringes and intravenous bags) to reconstitute and administer ABRAXANE may result in the formation of proteinaceous strands.

Visually inspect the reconstituted ABRAXANE suspension in the intravenous bag prior to administration. Discard the reconstituted suspension if proteinaceous strands, particulate matter or discoloration are observed.

2.8 Stability
Unopened vials of ABRAXANE are stable until the date indicated on the package when stored between 20°C to 25°C (68°F to 77°F) in the original package. Neither freezing nor refrigeration adversely affects the stability of the product.

Stability of Reconstituted Suspension in the Vial
Reconstituted ABRAXANE in the vial should be used immediately, but may be refrigerated at 2°C to 8°C (36°F to 46°F) for a maximum of 24 hours if necessary. If not used immediately, each vial of reconstituted suspension should be replaced in the original carton to protect it from bright light. Discard any unused portion.

Stability of Reconstituted Suspension in the Infusion Bag
The suspension for infusion when prepared as recommended in an infusion bag should be used immediately, but may be refrigerated at 2°C to 8°C (36°F to 46°F) and protected from bright light for a maximum of 24 hours.

The total combined refrigerated storage time of reconstituted ABRAXANE in the vial and in the infusion bag is 24 hours. This may be followed by storage in the infusion bag at ambient temperature (approximately 25°C) and lighting conditions for a maximum of 4 hours.

Reference ID: 3793488
3 DOSAGE FORMS AND STRENGTHS
For injectable suspension: lyophilized powder containing 100 mg of paclitaxel formulated as albumin-bound particles in single-use vial for reconstitution.

4 CONTRAINDICATIONS
- ABRAXANE should not be used in patients who have baseline neutrophil counts of < 1,500 cells/mm³.
- Patients who experience a severe hypersensitivity reaction to ABRAXANE should not be rechallenged with the drug.

5 WARNINGS AND PRECAUTIONS

5.1 Hematologic Effects
Bone marrow suppression (primarily neutropenia) is dose-dependent and a dose-limiting toxicity of ABRAXANE. In clinical studies, Grade 3-4 neutropenia occurred in 34% of patients with metastatic breast cancer (MBC), 47% of patients with non-small cell lung cancer (NSCLC), and 38% of patients with pancreatic cancer.

Monitor for myelotoxicity by performing complete blood cell counts frequently, including prior to dosing on Day 1 (for MBC) and Days 1, 8, and 15 (for NSCLC and for pancreatic cancer). Do not administer ABRAXANE to patients with baseline absolute neutrophil counts (ANC) of less than 1,500 cells/mm³. In the case of severe neutropenia (<500 cells/mm³ for seven days or more) during a course of ABRAXANE therapy, reduce the dose of ABRAXANE in subsequent courses in patients with either MBC or NSCLC.

In patients with MBC, resume treatment with every-3-week cycles of ABRAXANE after ANC recovers to a level >1,500 cells/mm³ and platelets recover to a level >100,000 cells/mm³.

In patients with NSCLC, resume treatment if recommended (see Dosage and Administration, Table 2) at permanently reduced doses for both weekly ABRAXANE and every-3-week carboplatin after ANC recovers to at least 1500 cells/mm³ and platelet count of at least 100,000 cells/mm³ on Day 1 or to an ANC of at least 500 cells/mm³ and platelet count of at least 50,000 cells/mm³ on Days 8 or 15 of the cycle [see Dosage and Administration (2.5)].

In patients with adenocarcinoma of the pancreas, withhold ABRAXANE and gemcitabine if the ANC is less than 500 cells/mm³ or platelets are less than 50,000 cells/mm³ and delay initiation of the next cycle if the ANC is less than 1500 cells/mm³ or platelet count is less than 100,000 cells/mm³ on Day 1 of the cycle. Resume treatment with appropriate dose reduction if recommended [see Dosage and Administration (2.5)].

5.2 Nervous System
Sensory neuropathy is dose- and schedule-dependent [see Adverse Reactions (6.1, 6.2, 6.3)]. The occurrence of Grade 1 or 2 sensory neuropathy does not generally require dose modification. If ≥ Grade 3 sensory neuropathy develops, withhold ABRAXANE treatment until resolution to Grade 1 or 2 for metastatic breast cancer or until resolution to ≤ Grade 1 for NSCLC and pancreatic cancer followed by a dose reduction for all subsequent courses of ABRAXANE [see Dosage and Administration (2.5)].

5.3 Sepsis
Sepsis occurred in 5% of patients with or without neutropenia who received ABRAXANE in combination with gemcitabine. Biliary obstruction or presence of biliary stent were risk factors for severe or fatal sepsis. If a patient becomes febrile (regardless of ANC) initiate treatment with broad spectrum antibiotics. For febrile neutropenia, interrupt ABRAXANE and gemcitabine until fever resolves and ANC ≥ 1500, then resume treatment at reduced dose levels [see Dosage and Administration (2.5)].

5.4 Pneumonitis
Pneumonitis, including some cases that were fatal, occurred in 4% of patients receiving ABRAXANE in combination with gemcitabine. Monitor patients for signs and symptoms of pneumonitis and interrupt ABRAXANE and gemcitabine during evaluation of suspected pneumonitis. After ruling out infectious etiology and upon making a diagnosis of pneumonitis, permanently discontinue treatment with ABRAXANE and gemcitabine.

5.5 Hypersensitivity
Severe and sometimes fatal hypersensitivity reactions, including anaphylactic reactions, have been reported. Patients who experience a severe hypersensitivity reaction to ABRAXANE should not be rechallenged with this drug.

Reference ID: 3793488
5.6 Hepatic Impairment
Because the exposure and toxicity of paclitaxel can be increased with hepatic impairment, administration of ABRAXANE in patients with hepatic impairment should be performed with caution. Patients with hepatic impairment may be at increased risk of toxicity, particularly from myelosuppression: such patients should be closely monitored for development of profound myelosuppression. ABRAXANE is not recommended in patients who have total bilirubin >5 x ULN or AST >10 x ULN. In addition, ABRAXANE is not recommended in patients with metastatic adenocarcinoma of the pancreas who have moderate to severe hepatic impairment (total bilirubin >1.5 x ULN and AST ≤10 x ULN). The starting dose should be reduced for patients with moderate or severe hepatic impairment [see Dosage and Administration (2.4), Use in Specific Populations (8.6) and Clinical Pharmacology (12.3)].

5.7 Albumin (Human)
ABRAXANE contains albumin (human), a derivative of human blood. Based on effective donor screening and product manufacturing processes, it carries a remote risk for transmission of viral diseases. A theoretical risk for transmission of Creutzfeldt-Jakob Disease (CJD) also is considered extremely remote. No cases of transmission of viral diseases or CJD have ever been identified for albumin.

5.8 Use in Pregnancy
ABRAXANE can cause fetal harm when administered to a pregnant woman. Administration of paclitaxel formulated as albumin-bound particles to rats during pregnancy at doses lower than the maximum recommended human dose, based on body surface area, caused embryo-fetal toxicities, including intrauterine mortality, increased resorptions, reduced numbers of live fetuses, and malformations.

There are no adequate and well-controlled studies in pregnant women receiving ABRAXANE. If this drug is used during pregnancy, or if the patient becomes pregnant while receiving this drug, the patient should be apprised of the potential hazard to the fetus. Women of childbearing potential should be advised to avoid becoming pregnant while receiving ABRAXANE [see Use in Specific Populations (8.1)].

5.9 Use in Men
Men should be advised not to father a child while receiving ABRAXANE [see Nonclinical Toxicology (13.1)].

6 ADVERSE REACTIONS
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The most common adverse reactions (≥ 20%) with single-agent use of ABRAXANE in metastatic breast cancer are alopecia, neutropenia, sensory neuropathy, abnormal ECG, fatigue/asthenia, myalgia/arthralgia, AST elevation, alkaline phosphatase elevation, anemia, nausea, infections, and diarrhea [see Adverse Reactions (6.1)].

