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Bempedoic Acid in Hypercholesterolemia Management: A New Approach

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Abstract:- Hypercholesterolemia, is a condition that increase cholesterol levels in body and it is major risk factor for cardiovascular disease (CVD). In the treatment of this condition statins, bile acid sequestrants, and cholesterol absorption inhibitors are use but they show side effects especially statin are cause muscle-related complications. Bempedoic acid is new drug that lower the lipid and it is alternative of other medicine. It is use in statin-intolerant patients or those with familial hypercholesterolemia. Bempedoic acid inhibit ATP-citrate lyase which is produce factor of cholesterol and reduce level of LDL-C without any muscle-related adverse effects which are show in statins. This review article explores Bempedoic acid's mechanism of action, its clinical efficacy in management of hypercholesterolemia, and its potential as a complementary or alternative therapy to traditional lipid-lowering treatments. Given its unique mechanism, Bempedoic acid offers a valuable advancement in the pharmacological management of hypercholesterolemia and cardiovascular risk.

Keywords:- *Bempedoic Acid, Hypercholesterolemia, Cholesterol Management, LDL-C Reduce.*

I. INTRODUCTION

Hypercholesterolemia is a condition where LDL cholesterol (LDL-C) levels are higher in the blood, which cause the risk of heart disease, especially coronary heart disease (CHD). Cholesterol is linked with problems with how the body processes fats. It is factor of atherosclerosis, where fat builds up into arteries, narrowing them and raising the risk of heart attacks, strokes, and other heart related problems. Main factor of Hypercholesterolemia is genetic (like familial hypercholesterolemia) or lifestyle such as poor diet, lack of exercise, and other health issues. So, imbalance of cholesterol can increase atherosclerosis, making it an important target for treatment. [1]

Hypercholesterolemia cause health conditions like heart disease, stroke, and atherosclerosis. Cholesterol is major factor of this problems which is related to heart. In the treatment of this condition and reduce LDL-C statins are used and they block the enzyme which generate the cholesterol. other options like bile acid sequestrants, fibrates, niacin, and ezetimibe are available for reduce cholesterol and manage lipid. The most common side effects of statins are mild liver enzyme enhance and muscle related problem. Recent studies show that long-term or high-dose statin use can developing type 2 diabetes in some people. [2]

Bempedoic acid is developed by Esperion Therapeutics. It is a non-statin oral medication for the management of high cholesterol. It is approved in U.S. in February 2020 and EU in April 2020. This medication is available standalone treatment and in a fixed-dose combination with ezetimibe. In Phase III CLEAR clinical trials, it shows lower the level of LDL cholesterol (LDL-C) in patients with hypercholesterolemia after that it was approved. [3]

II. INTRODUCTION OF BEMPEDOIC ACID

Bempedoic acid IUPAC 8-Hydroxy-2,2,14,14-tetramethylpentadecanedioic acid and it is an alpha, omega-dicarboxylic acid derived from pentadecanedioic acid, with methyl substitutions at positions 2 and 14, and a hydroxy group at position 8. Its Molecular formula $C_{19}H_{36}O_5$. Bempedoic acid is a fat-soluble molecule and its molecular weight is 350.8 g/mol. It is more soluble into organic solvents but insoluble in water that why it helps to absorbs in liver easily. It is stable in room temperature and simply take as a tablet. These properties help it lower cholesterol by targeting the liver, where fats are processed. Its chemical structure shown in figure 1: [4]

