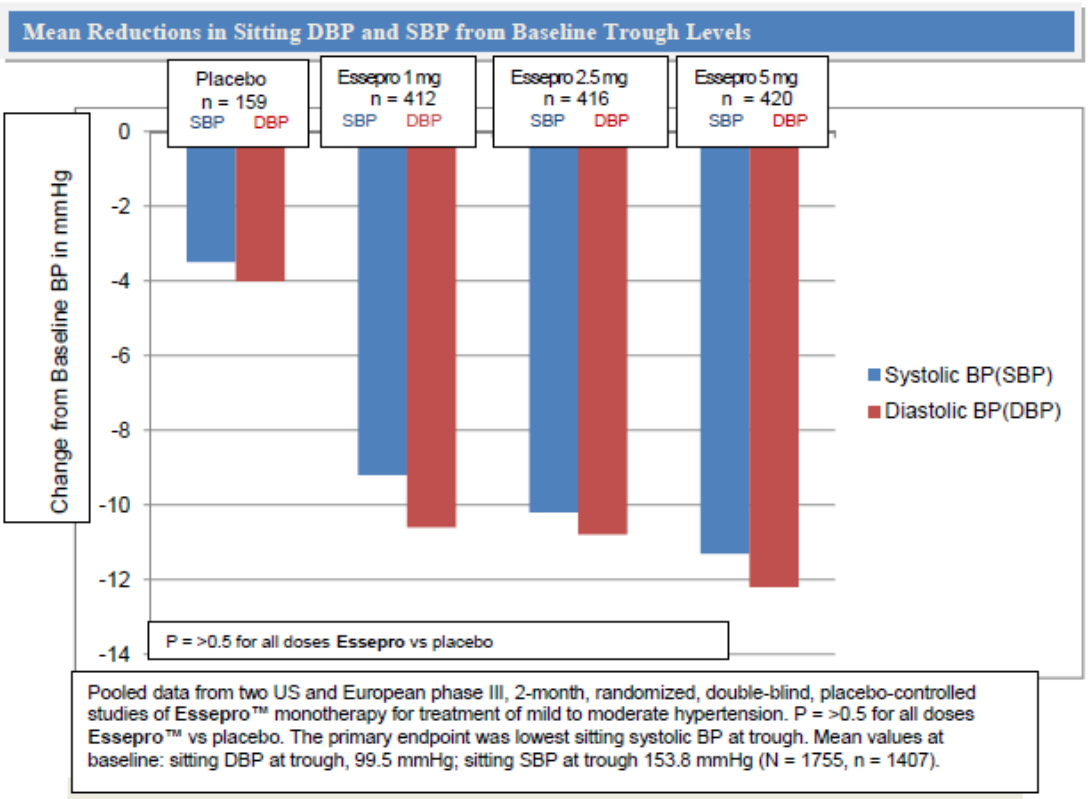
The pharmaceutical advertisement displayed on the next 2 pages is for use with the 2 items on the third page.

Essepro™ (lesystolol) Reduces Blood Pressure Significantly

In 2-month studies
Essepro™ therapy alone showed meaningful reductions in blood pressure[1]



Pooled data from two US and European phase III, 2-month, randomized, double-blind, placebo-controlled studies of **Essepro™** monotherapy for treatment of mild to moderate hypertension. P = >0.5 for all doses **Essepro™** vs placebo. The primary endpoint was lowest sitting systolic BP at trough. Mean values at baseline: sitting DBP at trough, 99.5 mmHg; sitting SBP at trough 153.8 mmHg (N = 1755, n = 1407).

In Clinical Studies **Essepro™** demonstrated:

- Significant reductions in heart rate[2]
  - Heart rate decreased 6-9 BPM across all dosing groups[1]
- Further BP reductions when used in combination with other BP medication[1,2]
  - In a separate combination treatment study of Essepro with ACRIs and/or diuretics
- Significant BP reductions in women
  - Similar BP reductions for women and men across dose groups
- Meaningful BP reductions in Black patients[3]
  - In a separate 2-month study, therapy with Essepro alone showed statistically significant reductions but less than those reductions seen in non-Black patients
  - Added BP reductions were seen when Essepro was combined with ACRIs and/or diuretics

Essepro is a beta-adrenergic blocking agent indicated for the treatment of hypertension.

