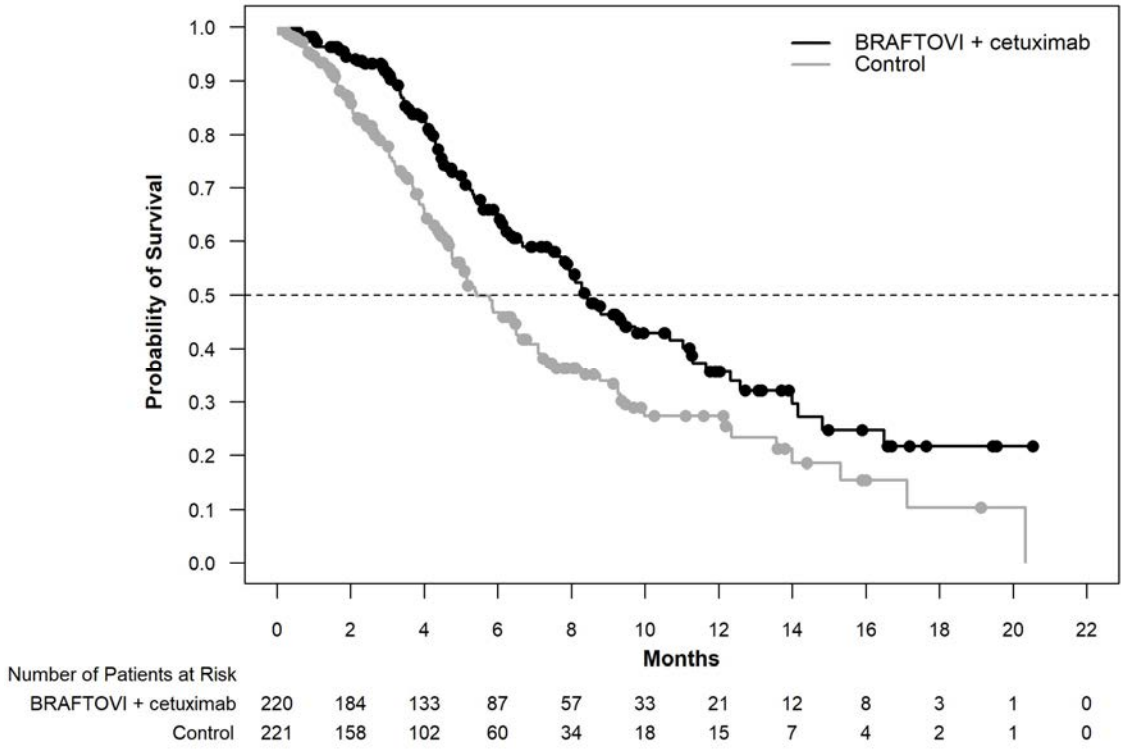
Figure 2: Kaplan-Meier Curves for Overall Survival in BEACON CRC



16 HOW SUPPLIED/STORAGE AND HANDLING

BRAFTOVI (encorafenib) is supplied as 75 mg hard gelatin capsules.

75 mg: stylized "A" on beige cap and "LGX 75mg" on white body, available in cartons (NDC 70255-025-01) containing two bottles of 90 capsules each (NDC 70255-025-02) and cartons (NDC 70255-025-03) containing two bottles of 60 capsules each (NDC 70255-025-04).

Store at 20°C to 25°C (68°F to 77°F); excursions permitted between 15°C and 30°C (59°F and 86°F) [see USP Controlled Room Temperature]. Do not use if safety seal under cap is broken or missing. Dispense in original bottle. Do not remove desiccant. Protect from moisture. Keep container tightly closed.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide).

Inform patients of the following:

New Primary Cutaneous Malignancies

Advise patients to contact their healthcare provider immediately for change in or development of new skin lesions *[see Warnings and Precautions (5.1)]*.

Hemorrhage

Advise patients to notify their healthcare provider immediately with any symptoms suggestive of hemorrhage, such as unusual bleeding *[see Warnings and Precautions (5.3)]*.

Uveitis

Advise patients to contact their healthcare provider if they experience any changes in their vision *[see Warnings and Precautions (5.4)]*.

QT Prolongation

Advise patients that BRAFTOVI can cause QTc interval prolongation and to inform their physician if they have any QTc interval prolongation symptoms, such as syncope *[see Warnings and Precautions (5.5)]*.

Embryo-Fetal Toxicity

- Advise females with reproductive potential of the potential risk to a fetus. Advise females to contact their healthcare provider if they become pregnant, or if pregnancy is suspected, during treatment with BRAFTOVI *[see Warnings and Precautions (5.6), Use in Specific Populations (8.1)]*.
- Advise females of reproductive potential to use effective non-hormonal contraception during treatment with BRAFTOVI and for 2 weeks after the final dose *[Use in Specific Populations (8.3)]*.

