

Aktiebolaget DRACO
Lund/SWEDEN

REPLACED SHEETS	SG
☒ Description : paged1.... to paged ..5.....	
☒ Claim(s) : paged4.... to paged7.....	
☐ Drawing(s) : paged to paged	
☒ Abstract : paged7.... to paged7.....	
DATE OF RECEIPT	

Inventors: Carl-Axel Bauer
Leif-Åke Svensson

D 1065-1
90-02-27
ML/ÅW

New use

D 1065-1

90-02-27

New useField of the invention

5

The present invention is related to the use of a pharmaceutically acceptable salt of the bis-dimethyl carbamate pro drug of terbutaline, namely 5-[2-(tert-butylamino)-1-hydroxyethyl]-m-phenylene-
10 bis(dimethylcarbamate), called bambuterol or a pharmaceutically acceptable salt thereof in the manufacture of pharmaceutical preparations with lipid lowering effects.

15 Background of the invention

Bambuterol, which is described in the European patent EP 43807 is a pro drug of a beta-2-adrenergic agonist (terbutaline) and can be used in the treatment of
20 asthmatic patients, no effect on the lipoprotein metabolism has been reported earlier.

A positive correlation between high risk for coronary heart disease and increased concentrations of low-density
25 lipoprotein (LDL) has been well documented, Castelli WP, Doyle JT, Gordon T, et al. HDL Cholesterol and other lipids in coronary heart disease. The Cooperative Lipoprotein Phenotyping Study. Circulation 55, 767-772 (1977). In contrast, it has been suggested that an
30 increased concentration of high-density lipoprotein (HDL) may confer a low risk for heart disease. A more recent study, Gordon T, Castelli WP, Hjortland MC, et al. High density lipoprotein as a protective factor against coronary heart disease. The Framingham Study. Am J Med 62,
35 707-714 (1977), however, suggests that the ratio between LDL cholesterol and HDL Cholesterol is a better indicator of risk rather than either of them alone, on the premise that LDL transports the cholesterol produced in the liver



to the extra-hepatic tissues and HDL brings it back into the liver for further metabolism.

Different kinds of cholesterol are present in the blood,
5 and the most important forms are HDL = High Density Lipoprotein, and LDL = Low Density Lipoprotein.

Prior art

10 In an earlier study the beta-2-adrenoreceptor agonist terbutaline was found to significantly increase the HDL-cholesterol levels in healthy nonobese man. Cf Hooper P.L et al N.Engl.J.Med 305, p.1455, 1981. Furthermore, it is known from Jain R et al.Clin. Chem 29, p.1031, 1983 that
15 there might be an interrelationship between plasma cholinesterase inhibition and lipoprotein metabolism, resulting in a decrease in LDL cholesterol. There is, however, always a risk with plasma cholinesterase inhibition, namely if the effect is not selective towards
20 the plasma cholinesterase. An unselective inhibitor gives toxic effects depending on the inhibition of acetylcholinesterase. Thus in order to obtain an effective lipid lowering effect, the combination of a HDL-cholesterol increasing effect and a plasma cholinesterase
25 inhibiting effect, which will lower LDL, is wanted.

Outline of the invention

With the background above it was decided to test the lipid
30 lowering effect of bambuterol, which is a specific inhibitor of plasma cholinesterase, which generates the beta-2-adrenoreceptor agonist terbutaline, which gives a significantly prolonged effect duration 24 h versus 8 h for conventional terbutaline tablets or 12 h for
35 terbutaline slow release tablets (compared to terbutaline). The lipid lowering preparation contains between 5-30 mg of bambuterol, preferably 10-20 mg. It is especially preferred to use the hydrochloride of



bambuterol. The pharmaceutical preparations are preferably in the form of tablets, but it is also possible to use other kinds of preparations such as capsules, oral solutions or injection solutions.

5

Conventional pharmaceutical preparations can be used.

