NEXLETOL® (bempedoic acid) tablets

NEXLIZET® (bempedoic acid and ezetimibe) tablets

When sufficient LDL-C reduction feels difficult to achieve,[1-3]

ADD EFFICACY. ADD POWER. ADD NEXLETOL or NEXLIZET

For appropriate patients currently on maximally tolerated statin therapy, with or without other lipid-lowering therapies[1,2]

In clinical trials, NEXLETOL delivered up to an 18% mean reduction, and NEXLIZET delivered a 38% mean reduction, in LDL-C (compared to placebo) when added to maximally tolerated statin dose (*P*<0.001)[1,2*†‡]

*LDL-C changes from baseline (LS mean) in CLEAR Harmony: NEXLETOL: -17% (n=1,488); placebo: +2% (n=742).[1,4]
†LDL-C changes from baseline (LS mean) in CLEAR Wisdom: NEXLETOL: -15% (n=522); placebo: +2% (n=257).[1,5]
‡LDL-C changes from baseline (LS mean) in 053 Trial: NEXLIZET: -36% (n=86); placebo: +2% (n=41). LDL-C changes from baseline (LS mean) for other drugs in the trial: NEXLETOL: -17% (n=88); ezetimibe: -23% (n=86).[2,3]

LDL-C=low-density lipoprotein cholesterol; LS=least squares.

INDICATION

NEXLETOL and NEXLIZET are indicated as adjuncts to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia or established atherosclerotic cardiovascular disease who require additional lowering of LDL-C.
Limitations of Use: The effect of NEXLETOL and NEXLIZET on cardiovascular morbidity and mortality has not been determined.

IMPORTANT SAFETY INFORMATION

Contraindications: NEXLETOL has no contraindications. NEXLIZET is contraindicated in patients with a known hypersensitivity to ezetimibe tablets. Hypersensitivity reactions including anaphylaxis, angioedema, rash, and urticaria have been reported with ezetimibe.

Please see additional Important Safety Information throughout and full Prescribing Information for NEXLETOL and NEXLIZET.

ADD NEXLETOL OR NEXLIZET: Powerful add-on LDL-C lowering[1-7]

SIGNIFICANT ADDITIONAL LDL-C REDUCTION FOR APPROPRIATE PATIENTS CURRENTLY ON MAXIMALLY TOLERATED STATIN THERAPY, WITH OR WITHOUT OTHER LIPID-LOWERING THERAPIES

High CV risk patients with ASCVD and/or HeFH not at LDL-C goal

Statin +/– Ezetimibe + NEXLETOL® (bempedoic acid) tablets

UP TO **18%**

MEAN LDL-C REDUCTION VS PLACEBO*†

High CV risk patients with ASCVD and/or HeFH not at LDL-C goal

Statin + NEXLIZET® (bempedoic acid and ezetimibe) tablets

38%

MEAN LDL-C REDUCTION VS PLACEBO‡

SAFETY PROFILES WITH INCIDENCE OF MOST COMMON ARs GENERALLY COMPARABLE TO PLACEBO[1,3]

ORAL, ONCE-DAILY TABLETS USED AS ADD-ONS TO MAXIMALLY TOLERATED STATIN THERAPY, WITH OR WITHOUT OTHER LIPID-LOWERING THERAPIES[1,2]

FIRST-IN-CLASS BEMPEDOIC ACID: THE ONLY ACL INHIBITOR WITH A MECHANISM COMPLEMENTARY TO STATINS[1,2,8-10]

- Bempedoic acid, the active ingredient in NEXLETOL and a component of NEXLIZET, has a targeted mechanism of action that works upstream from statins

*LDL-C changes from baseline (LS mean) at Week 12 in CLEAR Harmony: NEXLETOL: -17% (n=1,488); placebo: +2% (n=742) (*P*<0.001).[1,4]
†LDL-C changes from baseline (LS mean) at Week 12 in CLEAR Wisdom: NEXLETOL: -15% (n=522); placebo: +2% (n=257) (*P*<0.001).[1,5]
‡LDL-C changes from baseline (LS mean) at Week 12 in 053 Trial: NEXLIZET: -36% (n=86); placebo: +2% (n=41) (*P*<0.001). LDL-C changes from baseline (LS mean) at Week 12 for other drugs in the trial: NEXLETOL: -17% (n=88); ezetimibe: -23% (n=86).[2,3]

CLEAR Harmony (Study 1) was a 52-week, randomized, double-blind, Phase 3 trial in 2,230 patients randomized 2:1 to receive NEXLETOL (n=1,488) or placebo (n=742). CLEAR Harmony included patients aged ≥18 years with fasting LDL-C ≥70 mg/dL, and high-risk patients with ASCVD and/or HeFH. NEXLETOL was added to whatever patient's maximally tolerated statin dose was, either alone or with other lipid-lowering therapies. Primary endpoint was general safety, which included ARs, clinical safety laboratories, physical examinations, vital signs, and electrocardiogram. Secondary endpoint was % change from baseline to Week 12 in LDL-C.[4,6]

