PATIENT LEAFLET IN ACCORDANCE WITH THE
PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986
This medicine is dispensed with a doctor's prescription only

INSPRA® 25 mg
INSPRA® 50 mg
Film-coated tablets

Each tablet contains:
eplerenone 25 mg, 50 mg

Inactive ingredients and allergens: See section 2 under 'Important information about some of this medicine's ingredients' and section 6 'Further information'.

Read the entire leaflet carefully before using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, consult your doctor or 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 to yours.

1. WHAT IS THIS MEDICINE INTENDED FOR?

- In addition to standard therapy including beta-blockers, to reduce the risk of cardiovascular mortality and morbidity in stable patients with left ventricular dysfunction (LVEF < or = 40%) and clinical evidence of heart failure after recent myocardial infarction.
- In addition to standard optimal therapy, to reduce the risk of cardiovascular morbidity and mortality in adult patients with NYHA class II chronic heart failure and left ventricular systolic dysfunction (LVEF < or = 30%).

Therapeutic group:
Selective aldosterone antagonists.

2. BEFORE USING THIS MEDICINE

Do not use the medicine if:

- you are sensitive (allergic) to the active ingredient or to any of the additional ingredients contained in the medicine (see section 6).
- you suffer from high levels of potassium in the blood (hyperkalemia).
- you are taking medicines of the potassium-sparing diuretics group.
- you suffer from severe kidney disease.
- you suffer from severe liver disease.
- you are taking medicines that are used to treat fungal infection (ketoconazole or itraconazole).
- you are taking antiviral medicines for treating HIV (ritonavir or nelfinavir).
- you are taking antibiotics used to treat bacterial infections (telithromycin or clarithromycin).
- you are taking nefazodone used to treat depression.
- you are taking medicines used to treat certain heart conditions or hypertension called angiotensin converting enzyme inhibitors (ACE inhibitors) and an angiotensin receptor blockers (ARB) together.

Special warnings regarding use of the medicine

Before treatment with Inspra®, tell your doctor if:
- you suffer from a kidney or liver disease (see also 'Do not use the medicine if').
- you are taking lithium (usually given for treatment of manic-depressive disorder, also called bipolar disorder).
- you are taking tacrolimus or cyclosporine (medicines used to treat certain skin conditions such as psoriasis or eczema, and to prevent rejection after organ transplantation).

Children and adolescents
There is no information regarding the safety and effectiveness of using this preparation in children and adolescents.

Tests and follow-up
Blood potassium levels should be measured before starting Inspra® therapy, within the first week and at one month after the start of treatment or after a change in dose. The dose will be adjusted by your doctor, depending on the potassium levels in your blood.

Drug interactions
If you are taking or if you have recently taken, other medicines, including non-prescription medicines and dietary supplements, tell your doctor or pharmacist.
Particularly if you are taking:
- Itraconazole or ketoconazole (used to treat fungal infections), ritonavir, nelfinavir (antiviral medications for treating of HIV infection), clarithromycin, telithromycin (used to treat bacterial infections) or nefazodone (used to treat depression), as these drugs reduce the break-down of Inspra® and thereby prolonging its effect on the body.
- Potassium-sparing diuretics and potassium supplements, as these drugs increase the risk of high potassium levels in the blood.
- Angiotensin converting enzyme inhibitors (ACE inhibitors) and angiotensin receptor blockers (ARB) together (which are used to treat high blood pressure, heart disease or particular kidney conditions), as these drugs may increase the risk of high potassium levels in the blood.
- Lithium (usually given for treatment of manic-depressive disorder, also called bipolar disorder). Use of lithium together with diuretics and ACE inhibitors (used to treat high

blood pressure and heart disease) has been shown to cause levels of lithium in the blood to become too high which may cause side effects of: loss of appetite, visual impairment, tiredness, muscle weakness and muscle twitches.
- Cyclosporine or tacrolimus (used to treat certain skin conditions such as psoriasis or eczema and to prevent rejection after organ transplantation). These drugs can cause kidney problems, thereby increasing the risk of high potassium levels in the blood.
- Non-steroidal anti-inflammatory drugs (NSAIDs - certain pain killers such as ibuprofen used for relief of pain, stiffness and inflammation). These drugs may lead kidney problems, thereby increasing the risk of high potassium levels in the blood.
- Trimethoprim (used to treat bacterial infections) may increase the risk of high potassium levels in the blood.
- Alpha 1 receptor blockers such as prazosin or alfuzosin (used to treat high blood pressure and particular prostate gland conditions) may lead to a fall in blood pressure and dizziness upon standing.
- Tricyclic antidepressants such as amoxapine or amitriptyline (for treatment of depression), antipsychotics (also known as neuroleptics) such as chlorpromazine or haloperidol (for the treatment of psychiatric disorders), amifostine (used during chemotherapy treatments) and baclofen (used to treat muscle spasms).These drugs may lead to a fall in blood pressure and dizziness upon standing.
- Glucocorticoids such as hydrocortisone or prednisone (used to treat inflammations and certain skin conditions) and tetracosactide (used mainly for diagnosing and treating various disorders of the adrenal cortex) may reduce the blood pressure lowering effect of Inspra®.
- Digoxin (used in the treatment of heart conditions). Digoxin blood levels may be increased when taken together with Inspra®.
- Warfarin (anticoagulant): Caution is warranted when taking warfarin because high levels of warfarin in the blood may cause changes in the effect of Inspra® on the body.
- Erythromycin (an antibiotic used to treat bacterial infections), saquinavir (antiviral medication for treating HIV), fluconazole (used to treat fungal infections), amiodarone, diltiazem and verapamil (for the treatment of heart problems and high blood pressure) reduce the break-down of Inspra®, thereby prolonging the effect of the medicine on the body.
- St. John's Wort (herbal preparation), rifampicin (used to treat bacterial infections), carbamazepine, phenytoin and phenobarbital (used, among others to treat epilepsy) may increase the break-down of Inspra® and thus decrease its effect.