Biological test

10 In a study on the effects of bambuterol and terbutaline slow release on lipoprotein metabolism in healthy volunteers with normal lipoprotein status both bambuterol and terbutaline induced favourable changes in lipoprotein metabolism, and atherogenic index (s-LDL/s-HDL),
15 statistically significant and clinically relevant elevations were seen in HDL cholesterol and Apo A1 concentrations (in Apo A1 the major protein component is HDL), while plasma triglycerides levels decreased. In parallel the activity of lipoprotein lipase, increased,
20 suggesting that the alterations in plasma lipoprotein concentrations were mediated via an increase in the rate of turnover of triglyceride-rich lipoproteins. No effect on LDL cholesterol could be demonstrated with any of the drugs.

25

On the other hand, in a second placebo controlled study in 16 patients with diabetes mellitus with moderately impaired lipoprotein status, bambuterol 20 mg once daily for 5 weeks was found to significantly rise S-HDL-
30 cholesterol levels and to lower S-LDL-cholesterol levels compared to placebo. This was accompanied by a significant decrease in both S-cholesterol and S-triglyceride levels. Cf. Table 1.

This Sheet Has Been Replaced



Table 1. Effects of bambuterol on lipoprotein metabolism markers in 16 diabetes mellitus patients.

N = 16		Before treatment	After 3 weeks	After 6 weeks	
<u>S-HDL-Cholesterol</u> (mmol/L)	1.06 ± 0.31	P: 1.12 ± 0.34 B: 1.29 ± 0.35	1.18 ± 0.33 1.26 ± 0.35	p=0.0001	
<u>S-LDL-Cholesterol</u> (mmol/L)	4.04 ± 0.92	P: 4.11 ± 0.89 B: 3.85 ± 0.98	4.11 ± 0.93 3.90 ± 0.97	p=0.004	
<u>S-Cholesterol</u> (mmol/L)	5.92 ± 1.08	P: 6.02 ± 0.93 B: 5.76 ± 1.14	6.00 ± 0.89 5.78 ± 1.05	p=0.029	
<u>S-Triglyceride</u> (mmol/L)	1.86 ± 1.62	P: 1.69 ± 1.10 B: 1.38 ± 0.86	1.58 ± 0.98 1.36 ± 0.86	p=0.026	

P = Placebo
B = Bambuterol

This Sheet Has Been Replaced



Conclusion

From the results given in table 1, it can be concluded
5 that bambuterol gives beneficial effects on the
lipoprotein metabolism in patients with moderately
impaired lipoprotein status. The effect of bambuterol is
persistent and highly significant and of the same order as
seen with other well known lipid lowering drugs.
10 Bambuterol thus offers a new, convenient lipid lowering
therapy, since bambuterol is dosed only once daily.

15

20

25

30

35

This Sheet Has Been Replaced



Claims

1. Use of 5-[2-(tert-butylamino)-1-hydroxyethyl]-m-phenylene-bis(dimethylcarbamate), bambuterol, or a pharmaceutically acceptable salt thereof, in the manufacture of a pharmaceutical preparation with lipid lowering effects.
2. Use according to claim 1, wherein bambuterol is in the form of its hydrochloride.
3. A method for obtaining of lipid lowering effect whereby a lipid lowering effective amount of bambuterol or a pharmaceutically acceptable salt thereof is used.
4. A method according to claim 3 wherein the hydrochloride of bambuterol is used.
5. A pharmaceutical preparation for use as in lowering the lipid content of the blood, wherein the active ingredient is bambuterol or a pharmaceutically acceptable salt thereof.
6. A preparation according to claim 5 wherein the active ingredient is the hydrochloride of bambuterol.

This Sheet Has Been Replaced



Abstract

Use of bambuterol or a pharmaceutically acceptable salt thereof for the manufacture of a pharmaceutical
5 preparation with lipid lowering effect.