CLEAR Wisdom (Study 2) was a 52-week, randomized, double-blind, Phase 3 trial in 779 patients randomized 2:1 to receive NEXLETOL (n=522) or placebo (n=257). CLEAR Wisdom included patients aged ≥18 years with fasting LDL-C ≥70 mg/dL, and high-risk patients with ASCVD and/or HeFH. NEXLETOL was added to whatever patient's maximally tolerated statin dose was (including no statin at all) either alone or with other lipid-lowering therapies. Primary endpoint was % change from baseline to Week 12 in LDL-C. Secondary endpoints were % change from baseline to Week 24 in LDL-C, % change from baseline to Week 12 in non-HDL-C, total C, apolipoprotein B, and hsCRP, and absolute change from baseline to Weeks 12 and 24 in LDL-C.[5,7]

053 Trial (Study 1) was a 12-week, randomized, double-blind, Phase 3 trial in 301 patients randomized 2:2:2:1 to receive NEXLIZET (n=86), NEXLETOL (n=88), ezetimibe (n=86), or placebo (n=41). 053 Trial included patients aged ≥18 years with fasting LDL-C ≥100 mg/dL if they had ASCVD and/or HeFH, or ≥130 mg/dL if they had multiple CV risk factors. Therapies were added to whatever patient's maximally tolerated statin dose was (including no statin at all), either alone or with other lipid-lowering therapies. Primary endpoint was % change from baseline to Week 12 in LDL-C. Secondary endpoint was % change from baseline to Week 12 in hsCRP, non-HDL-C, total C, apolipoprotein B, HDL-C, and TGs.[2,3]

CV=cardiovascular; ASCVD=atherosclerotic cardiovascular disease; HeFH=heterozygous familial hypercholesterolemia; AR=adverse reaction; non-HDL-C=non-high-density lipoprotein cholesterol; total C=total cholesterol; hsCRP=high-sensitivity C-reactive protein; TGs=triglycerides.

IMPORTANT SAFETY INFORMATION (cont.)

Warnings and Precautions: *Hyperuricemia:* Bempedoic acid, a component of NEXLETOL and NEXLIZET, may increase blood uric acid levels. Hyperuricemia may occur early in treatment and persist throughout treatment, and may lead to the development of gout, especially in patients with a history of gout. Assess uric acid levels periodically as clinically indicated. Monitor for signs and symptoms of hyperuricemia, and initiate treatment with urate-lowering drugs as appropriate.

ACL=adenosine triphosphate citrate lyase.

IMPORTANT SAFETY INFORMATION (cont.)

Warnings and Precautions (cont.): *Tendon Rupture:* Bempedoic acid is associated with an increased risk of tendon rupture or injury. In clinical trials, tendon rupture occurred in 0.5% of patients treated with bempedoic acid versus 0% of patients treated with placebo, and involved the rotator cuff (the shoulder), biceps tendon, or Achilles tendon. Tendon rupture occurred within weeks to months of starting bempedoic acid. Tendon rupture may occur more frequently in patients over 60 years of age, patients taking corticosteroid or fluoroquinolone drugs, patients with renal failure, and patients with previous tendon disorders. Discontinue NEXLETOL or NEXLIZET at the first sign of tendon rupture. Avoid NEXLETOL and NEXLIZET in patients who have a history of tendon disorders or tendon rupture.

Please see additional Important Safety Information throughout and full Prescribing Information for NEXLETOL and NEXLIZET.

NEXLETOL® (bempedoic acid) tablets

NEXLIZET® (bempedoic acid and ezetimibe) tablets

ADD NEXLETOL: GET THEIR LDL-C CLOSER TO WHERE YOU WANT THEM TO BE

CLEAR Harmony and CLEAR Wisdom results showed up to a significant 18% mean LDL-C reduction compared to placebo at 12 weeks, for extra control[1,4,5]

CLEAR HARMONY

18% **LDL-C REDUCTION** VS PLACEBO

LDL-C changes from baseline (LS mean):
NEXLETOL: -17% (n=1,488); placebo: +2% (n=742) (*P*<0.001)

CLEAR WISDOM

17% **LDL-C REDUCTION** VS PLACEBO

LDL-C changes from baseline (LS mean):
NEXLETOL: -15% (n=522); placebo: +2% (n=257) (*P*<0.001)

CLEAR Harmony (Study 1) was a 52-week, randomized, double-blind, Phase 3 trial in 2,230 patients randomized 2:1 to receive NEXLETOL (n=1,488) or placebo (n=742). CLEAR Harmony included patients aged ≥18 years with fasting LDL-C ≥70 mg/dL, and high-risk patients with ASCVD and/or HeFH. NEXLETOL was added to whatever patient's maximally tolerated statin dose was, either alone or with other lipid-lowering therapies. Primary endpoint was general safety, which included ARs, clinical safety laboratories, physical examinations, vital signs, and electrocardiogram. Secondary endpoint was % change from baseline to Week 12 in LDL-C.[4,6]

