PATIENT LEAFLET IN ACCORDANCE WITH THE
PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986

The medicine is dispensed according
to a physician's prescription only

Triumeq, film-coated tablets

Each tablet contains:
dolutegravir (as sodium) 50 mg
abacavir (as sulfate) 600 mg
lamivudine 300 mg

For the list of inactive and allergenic ingredients in the preparation, see section 2 – "Important information about some of the ingredients of the medicine" and section 6 – "Additional information".

Read the entire leaflet carefully before using the medicine. This leaflet contains concise information about the medicine. If you have any other questions, refer to the physician or the pharmacist.

This medicine has been prescribed for you. Do not pass it on to others. It may harm them even if it seems to you that their medical condition is similar.

IMPORTANT – Hypersensitivity reactions

Triumeq contains abacavir and dolutegravir. Both of these active ingredients can cause a serious allergic reaction known as a hypersensitivity reaction, which can be life-threatening in people who continue to take abacavir-containing products.

- **! You must carefully read all the information under 'Hypersensitivity reactions' in the panel in Section 4.**

The Triumeq pack includes an **Alert Card**, to remind you and the medical staff about hypersensitivity to abacavir.
Detach this card and keep it with you at all times.
This card contains important safety information that you must know and act upon before starting and during treatment with Triumeq. Read the Alert Card and the patient leaflet before starting to use the preparation.

1. WHAT IS THE MEDICINE INTENDED FOR?

Triumeq is used to treat **HIV (human immunodeficiency virus) infection** in adults and adolescents over 12 years old who weigh at least 40 kg.

Before you are prescribed Triumeq your physician will arrange a test to find out whether you carry a particular type of gene called HLA-B*5701. Triumeq should not be used in patients who are known to carry the HLA-B*5701 gene. Patients with this gene are at a high risk of developing a serious hypersensitivity (allergic) reaction if they use Triumeq (see 'hypersensitivity reactions' in Section 4).

Triumeq does not cure HIV infection; it reduces the amount of virus in your body, and keeps it at a low level. It also increases the number of CD4 cells in your blood. CD4 cells are a type of white blood cells that are important in helping your body to fight infection.

Not everyone responds to treatment with Triumeq in the same way. Your physician will monitor the effectiveness of your treatment.

Therapeutic group: Triumeq is a medicine that contains three active ingredients used to treat HIV infection: abacavir, lamivudine and dolutegravir. Abacavir and lamivudine belong to a group of anti-retroviral medicines (medicines used to treat HIV infection) called *nucleoside analogue reverse transcriptase inhibitors (NRTIs)*, and dolutegravir belongs to a group of anti-retroviral medicines called *integrase inhibitors (INIs)*.

2. BEFORE USING THE MEDICINE

Do not use the medicine:

- if you are **sensitive** (allergic) to dolutegravir, abacavir (or any other medicine containing abacavir), or lamivudine, or any of the additional ingredients contained in the medicine (listed in Section 6).
  - **! Carefully read all the information about hypersensitivity reactions in Section 4**.
- if you are taking a medicine called **fampridine** (also known as dalfampridine; used to treat multiple sclerosis).

→ **Tell the physician** if you think any of these apply to you.

Special warnings regarding the use of the medicine

IMPORTANT – Hypersensitivity reactions

Triumeq contains abacavir and dolutegravir. Both of these active ingredients can cause a serious allergic reaction known as a hypersensitivity reaction. Never take abacavir or abacavir-containing products if you have a hypersensitivity reaction: it can be life-threatening.

! You must carefully read all the information under 'Hypersensitivity reactions' in the panel in Section 4.

The Triumeq pack includes an **Alert Card**, to remind you and the medical staff about hypersensitivity. **Detach this card and keep it with you at all times**.

Some people taking Triumeq or other combination treatments for HIV are more at risk of serious side effects than others. You need to be aware of the extra risks:

- if you have moderate or severe liver disease
- if you have ever had **liver disease,** including hepatitis B or C (if you have hepatitis B infection, do not stop using Triumeq without consulting your physician, as your hepatitis may come back)
- if you have a kidney problem

→ **Talk to your physician if any of these apply to you before using Triumeq.** You may need extra check-ups, including blood tests, while you are taking your medicine. See Section 4 for more information.

Abacavir hypersensitivity reactions

Even patients who do not have the HLA-B*5701 gene may still develop a **hypersensitivity reaction** (a serious allergic reaction).

