Patient Package Leaflet in Accordance With

the Pharmacists' Regulations (Preparations) – 1986

The medicine is dispensed with a doctor's prescription only

TAGRISSO® 40 mg

Tablets

Composition:

Each tablet contains:

Osimertinib (as mesylate) 40 mg

TAGRISSO® 80 mg

Tablets

Composition:

Each tablet contains:

Osimertinib (as mesylate) 80 mg

For inactive ingredients please refer to Section 6 – "Further Information".

Read this leaflet carefully in its entirety before using the medicine.

Keep this leaflet, you may need it again.

This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.

This medicine has been prescribed for the treatment of your ailment. Do not pass it on to others. It may harm them, even if it seems to you that their ailment is similar.

This medicine is not intended for children under the age of 18.

1. What is Tagrisso and what is it used for?

- TAGRISSO is indicated as adjuvant therapy after tumor resection in adult patients with non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R mutations.
- TAGRISSO in combination with pemetrexed and platinum-based chemotherapy is indicated for the first line treatment of adult patients with locally advanced or metastatic NSCLC whose tumors have EGFR exon 19 deletions or exon 21 L858R mutations.

Tagrisso as monotherapy is indicated for:

- the first-line treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with activating epidermal growth factor receptor (EGFR) mutations.
- the treatment of adult patients with locally advanced or metastatic EGFR (epidermal growth factor receptor) T790M mutation-positive NSCLC.

Therapeutic group

Anticancer medicine, protein kinase inhibitor.

This medicine will be prescribed by a doctor with experience in anticancer therapies.

2. Before using the medicine

Do not use the medicine if:

- you are hypersensitive to the active ingredient or any of the other ingredients of this medicine (see section 6 below – "Further Information").
- you are using St. John's Wort (*hypericum perforatum*) concomitantly.

Special warnings regarding use of Tagrisso:

Before treatment with this medicine, tell your doctor if:

- you have a history of inflammation of your lungs called 'interstitial lung disease'.
- you have ever had heart problems – you will probably need medical supervision.
- you have a history of eye problems.

If any of the above apply to you (or you are not sure), talk to your doctor or pharmacist before taking this medicine.

Tell your doctor straight away while taking this medicine if:

- you have sudden difficulty in breathing together with a cough or fever.
- you have severe peeling of your skin.
- you have rapid or irregular heartbeats, dizziness, light-headedness, chest discomfort, shortness of breath and fainting.
- you develop watery eyes, sensitivity to light, eye pain, eye redness or vision changes. See Side effects which require special attention in section 4 for more information.
- you develop persistent fever, bruising or bleeding more easily, increasing tiredness, pale skin and infection. See Side effects which require special attention in section 4 for more information.

Children and adolescents

There is no data regarding efficacy and safety of this preparation in children and adolescents.

If you are taking, or have recently taken, other medicines including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist, since Tagrisso can affect the way other medicines work, and other medicines can affect the way Tagrisso works.

Tell your doctor before taking Tagrisso if you are taking any of the following medicines:

The following medicines may reduce Tagrisso's activity:

- Phenytoin, carbamazepine or phenobarbital – used for epilepsy and fits.
- Rifabutin or rifampicin – used for tuberculosis.
- St. John's Wort (*Hypericum Perforatum*) – an herbal medicine used for depression.

Tagrisso may affect how well the following medicines work and/or increase side effects of these medicines:

- Rosuvastatin - used to lower cholesterol level.
- Oral hormonal contraceptive pill – used to prevent pregnancy.
- Bosentan – used for high blood pressure in the lungs.
- Efavirenz and etravirine – used to treat HIV infections/AIDS.
- Modafinil – used for sleep disorders.
- Dabigatran – used to prevent blood clots.
- Digoxin – used for irregular heart beat or heart failure.
- Aliskiren – used for high blood pressure.

If you are taking any of the medicines listed above, tell the attending doctor before taking Tagrisso. Your doctor will consider treatment options appropriate for you.

Pregnancy, contraception and breast-feeding – information for women and men

Pregnancy – information for women

- If you are pregnant, think you may be pregnant or are planning to become pregnant, inform your doctor before taking this medicine. If you do become pregnant during

treatment, tell your doctor straight away. Your doctor will decide with you whether you should carry on taking Tagrisso.

- You should not become pregnant while taking this medicine. You must use effective contraception while taking Tagrisso. See “Contraception - information for women and men” below.
- If you plan to become pregnant after taking the last dose of this medicine, ask your doctor for advice. This is because some medicine may remain in your body for some time after finishing treatment (see "Contraception" section below).