CLEAR Wisdom (Study 2) was a 52-week, randomized, double-blind, Phase 3 trial in 779 patients randomized 2:1 to receive NEXLETOL (n=522) or placebo (n=257). CLEAR Wisdom included patients aged ≥18 years with fasting LDL-C ≥70 mg/dL, and high-risk patients with ASCVD and/or HeFH. NEXLETOL was added to whatever patient's maximally tolerated statin dose was (including no statin at all) either alone or with other lipid-lowering therapies. Primary endpoint was % change from baseline to Week 12 in LDL-C. Secondary endpoints were % change from baseline to Week 24 in LDL-C, % change from baseline to Week 12 in non-HDL-C, total C, apolipoprotein B, and hsCRP, and absolute change from baseline to Weeks 12 and 24 in LDL-C.[5,7]

IMPORTANT SAFETY INFORMATION (cont.)

Adverse Reactions: In NEXLETOL clinical trials, the most commonly reported adverse reactions were upper respiratory tract infection, muscle spasms, hyperuricemia, back pain, abdominal pain or discomfort, bronchitis, pain in extremity, anemia, and elevated liver enzymes. Reactions reported less frequently, but still more often than with placebo, included benign prostatic hyperplasia and atrial fibrillation.

ADD NEXLETOL: A SAFETY PROFILE WITH INCIDENCE OF MOST COMMON ARs GENERALLY COMPARABLE TO PLACEBO

Based on a pooled analysis of 2 clinical studies of up to 52 weeks in duration[1]

ARs OCCURRING IN ≥2% OF PATIENTS WITH ASCVD AND HeFH USING NEXLETOL (AND MORE FREQUENTLY THAN PLACEBO)[1]

Adverse reaction	NEXLETOL* (n=2,009)	Placebo (n=999)
Upper respiratory tract infection	4.5%	4.0%
Muscle spasms	3.6%	2.3%
Hyperuricemia†	3.5%	1.1%
Back pain	3.3%	2.2%
Abdominal pain or discomfort‡	3.1%	2.2%
Bronchitis	3.0%	2.5%
Pain in extremity	3.0%	1.7%
Anemia	2.8%	1.9%
Elevated liver enzymes§	2.1%	0.8%

Discontinuation rates due to ARs[1]: NEXLETOL: 11%; placebo: 8%

*Patients received NEXLETOL 180 mg orally once daily plus maximally tolerated statin therapy alone or in combination with other lipid-lowering therapies.[1]
†Included patients with hyperuricemia and patients with increased blood uric acid.[1]
‡Included patients with abdominal pain, upper abdominal pain, lower abdominal pain, and abdominal discomfort.[1]
§Included patients with increased AST, increased ALT, increased hepatic enzyme, and increased liver function test.[1]

Tendon Rupture: NEXLETOL was associated with an increased risk of tendon rupture, occurring in 0.5% of NEXLETOL-treated patients versus 0% of placebo-treated patients. Gout: NEXLETOL was associated with an increased risk of gout, occurring in 1.5% of NEXLETOL-treated patients versus 0.4% of placebo-treated patients. Benign Prostatic Hyperplasia: NEXLETOL was associated with an increased risk of BPH or prostatomegaly in men with no reported history of BPH, occurring in 1.3% of NEXLETOL-treated patients versus 0.1% of placebo-treated patients. The clinical significance is unknown. Atrial Fibrillation: NEXLETOL was associated with an imbalance in atrial fibrillation, occurring in 1.7% of NEXLETOL-treated patients versus 1.1% of placebo-treated patients. Laboratory Tests: NEXLETOL was associated with persistent changes in multiple laboratory tests within the first 4 weeks of treatment. Laboratory test values returned to baseline following discontinuation of treatment.[1]

Incidence of skeletal muscle ARs comparable to placebo[1]

Muscle spasms: NEXLETOL: 3.6%; placebo: 2.3%

AST=aspartate aminotransferase; ALT=alanine aminotransferase; BPH=benign prostatic hyperplasia.

IMPORTANT SAFETY INFORMATION (cont.)

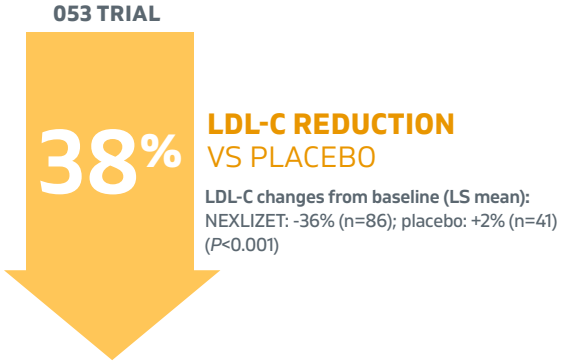
Adverse Reactions (cont.): In the NEXLIZET clinical trial, the most commonly reported adverse reactions observed with NEXLIZET, but not observed in clinical trials of bempedoic acid or ezetimibe, a component of NEXLIZET, and occurring more frequently than with placebo, were urinary tract infection, nasopharyngitis, and constipation.