The most common adverse reactions (≥ 20%) of ABRAXANE in combination with carboplatin for non-small cell lung cancer are anemia, neutropenia, thrombocytopenia, alopecia, peripheral neuropathy, nausea, and fatigue [see Adverse Reactions (6.2)]. The most common serious adverse reactions of ABRAXANE in combination with carboplatin for non-small cell lung cancer are anemia (4%) and pneumonia (3%). The most common adverse reactions resulting in permanent discontinuation of ABRAXANE are neutropenia (3%), thrombocytopenia (3%), and peripheral neuropathy (1%). The most common adverse reactions resulting in dose reduction of ABRAXANE are neutropenia (24%), thrombocytopenia (13%), and anemia (6%). The most common adverse reactions leading to withholding or delay in ABRAXANE dosing are neutropenia (41%), thrombocytopenia (30%), and anemia (16%).

In a randomized open-label trial of ABRAXANE in combination with gemcitabine for pancreatic adenocarcinoma [see Clinical Studies (14.3)], the most common (≥ 20%) selected (with a ≥ 5% higher incidence) adverse reactions of ABRAXANE are neutropenia, fatigue, peripheral neuropathy, nausea, alopecia, peripheral edema, diarrhea, pyrexia, vomiting, decreased appetite, rash, and dehydration. The most common serious adverse reactions of ABRAXANE (with a ≥ 1% higher incidence) are pyrexia (6%), dehydration (5%), pneumonia (4%) and vomiting (4%). The most common adverse reactions resulting in permanent discontinuation of ABRAXANE are peripheral neuropathy (8%), fatigue (4%) and thrombocytopenia (2%). The most common adverse reactions resulting in dose reduction of ABRAXANE are neutropenia (10%) and peripheral neuropathy (6%). The most common adverse reactions leading to withholding or delay in ABRAXANE dosing are neutropenia (16%), thrombocytopenia (12%), fatigue (8%), peripheral neuropathy (15%), anemia (5%) and diarrhea (5%).

6.1 Clinical Trials Experience in Metastatic Breast Cancer
Table 6 shows the frequency of important adverse events in the randomized comparative trial for the patients who received either single-agent ABRAXANE or paclitaxel injection for the treatment of metastatic breast cancer.
Table 6: Frequency\textsuperscript{a} of Important Treatment Emergent Adverse Events in the Randomized Metastatic Breast Cancer Study on an Every-3-Weeks Schedule

<table>
<thead>
<tr>
<th>Percent of Patients</th>
<th>ABRAXANE 260 mg/m\textsuperscript{2} over 30 min (n=229)</th>
<th>Paclitaxel Injection 175 mg/m\textsuperscript{2} over 3 h\textsuperscript{b} (n=225)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bone Marrow</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neutropenia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 2.0 x 10\textsuperscript{9}/L</td>
<td>80</td>
<td>82</td>
</tr>
<tr>
<td>&lt; 0.5 x 10\textsuperscript{9}/L</td>
<td>9</td>
<td>22</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 100 x 10\textsuperscript{9}/L</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>&lt; 50 x 10\textsuperscript{9}/L</td>
<td>&lt;1</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Anemia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 11 g/dL</td>
<td>33</td>
<td>25</td>
</tr>
<tr>
<td>&lt; 8 g/dL</td>
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<td>&lt;1</td>
</tr>
<tr>
<td>Infections</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>24</td>
<td>20</td>
</tr>
<tr>
<td>Febrile Neutropenia</td>
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</tr>
<tr>
<td></td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Neutropenic Sepsis</td>
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</tr>
<tr>
<td></td>
<td>&lt;1</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Bleeding</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td><strong>Hypersensitivity Reaction</strong>\textsuperscript{c}</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>4</td>
<td>12</td>
</tr>
<tr>
<td>Severe\textsuperscript{d}</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td><strong>Cardiovascular</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vital Sign Changes During Administration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bradycardia</td>
<td>&lt;1</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Hypotension</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Severe Cardiovascular Events\textsuperscript{e}</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td><strong>Abnormal ECG</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All Patients</td>
<td>60</td>
<td>52</td>
</tr>
<tr>
<td>Patients with Normal Baseline</td>
<td>35</td>
<td>30</td>
</tr>
<tr>
<td><strong>Respiratory</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cough</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>12</td>
<td>9</td>
</tr>
<tr>
<td><strong>Sensory Neuropathy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any Symptoms</td>
<td>71</td>
<td>56</td>
</tr>
<tr>
<td>Severe Symptoms\textsuperscript{f}</td>
<td>10</td>
<td>2</td>
</tr>
<tr>
<td><strong>Myalgia / Arthralgia</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any Symptoms</td>
<td>44</td>
<td>49</td>
</tr>
<tr>
<td>Severe Symptoms\textsuperscript{f}</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td><strong>Asthenia</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any Symptoms</td>
<td>47</td>
<td>39</td>
</tr>
<tr>
<td>Severe Symptoms\textsuperscript{f}</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td><strong>Fluid Retention/Edema</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any Symptoms</td>
<td>10</td>
<td>8</td>
</tr>
<tr>
<td>Severe Symptoms\textsuperscript{f}</td>
<td>0</td>
<td>&lt;1</td>
</tr>
<tr>
<td><strong>Gastrointestinal</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any Symptoms</td>
<td>30</td>
<td>22</td>
</tr>
<tr>
<td>Severe Symptoms\textsuperscript{f}</td>
<td>3</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Vomiting</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any Symptoms</td>
<td>18</td>
<td>10</td>
</tr>
<tr>
<td>Severe Symptoms\textsuperscript{f}</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Diarrhea</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any Symptoms</td>
<td>27</td>
<td>15</td>
</tr>
<tr>
<td>Severe Symptoms\textsuperscript{f}</td>
<td>&lt;1</td>
<td>1</td>
</tr>
<tr>
<td>Mucositis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any Symptoms</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>Severe Symptoms\textsuperscript{f}</td>
<td>&lt;1</td>
<td>0</td>
</tr>
<tr>
<td><strong>Alopecia</strong></td>
<td>90</td>
<td>94</td>
</tr>
<tr>
<td><strong>Hepatic (Patients with Normal Baseline)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bilirubin Elevations</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Alkaline Phosphatase Elevations</td>
<td>36</td>
<td>31</td>
</tr>
<tr>
<td>AST (SGOT) Elevations</td>
<td>39</td>
<td>32</td>
</tr>
</tbody>
</table>

Reference ID: 3793488
Percent of Patients

<table>
<thead>
<tr>
<th></th>
<th>ABRAXANE 260 mg/m² over 30 min (n=229)</th>
<th>Paclitaxel Injection 175 mg/m² over 3 h (n=225)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injection Site Reaction</td>
<td>&lt;1</td>
<td>1</td>
</tr>
</tbody>
</table>

*a* Based on worst grade by NCI Common Terminology Criteria for Adverse Events (CTCAE) version 2.

*b* Paclitaxel injection patients received premedication.

*c* Includes treatment-related events related to hypersensitivity (e.g., flushing, dyspnea, chest pain, hypotension) that began on a day of dosing.

*d* Severe events are defined as at least grade 3 toxicity.

**Adverse Event Experiences by Body System**

**Hematologic Disorders**

Neutropenia was dose dependent and reversible. Among patients with metastatic breast cancer in the randomized trial, neutrophil counts declined below 500 cells/mm³ (Grade 4) in 9% of the patients treated with a dose of 260 mg/m² compared to 22% in patients receiving paclitaxel injection at a dose of 175 mg/m². Pancytopenia has been observed in clinical trials.

**Infections**

Infectious episodes were reported in 24% of the patients treated with ABRAXANE. Oral candidiasis, respiratory tract infections and pneumonia were the most frequently reported infectious complications.

