This信访 highlighted the potential interaction with many medications, such as anticoagulants and antiplatelet agents, and provides guidelines for managing these interactions. The absence of bleeding events in the trials of FENOGLIDE demonstrates a different mechanism of action compared to clofibrate, which has been associated with increasing the risk of bleeding.  FENOGLIDE, however, has not been associated with an increased risk of bleeding when used in combination with anticoagulants. This finding is supported by the results of the FIELD study, which demonstrated a reduction in the primary outcome of cardiovascular disease with FENOGLIDE compared to placebo, with no increase in the risk of bleeding. 

8 USE IN SPECIFIC POPULATIONS

8.2 Pregnancy

FENOGLIDE is contraindicated in women who are or may become pregnant. If the patient becomes pregnant while on FENOGLIDE, treatment should be discontinued immediately. Caution should be exercised when FENOGLIDE is used in women of childbearing potential, as there is no information regarding the risk of fetal harm associated with its use. 

8.3 Nursing Mothers

FENOGLIDE is excreted in human milk. Although the amount of FENOGLIDE excreted in human milk is not known, it is unlikely that it would pose a risk to the nursing infant. However, due to the potential for serious adverse reactions in nursing infants, women should not use FENOGLIDE while nursing. 

9 DRUG INTERACTIONS

FENOGLIDE should be used with caution in patients taking medications that are known to be associated with an increased risk of bleeding, such as nonsteroidal anti-inflammatory drugs (NSAIDs) and other antiplatelet agents. FENOGLIDE should be administered with caution in patients taking warfarin (Coumadin), as there is evidence of in vitro interaction between FENOGLIDE and warfarin, resulting in an increase in AT-III activity and a potential risk of bleeding. 

10 ADVERSE REACTIONS

10.1 Overview

Adverse reactions to FENOGLIDE were generally mild to moderate in severity and were consistent with those expected for fibrate drugs. The most common adverse reactions were abdominal pain, flatulence, and diarrhea. 

11 CLINICAL PHARMACOLOGY

11.1 Mechanism of Action

FENOGLIDE is a fibrate that acts by activating peroxisome proliferator-activated receptor-alpha (PPAR-alpha) in the liver, which increases the synthesis of lipoprotein lipase (LPL) and decreases the synthesis of remnant lipoproteins (VLDL remnants). This leads to an increase in the clearance of triglycerides from the circulation. 

11.2 Pharmacokinetics

FENOGLIDE is absorbed rapidly and reaches peak plasma concentrations within 1-2 hours after oral administration. It is extensively metabolized in the liver and excreted primarily in the feces. The half-life of FENOGLIDE is about 12-18 hours. 

12 CLINICAL STUDIES

12.1 Mechanism of Action

FENOGLIDE has been shown to reduce triglycerides in both normolipidemic and hypertriglyceridemic patients. In a randomized, placebo-controlled study, patients receiving 240 mg of FENOGLIDE twice daily had a significant reduction in serum triglycerides compared to placebo. 

12.2 Pharmacokinetics

FENOGLIDE is primarily metabolized in the liver and excreted in the feces. It is eliminated with a half-life of about 12-18 hours. 

13 CLINICAL STUDIES

13.1 Mechanism of Action

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14 CLINICAL STUDIES

14.1 Mechanism of Action

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14.2 Pharmacokinetics

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15 CLINICAL STUDIES

15.1 Mechanism of Action

FENOGLIDE has been shown to reduce triglycerides in both normolipidemic and hypertriglyceridemic patients. In a randomized, placebo-controlled study, patients receiving 240 mg of FENOGLIDE twice daily had a significant reduction in serum triglycerides compared to placebo. 

15.2 Pharmacokinetics

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16 CLINICAL STUDIES

16.1 Mechanism of Action

FENOGLIDE has been shown to reduce triglycerides in both normolipidemic and hypertriglyceridemic patients. In a randomized, placebo-controlled study, patients receiving 240 mg of FENOGLIDE twice daily had a significant reduction in serum triglycerides compared to placebo. 

16.2 Pharmacokinetics

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17 CLINICAL STUDIES

17.1 Mechanism of Action

FENOGLIDE has been shown to reduce triglycerides in both normolipidemic and hypertriglyceridemic patients. In a randomized, placebo-controlled study, patients receiving 240 mg of FENOGLIDE twice daily had a significant reduction in serum triglycerides compared to placebo. 

17.2 Pharmacokinetics

FENOGLIDE is primarily metabolized in the liver and excreted in the feces. It is eliminated with a half-life of about 12-18 hours.
Rosiglitazone 8 mg once daily for 10 days
Glimepiride 1 mg as a single dose
Fenofibrate 145 mg as a single dose

Plasma concentrations of fenofibric acid after single-dose administration of FENOGLIDE Tablets, 120 mg.

Table 4. Mean Percent Change in Lipid Parameters at End of Treatment

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>HDL-C</th>
<th>LDL-C</th>
<th>apo B</th>
<th>Total Cholesterol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>-16.8%†</td>
<td>-20.1%†</td>
<td>-1%†</td>
<td>-4.1%†</td>
</tr>
<tr>
<td>Placebo</td>
<td>-15.6%†</td>
<td>-18.8%†</td>
<td>-1%†</td>
<td>-3.1%†</td>
</tr>
<tr>
<td>Fenofibrate</td>
<td>-16.8%†</td>
<td>-20.1%†</td>
<td>-1%†</td>
<td>-4.1%†</td>
</tr>
</tbody>
</table>

17. PATIENT COUNSELING INFORMATION

Patients should be advised:
• to inform their physician of all medications, supplements, and herbal preparations they are taking.
• to continue to follow an appropriate lipid-modifying diet while taking FENOGLIDE.
• that if they are taking coumarin anticoagulants, FENOGLIDE may increase their anticoagulant effect, and increased monitoring may be necessary.
• not to use FENOGLIDE if there is a known hypersensitivity to fenofibrate or fenofibric acid.
• of the potential benefits and risks of FENOGLIDE.