→ **Carefully read all the information about hypersensitivity reactions in Section 4 of this leaflet.**

Risk of cardiovascular events

It cannot be excluded that abacavir may increase the risk of having cardiovascular events.

→ **Tell your physician** if you have cardiovascular problems, if you smoke, or have other illnesses that may increase your risk of cardiovascular diseases such as high blood pressure or diabetes. Do not stop taking Triumeq unless your physician advises you to do so.

Look out for important symptoms

Some people taking medicines for HIV infection develop other medical conditions, which can be serious. These include:

- symptoms of infections and inflammation
- joint pain, stiffness and bone problems

You need to know about important signs and symptoms to look out for while you are taking Triumeq.

→ **Read the information 'Other possible side effects of combination therapy for HIV' in Section 4 of this leaflet.**

Children

This medicine is not intended for children under 12 years of age. The use of Triumeq in children under 12 years of age has not yet been studied.

Drug interactions

If you are taking, or have recently taken, or might take, other medicines including non-prescription medicines and nutritional supplements, tell the physician or the pharmacist.

Do not take Triumeq with the following medicine:

- fampridine (also known as dalfampridine), used to treat **multiple sclerosis**.

Some medicines can affect how Triumeq works, or make it more likely that you will have side effects. Triumeq can also affect how some other medicines work.

Tell your physician if you are taking any of the medicines *in the following list:*

- metformin, to treat **diabetes**
- medicines called **antacids**, to treat **indigestion** and **heartburn. Do not take an antacid** during the 6 hours before you take Triumeq, or for at least 2 hours after you take it *(see also Section 3)*.
- nutritional supplements or multivitamins containing calcium, iron or magnesium. **If you take Triumeq with food,** you can take nutritional supplements or multivitamins containing calcium, iron or magnesium at the same time as Triumeq. **If you do not take Triumeq with food, do not take nutritional supplements or multivitamins containing calcium, iron or magnesium** during the 6 hours before you take Triumeq, or for at least 2 hours after you take it *(see also Section 3)*.
- emtricitabine, etravirine, efavirenz, fosamprenavir/ritonavir, nevirapine or tipranavir/ritonavir, to treat **HIV infection**
- medicines (usually liquids) containing **sorbitol and other sugar alcohols** (such as xylitol, mannitol, lactitol or maltitol), if taken regularly

- other medicines containing lamivudine, used to treat **HIV infection** or **hepatitis B infection**
- cladribine, used to treat **hairy cell leukaemia**
- rifampicin, to treat tuberculosis (TB) and other **bacterial infections**
- trimethoprim/sulfamethoxazole, an antibiotic to treat **bacterial infections**
- phenytoin and phenobarbital, to treat **epilepsy**
- oxcarbazepine and carbamazepine, to treat **epilepsy** and **bipolar disorder**
- **St. John's wort** *(Hypericum perforatum)*, a herbal remedy to treat **depression**
- **methadone,** used as a **heroin substitute.** Abacavir increases the rate at which methadone is removed from the body. If you are taking methadone, you will be checked for any withdrawal symptoms. Your methadone dose may need to be changed.
- Riociguat, used to treat **high blood pressure in the blood vessels** (the pulmonary arteries) that carry blood from the heart to the lungs. Your physician may need to reduce your riociguat dose, as abacavir may increase riociguat blood levels.

→ **Tell your physician or pharmacist** if you are taking any of these. Your physician may decide to adjust your dose or that you need extra check-ups.

Pregnancy, breast-feeding and fertility

Pregnancy

If you are pregnant, think you may be pregnant, or if you are planning to become pregnant:

→ **Consult with your physician** about the risks and benefits of taking Triumeq.

Taking Triumeq at the time of becoming pregnant or during the first 6 weeks of pregnancy, may increase the risk of a type of birth defect, called neural tube defect, such as spina bifida (malformed spinal cord).

If you could get pregnant while taking Triumeq:

→ **Talk to your physician** and discuss whether there is a need for contraception, such as condom or pills.

Inform your physician immediately if you become pregnant or if you are planning to become pregnant. Your physician will review your treatment. Do not stop taking Triumeq without consulting your physician, as this may harm you and your unborn child.

Breast-feeding

Breast-feeding is **not recommended** in women living with HIV because HIV infection can be passed on to the baby in breast milk.

A small amount of the ingredients in Triumeq can also pass into your breast milk.

If you are breast-feeding, or thinking about breast-feeding, you should **consult with your physician as soon as possible.**

Driving and using machines

Triumeq can make you dizzy and have other side effects that make you less alert.

→ **Do not drive or operate machinery** unless you are sure your alertness has not been affected.

