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Statin Step Therapy Program Summary

FDA APPROVED INDICATIONS AND DOSAGE[1-12]
Single Ingredient Products

Agent(s)	Indication(s)	Dosage
Altoprev® (lovastatin extended release) Tablet	Adjunctive therapy to diet to: • Reduce the risk of MI, revascularization procedures, and angina in patients without CHD, but with multiple risk factors. • Slow the progression of coronary atherosclerosis in patients with CHD as part of a treatment strategy to lower Total-C and LDL-C. • Reduce elevated Total-C, LDL-C, Apo B, and TG levels and increase HDL-C in adult patients with primary hyperlipidemia (heterozygous familial and nonfamilial) and mixed dyslipidemia. Limitations of use: has not been studied in Fredrickson Types I, III, and V dyslipidemias.	The recommended dosing range is 20-60 mg once daily taken in the evening at bedtime.
Crestor® (rosuvastatin)[a] Tablet	Adjunctive therapy to diet for: • Adult patients with primary hyperlipidemia and mixed dyslipidemia to reduce elevated total-C, LDL-C, ApoB, nonHDL-C, and TG levels and to increase HDL-C • Pediatric patients 8 to 17 years of age with heterozygous familial hypercholesterolemia (HeFH) to reduce elevated total-C, LDL-C and ApoB after failing an adequate trial of diet therapy • Pediatric patients 7 to 17 years of age with homozygous familial hypercholesterolemia (HoFH) to reduce LDL-C, total-C, nonHDL-C and ApoB, either alone or with other lipid-lowering treatments • Adult patients with hypertriglyceridemia • Adult patients with primary dysbeta-lipoproteinemia (Type III hyperlipoproteinemia) • Slowing the progression of atherosclerosis as part of a treatment strategy to lower total-C and LDL-C Adult patients with homozygous familial hypercholesterolemia (HoFH) to reduce LDL-C, total-C, and ApoB	5-40 mg once daily. Use 40 mg dose only for patients not reaching LDL-C goal with 20 mg. Adult HoFH: starting dose 20 mg/day Pediatric patients with HeFH: 5 to 10 mg/day for patients 8 to less than 10 years of age, and 5 to 20 mg/day for patients 10 to 17 years of age. Pediatric patients with HoFH: 20 mg/day for patients 7 to 17 years of age.

 Effective: 12/01/2021

Agent(s)	Indication(s)	Dosage
	Risk reduction of MI, stroke, and arterial revascularization procedures in patients without clinically evident CHD, but with multiple risk factors Limitations of use: Not studied in Fredrickson Type I and V dyslipidemias	
Ezallor™ Sprinkle (rosuvastatin) Capsule	• Adult patients with hypertriglyceridemia as an adjunct to diet • Adult patients with primary dysbetalipoproteinemia (Type III hypercholesterolemia) as an adjunct to diet • Adult patients with homozygous familial hypercholesterolemia (HoFH) to reduce LDL-C, total-C, and ApoB Limitations of use: Not studied in Fredrickson Type I and V dyslipidemias	5-40 mg once daily. Use 40 mg dose only for patients not reaching LDL-C goal with 20 mg. Adult HoFH: Starting dose 20 mg once daily.
Flolipid™, Simvastatin oral suspension Oral suspension	Adjunctive therapy to diet to: • Reduce the risk of total mortality by reducing CHD deaths and reduce the risk of non-fatal MI, stroke, and the need for revascularization procedures in patients at high risk of coronary events. • Reduce elevated total-C, LDL-C, Apo B, TG and increase HDL-C in patients with primary hyperlipidemia (heterozygous familial and nonfamilial) and mixed dyslipidemia. • Reduce elevated TG in patients with hypertriglyceridemia and reduce TG and VLDL-C in patients with primary dysbetalipoproteinemia. • Reduce total-C and LDL-C in adult patients with homozygous familial hypercholesterolemia. • Reduce elevated total-C, LDL-C, and Apo B in boys and postmenarchal girls, 10 to 17 years of age with heterozygous familial hypercholesterolemia after failing an adequate trial of diet therapy. Limitations of use: Simvastatin has not been studied in Fredrickson Types I and V dyslipidemias.	Usual dosage range is 5 to 40 mg/day. The recommended usual starting dose is 10 or 20 mg once a day. Recommended starting dose for patients at high risk of a coronary heart disease event is 40 mg/day. Due to the increased risk of myopathy, use of the 80 mg dose of Flolipid should be restricted to patients who have been taking Flolipid 80 mg chronically