**Hypersensitivity Reactions (HSRs)**

Grade 1 or 2 HSRs occurred on the day of ABRAXANE administration and consisted of dyspnea (1%) and flushing, hypotension, chest pain, and arrhythmia (all <1%). The use of ABRAXANE in patients previously exhibiting hypersensitivity to paclitaxel injection or human albumin has not been studied.

**Cardiovascular**

Hypotension, during the 30-minute infusion, occurred in 5% of patients. Bradycardia, during the 30-minute infusion, occurred in <1% of patients. These vital sign changes most often caused no symptoms and required neither specific therapy nor treatment discontinuation.

Severe cardiovascular events possibly related to single-agent ABRAXANE occurred in approximately 3% of patients. These events included cardiac ischemia/infarction, chest pain, cardiac arrest, supraventricular tachycardia, edema, thrombosis, pulmonary thromboembolism, pulmonary emboli, and hypertension. Cases of cerebrovascular attacks (strokes) and transient ischemic attacks have been reported.

Electrocardiogram (ECG) abnormalities were common among patients at baseline. ECG abnormalities on study did not usually result in symptoms, were not dose-limiting, and required no intervention. ECG abnormalities were noted in 60% of patients. Among patients with a normal ECG prior to study entry, 35% of all patients developed an abnormal tracing while on study. The most frequently reported ECG modifications were non-specific repolarization abnormalities, sinus bradycardia, and sinus tachycardia.

**Respiratory**

Dyspnea (12%), cough (7%), and pneumothorax (<1%) were reported after treatment with ABRAXANE.

**Neurologic**

The frequency and severity of sensory neuropathy increased with cumulative dose. Sensory neuropathy was the cause of ABRAXANE discontinuation in 7/229 (3%) patients. Twenty-four patients (10%) treated with ABRAXANE developed Grade 3 peripheral neuropathy; of these patients, 14 had documented improvement after a median of 22 days; 10 patients resumed treatment at a reduced dose of ABRAXANE and 2 discontinued due to peripheral neuropathy. Of the 10 patients without documented improvement, 4 discontinued the study due to peripheral neuropathy.

No Grade 4 sensory neuropathies were reported. Only one incident of motor neuropathy (Grade 2) was observed in either arm of the controlled trial.

**Vision Disorders**

Ocular/visual disturbances occurred in 13% of all patients (n=366) treated with ABRAXANE and 1% were severe. The severe cases (keratitis and blurred vision) were reported in patients who received higher doses than those recommended (300 or 375 mg/m²). These effects generally have been reversible.

**Arthralgia/Myalgia**

The symptoms were usually transient, occurred two or three days after ABRAXANE administration, and resolved within a few days.

**Hepatic**

Grade 3 or 4 elevations in GGT were reported for 14% of patients treated with ABRAXANE and 10% of patients treated with paclitaxel injection in the randomized trial.
Renal
Overall 11% of patients experienced creatinine elevation, 1% severe. No discontinuations, dose reductions, or dose delays were caused by renal toxicities.

Other Clinical Events
Nail changes (changes in pigmentation or discoloration of nail bed) have been reported. Edema occurred in 10% of patients; no patients had severe edema. Dehydration and pyrexia were also reported.

6.2 Clinical Trials Experience in Non-Small Cell Lung Cancer
Adverse reactions were assessed in 514 ABRAXANE/carboplatin-treated patients and 524 paclitaxel injection/carboplatin-treated patients receiving first-line systemic treatment for locally advanced (stage IIIIB) or metastatic (IV) non-small cell lung cancer (NSCLC) in a multicenter, randomized, open-label trial. ABRAXANE was administered as an intravenous infusion over 30 minutes at a dose of 100 mg/m² on Days 1, 8, and 15 of each 21-day cycle. Paclitaxel injection was administered as an intravenous infusion over 3 hours at a dose of 200 mg/m², following premedication. In both treatment arms carboplatin at a dose of AUC = 6 mg•min/mL was administered intravenously on Day 1 of each 21-day cycle after completion of ABRAXANE/paclitaxel infusion. The differences in paclitaxel dose and schedule between the two arms limit direct comparison of dose- and schedule-dependent adverse reactions. Among patients evaluable for adverse reactions, the median age was 60 years, 75% were men, 81% were White, 49% had adenocarcinoma, 43% had squamous cell lung cancer, 76% were ECOG PS 1. Patients in both treatment arms received a median of 6 cycles of treatment.

The following common (≥ 10% incidence) adverse reactions were observed at a similar incidence in ABRAXANE plus carboplatin-treated and paclitaxel injection plus carboplatin-treated patients: alopecia 56%, nausea 27%, fatigue 25%, decreased appetite 17%, asthenia 16%, constipation 16%, diarrhea 15%, vomiting 12%, dyspnea 12%, and rash 10% (incidence rates are for the ABRAXANE plus carboplatin treatment group).

Table 7 provides the frequency and severity of laboratory-detected abnormalities which occurred with a difference of ≥ 5% for all grades (1-4) or ≥ 2% for Grade 3-4 toxicity between ABRAXANE plus carboplatin-treated patients or paclitaxel injection plus carboplatin-treated patients.

<table>
<thead>
<tr>
<th>System Organ Class</th>
<th>MedDRA v 12.1 Preferred Term</th>
<th>ABRAXANE (100 mg/m² weekly) + carboplatin (N=514)</th>
<th>Paclitaxel Injection (200 mg/m² every 3 weeks) + carboplatin (N=524)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nervous system disorders</td>
<td>Peripheral neuropathy*</td>
<td>Grade 1-4 Toxicity (%)</td>
<td>48</td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
<td>Edema peripheral</td>
<td>Grade 3-4 Toxicity (%)</td>
<td>10</td>
</tr>
<tr>
<td>Respiratory thoracic and mediastinal disorders</td>
<td>Epistaxis</td>
<td>Grade 1-4 Toxicity (%)</td>
<td>7</td>
</tr>
</tbody>
</table>

Table 8 provides the frequency and severity of adverse reactions, which occurred with a difference of ≥ 5% for all grades (1-4) or ≥ 2% for Grade 3-4 toxicity between either treatment group for the 514 ABRAXANE plus carboplatin-treated patients compared with the 524 patients who received paclitaxel injection plus carboplatin.

Reference ID: 3793488
Musculoskeletal and connective tissue disorders

<table>
<thead>
<tr>
<th>System Organ Class</th>
<th>MedDRA v 12.1 Preferred Term</th>
<th>ABRAXANE (100 mg/m² weekly) + carboplatin (N=514)</th>
<th>Paclitaxel Injection (200 mg/m² every 3 weeks) + carboplatin (N=524)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Grade 1-4 Toxicity (%)</td>
<td>Grade 3-4 Toxicity (%)</td>
<td>Grades 1-4 Toxicity (%)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>13</td>
<td>&lt;1</td>
<td>25</td>
</tr>
<tr>
<td>Myalgia</td>
<td>10</td>
<td>&lt;1</td>
<td>19</td>
</tr>
</tbody>
</table>

* Peripheral neuropathy is defined by the MedDRA Version 14.0 SMQ neuropathy (broad scope).

For the ABRAXANE plus carboplatin treated group, 17/514 (3%) patients developed Grade 3 peripheral neuropathy and no patients developed Grade 4 peripheral neuropathy. Grade 3 neuropathy improved to Grade 1 or resolved in 10/17 patients (59%) following interruption or discontinuation of ABRAXANE.

6.3 Clinical Trials Experience in Adenocarcinoma of the Pancreas

Adverse reactions were assessed in 421 patients who received ABRAXANE plus gemcitabine and 402 patients who received gemcitabine for the first-line systemic treatment of metastatic adenocarcinoma of the pancreas in a multicenter, multinational, randomized, controlled, open-label trial. Patients received a median treatment duration of 3.9 months in the ABRAXANE/gemcitabine group and 2.8 months in the gemcitabine group. For the treated population, the median relative dose intensity for gemcitabine was 75% in the ABRAXANE/gemcitabine group and 86% in the gemcitabine group. The median relative dose intensity of ABRAXANE was 81%.