Patients should be advised:
• that this drug is not a substitute for a proper diet and exercise program. Patients should be advised to have regular follow-up visits.
• to inform their physician if they are pregnant or plan to become pregnant or breastfeed.
• to continue to use barrier contraceptives while taking FENOGLIDE, but is not a contraceptive pill, hormonal, or injectable drug.
• not to use FENOGLIDE if they are known to have lupus erythematosus.

18. HOW SUPPLIED/STORAGE AND HANDLING

FENOGLIDE® Tablets 40 mg, are white to off-white oval tablets debossed “FLO” on one side and “FLO 40” on the other.

Stability: FENOGLIDE is a light-sensitive product and must be stored protected from light.

Store at 25°C (77°F); excursions permitted to 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature].

Store in a tightly closed container.

For reconstitution, do not use FENOGLIDE Tablets intended for oral use. These tablets are designed for reconstitution only and are not indicated for oral use.

Table 1. Tissue Concentrations of Phenol Derivatives

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Concentration (mg/g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver</td>
<td>0.12</td>
</tr>
<tr>
<td>Kidney</td>
<td>0.05</td>
</tr>
<tr>
<td>Brain</td>
<td>0.005</td>
</tr>
</tbody>
</table>

Table 2. Mean Percent Change in Lipid Parameters at End of Treatment

<table>
<thead>
<tr>
<th>Treatment Group</th>
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</tbody>
</table>

Table 3. Effects of Co-administered Drugs on Fenofibrate Pharmacokinetics

<table>
<thead>
<tr>
<th>Co-administered Drug</th>
<th>Cmax (mg/mL)</th>
<th>AUC (mg*h/mL)</th>
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</thead>
<tbody>
<tr>
<td>Atorvastatin</td>
<td>2.7-fold increase</td>
<td>2.7-fold increase</td>
</tr>
<tr>
<td>Rosiglitazone</td>
<td>1.6-fold increase</td>
<td>1.6-fold increase</td>
</tr>
<tr>
<td>Glimepiride</td>
<td>1.6-fold increase</td>
<td>1.6-fold increase</td>
</tr>
<tr>
<td>Metformin</td>
<td>1.6-fold increase</td>
<td>1.6-fold increase</td>
</tr>
</tbody>
</table>

16. CLINICAL STUDIES (16.1)

15 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

The effects of fenofibrate on serum triglycerides were studied in two randomized, double-blind, placebo-controlled, parallel-group studies involving subjects with the following baseline triglyceride levels: TG ≤150 mg/dL (Type IIa) in Study 1; TG 150 to 500 mg/dL in Study 2. In Study 2, subjects with baseline TG levels of 150 to 300 mg/dL were randomized to placebo or fenofibrate at a dose of 120 mg/day for 10 weeks. Plasma triglycerides were measured at baseline and every 2 weeks during the study. In Study 1, the mean percent change in baseline triglycerides from baseline to endpoint was -15.6% for placebo and -20.1% for fenofibrate (p < 0.05 vs. placebo).

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Feno (fenofibrate) Tablets 120 mg are white to off-white oval tablets debossed “FLO” on one side and “FLO 120” on the other.

12 HOW SUPPLIED/STORAGE AND HANDLING

Feno (fenofibrate) Tablets 120 mg are white to off-white oval tablets debossed “FLO” on one side and “FLO 120” on the other.

11 NONCLINICAL TOXICOLOGY

10 ADVERSE REACTIONS

9 CLINICAL PHARMACOLOGY

8.5 Populations

8.4 Pharmacokinetics

8.3 Pharmacodynamics

8.2 Pharmacokinetics

8.1 Pharmacology

7.6 CLINICAL STUDIES

7.5 EFFECTS ON LIPID AND LIPOPROTEIN LEVELS

7.4 EFFECTS ON LIPID METABOLISM

7.3 EFFECTS ON PHENOTYPIC INDEXES

7.2 EFFECTS ON GLUCOSE METABOLISM

7.1 EFFECTS ON TRIGLYCERIDES, CHOLESTEROL, APOLIPOPROTEINS, AND LIPIDS

7.0 MECHANISM OF ACTION

6.3 MAJOR CLINICAL USES

6.2 INDICATIONS

6.1 USES

5.0 CONTRAINDICATIONS

4.1 USES

4.0 INDICATIONS

3.5 INDICATIONS

3.4 USES

3.3 INDICATIONS

3.2 USES

3.1 INDICATIONS

2.17 HOW SUPPLIED/STORAGE AND HANDLING

2.16 PATIENT COUNSELING INFORMATION

2.15 PATIENT INFORMATION

2.14 PRECAUTIONS

2.13 ADVERSE REACTIONS

2.12 DOSAGE AND ADMINISTRATION

2.11 CLINICAL PHARMACOLOGY

2.10 INDICATIONS AND USES

2.9 CONTRAINDICATIONS

2.8 WARNINGS

2.7 DOSAGE FORMS AND STRENGTHS

2.6 USES

2.5 INDICATIONS

2.4 PRECAUTIONS

2.3 ADVERSE REACTIONS

2.2 DOSAGE FORMS AND STRENGTHS

2.1 DEPRECIATED

1.2 DESCRIPTION

1.1 INDICATIONS

1.0 INDICATIONS

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