Important information about some of the ingredients of the medicine
This medicine contains less than 1 mmol sodium (23 mg) per dosage unit, that is to say it is essentially 'sodium-free'.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use this preparation according to the physician's instructions. You should check with the physician or the pharmacist if you are uncertain about the dosage and treatment regimen of the preparation.
The dosage and treatment regimen will be determined only by the physician.

- **The usual dosage generally is one tablet once a day**

Swallow the tablet with some liquid. Triumeq can be taken with or without food.
There is no information regarding crushing/halving/chewing.
Use in children and adolescents
Children and adolescents aged between 12 and 17 years and weighing at least 40 kg can take the adult dose of one tablet once a day.
Do not exceed the recommended dose.
Do not take an antacid during the 6 hours before you take Triumeq, or for at least 2 hours after you take it. Other acid-lowering medicines like ranitidine and omeprazole can be taken at the same time as Triumeq.
→ Talk to your physician for further advice on taking antacid medicines with Triumeq.
If you take Triumeq with food, you can take nutritional supplements or multivitamins containing calcium, iron or magnesium at the same time as Triumeq. **If you do not take Triumeq with food,** do not take nutritional supplements or multivitamins containing calcium, iron or magnesium during the 6 hours before you take Triumeq, or for at least 2 hours after you take it.
→ Talk to your physician for further advice on taking nutritional supplements or multivitamins containing calcium, iron or magnesium with Triumeq.
If you accidentally have taken a higher dosage
If you take too many tablets of Triumeq, **contact your physician or pharmacist for advice**. If possible, show them the pack. If a child has accidentally swallowed the medicine, refer immediately to a physician or to a hospital emergency room and bring the package of the medicine with you.
If you forgot to take the medicine
If you miss a dose, take it as soon as you remember. But if your next dose is due within 4 hours, skip the dose you missed and take the next one at the usual time. Then continue your treatment as before.
→ **Do not take a double dose** to make up for a missed dose.
Persist with the treatment as recommended by the physician. Even if there is an improvement in your health, do not stop treatment with the medicine without consulting the physician.
If you stop taking the medicine
If you have stopped taking Triumeq for any reason – especially because you think you are having side effects, or because you have another illness:

→ **Talk to your physician before you start taking it again**. Your physician will check whether your symptoms were related to a hypersensitivity reaction. If the physician thinks they may be related to a hypersensitivity reaction, **you will be told never again to take Triumeq, or any other medicine containing abacavir or dolutegravir.** It is important that you follow this advice.

If your physician advises that you can start taking Triumeq again, you may be asked to take your first doses in a place where you will have ready access to medical care if you need it.

Do not take medicines in the dark! Check the label and the dose each time you take a medicine. Wear glasses if you need them.

If you have any other questions regarding the use of the medicine, consult the physician or the pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Triumeq may cause side effects in some of the users. Do not be alarmed by reading the list of side effects. You may not experience any of them.

When you are being treated for HIV, it can be hard to tell whether a symptom is a side effect of Triumeq or other medicines you are taking, or an effect of the HIV disease itself. **So it is very important to talk to your physician about any change in your health**.

! Abacavir can cause a hypersensitivity reaction (a serious allergic reaction), especially in people who carry a particular type of gene called: HLA-B*5701. Even patients who do not have the HLA-B*5701 gene may still develop **a hypersensitivity reaction**, described in this leaflet in the panel headed 'Hypersensitivity reactions'. **It is very important that you read and understand the information about this serious reaction**.

As well as the side effects listed below for Triumeq, other conditions can develop during combination therapy for HIV.

→ It is important to read the information in this section under the heading 'Other possible side effects of combination therapy for HIV'.

Hypersensitivity reactions

Triumeq contains abacavir and dolutegravir. Both of these active ingredients can cause a serious allergic reaction known as a hypersensitivity reaction.

These hypersensitivity reactions have been seen more frequently in people taking medicines that contain abacavir.

Who will develop these reactions?

Anyone taking Triumeq could develop a hypersensitivity reaction, which could be life-threatening if they continue to take Triumeq.

You are more likely to develop this reaction if you have a gene called HLA-B*5701 (but you can get a reaction even if you do not have this gene). You should have been tested for this gene before Triumeq was prescribed for you. If you know you have this gene, tell your physician.

What are the symptoms?

The most common symptoms are:

- **fever and skin rash**.

Other common symptoms are:

- **nausea**, vomiting, diarrhoea, abdominal pain, severe tiredness.