Table 9 provides the frequency and severity of laboratory-detected abnormalities which occurred at a higher incidence for Grades 1-4 (≥ 5%) or for Grade 3-4 (≥ 2%) toxicity in ABRAXANE plus gemcitabine-treated patients.

Table 10 provides the frequency and severity of adverse reactions which occurred with a difference of ≥ 5% for all grades or ≥ 2% for Grade 3 or higher in the ABRAXANE/Gemcitabine Arm compared to the gemcitabine group.

Reference ID: 3793488
**System Organ Class** | **Adverse Reaction** | **ABRAXANE (125 mg/m²) and gemcitabine (N=421)** | **Gemcitabine (N=402)** |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All Grades</td>
<td>Grade 3 or Higher</td>
<td>All Grades</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td>Alopecia</td>
<td>212 (50%)</td>
<td>6 (1%)</td>
</tr>
<tr>
<td></td>
<td>Rash</td>
<td>128 (30%)</td>
<td>8 (2%)</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td>Peripheral neuropathy&lt;sup&gt;a&lt;/sup&gt;</td>
<td>227 (54%)</td>
<td>70 (17%)</td>
</tr>
<tr>
<td></td>
<td>Dyseusia</td>
<td>68 (16%)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Headache</td>
<td>60 (14%)</td>
<td>1 (&lt;1%)</td>
</tr>
<tr>
<td>Metabolism and nutrition disorders</td>
<td>Decreased appetite</td>
<td>152 (36%)</td>
<td>23 (5%)</td>
</tr>
<tr>
<td></td>
<td>Dehydration</td>
<td>87 (21%)</td>
<td>31 (7%)</td>
</tr>
<tr>
<td></td>
<td>Hypokalemia</td>
<td>52 (12%)</td>
<td>18 (4%)</td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastinal disorders</td>
<td>Cough</td>
<td>72 (17%)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Epistaxis</td>
<td>64 (15%)</td>
<td>1 (&lt;1%)</td>
</tr>
<tr>
<td>Infections and infestations</td>
<td>Urinary tract infections&lt;sup&gt;b&lt;/sup&gt;</td>
<td>47 (11%)</td>
<td>10 (2%)</td>
</tr>
<tr>
<td>Musculoskeletal and connective tissue disorders</td>
<td>Pain in extremity</td>
<td>48 (11%)</td>
<td>3 (1%)</td>
</tr>
<tr>
<td></td>
<td>Arthralgia</td>
<td>47 (11%)</td>
<td>3 (1%)</td>
</tr>
<tr>
<td></td>
<td>Myalgia</td>
<td>44 (10%)</td>
<td>4 (1%)</td>
</tr>
<tr>
<td>Psychiatric disorders</td>
<td>Depression</td>
<td>51 (12%)</td>
<td>1 (&lt;1%)</td>
</tr>
</tbody>
</table>

<sup>a</sup> Peripheral neuropathy is defined by the MedDRA Version 15.0 Standard MedDRA Query neuropathy (broad scope).

<sup>b</sup> Urinary tract infections includes the preferred terms of: urinary tract infection, cystitis, urosepsis, urinary tract infection bacterial, and urinary tract infection enterococcal.

Additional clinically relevant adverse reactions that were reported in < 10% of the patients with adenocarcinoma of the pancreas who received ABRAXANE/gemcitabine included:

- Infections & infestations: oral candidiasis, pneumonia
- Vascular disorders: hypertension
- Cardiac disorders: tachycardia, congestive cardiac failure
- Eye disorders: cystoid macular edema

**Peripheral Neuropathy**

Grade 3 peripheral neuropathy occurred in 17% of patients who received ABRAXANE/gemcitabine compared to 1% of patients who received gemcitabine only; no patients developed grade 4 peripheral neuropathy. The median time to first occurrence of Grade 3 peripheral neuropathy in the ABRAXANE arm was 140 days. Upon suspension of ABRAXANE dosing, the median time to improvement from Grade 3 peripheral neuropathy to ≤ Grade 1 was 29 days. Of ABRAXANE-treated patients with Grade 3 peripheral neuropathy, 44% resumed ABRAXANE at a reduced dose.

**Sepsis**

Sepsis occurred in 5% of patients who received ABRAXANE/gemcitabine compared to 2% of patients who received gemcitabine alone. Sepsis occurred both in patients with and without neutropenia. Risk factors for sepsis included biliary obstruction or presence of biliary stent.

**Pneumonitis**

Pneumonitis occurred in 4% of patients who received ABRAXANE/gemcitabine compared to 1% of patients who received gemcitabine alone. Two of 17 patients in the ABRAXANE arm with pneumonitis died.

### 6.4 Postmarketing Experience with ABRAXANE and other Paclitaxel Formulations

Unless otherwise noted, the following discussion refers to the adverse reactions that have been identified during post-approval use of ABRAXANE. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. In some instances, severe events observed with paclitaxel injection may be expected to occur with ABRAXANE.

**Hypersensitivity Reactions**

Severe and sometimes fatal hypersensitivity reactions have been reported with ABRAXANE. The use of ABRAXANE in patients previously exhibiting hypersensitivity to paclitaxel injection or human albumin has not been studied.
Cardiovascular
There have been reports of congestive heart failure, left ventricular dysfunction, and atrioventricular block with ABRAXANE. Most of the individuals were previously exposed to cardiotoxic drugs, such as anthracyclines, or had underlying cardiac history.

Respiratory
There have been reports of pneumonitis, interstitial pneumonia and pulmonary embolism in patients receiving ABRAXANE and reports of radiation pneumonitis in patients receiving concurrent radiotherapy. Reports of lung fibrosis have been received as part of the continuing surveillance of paclitaxel injection safety and may also be observed with ABRAXANE.

Neurologic
Cranial nerve palsies and vocal cord paresis have been reported, as well as autonomic neuropathy resulting in paralytic ileus.

Vision Disorders
Reports in the literature of abnormal visual evoked potentials in patients treated with paclitaxel injection suggest persistent optic nerve damage. These may also be observed with ABRAXANE.

Reduced visual acuity due to cystoid macular edema (CME) has been reported during treatment with ABRAXANE as well as with other taxanes. After cessation of treatment, CME improves and visual acuity may return to baseline.

Hepatic
Reports of hepatic necrosis and hepatic encephalopathy leading to death have been received as part of the continuing surveillance of paclitaxel injection safety and may occur following ABRAXANE treatment.

Gastrointestinal (GI)
There have been reports of intestinal obstruction, intestinal perforation, pancreatitis, and ischemic colitis following ABRAXANE treatment. There have been reports of neutropenic enterocolitis (typhlitis), despite the coadministration of G-CSF, occurring in patients treated with paclitaxel injection alone and in combination with other chemotherapeutic agents.

Injection Site Reaction
There have been reports of extravasation of ABRAXANE. Given the possibility of extravasation, it is advisable to monitor closely the ABRAXANE infusion site for possible infiltration during drug administration.

Severe events such as phlebitis, cellulitis, induration, necrosis, and fibrosis have been reported as part of the continuing surveillance of paclitaxel injection safety. In some cases the onset of the injection site reaction in paclitaxel injection patients either occurred during a prolonged infusion or was delayed by a week to ten days. Recurrence of skin reactions at a site of previous extravasation following administration of paclitaxel injection at a different site, i.e., “recall”, has been reported.

Other Clinical Events
Skin reactions including generalized or maculopapular rash, erythema, and pruritus have been observed with ABRAXANE. There have been case reports of photosensitivity reactions, radiation recall phenomenon, and in some patients previously exposed to capecitabine, reports of palmar-plantar erythrodysesthesia. Stevens-Johnson syndrome and toxic epidermal necrolysis have been reported.