This Sheet Has Been Replaced



Aktiebolaget DRACO
Lund/SWEDEN

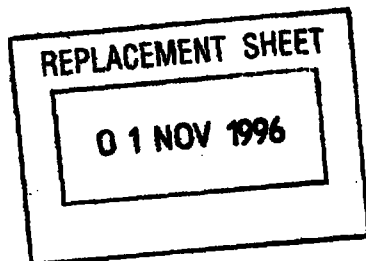
REPLACEMENT SHEETS		SG
☒	Description : paged ..1... to paged ..5...	
☒	Claim(s) : paged ..4... to paged	
☐	Drawing(s) : paged to paged	
☒	Abstract : paged ..7... to paged	
DATE OF RECEIPT 4/14/96		

REPLACED SHEETS		SG
☒	Description : paged1... to paged ..5.....	
☒	Claim(s) : paged4... to paged	
☐	Drawing(s) : paged to paged	
☒	Abstract : paged7... to paged	
DATE OF RECEIPT		

Inventors: Carl-Axel Bauer
Leif-Åke Svensson

D 1065-1
90-02-27
ML/ÅW

New use

**NEW USE OF BAMBUTEROL**Field of the invention

The present invention is related to the use of a pharmaceutically acceptable salt of the bis-dimethyl carbamate pro drug of terbutaline, namely 5-[2-(tert-butylamino)-1-hydroxyethyl]-m-phenylene-bis(dimethylcarbamate), called bambuterol or a pharmaceutically acceptable salt thereof in the manufacture of pharmaceutical preparations with lipid lowering effects.

Background of the invention

Bambuterol, which is described in the European patent EP 43807 is a pro drug of a beta-2-adrenergic agonist (terbutaline) and can be used in the treatment of asthmatic patients, no effect on the lipoprotein metabolism has been reported earlier.

A positive correlation between high risk for coronary heart disease and increased concentrations of low-density lipoprotein (LDL) has been well documented, Castelli WP, Doyle JT, Gordon T, et al. HDL Cholesterol and other lipids in coronary heart disease. The Cooperative Lipoprotein Phenotyping Study. Circulation 55, 767-772 (1977). In contrast, it has been suggested that an increased concentration of high-density lipoprotein (HDL) may confer a low risk for heart disease. A more recent study, Gordon T, Castelli WP, Hjortland MC, et al. High density lipoprotein as a protective factor against coronary heart disease. The Framingham Study. Am J Med 62, 707-714 (1977), however, suggests that the ratio between LDL cholesterol and HDL Cholesterol is a better indicator of risk rather than either of them alone, on the premise that LDL transports the cholesterol produced in the liver

2-566-1

01 NOV 1996

This Sheet Has Been Replaced



to the extra-hepatic tissues and HDL brings it back into the liver for further metabolism.

Different kinds of cholesterol are present in the blood, and the most important forms are HDL = High Density Lipoprotein, and LDL = Low Density Lipoprotein.

Prior art

In an earlier study the beta-2-adrenoreceptor agonist terbutaline was found to significantly increase the HDL-cholesterol levels in healthy nonobese man. Cf Hooper P.L et al N.Engl.J.Med 305, p.1455, 1981. Furthermore, it is known from Jain R et al.Clin. Chem 29, p.1031, 1983 that there might be an interrelationship between plasma cholinesterase inhibition and lipoprotein metabolism, resulting in a decrease in LDL cholesterol. There is, however, always a risk with plasma cholinesterase inhibition, namely if the effect is not selective towards the plasma cholinesterase. An unselective inhibitor gives toxic effects depending on the inhibition of acetylcholinesterase. Thus in order to obtain an effective lipid lowering effect, the combination of a HDL-cholesterol increasing effect and a plasma cholinesterase inhibiting effect, which will lower LDL, is wanted.