Other symptoms include:

- pains in the joints or muscles, swelling of the neck, shortness of breath, sore throat, cough, occasional headaches, inflammation of the eye (conjunctivitis), mouth ulcers, low blood pressure, tingling or numbness of the feet or hands.

When do these reactions happen?

Hypersensitivity reactions can start at any time during treatment with Triumeq, but are more likely during the first 6 weeks of treatment.

Contact your physician immediately if:

1 you get a skin rash, OR

2 you get symptoms from at least 2 of the following groups:

- **fever**
- **shortness of breath, sore throat or cough**
- **nausea or vomiting, diarrhoea or abdominal pain**
- **severe tiredness or aches and pains, or generally feeling ill.**

! Your physician may advise you to stop taking Triumeq.

If you stop taking Triumeq

! If you have stopped taking Triumeq because of a hypersensitivity reaction, **you must NEVER AGAIN take Triumeq, or any other medicine containing abacavir.** If you do, within hours, your blood pressure could fall dangerously low, which could result in death. You should also never again take medicines containing dolutegravir.

If you have stopped taking Triumeq for any reason – especially because you think you are having side effects, or because you have other illness:

→ **Talk to your physician before you start again.** Your physician will check whether your symptoms were related to a hypersensitivity reaction. If the physician thinks they may have been, **you will then be told never again to take Triumeq, or any other medicine containing abacavir.** You may also be told never again to take any other medicine containing dolutegravir. It is important that you follow this advice.

Occasionally, hypersensitivity reactions have developed in people who start taking abacavir-containing products again, and had only one symptom on the Alert Card before they stopped taking it.

Very rarely, patients who have taken medicines containing abacavir in the past without any symptoms of hypersensitivity have developed a hypersensitivity reaction when they start taking these medicines again.

If your physician advises that you can start taking Triumeq again, you may be asked to take your first doses in a place where you will have ready access to medical care if you need it.

If you are hypersensitive to Triumeq, return all your unused Triumeq tablets for safe disposal. Consult with the physician or pharmacist.
The Triumeq pack includes an **Alert Card**, to remind you and medical staff about hypersensitivity reactions. **Detach this card and keep it with you at all times.**

Very common side effects
These may occur in **more than 1 in 10** people:
- headache
- diarrhoea
- nausea *(feeling sick)*
- difficulty in sleeping *(insomnia)*
- lack of energy *(fatigue)*.

Common side effects
These may occur in **up to 1 in 10** people:
- hypersensitivity reaction *(see 'Hypersensitivity reactions' earlier in this section)*
- loss of appetite
- rash
- itching *(pruritus)*
- vomiting
- stomach pain
- stomach discomfort
- weight gain
- indigestion
- wind *(flatulence)*
- dizziness
- abnormal dreams
- nightmares
- depression (feelings of deep sadness and unworthiness)
- anxiety
- tiredness
- feeling drowsy
- fever
- cough
- irritated or runny nose
- hair loss
- muscle pain and discomfort
- joint pain
- feeling weak
- general feeling of being unwell.

Common side effects that may show up in blood tests are:
- an increase in the level of liver enzymes
- increase in the level of enzymes produced in the muscles *(creatine phosphokinase)*.

Uncommon side effects

These may occur in **up to 1 in 100** people:

- inflammation of the liver *(hepatitis)*
- suicidal thoughts and behaviours (particularly in patients who have had depression or mental health problems before)
- panic attack.

Uncommon side effects that may show up in blood tests are:

- a decreased number of cells involved in blood clotting *(thrombocytopenia)*
- a low red blood cell count *(anaemia)* or low white blood cell count *(neutropenia)*
- an increase in sugar (glucose) in the blood
- an increase in triglycerides (type of fat) in the blood.

Rare side effects

These may occur in **up to 1 in 1,000** people:

- inflammation of the pancreas *(pancreatitis)*
- breakdown of muscle tissue
- liver failure (signs may include yellowing of the skin and whites of the eyes, or darker urine than usual)
- suicide (particularly in patients who have had depression or mental health problems before).

→ **Tell your physician immediately** if you experience any mental health problems (see also other mental health problems above).

Rare side effects that may show up in blood tests are:

- increase in bilirubin level (a test of liver function)
- increase in an enzyme called *amylase*.