There have been reports of conjunctivitis, cellulitis, and increased lacrimation with paclitaxel injection.

6.5 Accidental Exposure
No reports of accidental exposure to ABRAXANE have been received. However, upon inhalation of paclitaxel, dyspnea, chest pain, burning eyes, sore throat, and nausea have been reported. Following topical exposure, events have included tingling, burning, and redness.

7 DRUG INTERACTIONS
The metabolism of paclitaxel is catalyzed by CYP2C8 and CYP3A4. Caution should be exercised when administering ABRAXANE concomitantly with medicines known to inhibit (e.g., ketoconazole and other imidazole antifungals, erythromycin, fluoxetine, gemfibrozil, cimetidine, ritonavir, saquinavir, indinavir, and nelfinavir) or induce (e.g., rifampicin, carbamazepine, phenytoin, efavirenz, and nevirapine) either CYP2C8 or CYP3A4.

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
Pregnancy Category D [see Warnings and Precautions (5.8)].

There are no adequate and well-controlled studies in pregnant women using ABRAXANE. Based on its mechanism of action and findings in animals, ABRAXANE can cause fetal harm when administered to a pregnant woman. If this drug is used during pregnancy, or if the patient becomes pregnant while receiving this drug, the patient should be apprised of the potential hazard to the fetus. Women of childbearing potential should be advised to avoid becoming pregnant while receiving ABRAXANE.

Administration of paclitaxel formulated as albumin-bound particles to rats during pregnancy, on gestation days 7 to 17 at doses of 6 mg/m² (approximately 2% of the daily maximum recommended human dose on a mg/m² basis) caused embryofetal toxicities, as indicated by intrauterine mortality, increased resorptions (up to 5-fold), reduced numbers of litters and live fetuses, reduction in fetal body weight and increase in fetal anomalies. Fetal anomalies included soft tissue and skeletal malformations, such as eye bulge,
folded retina, microphthalmia, and dilation of brain ventricles. A lower incidence of soft tissue and skeletal malformations were also exhibited at 3 mg/m² (approximately 1% of the daily maximum recommended human dose on a mg/m² basis).

8.3 Nursing Mothers
It is not known whether paclitaxel is excreted in human milk. Paclitaxel and/or its metabolites were excreted into the milk of lactating rats. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants, a decision should be made to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

8.4 Pediatric Use
The safety and effectiveness of ABRAXANE in pediatric patients have not been evaluated.

8.5 Geriatric Use
Of the 229 patients in the randomized study who received ABRAXANE for the treatment of metastatic breast cancer, 13% were at least 65 years of age and < 2% were 75 years or older. No toxicities occurred notably more frequently among patients who received ABRAXANE.

A subsequent pooled analysis was conducted in 981 patients receiving ABRAXANE monotherapy for metastatic breast cancer, of which 15% were 65 years of age or older and 2% were 75 years of age or older. A higher incidence of epistaxis, diarrhea, dehydration, fatigue and peripheral edema was found in patients 65 years of age or older.

Of the 514 patients in the randomized study who received ABRAXANE and carboplatin for the first-line treatment of non-small cell lung cancer, 31% were 65 years or older and 3.5% were 75 years or older. Myelosuppression, peripheral neuropathy, and arthralgia were more frequent in patients 65 years or older compared to patients younger than 65 years old. No overall difference in effectiveness, as measured by response rates, was observed between patients 65 years or older compared to patients younger than 65 years old.

Of the 431 patients in the randomized study who received ABRAXANE and gemcitabine for the first-line treatment of pancreatic adenocarcinoma, 41% were 65 years or older and 10% were 75 years or older. No overall differences in effectiveness were observed between patients who were 65 years of age or older and younger patients. Diarrhea, decreased appetite, dehydration and epistaxis were more frequent in patients 65 years or older compared with patients younger than 65 years old. Clinical studies of ABRAXANE did not include sufficient number of patients with pancreatic cancer who were 75 years and older to determine whether they respond differently from younger patients.

8.6 Patients with Hepatic Impairment
The exposure to paclitaxel may be higher in patients with hepatic impairment than in patients with normal hepatic function. Reduce ABRAXANE starting dose in patients with moderate to severe hepatic impairment. Do not administer ABRAXANE to patients with total bilirubin > 5 x ULN or AST > 10 x ULN [see Dosage and Administration (2.4), Warnings and Precautions (5.6) and Clinical Pharmacology (12.3)]. Do not administer to patients with metastatic adenocarcinoma of the pancreas who have moderate to severe hepatic impairment [see Dosage and Administration (2.4)].

8.7 Patients with Renal Impairment
Adjustment of the starting ABRAXANE dose is not required for patients with mild to moderate renal impairment (estimated creatinine clearance ≥30 to <90 mL/min) [see Clinical Pharmacology (12.3)]. There are insufficient data to permit dosage recommendations in patients with severe renal impairment or end stage renal disease (estimated creatinine clearance <30 mL/min).

10 OVERDOSAGE
There is no known antidote for ABRAXANE overdosage. The primary anticipated complications of overdosage would consist of bone marrow suppression, sensory neurotoxicity, and mucositis.

11 DESCRIPTION
ABRAXANE for Injectable Suspension (paclitaxel protein-bound particles for injectable suspension) (albumin-bound) is paclitaxel formulated as albumin-bound nanoparticles with a mean particle size of approximately 130 nanometers. Paclitaxel exists in the particles in a non-crystalline, amorphous state. ABRAXANE is supplied as a white to yellow, sterile, lyophilized powder for reconstitution with 20 mL of 0.9% Sodium Chloride Injection, USP prior to intravenous infusion. Each single-use vial contains 100 mg of paclitaxel (bound to human albumin) and approximately 900 mg of human albumin (containing sodium caprylate and sodium acetyltryptophanate). Each milliliter (mL) of reconstituted suspension contains 5 mg paclitaxel formulated as albumin-bound particles. ABRAXANE is free of solvents.

The active agent in ABRAXANE is paclitaxel, a microtubule inhibitor. The chemical name for paclitaxel is 5β,20-Epoxy-1,2α,4,7β,10β,13α-hexahydroxytax-11-en-9-one 4,10-diacetate 2-benzoate 13-ester with (2R,3S)-N-benzyol-3-phenylisoserine.
Paclitaxel has the following structural formula:

Paclitaxel is a white to off-white crystalline powder with the empirical formula C_{47}H_{51}NO_{14} and a molecular weight of 853.91. It is highly lipophilic, insoluble in water, and melts at approximately 216°C to 217°C.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action
ABRAXANE is a microtubule inhibitor that promotes the assembly of microtubules from tubulin dimers and stabilizes microtubules by preventing depolymerization. This stability results in the inhibition of the normal dynamic reorganization of the microtubule network that is essential for vital interphase and mitotic cellular functions. Paclitaxel induces abnormal arrays or “bundles” of microtubules throughout the cell cycle and multiple asters of microtubules during mitosis.

12.3 Pharmacokinetics

Absorption
The pharmacokinetics of total paclitaxel following 30 and 180-minute infusions of ABRAXANE at dose levels of 80 to 375 mg/m² were determined in clinical studies. Dose levels of mg/m² refer to mg of paclitaxel in ABRAXANE. Following intravenous administration of ABRAXANE, paclitaxel plasma concentrations declined in a biphasic manner, the initial rapid decline representing distribution to the peripheral compartment and the slower second phase representing drug elimination.

The drug exposure (AUCs) was dose proportional over 80 to 300 mg/m² and the pharmacokinetics of paclitaxel for ABRAXANE were independent of the duration of intravenous administration.