Agent(s)	Indication(s)	Dosage
Lescol XL® (fluvastatin)[a] Extended release tablet	Adjunctive therapy to diet to: • Reduce elevated TC, LDL-C, Apo B, and TG, and to increase HDL-C in adult patients with primary hypercholesterolemia and mixed dyslipidemia • Reduce elevated TC, LDL-C, and Apo B levels in boys and postmenarchal girls, 10 to 16 years of age, with heterozygous familial hypercholesterolemia after failing an adequate trial of diet therapy • Reduce the risk of undergoing revascularization procedures in patients with clinically evident CHD • Slow the progression of atherosclerosis in patients with clinically evident CHD Limitations of use: Not studied in conditions where the major abnormality is elevation of chylomicrons, VLDL, or IDL (i.e., hyperlipoproteinemia Types I, III, IV, or V)	Dose range is 20 to 80 mg/day. For patients requiring LDL-C reduction to a goal of ≥ 25%, the recommended starting dose is 40 mg in the evening, 80 mg of Lescol XL any time of the day, or 80 mg in divided doses of 40 mg twice daily). For patients requiring a LDL-C reduction to a goal of < 25% a starting dose of 20 mg may be used. Children with HeFH, ages 10 to 16: Recommended starting dose is 20 mg once daily. Adjust dose at 6 week intervals to a maximum of 40 mg twice daily or Lescol XL 80 mg once daily.
Lipitor® (atorvastatin)[a] Tablet	Adjunct therapy to diet to: • Reduce the risk of MI, stroke, revascularization procedures, and angina in patients without CHD, but with multiple risk factors • Reduce the risk of MI and stroke in patients with type 2 diabetes without CHD, but with multiple risk factors • Reduce the risk of non-fatal MI, fatal and non-fatal stroke, revascularization procedures, hospitalization for CHF, and angina in patients with CHD • Reduce elevated total-C, LDL-C, apo B, and TG levels and increase HDL-C in adult patients with primary hyperlipidemia (heterozygous familial and nonfamilial) and mixed dyslipidemia • Reduce elevated TG in patients with hypertriglyceridemia and primary dysbetalipoproteinemia • Reduce total-C and LDL-C in patients with homozygous familial hypercholesterolemia (HoFH) • Reduce elevated total-C, LDL-C, and apo B levels in boys and postmenarchal girls, 10 to 17 years of age, with heterozygous familial hypercholesterolemia after failing an adequate trial of diet therapy	Hyperlipidemia and mixed dyslipidemia: The recommended starting dose is 10 or 20 mg once daily. Patients requiring large LDL-C reduction (> 45%) may start at 40 mg once daily. The dosage range is 10 to 80 mg once daily. Pediatric patients with HeFH: Recommended starting dose is 10 mg once daily; usual dose range is 10 to 20 mg/day. Homozygous Familial Hypercholesterolemia: 10 to 80 mg daily.