Please see additional Important Safety Information throughout and full Prescribing Information for NEXLETOL and NEXLIZET.

NEXLETOL® (bempedoic acid) tablets

ADD NEXLIZET: A SINGLE TABLET THAT COMBINES THE BENEFITS OF NEXLETOL AND EZETIMIBE

Significant 38% mean LDL-C reduction compared to placebo at 12 weeks, for extra control[2,3]



LDL-C reductions from baseline (LS mean) for other drugs in the trial:
- NEXLETOL: -17% (n=88); ezetimibe: -23% (n=86)

053 Trial (Study 1) was a 12-week, randomized, double-blind, Phase 3 trial in 301 patients randomized 2:2:2:1 to receive NEXLIZET (n=86), NEXLETOL (n=88), ezetimibe (n=86), or placebo (n=41). 053 Trial included patients aged ≥18 years with fasting LDL-C ≥100 mg/dL if they had ASCVD and/or HeFH, or ≥130 mg/dL if they had multiple CV risk factors. Therapies were added to whatever patient's maximally tolerated statin dose was (including no statin at all), either alone or with other lipid-lowering therapies. Primary endpoint was % change from baseline to Week 12 in LDL-C. Secondary endpoint was % change from baseline to Week 12 in hsCRP, non-HDL-C, total C, apolipoprotein B, HDL-C, and TGs.[2,3]

APPROVED

NEXLIZET: THE ONLY FDA-APPROVED LIPID-LOWERING THERAPY COMBINING THE POWER OF NEXLETOL AND EZETIMIBE[2]

IMPORTANT SAFETY INFORMATION (cont.)

Adverse Reactions (cont.): Adverse reactions reported in clinical trials of ezetimibe, and occurring at an incidence greater than with placebo, included upper respiratory tract infection, diarrhea, arthralgia, sinusitis, pain in extremity, fatigue, and influenza. Other adverse reactions reported in postmarketing use of ezetimibe included hypersensitivity reactions, including anaphylaxis, angioedema, rash, and urticaria; erythema multiforme; myalgia; elevated creatine phosphokinase; myopathy/rhabdomyolysis; elevations in liver transaminases; hepatitis; abdominal pain; thrombocytopenia; pancreatitis; nausea; dizziness; paresthesia; depression; headache; cholelithiasis; cholecystitis.

ADD NEXLIZET: A SAFETY PROFILE WITH INCIDENCE OF MOST COMMON ARs GENERALLY COMPARABLE TO PLACEBO

Based on a 4-arm, 12-week, randomized, double-blind, placebo-controlled, parallel group, factorial trial[2]

ARs OCCURRING IN ≥3% OF PATIENTS IN THE NEXLIZET GROUP[3]

Adverse reaction	NEXLIZET (n=85)	NEXLETOL (n=88)	Ezetimibe (n=86)	Placebo (n=41)
Urinary tract infection	5.9%	3.4%	2.3%	2.4%
Nasopharyngitis	4.7%	6.8%	4.7%	0.0%
Constipation	4.7%	0.0%	2.3%	0.0%
Back pain	3.5%	3.4%	2.3%	4.9%
Fatigue	3.5%	2.3%	1.2%	0.0%
Upper respiratory tract infection	3.5%	1.1%	0.0%	0.0%
Blood creatinine increased	3.5%	1.1%	0.0%	0.0%
Blood uric acid increased	3.5%	1.1%	0.0%	0.0%
Bronchitis	3.5%	0.0%	3.5%	0.0%

Discontinuation rates due to ARs[2]: NEXLIZET: 8%; NEXLETOL: 10%; ezetimibe: 12%; placebo: 5%
- Most common reason for NEXLIZET treatment discontinuation was oral discomfort (NEXLIZET: 2%; placebo: 0%)

Incidence of ARs occurring in pivotal trials of NEXLETOL or ezetimibe that did not occur at a significant rate in the pivotal trial of NEXLIZET above[2]

- **Pivotal trials for NEXLETOL:** ARs occurring in ≥2% of patients with ASCVD and HeFH using NEXLETOL* (and more frequently than placebo) included muscle spasms (NEXLETOL: 3.6%; placebo: 2.3%), hyperuricemia† (3.5%; 1.1%), abdominal pain or discomfort‡ (3.1%; 2.2%), pain in extremity (3.0%; 1.7%), anemia (2.8%; 1.9%), and elevated liver enzymes§ (2.1%; 0.8%). For more information, please see page 5 of this Visual Aid
- **Pivotal trials for ezetimibe:** ARs occurring in ≥2% of patients using ezetimibe (and at an incidence greater than placebo), regardless of causality, included diarrhea (ezetimibe: 4.1%; placebo: 3.7%), arthralgia (3.0%; 2.2%), sinusitis (2.8%; 2.2%), pain in extremity (2.7%; 2.5%), and influenza (2.0%; 1.5%)