Lactation

Advise women not to breastfeed during treatment with BRAFTOVI and for 2 weeks after the final dose *[see Use in Specific Populations (8.2)]*.

Infertility

Advise males of reproductive potential that BRAFTOVI may impair fertility *[see Use in Specific Populations (8.3)]*.

Strong or Moderate CYP3A Inducers or Inhibitors

Coadministration of BRAFTOVI with a strong or moderate CYP3A inhibitor may increase encorafenib concentrations; coadministration of BRAFTOVI with a strong or moderate CYP3A inducer may decrease encorafenib concentrations. Advise patients that they may need to avoid certain medications while taking BRAFTOVI and to inform their healthcare provider of all concomitant medications, including prescription medicines, over-the-counter drugs, vitamins, and herbal products. Advise patients to avoid grapefruit and grapefruit juice while taking BRAFTOVI *[see Drug Interactions (7.1)]*.

Storage

BRAFTOVI is moisture sensitive. Advise patients to store BRAFTOVI in the original bottle with desiccant and to keep the cap of the bottle tightly closed. Do not remove the desiccants from the bottle.

This product's labeling may have been updated. For the most recent prescribing information, please visit www.pfizer.com.

Distributed by:

Array BioPharma Inc., a wholly owned subsidiary of Pfizer Inc.
3200 Walnut Street
Boulder, CO 80301

LAB-1428-1.2

MEDICATION GUIDE

BRAFTOVI® (braf-TOE-vee)
(encorafenib)
capsules

Important information: BRAFTOVI is used with other medicines, either binimetinib or cetuximab. Read the Patient Information leaflet that comes with binimetinib if used with binimetinib, and talk to your healthcare provider about cetuximab if used with cetuximab.

What is the most important information I should know about BRAFTOVI?

BRAFTOVI may cause serious side effects, including:

- **Risk of new skin cancers.** BRAFTOVI when used alone, or with binimetinib or cetuximab, may cause skin cancers called cutaneous squamous cell carcinoma or basal cell carcinoma.

  Talk to your healthcare provider about your risk for these cancers.

  Check your skin and tell your healthcare provider right away about any skin changes, including a:

  - new wart
  - skin sore or reddish bump that bleeds or does not heal
  - change in size or color of a mole

  Your healthcare provider should check your skin before treatment with BRAFTOVI, every 2 months during treatment, and for up to 6 months after you stop treatment with BRAFTOVI to look for any new skin cancers.

  Your healthcare provider should also check for cancers that may not occur on the skin. Tell your healthcare provider about any new symptoms that develop during treatment with BRAFTOVI.

  See "**What are the possible side effects of BRAFTOVI?**" for more information about side effects.

What is BRAFTOVI?

BRAFTOVI is a prescription medicine used:

- in combination with a medicine called binimetinib to treat people with a type of skin cancer called melanoma:
  - that has spread to other parts of the body or cannot be removed by surgery, **and**
  - that has a certain type of abnormal "BRAF" gene
- in combination with a medicine called cetuximab, for the treatment of adults with cancer of your colon or rectum (colorectal cancer):
  - that has been previously treated, **and**
  - that has spread to other parts of the body, **and**
  - that has a certain type of abnormal “BRAF” gene

BRAFTOVI should not be used to treat people with wild-type BRAF melanoma or wild-type BRAF colorectal cancer. Your healthcare provider will perform a test to make sure that BRAFTOVI is right for you.

It is not known if BRAFTOVI is safe and effective in children.

Before taking BRAFTOVI, tell your healthcare provider about all of your medical conditions, including if you:

- have had bleeding problems
- have eye problems
- have heart problems, including a condition called long QT syndrome
- have been told that you have low blood levels of potassium, calcium, or magnesium
- have liver or kidney problems
- are pregnant or plan to become pregnant. BRAFTOVI can harm your unborn baby.
  - Females who are able to become pregnant should use effective non-hormonal birth control (contraception) during treatment with BRAFTOVI and for 2 weeks after the final dose of BRAFTOVI. Birth control methods that contain hormones (such as birth control pills, injections or transdermal systems) may not work as well during treatment with BRAFTOVI.
  - Talk to your healthcare provider about birth control methods that may be right for you during this time.
  - Your healthcare provider will do a pregnancy test before you start taking BRAFTOVI. Tell your healthcare provider right away if you become pregnant or think you might be pregnant during treatment with BRAFTOVI.
- are breastfeeding or plan to breastfeed. It is not known if BRAFTOVI passes into your breast milk. Do not breastfeed during treatment with BRAFTOVI and for 2 weeks after the final dose of BRAFTOVI. Talk to your healthcare provider about the best way to feed your baby during this time.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

BRAFTOVI and certain other medicines can affect each other, causing side effects or affecting how BRAFTOVI or the other medicines work.

Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

How should I take BRAFTOVI?