Pregnancy – information for men

- If your partner becomes pregnant while you are taking Tagrisso, tell your doctor straight away.

Contraception – information for women and men

- You must use effective contraception during treatment with Tagrisso.
- Tagrisso may interfere with how well oral hormonal contraceptives work. Discuss with your doctor the most appropriate methods of contraception.
- Tagrisso may pass into semen. Therefore, it is important that men also use effective contraception.

After completing treatment with Tagrisso follow the instructions below:

- **Women** – keep using contraception for an additional 2 months after stopping treatment with Tagrisso.
- **Men** – keep using contraception for an additional 4 months after stopping treatment with Tagrisso.

Breast-feeding

Do not breast-feed while taking this medicine. This is because it is not known if there is a risk to your baby.

Driving and using machines

Tagrisso has no marked influence on the ability to drive and use machines.

Important information regarding some of the ingredients of the medicine

Tagrisso contains less than 1 mmol sodium (23 mg) per tablet, this means that the medicine is essentially ‘sodium-free’.

3. How should you use the medicine?

- Always use according to the doctor's instructions. Check with the doctor or pharmacist if you not sure.
- The dosage and course of treatment will be determined only by the doctor.

Dosage

- The recommended dose is usually one 80 mg tablet each day.
- If necessary, your doctor may reduce your daily dose to one 40 mg tablet each day.
- The recommended dose of Tagrisso is usually one 80 mg tablet each day when taken with pemetrexed and a platinum-containing chemotherapy.

Do not exceed the recommended dosage.

Method of administration

- Swallow the tablet whole with water. Do not crush, split or chew the tablet.
- Take every day at about the same time.
- You can take this medicine with food or on an empty stomach.
- If you have trouble swallowing the tablet, you can mix it in water:
  - Put the tablet in a glass.
  - Add 50 mL of water (non-fizzy) – do not use any other liquids.
  - Stir the water until the tablet breaks up into very small pieces - the tablet will not completely dissolve.
  - Drink the liquid straight away.
  - To make sure you have taken all of the medicine, rinse the glass thoroughly with another 50 mL of water and drink it.

If you accidentally take a higher dose

If you take an overdose, or if a child has accidently swallowed the medicine, refer immediately to a doctor or proceed to a hospital emergency room and bring the package of the medicine with you.

If you forget to take the medicine

If you forget a dose, take it as soon as you remember it. However, if it is less than 12 hours until your next dose is due, skip the missed dose. Take your next normal dose at its scheduled time.

Adhere to the treatment recommended by your doctor.

If you stop taking the medicine

Do not stop taking this medicine without consulting your doctor. It is important to take this medicine every day, for as long as your doctor prescribes it for you.

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

If you have any further questions regarding the use of this medicine, ask your doctor or pharmacist.

4. Side effects

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

Side effects which require special attention:

Refer immediately to your doctor if you notice any of the following serious side effects (also see section 2):

- Sudden difficulty in breathing together with a cough or fever. This may be a sign of inflamed lungs called 'interstitial lung disease'. Most cases can be treated but some can be life threatening. Your doctor may stop treatment with Tagrisso if you get this side effect. This side effect is common (affect up to 1 in 10 users).
- Stevens-Johnson syndrome or toxic epidermal necrolysis (TEN), which can appear as reddish target-like macules or circular patches often with central blisters on the trunk, skin peeling, ulcers of mouth, throat, nose, genitals and eyes and be preceded by fever and flu-like symptoms. Stevens-Johnson syndrome is a rare side effect (affect up to 1 in 1,000 users). Please see also Section 2. The frequency of toxic epidermal necrolysis cannot be determined as cases have only been reported since marketing Tagrisso.
- Changes in the electrical activity in the heart (QT prolongation) such as rapid or irregular heartbeats, dizziness, light-headedness, chest discomfort, shortness of breath and fainting. This side effect is uncommon (affect up to 1 in 100 users).
- If you develop watery eyes, sensitivity to light, eye pain, eye redness, or vision changes. This side effect is uncommon (affect up to 1 in 100 users).
- A blood disorder called aplastic anaemia, when bone marrow stops producing new blood cells – signs suggestive of this blood disorder may include persistent

fever, bruising or bleeding more easily, increased tiredness and a decrease in your ability to fight infection. This side effect is rare (affect up to 1 in 1,000 users).

- A condition in which the heart does not pump enough blood out of the heart in one beat as well as it should which could result in shortness of breath, tiredness and ankle swelling (suggestive of heart failure or left ventricular ejection fraction decreased).

Tell your doctor straight away if you notice the serious side effects listed above.