*Patients received NEXLETOL 180 mg orally once daily plus maximally tolerated statin therapy alone or in combination with other lipid-lowering therapies.[2]
†Included patients with hyperuricemia and patients with increased blood uric acid.[2]
‡Included patients with abdominal pain, upper abdominal pain, lower abdominal pain, and abdominal discomfort.[2]
§Included patients with increased AST, increased ALT, increased hepatic enzyme, and increased liver function test.[2]

IMPORTANT SAFETY INFORMATION (cont.)

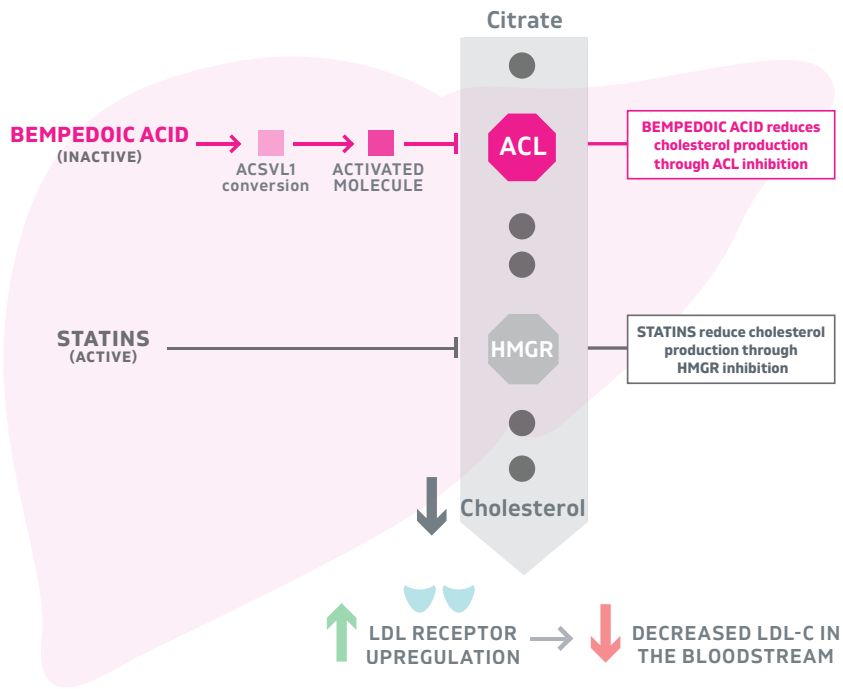
Drug Interactions: *Simvastatin and Pravastatin:* Concomitant use with bempedoic acid results in increased concentrations and increased risk of simvastatin or pravastatin-related myopathy. Use of either NEXLETOL or NEXLIZET with greater than 20 mg of simvastatin or 40 mg of pravastatin should be avoided.

Please see additional Important Safety Information throughout and full Prescribing Information for NEXLETOL and NEXLIZET.

NEXLIZET® (bempedoic acid and ezetimibe) tablets

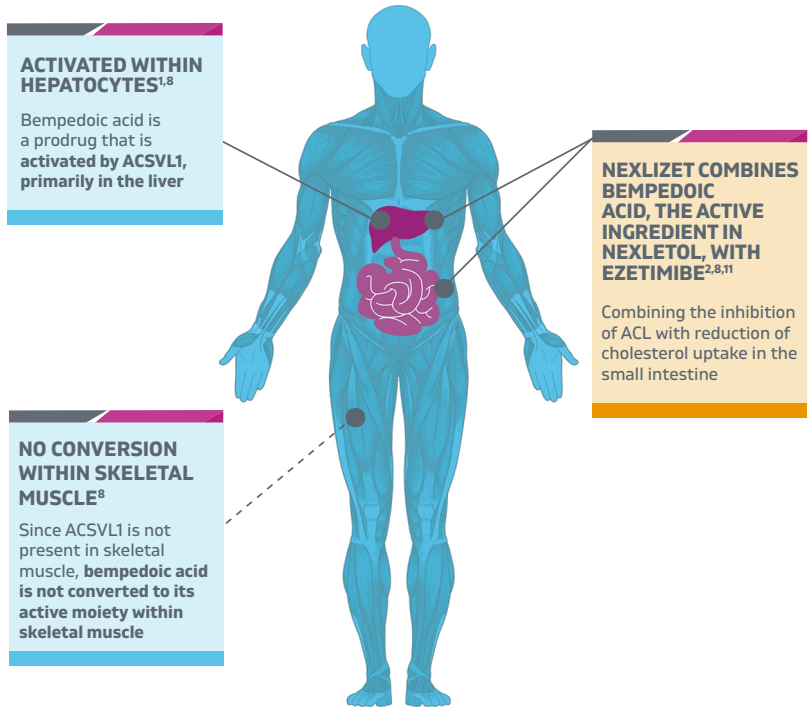
Bempedoic acid, the active ingredient in NEXLETOL, and a component of NEXLIZET, has a targeted mechanism of action that works upstream from statins[1,2,8-10]

BEMPEDOIC ACID REDUCES CHOLESTEROL BIOSYNTHESIS TO LOWER LDL-C



ACSVL1=very long-chain acyl-coenzyme A synthetase-1; HMGR=3-hydroxy-3-methyl-glutaryl-coenzyme A reductase.