Outline of the invention

With the background above it was decided to test the lipid lowering effect of bambuterol, which is a specific inhibitor of plasma cholinesterase, which generates the beta-2-adrenoreceptor agonist terbutaline, which gives a significantly prolonged effect duration 24 h versus 8 h for conventional terbutaline tablets or 12 h for terbutaline slow release tablets (compared to terbutaline). The lipid lowering preparation contains between 5-30 mg of bambuterol, preferably 10-20 mg. It is especially preferred to use the hydrochloride of

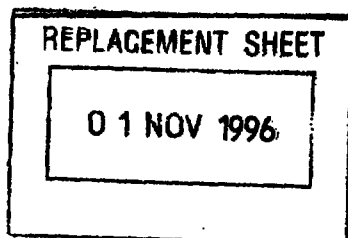
bambuterol. The pharmaceutical preparations are preferably in the form of tablets, but it is also possible to use other kinds of preparations such as capsules, oral solutions or injection solutions.

Conventional pharmaceutical preparations can be used.

Biological test

In a study on the effects of bambuterol and terbutaline slow release on lipoprotein metabolism in healthy volunteers with normal lipoprotein status both bambuterol and terbutaline induced favourable changes in lipoprotein metabolism, and atherogenic index (s-LDL/s-HDL), statistically significant and clinically relevant elevations were seen in HDL cholesterol and Apo A1 concentrations (in Apo A1 the major protein component is HDL), while plasma triglycerides levels decreased. In parallel the activity of lipoprotein lipase, increased, suggesting that the alterations in plasma lipoprotein concentrations were mediated via an increase in the rate of turnover of triglyceride-rich lipoproteins. No effect on LDL cholesterol could be demonstrated with any of the drugs.

On the other hand, in a second placebo controlled study in 16 patients with diabetes mellitus with moderately impaired lipoprotein status, bambuterol 20 mg once daily for 6 weeks was found to significantly rise S-HDL-cholesterol levels and to lower S-LDL-cholesterol levels compared to placebo. This was accompanied by a significant decrease in both S-cholesterol and S-triglyceride levels. Cf Table 1.



This Sheet Has Been Replaced



Table 1. Effects of bambuterol on lipoprotein metabolism markers in 16 diabetes mellitus patients.

N = 16		Before treatment	After 3 weeks	After 6 weeks	
4	<u>S-HDL-Cholesterol</u> (mmol/L)	1.06 ± 0.31	P: 1.12 ± 0.34 B: 1.29 ± 0.35	1.18 ± 0.33 1.26 ± 0.35	p=0.0001
	<u>S-LDL-Cholesterol</u> (mmol/L)	4.04 ± 0.92	P: 4.11 ± 0.89 B: 3.85 ± 0.98	4.11 ± 0.93 3.90 ± 0.97	p=0.004
	<u>S-Cholesterol</u> (mmol/L)	5.92 ± 1.08	P: 6.02 ± 0.93 B: 5.76 ± 1.14	6.00 ± 0.89 5.78 ± 1.05	p=0.029
	<u>S-Triglyceride</u> (mmol/L)	1.86 ± 1.62	P: 1.69 ± 1.10 B: 1.38 ± 0.86	1.58 ± 0.98 1.36 ± 0.86	p=0.026

P = Placebo
B = Bambuterol

REPLACEMENT SHEET

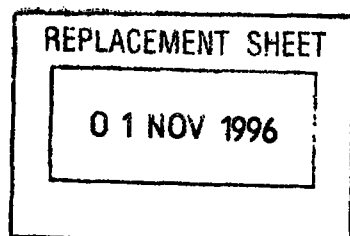
01 NOV 1996

This Sheet Has Been Replaced



Conclusion

From the results given in table 1, it can be concluded that bambuterol gives beneficial effects on the lipoprotein metabolism in patients with moderately impaired lipoprotein status. The effect of bambuterol is persistent and highly significant and of the same order as seen with other well known lipid lowering drugs. Bambuterol thus offers a new, convenient lipid lowering therapy, since bambuterol is dosed only once daily.