Other side effects:

Very common side effects (affect more than 1 in 10 users):

- Diarrhea - this may come and go during treatment. Tell your doctor if your diarrhea does not go away or worsens.
- Skin and nail problems - signs may include pain, itching, dry skin, rash, redness around the fingernails. This is more likely in areas exposed to the sun. Using moisturizers regularly on your skin and nails can help with this. Tell your doctor if your skin or nail problems get worse.
- Inflammation of the inner lining of the mouth or ulcers forming in the mouth (Stomatitis).
- Loss of appetite.
- Reduction in the number of white blood cells (leukocytes, lymphocytes or neutrophils).
- Reduction in the number of platelets in the blood.

Common side effects (affect up to 1 of 10 users):

- Nose bleed (epistaxis).
- Hair thinning (alopecia).
- Hives (urticaria) - itchy, raised patches anywhere on the skin, which may be pink or red and round in shape. Tell your doctor if you notice this side effect.
- Skin greying or darkening (hyperpigmentation).
- Hand-foot syndrome – this may include redness, swelling, tingling or burning sensation with cracking of the skin on the palms of hands and/or soles of feet.
- Increase in the blood creatinine (produced by the body and removed by the kidney).

- Increase of a substance in the blood called creatine phosphokinase (an enzyme released into the blood when muscle is damaged).

Uncommon side effects (effects occurring in up to 1 of 100 users):

- Target lesions, which are skin reactions that look like rings (suggestive of Erythema multiforme).
- Inflammation of the blood vessels in the skin. This may give the appearance of bruising or patches of non-blanching rash on the skin.
- Inflammation of the muscle which may result in muscle pain or weakness

The following side effects have been reported in a clinical trial with patients receiving TAGRISSO in combination with pemetrexed and a platinum-containing chemotherapy:

Very common side effects (affect more than 1 in 10 users):

- Diarrhea - this may come and go during treatment. Tell your doctor if your diarrhea does not go away or becomes severe.
- Skin and nail problems - signs may include pain, itching, dry skin, rash, redness around the fingernails. This is more likely in areas exposed to the sun. Using moisturizers regularly on your skin and nails can help with this. Tell your doctor if your skin or nail problems get worse.
- Stomatitis - inflammation of the inner lining of the mouth or ulcers forming in the mouth.
- Loss of appetite.
- Reduction in the number of white blood cells (leukocytes, lymphocytes or neutrophils).
- Reduction in the number of platelets in the blood.
- Increase of a substance in the blood called creatinine (produced by your body and removed by the kidney).

Common side effects (affect up to 1 of 10 users):

- Nose bleed (epistaxis)
- Itchy skin (pruritus) - Using moisturizers regularly on your skin can help with this
- Hair thinning (alopecia)

- Target lesions, which are skin reactions that look like rings (suggestive of Erythema multiforme)
- Hives (urticaria) - itchy, raised patches anywhere on the skin, which may be pink or red and round in shape. Tell your doctor if you notice this side effect.
- Skin greying or darkening (hyperpigmentation).
- Hand-foot syndrome - this may include redness, swelling, tingling or burning sensation with cracking of the skin on the palms of hands and/or soles of feet.
- Increase of a substance in the blood called creatine phosphokinase (an enzyme released into the blood when muscle is damaged).

If any side effect appears, if one of the side effects worsens or if you suffer from a side effect not mentioned in the leaflet, consult with the doctor.

Reporting of 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 should the medicine be stored?

- Avoid Poisoning! This medicine, and any other medicine, should be kept in a safe place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.
- 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 use any pack that is damaged or shows signs of tampering.
- Store below 30°C in the original package.

6. Further information

In addition to the active ingredient, the medicine also contains:
Tablet core:
Mannitol

Microcrystalline cellulose
Low-substituted hydroxypropyl cellulose
Sodium stearyl fumarate

Tablet coating:
Polyvinyl alcohol
Titanium dioxide
Macrogol 3350
Talc
Yellow iron oxide
Red iron oxide
Black iron oxide

- **What does the medicine look like?**
  The medicine pack contains 30 tablets.
  Tagrisso 40 mg: beige, film-coated, round and biconvex tablets, marked with “AZ” and “40” on one side, and plain on the other.
  Tagrisso 80 mg: beige, film-coated, oval and biconvex tablets, marked with “AZ” and “80” on one side, and plain on the other.

Manufacturer:
AstraZeneca A.B, Södertälje, Sweden.

License holder:
AstraZeneca (Israel) Ltd.,
1 Atirei Yeda St., Kfar Saba 4464301.

Registration number of the medicine in the National Drug Registry of the Ministry of Health:
Tagrisso 40 mg: 155-86-34627-00
Tagrisso 80 mg: 155-87-34654-00

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