Bempedoic acid is primarily activated in the liver[1,8]



IMPORTANT SAFETY INFORMATION (cont.)

Drug Interactions (cont.): *Cyclosporine:* Caution should be exercised when using NEXLIZET and cyclosporine concomitantly due to increased exposure to both ezetimibe and cyclosporine. Monitor cyclosporine concentrations in patients receiving NEXLIZET and cyclosporine. In patients treated with cyclosporine, the potential effects of the increased exposure to ezetimibe from concomitant use should be carefully weighed against the benefits of alterations in lipid levels provided by NEXLIZET.

Please see additional Important Safety Information throughout and full Prescribing Information for NEXLETOL and NEXLIZET.

NEXLETOL® (bempedoic acid) tablets

NEXLIZET® (bempedoic acid and ezetimibe) tablets

NEXLETOL and NEXLIZET have the flexibility to be combined with other lipid-lowering medications for appropriate patients[1,2†]

- ORAL, ONCE-DAILY TABLETS
- TAKEN WITH OR WITHOUT FOOD
- DO NOT NEED TO BE TITRATED*
- DO NOT REQUIRE REFRIGERATION FOR STORAGE

*Concomitant use of simvastatin or pravastatin with NEXLETOL, or of simvastatin, pravastatin, cyclosporine, fibrates, or cholestyramine with NEXLIZET, may require adjustments for these medications.[1,2]

NEXLETOL	NEXLIZET
 One 180-mg tablet for all appropriate patients[1]	 One 180-mg bempedoic acid/ 10-mg ezetimibe tablet for all appropriate patients[2]

Pill images are not actual size.

Lipid levels should be analyzed within 8 to 12 weeks after initiation of NEXLETOL or NEXLIZET.[1,2]

NEXLETOL and NEXLIZET are appropriate for patients with ASCVD and/or HeFH requiring additional LDL-C lowering[1,2‡§]

†Administer NEXLIZET either at least 2 hours before, or at least 4 hours after, bile acid sequestrants.[2]
‡ASCVD is defined as acute coronary syndromes, a history of MI, stable or unstable angina, coronary or other arterial revascularization, stroke, TIA, or PAD presumed to be of atherosclerotic origin.[3,4,12]
§HeFH is defined as patients with a family history of elevated LDL-C or premature CAD, and with LDL-C ≥190 mg/dL without lipid-lowering therapies.[3,4,13,14]

MI=myocardial infarction; TIA=transient ischemic attack; PAD=peripheral arterial disease; CAD=coronary artery disease.

IMPORTANT SAFETY INFORMATION (cont.)

Drug Interactions (cont.): *Fibrates:* Coadministration of NEXLIZET with fibrates other than fenofibrate is not recommended. Fenofibrate and ezetimibe may increase cholesterol excretion into the bile, leading to cholelithiasis. If cholelithiasis is suspected in a patient receiving NEXLIZET and fenofibrate, gallbladder studies are indicated and alternative lipid-lowering therapy should be considered.

NEXLETOL and NEXLIZET have broad coverage for your patients on both commercial and Medicare Part D plans

WITH THE CO-PAY CARD, ELIGIBLE PATIENTS MAY PAY AS LITTLE AS $10 PER FILL FOR UP TO A 3-MONTH SUPPLY OF NEXLETOL OR NEXLIZET‖

‖Certain restrictions apply. See Terms and Conditions at NEXLETOLHCP.com/access.

IMPORTANT SAFETY INFORMATION (cont.)

Drug Interactions (cont.): *Cholestyramine:* Concomitant use of NEXLIZET and cholestyramine decreases ezetimibe concentration. This may result in a reduction of efficacy. Administer NEXLIZET either at least 2 hours before, or at least 4 hours after, bile acid sequestrants.

Lactation and Pregnancy: It is not recommended that NEXLETOL or NEXLIZET be taken during breastfeeding. Discontinue NEXLETOL or NEXLIZET when pregnancy is recognized, unless the benefits of therapy outweigh the potential risks to the fetus. Based on the mechanism of action of bempedoic acid, NEXLETOL and NEXLIZET may cause fetal harm.

Please see additional Important Safety Information throughout and full Prescribing Information for NEXLETOL and NEXLIZET.