- Take BRAFTOVI exactly as your healthcare provider tells you. Do not change your dose or stop taking BRAFTOVI unless your healthcare provider tells you to.
- Your healthcare provider may change your dose of BRAFTOVI, temporarily stop, or completely stop your treatment with BRAFTOVI if you develop certain side effects.
- For melanoma, take BRAFTOVI in combination with binimetinib by mouth one time each day.
- For colorectal cancer, take BRAFTOVI by mouth one time each day. You will also receive cetuximab through a vein in your arm (intravenously) given by your healthcare provider.
- BRAFTOVI may be taken with or without food.
- Avoid grapefruit during treatment with BRAFTOVI. Grapefruit products may increase the amount of BRAFTOVI in your body.
- If you miss a dose of BRAFTOVI, take it as soon as you remember. If it is within 12 hours of your next scheduled dose, take your next dose at your regular time. Do not make up for the missed dose.
- Do not take an extra dose if you vomit after taking your scheduled dose. Take your next dose at your regular time.
- If you stop treatment with binimetinib or cetuximab, talk to your healthcare provider about your BRAFTOVI treatment. Your BRAFTOVI dose may need to be changed or stopped.

What are the possible side effects of BRAFTOVI?

BRAFTOVI may cause serious side effects, including:

See "**What is the most important information I should know about BRAFTOVI?**"

- **Bleeding problems.** BRAFTOVI, when taken with binimetinib or cetuximab, can cause serious bleeding problems, including in your stomach or brain, that can lead to death. Call your healthcare provider and get medical help right away if you have any signs of bleeding, including:
  - headaches, dizziness, or feeling weak
  - cough up blood or blood clots
  - vomit blood or your vomit looks like "coffee grounds"
  - red or black stools that look like tar
- **Eye problems.** Tell your healthcare provider right away if you develop any of these symptoms of eye problems:
  - blurred vision, loss of vision, or other vision changes
  - see colored dots
  - see halos (blurred outline around objects)
  - eye pain, swelling, or redness
- **Changes in the electrical activity of your heart called QT prolongation.** QT prolongation can cause irregular heartbeats that can be life threatening. Your healthcare provider should do tests before you start taking BRAFTOVI with binimetinib or cetuximab and during your treatment to check your body salts (electrolytes). Tell your healthcare provider right away if you feel faint, lightheaded, dizzy or if you feel your heart beating irregularly or fast while taking BRAFTOVI with binimetinib or cetuximab. These symptoms may be related to QT prolongation.

The most common side effects of BRAFTOVI when taken in combination with binimetinib, include:

- fatigue
- nausea
- vomiting
- abdominal pain
- pain or swelling of your joints (arthralgia)

The most common side effects of BRAFTOVI when taken in combination with cetuximab, include:

- fatigue
- nausea
- diarrhea

- acne-like rash (dermatitis acneiform)
- abdominal pain
- decreased appetite
- pain or swelling of your joints (arthralgia)
- rash

BRAFTOVI may cause fertility problems in males. Talk to your healthcare provider if this is a concern for you.

These are not all the possible side effects of BRAFTOVI.

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

You may also report side effects to Array BioPharma Inc. at 1-844-792-7729.

How should I store BRAFTOVI?

- Store BRAFTOVI at room temperature between 68°F to 77°F (20°C to 25°C).
- Store BRAFTOVI in the original bottle.
- Keep the BRAFTOVI bottle tightly closed and protect it from moisture.
- BRAFTOVI comes with a desiccant packet in the bottle to help protect your medicine from moisture. Do not remove the desiccant packet from the bottle.

Keep BRAFTOVI and all medicines out of the reach of children.

General information about the safe and effective use of BRAFTOVI.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use BRAFTOVI for a condition for which it was not prescribed. Do not give BRAFTOVI to other people, even if they have the same symptoms that you have. It may harm them. You can ask your healthcare provider or pharmacist for information about BRAFTOVI that is written for health professionals.

What are the ingredients in BRAFTOVI?

Active ingredient: encorafenib

Inactive ingredients: copovidone, poloxamer 188, microcrystalline cellulose, succinic acid, crospovidone, colloidal silicon dioxide, and magnesium stearate of vegetable origin

Capsule shell: gelatin, titanium dioxide, iron oxide red, iron oxide yellow, ferrosoferric oxide, monogramming ink (pharmaceutical glaze, ferrosoferric oxide, propylene glycol)

Distributed by: Array BioPharma Inc., a wholly owned subsidiary of Pfizer Inc. Boulder, Colorado 80301.

BRAFTOVI® is a registered trademark of Array BioPharma Inc. in the United States and various other countries.

LAB-1429-1.1

For more information, go to www.BRAFTOVIMEKTOVI.com or call 1-844-792-7729.

This Medication Guide has been approved by the U.S. Food and Drug Administration. Revised: 2/2022