The pharmacokinetic data of 260 mg/m² ABRAXANE administered over a 30-minute infusion was compared to the pharmacokinetics of 175 mg/m² paclitaxel injection over a 3-hour infusion. Clearance was larger (43%) and the volume of distribution was higher (53%) for ABRAXANE than for paclitaxel injection. There were no differences in terminal half-lives.

Distribution
Following ABRAXANE administration to patients with solid tumors, paclitaxel is evenly distributed into blood cells and plasma and is highly bound to plasma proteins (94%). In a within-patient comparison study, the fraction of unbound paclitaxel in plasma was significantly higher with ABRAXANE (6.2%) than with solvent-based paclitaxel (2.3%). This contributes to significantly higher exposure to unbound paclitaxel with ABRAXANE compared with solvent-based paclitaxel, when the total exposure is comparable. In vitro studies of binding to human serum proteins, using paclitaxel concentrations ranging from 0.1 to 50 µg/mL, indicated that the presence of cimetidine, ranitidine, dexamethasone, or diphenhydramine did not affect protein binding of paclitaxel. The total volume of distribution is approximately 1741 L; the large volume of distribution indicates extensive extravascular distribution and/or tissue binding of paclitaxel.

Metabolism
In vitro studies with human liver microsomes and tissue slices showed that paclitaxel was metabolized primarily to 6α-hydroxy-paclitaxel by CYP2C8; and to two minor metabolites, 3′-p-hydroxy-paclitaxel and 6α, 3′-p-dihydroxy-paclitaxel, by CYP3A4. In vitro, the metabolism of paclitaxel to 6α-hydroxy-paclitaxel was inhibited by a number of agents (ketoconazole, verapamil, diazepam, quinidine, dexamethasone, cyclosporin, teniposide, etoposide, and vincristine), but the concentrations used exceeded those found in vivo following normal therapeutic doses. Testosterone, 17α-ethyl estradiol, retinoic acid, and quercetin, a specific inhibitor of CYP2C8, also inhibited the formation of 6α-hydroxy-paclitaxel in vitro. The pharmacokinetics of paclitaxel may also be altered in vivo as a result of interactions with compounds that are substrates, inducers, or inhibitors of CYP2C8 and/or CYP3A4 [see Drug Interactions (7)].

Elimination
At the clinical dose range of 80 to 300 mg/m², the mean total clearance of paclitaxel ranges from 13 to 30 L/h/m², and the mean terminal half-life ranges from 13 to 27 hours.

After a 30-minute infusion of 260 mg/m² doses of ABRAXANE, the mean values for cumulative urinary recovery of unchanged drug (4%) indicated extensive non-renal clearance. Less than 1% of the total administered dose was excreted in urine as the metabolites 6α-hydroxy-paclitaxel and 3′-p-hydroxy-paclitaxel.

Fecal excretion was approximately 20% of the total dose administered.
Specific Populations

Pharmacokinetics in Hepatic Impairment
The effect of hepatic impairment on the pharmacokinetics of paclitaxel following ABRAXANE administration was studied in patients with advanced solid tumors. The results showed that mild hepatic impairment (total bilirubin >1 to ≤1.5 x ULN, AST ≤10 x ULN, n=8) had no clinically important effect on pharmacokinetics of paclitaxel. Patients with moderate (total bilirubin >1.5 to ≤ 3 x ULN, AST ≤10 x ULN, n=7) or severe (total bilirubin >3 to ≤5 x ULN, n=5) hepatic impairment had a 22% to 26% decrease in the maximum elimination rate of paclitaxel and approximately 20% increase in mean paclitaxel AUC compared with patients with normal hepatic function (total bilirubin ≤ULN, AST ≤ULN, n=130). [see Dosage and Administration (2.4) and Use in Specific Populations (8.6)].

Elimination of paclitaxel shows an inverse correlation with total bilirubin and a positive correlation with serum albumin. Pharmacokinetic/pharmacodynamic modeling indicates that there is no correlation between hepatic function (as indicated by the baseline albumin or total bilirubin level) and neutropenia after adjusting for ABRAXANE exposure. Pharmacokinetic data are not available for patients with total bilirubin >5 x ULN or for patients with metastatic adenocarcinoma of the pancreas [see Dosage and Administration (2.4) and Use in Specific Populations (8.6)].

Pharmacokinetics in Renal Impairment
The effect of pre-existing mild (creatinine clearance ≥60 to <90 mL/min, n=61) or moderate (creatinine clearance ≥30 to <60 mL/min, n=23) renal impairment on the pharmacokinetics of paclitaxel following ABRAXANE administration was studied in patients with advanced solid tumors. Mild to moderate renal impairment had no clinically important effect on the maximum elimination rate and systemic exposure (AUC and Cmax) of paclitaxel [see Use in Specific Populations (8.7)].

Other Intrinsic Factors
Population pharmacokinetic analyses for ABRAXANE show that body weight (40 to 143 kg), body surface area (1.3 to 2.4 m²), gender, race (Asian vs. White), age (24 to 85 years) and type of solid tumors do not have a clinically important effect on the maximum elimination rate and systemic exposure (AUC and Cmax) of paclitaxel.

Pharmacokinetic Interactions between ABRAXANE and Carboplatin
Administration of carboplatin immediately after the completion of the ABRAXANE infusion to patients with NSCLC did not cause clinically meaningful changes in paclitaxel exposure. The observed mean AUCinf of free carboplatin was approximately 23% higher than the targeted value (6 min*mg/mL), but its mean half-life and clearance were consistent with those reported in the absence of paclitaxel.

Pharmacokinetic Interactions between ABRAXANE and Gemcitabine
Pharmacokinetic interactions between ABRAXANE and gemcitabine have not been studied in humans.

13  NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
The carcinogenic potential of ABRAXANE has not been studied.

Paclitaxel was clastogenic in vitro (chromosome aberrations in human lymphocytes) and in vivo (micronucleus test in mice). ABRAXANE was not mutagenic in the Ames test or the CHO/HGPRT gene mutation assay.

Administration of paclitaxel formulated as albumin-bound particles to male rats at 42 mg/m² on a weekly basis (approximately 16% of the daily maximum recommended human exposure on a body surface area basis) for 11 weeks prior to mating with untreated female rats resulted in significantly reduced fertility accompanied by decreased pregnancy rates and increased loss of embryos in mated females. A low incidence of skeletal and soft tissue fetal anomalies was also observed at doses of 3 and 12 mg/m²/week in this study (approximately 1 to 5% of the daily maximum recommended human exposure on a mg/m² basis). Testicular atrophy/degeneration was observed in single-dose toxicity studies in rodents administered paclitaxel formulated as albumin-bound particles at doses lower than the recommended human dose; doses were 54 mg/m² in rodents and 175 mg/m² in dogs.

14  CLINICAL STUDIES

14.1 Metastatic Breast Cancer
Data from 106 patients accrued in two single arm open label studies and from 460 patients enrolled in a randomized comparative study were available to support the use of ABRAXANE in metastatic breast cancer.

Single Arm Open Label Studies
In one study, ABRAXANE was administered as a 30-minute infusion at a dose of 175 mg/m² to 43 patients with metastatic breast cancer. The second trial utilized a dose of 300 mg/m² as a 30-minute infusion in 63 patients with metastatic breast cancer. Cycles were administered at 3-week intervals. Objective responses were observed in both studies.

Randomized Comparative Study
This multicenter trial was conducted in 460 patients with metastatic breast cancer. Patients were randomized to receive ABRAXANE at a dose of 260 mg/m² given as a 30-minute infusion, or paclitaxel injection at 175 mg/m² given as a 3-hour infusion. Sixty-four percent of patients had impaired performance status (ECOG 1 or 2) at study entry; 79% had visceral metastases; and 76% had > 3 sites of metastases. Fourteen percent of the patients had not received prior chemotherapy; 27% had received chemotherapy in the adjuvant setting, 40% in the metastatic setting and 19% in both metastatic and adjuvant settings. Fifty-nine
percent received study drug as second or greater than second-line therapy. Seventy-seven percent of the patients had been previously exposed to anthracyclines.

