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Dear provider of pharmaceutical services,

In recent years lipid lowering treatment has been transformed by the addition of protein convertase subtilisin kexin type 9 (PCSK9) inhibitors. This pharmacologic category comprises human monoclonal antibodies that bind to PCSK9 and block its binding to low-density lipoprotein receptors (LDLR) whose job it is to clear LDL from the body. Currently there are two available PCSK9 inhibitors on the market: Evolocumab (*Repatha*™) and Alirocumab (*Praluent*™).

Last year, the American College of Cardiology (ACC) released a Focused Update to define the role of non-statin therapies in lipid lowering treatment and Atherosclerotic Cardiovascular Disease (ASCVD) management.

It's important to remember that statins have dual role in ASCVD management: (1) lipid lowering and (2) plaque stabilization. Statins should remain in the highest tolerable intensity as part of the patient therapy if there is no contraindication or intolerance reported.

If statin therapy alone fails to lower LDL the desired percentage, it's important to evaluate adherence, statin intensity and life style modifications before modifying or adding non-statin therapies to the medication regimen. After evaluation of these factors, depending on the patient group, the recommendation for non-statin therapy addition will vary. The following table summarizes ACC recommendations for different patient groups.

ACC Recommendation	Patient Group
Addition of ezetimibe	1. Patients from 40-75 years of age without clinical ASCVD, with diabetes and LDL 70-189 mg/dl 2. Patients from 40-75 years of age without clinical ASCVD or Diabetes with LDL 70-189 mg/dl and 10-year ASCVD risk $\geq$ 7.5%
Addition of ezetimibe FIRST Consider replacing ezetimibe with PCSK9 inhibitor if statin-ezetimibe treatment fails to lower LDL	1. Patients over 21 years of age with stable clinical ASCVD and without comorbidities
Addition of EITHER ezetimibe or PCSK9 inhibitor Decision between ezetimibe and PCSK9 inhibitors should be based on factors like: additional % of LDL reduction needed, patient renal function (GFR), smoking status and other health conditions (recent ACS, HF, DM, CABG, others). Please refer to the complete 2017 focused update for details.	1. Patients over 21 years of age without clinical ASCVD and LDL $\geq$ 190 mg/d 2. Patients over 21 years of age with clinical ASCVD and LDL $\geq$ 190 mg/d 3. Patients over 21 years of age with clinical ASCVD and comorbidities

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The following table summarizes information regarding these two PCSK9 inhibitors.

	Evolocumab *Repatha™*	**Alirocumab** *Praluent™*
FDA-Approved Indications and Dosing	**Treatment of HoFH who require additional lowering of LDL-C, as an adjunct to diet and other LDL-lowering therapies** • 420 mg once monthly **Treatment of primary hyperlipidemia (including HeFH) to reduce LDL-C, as an adjunct to diet, alone or in combination with other lipid-lowering therapies** • 140 mg every 2 weeks or 420 mg once monthly **To reduce the risk of myocardial infarction, stroke, and coronary revascularization in adults with established cardiovascular disease** • 140 mg every 2 weeks or 420 mg once monthly	**Treatment of HeFH or clinical ASCVD, as adjunct to diet and maximally tolerated statin therapy** • 75 mg every 2 weeks or 300 mg every 4 weeks ○ Max dose: 150 mg every 2 weeks
Administration	Subcutaneous administration in fatty part of skin like thigh, belly area or upper arm; rotating injection site to avoid injection site reactions. Avoid: (1) using the same place and (2) administering in skin that is irritated, bruised, red, infected, or scarred.	
Missed Doses	**Never take 2 doses at the same time.** Administration frequency every 2 weeks: • Take the dose as quickly as possible if it has been less than 7 days and continue with next scheduled dose. • If more than 7 days have passed, skip missed dose and continue with next scheduled dose. Administration frequency every month: • Take the dose as quickly as possible if it has been less than 7 days and continue with next scheduled dose. • If more than 7 days have passed, take missed dose and start new schedule based on this dose.	
Adverse Effects (*most common*)	Irritation where shot is given; back pain; flu-like symptoms; nose or throat irritation	Irritation, itching or pain where shot is given; flu-like symptoms; nose or throat irritation
Abbreviations: ASCVD – Arteriosclerotic cardiovascular disease; HeFH - Heterozygous familial hypercholesterolemia; HoFH - Homozygous familial hypercholesterolemia; LDL-C - Low-density lipoprotein cholesterol.		

If you're dispensing PCSK9 inhibitors at your pharmacy remember to counsel patients on:

- Subcutaneous administration;
- Importance of adherence to all dyslipidemia medication;
- What response to expect from their medications; and
- Storage at 2-8 ºC (refrigerated), avoiding extreme heat or freezing temperature, and protected from light. Both medications could also be stored at room temperature (20-25ºC), but once product is stored at these temperatures it cannot be returned to the refrigerator and MUST be used prior to 30 days. Any remaining product after 30 days at room temperature must be discarded.

For more details on guidelines recommendations, please refer to the complete focused update available at http://www.onlinejacc.org/content/early/2017/08/30/j.jacc.2017.07.745#F3. For more specific information on both medications available, please reference package inserts.

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Medical literature is dynamic and is continuously changing as new scientific knowledge is developed. We exhort the frequent revision of treatment guidelines to assure that your recommendations are consistent with the most actualized information.

On PharmPix we are compromised with the health and wellness of our insured. It is our priority to offer high quality services and to promote practices for health promotion and diseases prevention. If you have any doubt or wish to have more information regarding this document, you can call us to 787-522-5252, extension 138.

Regards,

Pharmacy Department

References:

1. Lambert, M. (2014, August 15). ACC/AHA Release Updated Guideline on the Treatment of Blood Cholesterol to Reduce ASCVD Risk. Retrieved March 22, 2018, from https://www.aafp.org/afp/2014/0815/p260.html
2. Lloyd-Jones, D. M., Morris, P. B., Ballantyne, C. M., Birtcher, K. K., Daly, D. D., DePalma, S. M., et. al. (2017, September 05). 2017 Focused Update of the 2016 ACC Expert Consensus Decision Pathway on the Role of Non-Statin Therapies for LDL-Cholesterol Lowering in the Management of Atherosclerotic Cardiovascular Disease Risk. Retrieved March 23, 2018, from http://www.onlinejacc.org/content/early/2017/08/30/j.jacc.2017.07.745
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