References: 1. **Essepro** [package insert]. Radnor ,PA: NB Pharma Inc, 2009. 2. Data on file, NB Pharma, Inc. 3. Jones RF, Smith PL, Green, MM. Efficacy and safety of lesystolol alone and in combination therapy in African-American patients. J Hypertens 2008;7:655-661.

Essepro §™
(lesystolol) capsules
www.essepro.com

Well-tolerated at all doses with low rate of side effects

Percentage of Adverse Events by Dose, Occurring More Frequently in **Essepro™** than Placebo Patients, and in ≥1% of Patients

	Placebo n = 208	Essepro 1 mg n = 461	Essepro 2.5 mg n = 464	Essepro 5 mg n = 622
Adverse Event	%	%	%	%
Dizziness	2	6	5	8
Headache	1	5	7	6
Fatigue	1	2	3	3
Nausea	1	0	2	2
Dyspnea	0	1	1	1
Chest Pain	1	0	2	1
Peripheral Edema	1	1	0	2
Bradycardia	0	2	0	1
Rash	0	0	1	1

Pooled results from three US and European, phase III, 2-month, randomized, double-blind, placebo-controlled studies of Essepro in the treatment of mild to moderate hypertension (N = 2043, n = 1862).

Most side effects were mild and did not require discontinuation of Essepro™[1]

- Most adverse events were assessed as mild by investigators and treatment was continued[1]
- Few patients discontinued treatment due to adverse events, 2.6% for Essepro vs 2.1% for placebo[1]

No significant interactions with commonly used medications were observed[1]

- No significant interactions with hydrochlorothiazide, furosemide, losartan or lisinopril[1]
- No significant interactions with digoxin, warfarin or simvastatin[1]
- Drugs that inhibit CYP2C9 can increase plasma levels of Essepro. Patients on Essepro who are also treated with drugs that inhibit or induce this enzyme should be monitored closely, and dosage of Essepro may need to be adjusted based on blood pressure response[1]

Important Safety Information

Patients treated with Essepro should be advised against sudden discontinuation of therapy. When discontinuing therapy, dosage should be gradually tapered over 2 weeks.

Essepro is contraindicated in patients with bradycardia, heart block greater than first degree, cardiogenic shock, decompensated cardiac failure, severe hepatic impairment, and in patients who are hypersensitive to any component of this product.

Essepro should be used with caution in patients with peripheral vascular disease, renal impairment or thyrotoxicosis. Caution should be used in diabetics, as beta blockers may mask some manifestations of hypoglycemia.

In general, patients with bronchospastic disease should not receive beta blockers.

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A 65-year-old woman comes to the office for blood pressure medication management. Medical history is significant for poorly controlled hypertension, psoriasis, and psoriatic arthritis previously treated with methotrexate. Additional medical history is significant for alcohol use disorder and elevated liver function tests. Medications include enalapril, spironolactone, and topical corticosteroids. Vital signs are normal except for a blood pressure of 160/104 mm Hg. Physical examination discloses thick, scaly plaques on the scalp, buttocks, and upper and lower extremities. There are several spider angiomata on the chest and abdomen. The abdomen is distended and a fluid wave is noted. She has 2+ lower extremity edema. The patient says she would like to try a new drug called Essepro to treat her hypertension because she can get a 3-month supply of the medication for free.

1. Which of the following is the most appropriate response to the patient's request for the medication?

   (A) Essepro should be prescribed because she can get it for free
   (B) Essepro should not be prescribed because it can worsen her psoriasis
   (C) Essepro should not be prescribed because it is similar to her other medications
   (D) Essepro should not be prescribed because the patient has severe liver disease
   (E) Essepro should only be used for hypertensive emergencies

(Answer: D)

2. Which of the following interpretations can be made correctly from the graph on blood pressure reduction in the advertisement?

   (A) Blood pressure reduction from the three doses of Essepro cannot be compared to reduction with placebo because the number of patients on active drugs are higher than the number of patients on placebo
   (B) Doubling the highest dose of Essepro will decrease diastolic pressure from baseline by at least 15 mm Hg
   (C) The highest dose of Essepro should be used because it offers the greatest benefit
   (D) There is no clinically important difference in blood pressure reduction between the three dose groups
   (E) The significance of drug effect vs placebo cannot be determined because of the low P value

(Answer: D)