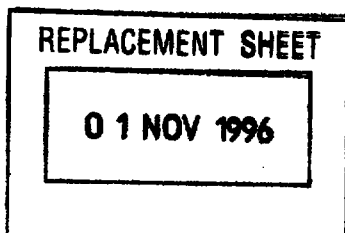


This Sheet Has Been Replaced



Claims

1. Use of 5-[2-(tert-butylamino)-1-hydroxyethyl]-m-phenylene-bis(dimethylcarbamate), bambuterol, or a pharmaceutically acceptable salt thereof, in the manufacture of a pharmaceutical preparation with lipid lowering effects.
2. Use according to claim 1, wherein bambuterol is in the form of its hydrochloride.
3. A method for obtaining of lipid lowering effect whereby a lipid lowering effective amount of bambuterol or a pharmaceutically acceptable salt thereof is used.
4. A method according to claim 3 wherein the hydrochloride of bambuterol is used.
5. A pharmaceutical preparation for use as in lowering the lipid content of the blood, wherein the active ingredient is bambuterol or a pharmaceutically acceptable salt thereof.
6. A preparation according to claim 5 wherein the active ingredient is the hydrochloride of bambuterol.



NEW USE OF BAMBUTEROL

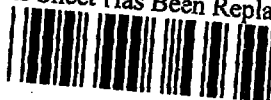
Abstract

Use of bambuterol or a pharmaceutically acceptable salt thereof for the manufacture of a pharmaceutical preparation with lipid lowering effect.

REPLACEMENT SHEET

01 NOV 1996

This Sheet Has Been Replaced



REPLACEMENT SHEET

21 JUL 1997

9103404-2 JP05

- 1 -

NEW USE OF BAMBUTEROL

Description

Field of the invention

The present invention is related to the use of the bis-dimethyl carbamate pro drug of terbutaline, namely 5-[2-(tert-butylamino)-1-hydroxyethyl]-m-phenylene-bis(dimethylcarbamate), called bambuterol, or a pharmaceutically acceptable salt thereof, in the manufacture of pharmaceutical preparations with lipid lowering effects.

Background of the invention

Bambuterol, which is described in the European patent EP 43807 is a pro drug of a beta-2-adrenergic agonist (terbutaline) and can be used in the treatment of asthmatic patients; no effect on the lipoprotein metabolism has been reported earlier.

A positive correlation between high risk for coronary heart disease and increased concentrations of low-density lipoprotein (LDL) has been well documented, Castelli WP, Doyle JT, Gordon T, et al. HDL Cholesterol and other lipids in coronary heart disease. The Cooperative Lipoprotein Phenotyping Study. Circulation 55, 767-772 (1977). In contrast, it has been suggested that an increased concentration of high-density lipoprotein (HDL) may confer a low risk for heart disease. A more recent study Gordon T, Castelli WP, Hjortland MC, et al. High density lipoprotein as a protective factor against coronary heart disease. The Framingham Study. Am J Med 62, 707-714 (1977), however, suggests that the ratio between LDL cholesterol and HDL Cholesterol is a better indicator of risk rather than either of them alone, on the premise that LDL transports the cholesterol produced in the liver to the extra-hepatic tissues and HDL brings it back into the liver for further metabolism.

Different kinds of cholesterol are present in the blood, and the most important forms are HDL = High Density Lipoprotein, and LDL = Low Density Lipoprotein.

Prior art

In an earlier study the beta-2-adrenoreceptor agonist terbutaline was found to significantly increase the HDL-cholesterol levels in healthy nonobese man. Cf Hooper P.L. et al N.Engl.J.Med 305, p.1455, 1981. Furthermore, it is known from Jain R et al.Clin. Chem 29, p.1031, 1983 that there might be an interrelationship between plasma cholinesterase inhibition and lipoprotein metabolism, resulting in a decrease in LDL cholesterol. There is, however, always a risk with plasma cholinesterase inhibition, namely if the effect is not selective towards the plasma cholinesterase. An unselective inhibitor gives toxic effects depending on the inhibition of acetylcholinesterase. Thus in order to obtain an effective lipid lowering effect, the combination of a HDL-cholesterol increasing effect and a plasma cholinesterase inhibiting effect, which will lower LDL, is wanted.

