Lipanthyl Penta 145 mg

15.9.2015, Version 3

PUBLIC SUMMARY OF THE RISK MANAGEMENT PLAN

VI.2 Fenofibrate: Elements for a Public Summary

VI.2.1 Fenofibrate: Overview of Disease Epidemiology

An estimated 15% of the population in developed countries have a combination of blood lipid disorders. Elevated cholesterol levels play a dominant role in both the initiation and progression of atherosclerosis, as well as in the clinical consequences such as myocardial infarction, stroke, peripheral vascular disease, and heart failure. Both increased blood cholesterol levels and increased blood triglyceride levels have been linked to a higher risk of heart disease and arteriosclerosis. Hyperlipidemia tends to increase with age. Heart disease is the leading cause of death among both white and non-white US population. Severe elevations of triglycerides (> 2000 mg/dL) may cause acute pancreatitis.

VI.2.2 Fenofibrate: Summary of Treatment Benefits

Decreasing blood cholesterol and triglyceride levels with diet in combination with medication, decreases the risk of cardiovascular disease or reduces its progression.

VI.2.3 Fenofibrate: Unknowns Relating to Treatment Benefits

Fenofibrate use has been studied in more than 11 thousand adult and elderly patients. Only limited numbers of children have been studied. The available strengths for fenofibrate only allow limited dosage adjustment for children. Only limited data is available for patients with significant liver or kidney disease, or for patients who are pregnant or breast-feeding.

VI.2.4 Fenofibrate: Summary of Safety Concerns

Summary of the Risk Management Plan

Table 64. Fenofibrate: Summary of the Risk Management Plan

Safety Concern	Proposed Pharmacovigilance Activities (Routine and Additional)	Proposed Risk Minimization Activities (Routine and Additional)
Important identified risks		
Cholelithiasis	Routine pharmacovigilance	• Gallbladder disease is a contraindication • Labeled undesirable effect
Pancreatitis	Routine pharmacovigilance	• Chronic or acute pancreatitis (with the exception of acute pancreatitis due to severe hypertriglyceridemia) is a contraindication • Warning about pancreatitis risk is included in SPC • Labeled undesirable effect
Myopathy/rhabdomyolysis	Routine pharmacovigilance	• Warning about this risk, including description of risk factors, symptoms and risk minimization recommendations is included in SPC • Labeled undesirable effect
Drug-induced hepatitis	Routine pharmacovigilance	• Warning about this risk, including description of risk factors, monitoring recommendations, symptoms, and risk minimization measures is included in SPC • Labeled undesirable effect
Elevations in serum creatinine	Routine pharmacovigilance	• Warning about this risk, including monitoring recommendations is included in

Table 64. Fenofibrate: Summary of the Risk Management Plan

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		SPC • Labeled undesirable effect
Photosensitivity	Routine pharmacovigilance	• Known photoallergy or phototoxic reaction during treatment with fibrates or ketoprofen is a contraindication • Labeled undesirable effect
Venothromboembolic disease	Routine pharmacovigilance	• Results of FIELD study are communicated in Undesirable Effects section of the SPC
Severe cutaneous reactions	Routine pharmacovigilance	• Labeled undesirable effect
Interstitial lung disease	Routine pharmacovigilance	• Labeled undesirable effect
Important potential risks		
Increased risk of Major Adverse Cardiac Events in women on combined treatment	Routine pharmacovigilance Performance of an additional clinical trial in high risk patients	• Summary results of the subgroup analysis of the ACCORD Lipid study are included in the US and EU labeling
Increased homocysteine blood levels	Routine pharmacovigilance	• Labeled undesirable effect
Missing information		
Children/adolescents (< 18 years)	Routine pharmacovigilance	• Lack of data is appropriately communicated in the SPC
Pregnant/lactating women	Routine pharmacovigilance	• Lack of data is appropriately communicated in the SPC
Patients with severe renal impairment	Routine pharmacovigilance	• Severe chronic kidney disease is a contraindication for fenofibrate • Dosing recommendations for patients with (non-severe) renal

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Safety Concern	Proposed Pharmacovigilance Activities (Routine and Additional)	Proposed Risk Minimization Activities (Routine and Additional)
		impairment
Patients with hepatic insufficiency	Routine pharmacovigilance	• Hepatic insufficiency (including biliary cirrhosis and unexplained persistent liver function abnormality) is a contraindication

VI.2.5 Fenofibrate: Summary of Additional Risk Minimization Measures by Safety Concern

No additional risk minimization measures are foreseen.

VI.2.6 Fenofibrate: Planned Post-Authorization Development Plan

No post-authorization efficacy studies are planned.

VI.2.7 Fenofibrate: Summary of Changes to the Risk Management Plan over Time

Table 65. Fenofibrate: List of Major Changes to the Risk Management Plan

Version	Date	Safety Concerns	Comment
1	January 2012	New data for fenofibric acid treatment with or without various statins was added (Studies M06-844, M06-884 and M10-667). Post-marketing safety data and information on labeling for other similar products was updated to reflect currently available information.	The RMP for fenofibrate, fenofibric acid and fenofibrate/simvastatin, concerned a merge of the information from the originally separate RMPs for the individual products fenofibrate, fenofibrate/simvastatin and fenofibric acid.

Table 65. Fenofibrate: List of Major Changes to the Risk Management Plan

Version	Date	Safety Concerns	Comment
1.1	September 2012	-	Comments and requests from the PRAC/CHMP assessments were addressed.
2	08 MAY 2013	No significant changes to the information contained occurred, other than inserting existing sections into the changed sequence in the new template with correction of references to tables and sections and some other resultant minor edits.	Edition 2 of the RMP for fenofibrate, fenofibric acid and fenofibrate/simvastatin merged the comments and requests of the PRAC /CHMP, as included in version 1.1 for fenofibrate/simvastatin into the combined RMP in new RMP format. The numbers of post-marketing case reports in the sections on identified and potential risks were updated from the data lock date of Oct 2011 to 28 February 2013. Due to the limited changes in numbers of reports, these changes did not impact the benefit - risk balance.
2.1	05 DEC 2013	-	Edition 2.1 of the RMP included one section VI for each product.
3	15 SEP 2015	Addition of important identified risks: • Severe cutaneous reactions • Interstitial lung disease	Edition 3 included addition of two important identified risks as requested by the Preliminary Variation Assessment Report procedure: DE/H/0497/001/II/043 DE/H/0498/001/II/042 DE/H/0500/001/II/041. None of the new added risks was however added in response to newly received or analyzed safety data, or because of emergence of a new safety concern for the marketed product or for any other reason. All information specific for the combination product fenofibrate/simvastatin has been removed and will be included in the existing separate RMP for fenofibrate/simvastatin. This is in

Table 65. Fenofibrate: List of Major Changes to the Risk Management Plan

Version	Date	Safety Concerns	Comment
			line with separate PSURs for fenofibrate/fenofibric acid and for fenofibrate/simvastatin (the simvastatin component may result in a different adverse event reporting pattern). Study data for Study M10-313 were updated due to study report finalization. The fact that the FDA has relieved AbbVie from the study requirement to study the risk of Major Adverse Cardiac Events in women on combined treatment was included. The numbers of post-marketing exposure data and case reports in Part II were updated from the data lock point of 28 February 2013 to 31 July 2015. Due to the limited changes in numbers of reports, these changes did not impact the benefit - risk balance. Beyond that, further modifications of corrective/administrative nature were also implemented.