Agent(s)	Indication(s)	Dosage
	Limitations of use: has not been studied in Fredrickson Types I and V dyslipidemias.	
Livalo® (pitavastatin) Tablet	Adjunctive therapy to diet in: • Adult patients with primary hyperlipidemia or mixed dyslipidemia as an adjunctive therapy to diet to reduce elevated total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), apolipoprotein B (Apo B), triglycerides (TG), and to increase high-density lipoprotein cholesterol (HDL-C) • Pediatric patients aged 8 years and older with heterozygous familial hypercholesterolemia (HeFH) to reduce elevated TC, LDL-C, and ApoB. Limitations of use: The effect of Livalo on cardiovascular morbidity and mortality has not been determined.	The recommended starting dosage is 2 mg once daily, the maximum is 4 mg once daily.
Pravachol® (pravastatin)[a] Tablet	Adjunctive therapy to diet to: • Reduce the risk of MI, revascularization, and cardiovascular mortality in hypercholesterolemic patients without clinically evident CHD. • Reduce the risk of total mortality by reducing coronary death, MI, revascularization, stroke/TIA, and the progression of coronary atherosclerosis in patients with clinically evident CHD. • Reduce elevated Total-C, LDL-C, ApoB, and TG levels and to increase HDL-C in patients with primary hypercholesterolemia and mixed dyslipidemia. • Reduce elevated serum TG levels in patients with hypertriglyceridemia. • Treat patients with primary dysbetalipoproteinemia who are not responding to diet. • Treat children and adolescent patients ages 8 years and older with heterozygous familial hypercholesterolemia after failing an adequate trial of diet therapy Limitations of use: Has not been studied in Fredrickson Types I and V dyslipidemias.	Adults: the recommended starting dose is 40 mg once daily. If a 40 mg dose does not achieve desired cholesterol levels, 80 mg once daily is recommended. Children (ages 8 to 13): The recommended starting dose is 20 mg once daily. Doses greater than 20 mg have not been studied in this population. Adolescents (ages 14 to 18 years): The recommended starting dose is 40 mg once daily. Doses greater than 40 mg have not been studied in this patient population.

Agent(s)	Indication(s)	Dosage
Zocor® (simvastatin)[a] Tablet	Adjunctive therapy to diet to: • Reduce the risk of total mortality by reducing CHD deaths and reduce the risk of non-fatal MI, stroke, and the need for revascularization procedures in patients at high risk of coronary events. • Reduce elevated total-C, LDL-C, Apo B, TG and increase HDL-C in patients with primary hyperlipidemia (heterozygous familial and nonfamilial) and mixed dyslipidemia. • Reduce elevated TG in patients with hypertriglyceridemia and reduce TG and VLDL-C in patients with primary dysbetalipoproteinemia. • Reduce total-C and LDL-C in adult patients with homozygous familial hypercholesterolemia. • Reduce elevated total-C, LDL-C, and Apo B in boys and postmenarchal girls, 10 to 17 years of age with heterozygous familial hypercholesterolemia after failing an adequate trial of diet therapy. Limitations of use: Has not been studied in Fredrickson Types I and V dyslipidemias.	The usual dosage range is 5 mg to 40 mg/day. daily. The recommended usual starting dose is 10 or 20 mg once a day in the evening. For patients at high risk for a CHD event due to existing CHD, diabetes, peripheral vessel disease, history of stroke or other cerebrovascular disease, the recommended starting dose is 40 mg/day. For patients with Homozygous Familial Hypercholesteremia the recommended dose is 40 mg/day in the evening. Due to the increased risk of myopathy, use of the 80 mg dose should be restricted to patients who have been taking simvastatin 80 mg chronically. Adolescents (10-17 years of age) with HeFH: The recommended starting dose 10 mg once a day in the evening. The recommended dosing range is 10 to 40 mg/day; the maximum recommended dose is 40 mg/day.
Zypitamag™ (pitavastatin) tablet	Patients with primary hyperlipidemia or mixed dyslipidemia as an adjunctive therapy to diet to reduce elevated total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), apolipoprotein B (Apo B), triglycerides (TG), and to increase high-density lipoprotein cholesterol (HDL-C) Limitations of use: The effect of Zypitamag on cardiovascular morbidity and mortality has not been determined.	Dose range is 1-4 mg once daily. The recommended starting dose is 2 mg. The maximum dose is 4 mg per day.