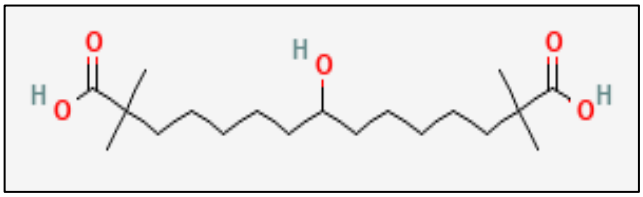

Fig 1: Chemical Structure of Bempedoic Acid

III. MECHANISM OF ACTION

Bempedoic acid is convert into its active form ETC-1002-CoA and ESP15228-CoA by the help of an enzyme called very long chain acyl-CoA synthetase 1 (ACSVL1). Now activated Bempedoic acid is inhibit another enzyme which is ATP citrate lyase (ACL), it is plays a major role in cholesterol and fat metabolism. ACL is converting citric acid (citrate) into acetyl-CoA, a key building block for making both fatty acids and cholesterol. Bempedoic acid reduce of the cholesterol in the liver and increases the removal of LDL cholesterol from the bloodstream. In the liver it helps to lower LDL-C. when statins, block cholesterol production in muscles and other tissues but Bempedoic acid only activate into liver and dose not effects on muscle tissue. So Bempedoic acid is use for people which is statin Bempedoic

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acid a useful alternative for people who can't tolerate statins. [5]

➢ *Pharmacokinetics*

When Bempedoic acid is taken regularly for 7 days 180 mg, steady blood levels are reached, with peak concentrations occurring around 3.5 hours after dosing. It is highly protein-bound (99.3%) and it has a half-life of 15 to 24 hours. Bempedoic acid is mainly excreted 70% in urine and 30% in feces. [6]

➢ *Pharmacodynamics*

Bempedoic acid prevent production of cholesterol in the liver by reduce level of LDL-C. This also reduce CVD events into the body. Compared to the statins it not shown any side effects. Recent clinical trials show that this drug reduce LDL-C levels in 12 weeks after therapy. [7]

➢ *Therapeutic Uses*

Bempedoic acid helps to reduce LDL cholesterol, especially when statins aren't effective or cause side effects. It also used with statins to reduce cholesterol and lower the risk of heart attacks and strokes. Bempedoic acid is useful for preventing further heart problems in people with a history of heart disease or stroke and can help dyslipidemia. It's an important treatment for management high cholesterol and reducing heart disease risk. [7]

➢ *Adverse Effects*

Bempedoic acid can lower LDL cholesterol but may cause some side effects. Common side effects are Upper respiratory tract infection, muscle spasms, hyperuricaemia, back pain, abdominal pain, high uric acid levels. Some people may also experience mild side effects such as muscle pain, fatigue, and headaches. While Bempedoic acid is effective at lowering LDL-C, its long-term impact on heart health is still being studied. [8]

➢ *Contraindications*

Bempedoic acid should be avoided in people who are sensitive to it or have severe liver problems as it could make liver function worse. Its safety during pregnancy and breastfeeding isn't known, so it should only be used if absolutely necessary. It can also increase uric acid levels, so those with gout or high uric acid should use it with care. [9]

Table 1: Summary of Bempedoic acid [10]

Alternative name	**ETC-1002, ESP-55016**
Chemical Name	**8-Hydroxy-2,2,14,14-** tetramethylpentadecanedioic acid
Category	Hypolipidemic Agents
Mechanism of action	Adenosine triphosphate citrate lyase (ACL) Inhibiter
Pharmacokinetic	**Steady state concentration:** 180 mg orally for 7 days. **Excretion:** 70% from urine and 30% from faeces
Therapeutic Uses	Hypercholesterolemia, Hypelipdaemia
Adverse effects	**Most common:** Upper respiratory tract infection, muscle spasms, hyperuricaemia, back pain, abdominal pain **Rare:** Tendon rupture, hyperplasia, gout

IV. CONCLUSION

Bempedoic acid is given for cure of hypercholesterolemia because it reduces LDL cholesterol (LDL-C). Clinical trials discovered that Bempedoic acid drop level of LDL cholesterol while not rise in adverse actions. Its only aftereffect are hyperuricemia and tendon rupture. Other side effects are mild to moderate. Thus, Bempedoic acid is a capable treatment alternate for people with hypercholesterolemia, providing an extra choice for those who require more LDL-C reduction while reducing the risk of statin-related adverse effects.

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