In this trial, patients in the ABRAXANE treatment arm had a statistically significantly higher reconciled target lesion response rate (the trial primary endpoint) of 21.5% (95% CI: 16.2% to 26.7%), compared to 11.1% (95% CI: 6.9% to 15.1%) for patients in the paclitaxel injection treatment arm. See Table 11. There was no statistically significant difference in overall survival between the two study arms.

### Table 11: Efficacy Results from Randomized Metastatic Breast Cancer Trial

<table>
<thead>
<tr>
<th></th>
<th>ABRAXANE 260 mg/m²</th>
<th>Paclitaxel Injection 175 mg/m²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reconciled Target Lesion Response Rate (primary endpoint)*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All randomized patients</td>
<td>Response Rate</td>
<td>50/233 (21.5%)</td>
</tr>
<tr>
<td></td>
<td>[95% CI]</td>
<td>[16.19% – 26.73%]</td>
</tr>
<tr>
<td></td>
<td>p-value</td>
<td>0.003</td>
</tr>
<tr>
<td>Patients who had failed combination chemotherapy or relapsed within 6 months of adjuvant chemotherapy c</td>
<td>Response Rate</td>
<td>20/129 (15.5%)</td>
</tr>
<tr>
<td></td>
<td>[95% CI]</td>
<td>[9.26% – 21.75%]</td>
</tr>
</tbody>
</table>

* Reconciled Target Lesion Response Rate (TLRR) was the prospectively defined protocol specific endpoint, based on independent radiologic assessment of tumor responses reconciled with investigator responses (which also included clinical information) for the first 6 cycles of therapy. The reconciled TLRR was lower than the investigator Reported Response Rates, which are based on all cycles of therapy.

b From Cochran-Mantel-Haenszel test stratified by 1st line vs. > 1st line therapy.

c Prior therapy included an anthracycline unless clinically contraindicated.

### 14.2 Non-Small Cell Lung Cancer

A multicenter, randomized, open-label study was conducted in 1052 chemonaive patients with Stage IIIb/IV non-small cell lung cancer to compare ABRAXANE in combination with carboplatin to paclitaxel injection in combination with carboplatin as first-line treatment in patients with advanced non-small cell lung cancer. ABRAXANE was administered as an intravenous infusion over 30 minutes at a dose of 100 mg/m² on Days 1, 8, and 15 of each 21-day cycle. Paclitaxel injection was administered as an intravenous infusion over 3 hours at a dose of 200 mg/m², following premedication. In both treatment arms carboplatin at a dose of AUC = 6 mg•min/mL was administered intravenously on Day 1 of each 21-day cycle after completion of ABRAXANE/paclitaxel infusion. Treatment was administered until disease progression or development of an unacceptable toxicity. The major efficacy outcome measure was overall response rate as determined by a central independent review committee using RECIST guidelines (Version 1.0).

In the intent-to-treat (all-randomized) population, the median age was 60 years, 75% were men, 81% were White, 49% had adenocarcinoma, 43% had squamous cell lung cancer, 76% were ECOG PS 1, and 73% were current or former smokers. Patients received a median of 6 cycles of treatment in both study arms.

Patients in the ABRAXANE/carboplatin arm had a statistically significantly higher overall response rate compared to patients in the paclitaxel injection/carboplatin arm (33% versus 25%) see Table 12. There was no statistically significant difference in overall survival between the two study arms.

### Table 12: Efficacy Results from Randomized Non-Small Cell Lung Cancer Trial (Intent-to-Treat Population)

<table>
<thead>
<tr>
<th>Overall Response Rate (ORR)</th>
<th>ABRAXANE (100 mg/m² weekly) + carboplatin (N=521)</th>
<th>Paclitaxel Injection (200 mg/m² every 3 weeks) + carboplatin (N=531)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confirmed complete or partial overall response, n (%)</td>
<td>170 (33%)</td>
<td>132 (25%)</td>
</tr>
<tr>
<td>95% CI</td>
<td>28.6, 36.7</td>
<td>21.2, 28.5</td>
</tr>
<tr>
<td>P-value (Chi-Square test)</td>
<td>0.005</td>
<td></td>
</tr>
<tr>
<td>Median DoR in months (95% CI)</td>
<td>6.9 (5.6, 8.0)</td>
<td>6.0 (5.6, 7.1)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Overall Response Rate by Histology</th>
<th>ABRAXANE (100 mg/m² weekly) + carboplatin</th>
<th>Paclitaxel Injection (200 mg/m² every 3 weeks) + carboplatin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carcinoma/Adenocarcinoma</td>
<td>66/254 (26%)</td>
<td>71/264 (27%)</td>
</tr>
<tr>
<td>Squamous Cell Carcinoma</td>
<td>94/229 (41%)</td>
<td>54/221 (24%)</td>
</tr>
<tr>
<td>Large Cell Carcinoma</td>
<td>3/9 (33%)</td>
<td>2/13 (15%)</td>
</tr>
<tr>
<td>Other</td>
<td>7/29 (24%)</td>
<td>5/33 (15%)</td>
</tr>
</tbody>
</table>

CI = confidence interval; DoR= Duration of response
14.3 Adenocarcinoma of the Pancreas

A multicenter, multinational, randomized, open-label study was conducted in 861 patients comparing ABRAXANE plus gemcitabine versus gemcitabine monotherapy as first-line treatment of metastatic adenocarcinoma of the pancreas. Key eligibility criteria were Karnofsky Performance Status (KPS) ≥70, normal bilirubin level, transaminase levels ≤2.5 times the upper limit of normal (ULN) or ≤5 times the ULN for patients with liver metastasis, no prior cytotoxic chemotherapy in the adjuvant setting or for metastatic disease, no ongoing active infection requiring systemic therapy, and no history of interstitial lung disease. Patients with rapid decline in KPS (≥10%) or serum albumin (≥20%) during the 14 day screening period prior to study randomization were ineligible.

A total of 861 patients were randomized (1:1) to the ABRAXANE/gemcitabine arm (N=431) or to the gemcitabine arm (N=430). Randomization was stratified by geographic region (Australia, Western Europe, Eastern Europe, or North America), KPS (70 to 80 versus 90 to 100), and presence of liver metastasis (yes versus no). Patients randomized to ABRAXANE/gemcitabine received ABRAXANE 125 mg/m² as an intravenous infusion over 30-40 minutes followed by gemcitabine 1000 mg/m² as an intravenous infusion over 30-40 minutes on Days 1, 8, and 15 of each 28-day cycle. Patients randomized to gemcitabine received 1000 mg/m² as an intravenous infusion over 30-40 minutes weekly for 7 weeks followed by a 1-week rest period in Cycle 1 then as 1000 mg/m² on Days 1, 8 and 15 of each subsequent 28-day cycle. Patients in both arms received treatment until disease progression or unacceptable toxicity. The major efficacy outcome measure was overall survival (OS). Additional outcome measures were progression-free survival (PFS) and overall response rate (ORR), both assessed by independent, central, blinded radiological review using RECIST (version 1.0).

In the intent to treat (all randomized) population, the median age was 63 years (range 27-88 years) with 42% ≥ 65 years of age; 58% were men; 93% were White and KPS was 90-100 in 60%. Disease characteristics included 46% of patients with 3 or more metastatic sites; 84% of patients had liver metastasis; and the location of the primary pancreatic lesion was in the head of pancreas (43%), body (31%), or tail (25%).