a - Generic equivalent available

Combination Products

Agent(s)	Indication(s)	Dosage
Roszet™, Ezetimibe/rosuvastatin	Adjunctive therapy to diet in patients with primary non-familial hyperlipidemia to reduce low-density lipoprotein cholesterol (LDL-C) Alone or as an adjunct to other LDL-C lowering therapies in patients with homozygous familial hypercholesterolemia (HoFH) to reduce LDL-C	Dosage range is 5 mg/10 mg to 40 mg/10 mg once daily
Vytorin® (ezetimibe/ simvastatin)[a] Tablet	Adjunctive therapy to diet to: • Reduce elevated TC, LDL-C, Apo B, TG, and non-HDL-C, and to increase HDL-C in patients with primary (heterozygous familial and non-familial) hyperlipidemia or mixed hyperlipidemia. • Reduce elevated total-C and LDL-C in patients with homozygous familial hypercholesterolemia (HoFH), as an adjunct to other lipid lowering treatments Limitations of use: • No incremental benefit of ezetimibe/simvastatin on cardiovascular morbidity and mortality over and above that demonstrated for simvastatin has been established. • Ezetimibe/simvastatin has not been studied in Fredrickson Type I, III, IV, and V dyslipidemias	The usual dosage range is 10 mg/10 mg to 10 mg/40 mg/day. Recommended usual starting dose is 10/10 or 10/20 mg/day. Patients who require a larger reduction in LDL-C may be started at 10/40 mg/day in the absence of moderate to severe renal impairment. Due to the increased risk of myopathy, use of the 10/80 mg dose of Vytorin should be restricted to patients who have been taken Vytorin 10/80 mg chronically without evidence of muscle toxicity.

a – Generic equivalent available

CLINICAL RATIONALE

Among lipid-lowering drugs, statins are the cornerstone of LDL-C lowering therapy, in addition to healthy lifestyle interventions. Statins are recommended as first-line treatment to prevent atherosclerotic cardiovascular disease events (ASCVD) [Clinical ASCVD is defined as acute coronary syndromes, or a history of myocardial infarction (MI), or stable or unstable angina, coronary or other arterial revascularization, stroke, TIA, or peripheral arterial disease presumed to be of atherosclerotic origin]. Both high intensity and medium intensity statin therapy reduce primary and secondary ASCVD events.[13]

Safety

All statin and statin combinations are contraindicated in active liver disease, pregnancy, and lactation. Livalo and Zypitamag are also contraindicated with the concomitant use of cyclosporine. Altoprev, Flolipid, Vytorin, and Zocor are contraindicated with concomitant administration of strong CTP3A4 inhibitors. Flolipid, Vytorin, and Zocor are also contraindicated with the concomitant use of gemfibrozil, cyclosporine, or danazol, while Altoprev is

contraindicated with the concomitant use of erythromycin.[1-11]

For additional clinical information see Prime Therapeutics Formulary Chapters 5.9C: HMG-CoA Reductase Inhibitors and 5.9D HMG-CoA Reductase Inhibitor Combinations, and Prime Therapeutics Formulary Monograph: Livalo (pitavastatin).

REFERENCES

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3. Ezallor Sprinkle Prescribing Information. Sun Pharmaceutical Industries, Inc. October 2020.
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6. Lipitor Prescribing Information. Pfizer. December 2020.
7. Livalo prescribing information. Kowa Pharmaceuticals America, Inc./Lilly USA LLC. May 2019.
8. Pravachol Prescribing Information. Bristol-Myers Squibb Company. October 2020.
9. Zocor Prescribing Information. Merck & Co. December 2020.
10. Vytorin prescribing information. Merck & Co, Inc.. September 2020.
11. Zypitamag Prescribing Information. Medicure. September 2020.
12. Roszet Prescribing Information. Althera Pharmaceuticals LLC. March 2021.
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Statin Step Therapy

TARGET AGENT(S)	PREREQUISITE AGENT(S)
Altoprev® (lovastatin extended release) **Ezallor™ Sprinkle** (rosuvastatin) **Ezetimibe/rosuvastatin** **Flolipid™** (simvastatin oral suspension) **Livalo®** (pitavastatin) **Roszet™** (ezetimibe/rosuvastatin) **Simvastatin oral suspension 20 mg/5 mL** **Zypitamag** (pitavastatin)	Any generic statin or statin combination

a - available as a generic

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL

Target Agent(s) will be approved when ANY ONE of the following is met:

1. The requested agent is eligible for continuation of therapy AND ONE of the following:
    a. Information has been provided that indicates the patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days
    OR
    b. The prescriber states the patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days AND is at risk if therapy is changed

Agents Eligible for Continuation of Therapy
Livalo

    OR
2. The patient's medication history includes use of a prerequisite agent within the past 90 days
    OR
3. The patient has an intolerance or hypersensitivity to a prerequisite agent
    OR
4. The patient has an FDA labeled contraindication to ALL prerequisite agents

Length of Approval: 12 months