Very rare side effects

These may occur in **up to 1 in 10,000** people:

- numbness, tingly feelings in the skin (pins and needles)
- sensation of weakness in the limbs
- skin rash, which may form blisters and looks like small targets (central dark spots surrounded by a paler area, with a dark ring around the edge) *(erythema multiforme)*
- a widespread rash with blisters and peeling skin, particularly around the mouth, nose, eyes and genitals *(Stevens-Johnson syndrome)*, and a more severe form causing skin peeling in more than 30% of the body surface *(toxic epidermal necrolysis)*
- lactic acidosis (excess lactic acid in the blood).

Very rare side effects that may show up in blood tests are:

- a failure of the bone marrow to produce new red blood cells *(pure red cell aplasia)*.

If you get any side effects

→ **Talk to your physician**. This includes any possible side effect not listed in this leaflet.

Other possible side effects of combination therapy for HIV

Combination therapy such as Triumeq may cause other conditions to develop during HIV treatment.

Symptoms of infection and inflammation

People with advanced HIV infection or AIDS have weak immune systems, and are more likely to develop serious infections *(opportunistic infections)*. Such infections may have been "silent" and not detected by the weak immune system before treatment was started. After starting treatment, the immune system becomes stronger, and may attack the infections, which can cause symptoms of infection or inflammation. Symptoms usually include **fever**, plus some of the following:

- headache
- stomach ache
- difficulty breathing.

In rare cases, as the immune system becomes stronger, it can also attack healthy body tissue *(autoimmune disorders)*. The symptoms of autoimmune disorders may develop many months after you start taking medicine to treat your HIV infection. Symptoms may include:

- palpitations (rapid or irregular heartbeat) or tremor
- hyperactivity (excessive restlessness and movement)
- weakness beginning in the hands and feet and moving up towards the trunk of the body.

If you get any symptoms of infection and inflammation or if you notice any of the symptoms above:

→ **Tell your physician immediately**. Do not take other medicines for the infection without consulting your physician.

Joint pain, stiffness and bone problems

Some people taking combination therapy for HIV develop a condition called *osteonecrosis*. In this condition, parts of the bone tissue die because of reduced blood supply to the bone. People may be more likely to get this condition if:

- they have been taking combination therapy for a long time
- they are also taking anti-inflammatory medicines called corticosteroids
- they drink alcohol
- their immune system is very weak
- they are overweight.

Signs of osteonecrosis include:

- stiffness in the joints
- aches and pains (especially in the hip, knee or shoulder)
- difficulty moving.

If you notice any of these symptoms:

→ **Tell your physician**.

Weight, blood lipids and blood glucose effects

During HIV therapy there may be an increase in weight and in levels of blood lipids and glucose. These effects are partly linked to restored health and lifestyle, and

sometimes to the HIV medicines themselves. Your physician will test for these changes.

If a side effect has appeared, if any of the side effects get worse or when you suffer from a side effect that has not been mentioned in the leaflet, you should consult the physician.

Reporting side effects

Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link:
https://sideeffects.health.gov.il

5. HOW TO STORE THE MEDICINE?

Avoid poisoning! This medicine and any other medicine should be kept in a closed place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting without an explicit instruction from the physician.

Do not use the medicine after the expiry date (exp. date) appearing on the package. The expiry date refers to the last day of that month.

Do not store above 30°C.

Store in the original package in order to protect from moisture. Keep the bottle tightly closed. Do not remove the *desiccant*.

Do not discard medicines via wastewater or household waste. Consult with the pharmacist on how to throw away medicines that are not in use. These steps will help protect the environment.

6. ADDITIONAL INFORMATION

In addition to the active ingredients the medicine also contains -

Microcrystalline cellulose, D-mannitol (E421), sodium starch glycolate, magnesium stearate, povidone K29/32, Opadry II Purple 85F90057 (containing polyvinyl alcohol – part hydrolyzed (E1203), titanium dioxide (E171), macrogol/PEG, talc, iron oxide black (E172) and iron oxide red (E172)).

What does the medicine look like and what is the content of the package: Triumeq film-coated tablets are purple, biconvex, oval tablets, debossed with "572 Tri" on one side. They are provided in bottles containing 30 tablets. The bottle is closed with a child-resistant cap.

Opening instructions - to remove the cap, press down, while simultaneously twisting to the left (turning counterclockwise).

Closing instructions - place cap on top of open end and twist to the right (turning clockwise) until it locks.

The bottle contains a *desiccant* to reduce the moisture. Once the bottle has been opened keep the *desiccant* in the bottle and do not remove it.

License Holder: GlaxoSmithKline (Israel) Ltd., 25 Basel St., Petach Tikva.

Manufacturer: ViiV Healthcare UK Limited, Brentford, UK.

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 153-49-34304

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