Results for overall survival, progression-free survival, and overall response rate are shown in Table 13.

| Efficacy Results from Randomized Study in Patients with Adenocarcinoma of the Pancreas (ITT Population) |
|--------------------------------------------------|--------------------------------------------------|
| ABRAXANE(125 mg/m²) and gemcitabine (N = 431) | Gemcitabine (N = 430) |
| Overall Survival | |
| Number of deaths, n (%) | 333 (77) | 359 (83) |
| Median Overall Survival (months) | 8.5 | 6.7 |
| 95% CI | 7.9, 9.5 | 6.0, 7.2 |
| HR (95% CI) | 0.72 (0.62, 0.83) |
| P-value | <0.0001 |
| Progression-free Survival | |
| Death or progression, n (%) | 277 (64) | 265 (62) |
| Median Progression-free Survival (months) | 5.5 | 3.7 |
| 95% CI | 4.5, 5.9 | 3.6, 4.0 |
| HR (95% CI) | 0.69 (0.58, 0.82) |
| P-value | <0.0001 |
| Overall Response Rate | |
| Confirmed complete or partial overall response, n (%) | 99 (23) | 31 (7) |
| 95% CI | 19.1, 27.2 | 5.0, 10.1 |
| P-value a | <0.0001 |

CI = confidence interval, HR = hazard ratio of ABRAXANE plus gemcitabine / gemcitabine, ITT = intent-to-treat population.

a Stratified Cox proportional hazard model.

b Stratified log-rank test stratified by geographic region (North America versus Others), Karnofsky performance score (70 to 80 versus 90 to 100), and presence of liver metastasis (yes versus no).

c Based on Independent Radiological Reviewer Assessment.

d Chi-square test.

In exploratory analyses conducted in clinically relevant subgroups with a sufficient number of subjects, the treatment effects on overall survival were similar to that observed in the overall study population.
15 REFERENCES


16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied
Product No.: 103450
NDC No.: 68817-134-50 100 mg of paclitaxel in a single-use vial, individually packaged in a carton.

16.2 Storage
Store the vials in original cartons at 20ºC to 25ºC (68ºF to 77ºF). Retain in the original package to protect from bright light.

16.3 Handling and Disposal
Procedures for proper handling and disposal of anticancer drugs should be considered. Several guidelines on this subject have been published [see References (15)]. There is no general agreement that all of the procedures recommended in the guidelines are necessary or appropriate.

17 PATIENT COUNSELING INFORMATION
See FDA-approved patient labeling

- ABRAXANE injection may cause fetal harm. Advise patients to avoid becoming pregnant while receiving this drug. Women of childbearing potential should use effective contraceptives while receiving ABRAXANE [see Warnings and Precautions (5.8) and Use in Specific Populations (8.1)].
- Advise men not to father a child while receiving ABRAXANE [see Warnings and Precautions (5.9)].
- Patients must be informed of the risk of low blood cell counts and severe and life-threatening infections and instructed to contact their physician immediately for fever or evidence of infection. [see Warnings and Precautions (5.1), (5.3)].
- Patients should be instructed to contact their physician for persistent vomiting, diarrhea, or signs of dehydration.
- Patients must be informed that sensory neuropathy occurs frequently with ABRAXANE and patients should advise their physicians of numbness, tingling, pain or weakness involving the extremities [see Warnings and Precautions (5.2)].
- Explain to patients that alopecia, fatigue/asthenia, and myalgia/arthritis occur frequently with ABRAXANE.
- Instruct patients to contact their physician for signs of an allergic reaction, which could be severe and sometimes fatal. [see Warnings and Precautions (5.5)].
- Instruct patients to contact their physician immediately for sudden onset of dry persistent cough, or shortness of breath [see Warnings and Precautions (5.4)].
Patient Information
ABRAXANE® (ah-BRAKS-ane)
(paclitaxel protein-bound particles for injectable suspension)
(albumin-bound)

Read this Patient Information before you start receiving ABRAXANE and before each infusion. This information does not take the place of talking with your doctor about your medical condition or your treatment.

What is ABRAXANE?
ABRAXANE is a prescription medicine used to treat:

- advanced breast cancer in people who have already received certain other medicines for their cancer.
- advanced non-small cell lung cancer, in combination with carboplatin in people who cannot be treated with surgery or radiation.
- and advanced pancreatic cancer, when used in combination with gemcitabine as the first medicine for advanced pancreatic cancer.

It is not known if ABRAXANE is safe or effective in children.

Who should not receive ABRAXANE?
Do not receive ABRAXANE if:

- your white blood cell count is below 1,500 cells/ mm³.
- you have had a severe allergic reaction to ABRAXANE.

What should I tell my doctor before receiving ABRAXANE?
Before you receive ABRAXANE, tell your doctor if you:

- have liver or kidney problems.
- have any other medical conditions.
- are a man planning to father a child. You should not father a child during your treatment with ABRAXANE. ABRAXANE can harm the unborn baby of your partner. Talk to your doctor if this is a concern to you.
- are pregnant or plan to become pregnant. ABRAXANE can harm your unborn baby. You should not become pregnant while receiving ABRAXANE. Women who may become pregnant should use effective birth control (contraception). Talk to your doctor about the best way to prevent pregnancy while receiving ABRAXANE.
- are breastfeeding or plan to breastfeed. It is not known if ABRAXANE passes into your breast milk. You and your doctor should decide if you will receive ABRAXANE or breastfeed.
Tell your doctor about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

Know the medicines you take. Keep a list to show your doctor and pharmacist when you get a new medicine.

How will I receive ABRAXANE?

- Your doctor will prescribe ABRAXANE in an amount that is right for you.
- Premedication to prevent allergic reactions is generally not needed to receive ABRAXANE. Premedication may be needed if you have had an allergic reaction to ABRAXANE. In case of severe allergic reaction, ABRAXANE should not be used again.
- ABRAXANE will be given to you by intravenous infusion into your vein.
- Your doctor should do regular blood tests while you receive ABRAXANE.

What are the possible side effects of ABRAXANE?

ABRAXANE may cause serious side effects, including:

- decreased blood cell counts. ABRAXANE can cause a severe decrease in neutrophils (a type of white blood cells important in fighting against bacterial infections) and platelets (important for clotting and to control bleeding). Your doctor will check your blood cell count during your treatment with ABRAXANE and after you have stopped your treatment.
- numbness, tingling, pain, or weakness in your hands or feet (neuropathy).
- severe infection (sepsis). If you receive ABRAXANE in combination with gemcitabine, infections can be severe and lead to death. Tell your doctor right away if you have a fever (temperature of greater than 100.4°F) or develop signs of infection.
- lung or breathing problems. If you receive ABRAXANE in combination with gemcitabine, lung or breathing problems may be severe and can lead to death. Tell your doctor right away if you have a sudden onset of persistent dry cough or shortness of breath.
- allergic reactions. Allergic reactions to ABRAXANE may be severe and can lead to death.

The most common side effects of ABRAXANE include:

- hair loss
- numbness, tingling, pain, or weakness in the hands or feet
- abnormal heart beat
- tiredness
- joint and muscle pain
- changes in your liver function tests
- rash
- low red blood cell count (anemia). Red blood cells carry oxygen to your body tissues. Tell your doctor if you feel weak, tired or short of breath.
- nausea and vomiting
- infections. If you have a fever (temperature of greater than 100.4°F) or other signs of infection, tell your doctor right away.
• Diarrhea
• Loss of body fluid (dehydration)
• Swelling in the hands or feet

These are not all the possible side effects of ABRAXANE. For more information, ask your doctor or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of ABRAXANE.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet.

This Patient Information leaflet summarizes the important information about ABRAXANE. If you would like more information, talk to your doctor. You can ask your doctor or pharmacist for information about ABRAXANE that is written for health professionals.

For more information, call 1-888-423-5436.

What are the ingredients in ABRAXANE?
Active ingredient: paclitaxel (bound to human albumin).
Other ingredient: human albumin (containing sodium caprylate and sodium acetyltryptophanate).

This Patient Information has been approved by the U.S. Food and Drug Administration.

Revised: July 2015

Manufactured for: Celgene Corporation
Summit, NJ 07901

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