Annex III

Amendments to the summaries of product characteristics and package leaflets

Note: These amendments to the summary of product characteristics and package leaflet are valid at the time of the Commission Decision.
After the Commission Decision the National Competent Authorities will update the product information as required.

Amendments to be included in the relevant sections of the summary of product characteristics for fenofibrate (100, 300, 67, 200, 250 mg capsules and 160 and 145 mg film coated tablets) containing medicinal products

Section 4.1 – Therapeutic indications (to replace current text)

[Product name] is indicated as an adjunct to diet and other non-pharmacological treatment (e.g. exercise, weight reduction) for the following:
- Treatment of severe hypertriglyceridaemia with or without low HDL cholesterol.
- Mixed hyperlipidaemia when a statin is contraindicated or not tolerated.
- Mixed hyperlipidaemia in patients at high cardiovascular risk in addition to a statin when triglycerides and HDL cholesterol are not adequately controlled.

Section 5.1 – Pharmacodynamic properties (in addition to current text)

There is evidence that treatment with fibrates may reduce coronary heart disease events but they have not been shown to decrease all cause mortality in the primary or secondary prevention of cardiovascular disease.

The Action to Control Cardiovascular Risk in Diabetes (ACCORD) lipid trial was a randomized placebo-controlled study of 5518 patients with type 2 diabetes mellitus treated with fenofibrate in addition to simvastatin. Fenofibrate plus simvastatin therapy did not show any significant differences compared to simvastatin monotherapy in the composite primary outcome of non-fatal myocardial infarction, non-fatal stroke, and cardiovascular death (hazard ratio [HR] 0.92, 95% CI 0.79-1.08, p = 0.32 ; absolute risk reduction: 0.74%). In the pre-specified subgroup of dyslipidaemic patients, defined as those in the lowest tertile of HDL-C (≤34 mg/dl or 0.88 mmol/L) and highest tertile of TG (≥204 mg/dl or 2.3 mmol/L) at baseline, fenofibrate plus simvastatin therapy demonstrated a 31% relative reduction compared to simvastatin monotherapy for the composite primary outcome (hazard ratio [HR] 0.69, 95% CI 0.49-0.97, p = 0.03 ; absolute risk reduction: 4.95%). Another prespecified subgroup analysis identified a statistically significant treatment-by-gender interaction (p = 0.01) indicating a possible treatment benefit of combination therapy in men (p=0.037) but a potentially higher risk for the primary outcome in women treated with combination therapy compared to simvastatin monotherapy (p=0.069). This was not observed in the aforementioned subgroup of patients with dyslipidaemia but there was also no clear evidence of benefit in dyslipidaemic women treated with fenofibrate plus simvastatin, and a possible harmful effect in this subgroup could not be excluded.

Amendments to be included in the relevant sections of the package leaflet for fenofibrate (100, 300, 67, 200, 250 mg capsules and 160 and 145 mg film coated tablets) containing medicinal products

Section 1. What is [Product name] and what it is used for

[Product name] belongs to a group of medicines, commonly known as fibrates. These medicines are used to lower the level of fats (lipids) in the blood. For example the fats known as triglycerides.

[Product name] is used, alongside a low fat diet and other non-medical treatments such as exercise and weight loss, to lower levels of fats in the blood.

[Product name] can be used in addition to other medicines [statins] in some circumstances when levels of fats in the blood are not controlled with a statin alone.

Amendments to be included in the relevant sections of the summary of product characteristics for bezafibrate, ciprofibrate and fenofibrate (267 mg capsules and 215 mg film coated tablets) containing medicinal products

Section 4.1 Therapeutic indications (to replace current text)

[Product name] is indicated as an adjunct to diet and other non-pharmacological treatment (e.g. exercise, weight reduction) for the following:
- Treatment of severe hypertriglyceridaemia with or without low HDL cholesterol.
- Mixed hyperlipidaemia when a statin is contraindicated or not tolerated.

Section 5.1 – Pharmacodynamic properties (in addition to current text)

There is evidence that treatment with fibrates may reduce coronary heart disease events but they have not been shown to decrease all cause mortality in the primary or secondary prevention of cardiovascular disease.

Amendments to be included in the relevant sections of the package leaflet bezafibrate, ciprofibrate and fenofibrate (267 mg capsules and 215 mg film coated tablets) containing medicinal products

Section 1. What is [Product name] and what it is used for

[Product name] belongs to a group of medicines, commonly known as fibrates. These medicines are used to lower the level of fats (lipids) in the blood. For example the fats known as triglycerides.

[Product name] is used, alongside a low fat diet and other non-medical treatments such as exercise and weight loss, to lower levels of fats in the blood.

Amendments to be included in the relevant sections of the summary of product characteristics for gemfibrozil containing medicinal products

Section 4.1 – Therapeutic indications (to replace current text)

[Product name] is indicated as an adjunct to diet and other non-pharmacological treatment (e.g. exercise, weight reduction) for the following:
- Treatment of severe hypertriglyceridaemia with or without low HDL cholesterol.
- Mixed hyperlipidaemia when a statin is contraindicated or not tolerated.
- Primary hypercholesterolaemia when a statin is contraindicated or not tolerated.

Primary prevention
Reduction of cardiovascular morbidity in males with increased non-HDL cholesterol and at high risk for a first cardiovascular event when a statin is contraindicated or not tolerated (see section 5.1).

Section 5.1 – Pharmacodynamic properties (in addition to current text)

There is evidence that treatment with fibrates may reduce coronary heart disease events but they have not been shown to decrease all cause mortality in the primary or secondary prevention of cardiovascular disease

The VA-HIT study was a double-blind study comparing gemfibrozil (1200 mg per day) with placebo in 2531 men with a history of coronary heart disease, HDL-C levels of < 40 mg/dL (1.0 mmol/L), and normal LDL C levels. After one year, the mean HDL-C level was 6% higher and the mean triglyceride level was 31% lower in the gemfibrozil group than in the placebo group. The primary event of non-fatal myocardial infarction or cardiac death occurred in 17.3% of gemfibrozil-treated and 21.7% of placebo-treated patients (reduction in relative risk 22%; 95% CI, 7 to 35 %; P=0.006). Among secondary outcomes, patients treated with gemfibrozil experienced relative risk reductions of 25% (95% CI –6-47%, p=0.10) for stroke, 24% (95% CI 11-36%, p< 0.001) for the combined outcome of death from CHD, non-fatal myocardial infarction, or confirmed stroke, 59% (95% CI 33-75%, p< 0.001) for transient ischaemic attack, and 65% (95% CI 37-80%, p< 0.001) for carotid endarterectomy.

Amendments to be included in the relevant sections of the package leaflet for gemfibrozil containing medicinal products

Section 1. What is [Product name] and what it is used for

[Product name] belongs to a group of medicines commonly known as fibrates. These medicines are used to lower the level of fats (lipids) in the blood. For example the fats known as triglycerides.

[Product name] is used, alongside a low fat diet and other non-medical treatment such as exercise and weight loss, to lower levels of fat in the blood. [Product name] can be used when other medicines [statins] are unsuitable, to reduce the occurrence of heart problems in men who are at high risk and who have increased 'bad cholesterol'

[Product name] may also be prescribed to people who cannot be prescribed other lipid-lowering medicines for lowering blood cholesterol levels.