NEXLETOL® (bempedoic acid) tablets

NEXLIZET® (bempedoic acid and ezetimibe) tablets

INDICATION

NEXLETOL and NEXLIZET are indicated as adjuncts to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia or established atherosclerotic cardiovascular disease who require additional lowering of LDL-C.

Limitations of Use: The effect of NEXLETOL and NEXLIZET on cardiovascular morbidity and mortality has not been determined.

IMPORTANT SAFETY INFORMATION

Contraindications: NEXLETOL has no contraindications. NEXLIZET is contraindicated in patients with a known hypersensitivity to ezetimibe tablets. Hypersensitivity reactions including anaphylaxis, angioedema, rash, and urticaria have been reported with ezetimibe.

Warnings and Precautions: *Hyperuricemia:* Bempedoic acid, a component of NEXLETOL and NEXLIZET, may increase blood uric acid levels. Hyperuricemia may occur early in treatment and persist throughout treatment, and may lead to the development of gout, especially in patients with a history of gout. Assess uric acid levels periodically as clinically indicated. Monitor for signs and symptoms of hyperuricemia, and initiate treatment with urate-lowering drugs as appropriate.

Tendon Rupture: Bempedoic acid is associated with an increased risk of tendon rupture or injury. In clinical trials, tendon rupture occurred in 0.5% of patients treated with bempedoic acid versus 0% of patients treated with placebo, and involved the rotator cuff (the shoulder), biceps tendon, or Achilles tendon. Tendon rupture occurred within weeks to months of starting bempedoic acid. Tendon rupture may occur more frequently in patients over 60 years of age, patients taking corticosteroid or fluoroquinolone drugs, patients with renal failure, and patients with previous tendon disorders. Discontinue NEXLETOL or NEXLIZET at the first sign of tendon rupture. Avoid NEXLETOL and NEXLIZET in patients who have a history of tendon disorders or tendon rupture.

Adverse Reactions: In NEXLETOL clinical trials, the most commonly reported adverse reactions were upper respiratory tract infection, muscle spasms, hyperuricemia, back pain, abdominal pain or discomfort, bronchitis, pain in extremity, anemia, and elevated liver enzymes. Reactions reported less frequently, but still more often than with placebo, included benign prostatic hyperplasia and atrial fibrillation.

In the NEXLIZET clinical trial, the most commonly reported adverse reactions observed with NEXLIZET, but not observed in clinical trials of bempedoic acid or ezetimibe, a component of NEXLIZET, and occurring more frequently than with placebo, were urinary tract infection, nasopharyngitis, and constipation.

Adverse reactions reported in clinical trials of ezetimibe, and occurring at an incidence greater than with placebo, included upper respiratory tract infection, diarrhea, arthralgia, sinusitis, pain in extremity, fatigue, and influenza. Other adverse reactions reported in postmarketing use of ezetimibe included hypersensitivity reactions, including anaphylaxis, angioedema, rash, and urticaria; erythema multiforme; myalgia; elevated creatine phosphokinase; myopathy/rhabdomyolysis; elevations in liver transaminases; hepatitis; abdominal pain; thrombocytopenia; pancreatitis; nausea; dizziness; paresthesia; depression; headache; cholelithiasis; cholecystitis.

Drug Interactions: *Simvastatin and Pravastatin:* Concomitant use with bempedoic acid results in increased concentrations and increased risk of simvastatin or pravastatin-related myopathy. Use of either NEXLETOL or NEXLIZET with greater than 20 mg of simvastatin or 40 mg of pravastatin should be avoided.

Cyclosporine: Caution should be exercised when using NEXLIZET and cyclosporine concomitantly due to increased exposure to both ezetimibe and cyclosporine. Monitor cyclosporine concentrations in patients receiving NEXLIZET and cyclosporine. In patients treated with cyclosporine, the potential effects of the increased exposure to ezetimibe from concomitant use should be carefully weighed against the benefits of alterations in lipid levels provided by NEXLIZET.

Fibrates: Coadministration of NEXLIZET with fibrates other than fenofibrate is not recommended. Fenofibrate and ezetimibe may increase cholesterol excretion into the bile, leading to cholelithiasis. If cholelithiasis is suspected in a patient receiving NEXLIZET and fenofibrate, gallbladder studies are indicated and alternative lipid-lowering therapy should be considered.

Cholestyramine: Concomitant use of NEXLIZET and cholestyramine decreases ezetimibe concentration. This may result in a reduction of efficacy. Administer NEXLIZET either at least 2 hours before, or at least 4 hours after, bile acid sequestrants.

Lactation and Pregnancy: It is not recommended that NEXLETOL or NEXLIZET be taken during breastfeeding. Discontinue NEXLETOL or NEXLIZET when pregnancy is recognized, unless the benefits of therapy outweigh the potential risks to the fetus. Based on the mechanism of action of bempedoic acid, NEXLETOL and NEXLIZET may cause fetal harm.