Using this medicine and food
The medicine can be taken with or without food. Swallow the tablet with plenty of water.

Pregnancy and breastfeeding
If you are pregnant or breastfeeding, think you are pregnant or are planning to become pregnant, consult your doctor or pharmacist before taking this medicine. The effect of Inspra® has not been evaluated during pregnancy in humans.
It is not known whether the active ingredient of the medicine is excreted into breast milk. A decision should be made with your doctor, whether to discontinue breastfeeding or to discontinue the drug.

Driving and using machines
You may feel dizziness after taking Inspra®. If this should happen, do not drive or operate machinery.

Important information about some of this medicine's ingredients
Inspra® contains lactose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.
Inspra® contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

3. HOW TO USE THIS MEDICINE?

Always use this preparation according to your doctor's instructions. Check with the doctor or pharmacist if you are uncertain about the dosage and treatment regimen of the preparation. The dosage and treatment regimen will be determined by your doctor only.
Do not exceed the recommended dose.
The medicine can be taken with food or on an empty stomach. Swallow the tablet whole with plenty of water.
Do not crush/split/chew, since the tablet is film-coated.

If you have accidentally taken a higher dosage
If you have taken too much of the medicine, the most likely symptoms will be low blood pressure (expressed as light feeling in your head, dizziness, blurred vision, weakness, acute loss of consciousness) or hyperkalemia – high potassium levels in the blood (expressed by muscle cramps, diarrhea, nausea, dizziness and headache).

If you have taken an overdose, or if a child has accidentally swallowed some medicine, immediately see a doctor or go to a hospital emergency room and bring the medicine package with you.

If you forget to take the medicine
If it is time to take your next tablet, skip the tablet you missed and take your next tablet when it is due.
Otherwise take the tablet as soon as you remember, provided that there is more than 12 hours to when you are due to take your next tablet. Then go back to taking your medicine as you would normally.
Do not take a double dose to make up for the forgotten tablet.

Adhere to the treatment as recommended by your doctor.
Even if your health improves, do not stop taking this medicine without consulting your doctor.

Do not take medicines in the dark! Check the label and the dose <u>each time</u> you take medicine. Wear glasses if you need them.
If you have any further questions about using this medicine, consult your doctor or pharmacist.

4. SIDE EFFECTS

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

Immediately seek medical treatment in case of:

- swelling of the face, tongue or throat
- difficulty swallowing
- hives and difficulties breathing

These are the symptoms of angioneurotic oedema, an uncommon side effect occurring in 1-10 of 1,000 users.

Additional side effects

Common side effects occurring in 1-10 of 100 users:

- high potassium levels in the blood (symptoms include muscle cramps, diarrhea, nausea, dizziness or headache)
- fainting
- dizziness
- elevated quantity of cholesterol in the blood
- insomnia
- headache
- heart-related problems e.g. irregular heartbeat and heart failure
- cough
- constipation
- low blood pressure
- diarrhea
- nausea
- vomiting
- abnormal functioning of the kidney
- rash
- itching
- back pain
- feeling weak
- muscle spasms
- increased urea levels in the blood
- increased creatinine blood levels which may indicate kidney problems

Uncommon side effects occurring in 1-10 of 1,000 users:

- infection
- eosinophilia (increase in certain white blood cells)
- low sodium blood levels
- dehydration
- elevated levels of triglycerides (fats) in the blood
- fast heartbeat
- inflammation of the gallbladder
- decreased blood pressure that may cause dizziness upon standing
- thrombosis (blood clot) in the leg
- sore throat
- flatulence
- underactive thyroid
- increase in blood glucose levels
- reduced sense of touch
- increased sweating
- musculoskeletal pain
- feeling generally unwell
- kidney inflammation
- enlargement of breasts in men

- changes in some blood test results

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health homepage (www.health.gov.il) which links to an online form for reporting side effects, or by using the link: https://sideeffects.health.gov.il

5. HOW TO STORE THE MEDICINE?

- Prevent poisoning! This 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 unless explicitly instructed to do so by a doctor.
- Do not use the medicine after the expiry date (exp. date) which is stated on the package. The expiry date refers to the last day of that month.

Storage conditions

- Store the medicine below 25°C.

6. FURTHER INFORMATION

In addition to the active ingredient, the medicine also contains:
lactose monohydrate, microcrystalline cellulose, croscarmellose sodium, hypromellose, sodium lauryl sulfate, talc, magnesium stearate, titanium dioxide, macrogol 400, polysorbate 80, iron oxide yellow, iron oxide red.

The medicine contains lactose:
Inspra® 25 mg: 35.7 mg lactose monohydrate.
Inspra® 50 mg: 71.4 mg lactose monohydrate.

What the medicine looks like and contents of the package:
Inspra® 25 mg: A yellow-colored, film-coated tablet with 'Pfizer' imprinted on one side and 'NSR' and '25' on the other side.
Inspra® 50 mg: A yellow-colored, film-coated tablet with 'Pfizer' imprinted on one side and 'NSR' and '50' on the other side.

Authorized pack sizes: 10, 20, 28, 30, 50, 100, 200 tablets.
Not all package sizes may be marketed.

Registration holder: Pfizer PFE Pharmaceuticals Israel Ltd., 9 Shenkar St., Herzliya Pituach 46725.

Registration number of the medicine in the Ministry of Health's National Drug Registry:
Inspra® 25 mg: 134.67.31192
Inspra® 50 mg: 134.68.31193

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