References:
1. NEXLETOL. Prescribing information. ESPERION Therapeutics, Inc.; 2020. **2.** NEXLIZET. Prescribing information. ESPERION Therapeutics, Inc.; 11/2020. **3.** Data on file. CSR 1002-053. January 2019. **4.** Data on file. CSR 1002-040. October 2018. **5.** Data on file. CSR 1002-047. January 2019. **6.** Ray KK, Bays HE, Catapano AL, et al. Safety and efficacy of bempedoic acid to reduce LDL cholesterol. *N Engl J Med.* 2019;380(11):1022-1032. **7.** Goldberg AC, Leiter LA, Stroes ESG, et al. Effect of bempedoic acid vs placebo added to maximally tolerated statins on low-density lipoprotein cholesterol in patients at high risk for cardiovascular disease: the CLEAR Wisdom randomized clinical trial. *JAMA.* 2019;322(18):1780-1788. **8.** Pinkosky SL, Newton RS, Day EA, et al. Liver-specific ATP-citrate lyase inhibition by bempedoic acid decreases LDL-C and attenuates atherosclerosis. *Nat Commun.* 2016;7(13457):1-13. **9.** Pinkosky SL, Filippov S, Srivastava RA, et al. AMP-activated protein kinase and ATP-citrate lyase are two distinct molecular targets for ETC-1002, a novel small molecule regulator of lipid and carbohydrate metabolism. *J Lipid Res.* 2013;54(1):134-151. **10.** Saeed A, Ballantyne CM. Bempedoic acid (ETC-1002): a current review. *Cardiol Clin.* 2018;36(2):257-264. **11.** ZETIA. Prescribing information. Merck & Co., Inc.; 2013. **12.** Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol.* 2019;73(24):e285-e350. **13.** Diagnosis & Management. The FH Foundation. Accessed February 19, 2020. https://thefhfoundation.org/diagnosis-management **14.** Gidding SS, Champagne MA, de Ferranti SD, et al. The agenda for familial hypercholesterolemia: a scientific statement from the American Heart Association. *Circulation.* 2015;132(22):2167-2192.

Please see full Prescribing Information for NEXLETOL and NEXLIZET.

NEXLETOL® (bempedoic acid) tablets

NEXLIZET® (bempedoic acid and ezetimibe) tablets

ADD EFFICACY. ADD POWER. **ADD NEXLETOL OR NEXLIZET FOR APPROPRIATE PATIENTS**

SIGNIFICANT ADDITIONAL LDL-C REDUCTION FOR APPROPRIATE PATIENTS CURRENTLY ON MAXIMALLY TOLERATED STATIN THERAPY, WITH OR WITHOUT OTHER LIPID-LOWERING THERAPIES[1-7]

NEXLETOL	NEXLIZET
UP TO 18% MEAN LDL-C REDUCTION VS PLACEBO[1]	38% MEAN LDL-C REDUCTION VS PLACEBO[2]

SAFETY PROFILES WITH INCIDENCE OF MOST COMMON ARs GENERALLY COMPARABLE TO PLACEBO[1,3]

ORAL, ONCE-DAILY TABLETS, TAKEN WITH OR WITHOUT FOOD[1,2]

BEMPEDOIC ACID IS THE FIRST AND ONLY ACL INHIBITOR, WITH A MECHANISM COMPLEMENTARY TO STATINS[1,2,10]

NEXLETOL	NEXLIZET
• Works along the cholesterol biosynthesis pathway, 2 steps upstream from the target of statins[8] • Not activated in skeletal muscle[8]	• Combines bempedoic acid, the active ingredient in NEXLETOL, with ezetimibe for dual complementary mechanisms of action[2,8,11] • The only **FDA-approved** lipid-lowering therapy combining the power of NEXLETOL and ezetimibe[2]

Savings and Resources

Your patients may be eligible to pay less for their prescription. For more information, speak to your representative, or visit **NEXLETOLHCP.com/access**.

Need more info?

If you need more information about NEXLETOL or NEXLIZET, speak to your representative, call **1-833-377-7633** (8:00AM-8:00PM ET, Monday-Friday, excluding holidays), or visit **NEXLETOLHCP.com**.

INDICATION

NEXLETOL and NEXLIZET are indicated as adjuncts to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia or established atherosclerotic cardiovascular disease who require additional lowering of LDL-C.

Limitations of Use: The effect of NEXLETOL and NEXLIZET on cardiovascular morbidity and mortality has not been determined.

IMPORTANT SAFETY INFORMATION

Contraindications: NEXLETOL has no contraindications. NEXLIZET is contraindicated in patients with a known hypersensitivity to ezetimibe tablets. Hypersensitivity reactions including anaphylaxis, angioedema, rash, and urticaria have been reported with ezetimibe.

Please see additional Important Safety Information throughout and full Prescribing Information for NEXLETOL and NEXLIZET.

ESPERION

NEXLETOL® (bempedoic acid) tablets

NEXLIZET® (bempedoic acid and ezetimibe) tablets