Outline of the invention

With the background above it was decided to test the lipid lowering effect of bambuterol, which is a specific inhibitor of plasma cholinesterase, which generates the beta-2-adrenoreceptor agonist terbutaline and which gives a significantly prolonged effect duration; 24 h versus 8 h for conventional terbutaline tablets or 12 h for terbutaline slow release tablets (compared to terbutaline). The lipid lowering preparation contains between 5-30 mg of bambuterol, preferably 10-20 mg. It is especially preferred to use the hydrochloride of bambuterol. The pharmaceutical preparations are preferably in the form of tablets, but it is also possible to use other kinds of preparations such as capsules, oral solutions or injection solutions.

Conventional pharmaceutical preparations can be used.

Biological test

In a study on the effects of bambuterol and terbutaline slow release on lipoprotein metabolism in healthy volunteers with normal lipoprotein status both bambuterol and terbutaline induced favourable changes in lipoprotein metabolism, and atherogenic index (s-LDL/s-HDL), statistically significant and clinically relevant elevations were seen in HDL cholesterol and Apo A1 concentrations (in Apo A1 the major protein component is HDL), while plasma triglycerides levels decreased. In parallel the activity of lipoprotein lipase, increased, suggesting that the alterations in plasma lipoprotein concentrations were mediated via an increase in the rate of turnover of triglyceride-rich lipoproteins. No effect on LDL cholesterol could be demonstrated with any of the drugs.

On the other hand, in a second placebo controlled study in 16 patients with diabetes mellitus with moderately impaired lipoprotein status, bambuterol 20 mg once daily for 6 weeks was found to significantly rise S-HDL-cholesterol

REPLACEMENT SHEETS SG
☒ Description : paged ..1.. to paged ..2..
☒ Claim(s) : paged ..2.. to paged
☐ Drawing(s) : paged to paged
☒ Abstract : paged ..3.. to paged

DATE OF RECEIPT ...21/7/97.....

THIS SHEET HAS BEEN
REPLACED

levels and to lower S-LDL-cholesterol levels compared to placebo. This was accompanied by a significant decrease in both S-cholesterol and S-triglyceride levels. Cf Table 1.

Table 1.

Effects of bambuterol on lipoprotein metabolism markers in 16 diabetes mellitus patients.				
N = 16	Before treatment	After 3 weeks	After 6 weeks	
<u>S-HDL-Cholesterol</u> (mmol/L)	1.06 ± 0.31	P: 1.12 ± 0.34 B: 1.29 ± 0.35	1.18 ± 0.33 1.26 ± 0.35	p=0.0001
<u>S-LDL-Cholesterol</u> (mmol/L)	4.04 ± 0.92	P: 4.11 ± 0.89 B: 3.85 ± 0.98	4.11 ± 0.93 3.90 ± 0.97	
<u>S-Cholesterol</u> (mmol/L)	5.92 ± 1.08	P: 6.02 ± 0.93 B: 5.76 ± 1.14	6.00 ± 0.89 5.78 ± 1.05	p=0.004
<u>S-Triglyceride</u> (mmol/L)	1.86 ± 1.62	P: 1.69 ± 1.10 B: 1.38 ± 0.86	1.58 ± 0.98 1.36 ± 0.86	p=0.029
P = Placebo B = Bambuterol				

Conclusion

From the results given in Table 1, it can be concluded that bambuterol gives beneficial effects on the lipoprotein metabolism in patients with moderately impaired lipoprotein status. The effect of bambuterol is persistent and highly significant and of the same order as seen with other well known lipid lowering drugs. Bambuterol thus offers a new, convenient lipid lowering therapy, since bambuterol is dosed only once daily.

Claims

1. Use of bambuterol, or a pharmaceutically acceptable salt thereof, in the manufacture of a pharmaceutical preparation with lipid lowering effects.
2. Use according to claim 1, wherein bambuterol is in the form of its hydrochloride.
3. Use according to either claim 1 or claim 2, wherein the preparation contains between 5-30 mg of bambuterol.
4. Use according to claim 3, wherein the preparation contains 10-20 mg of bambuterol.
5. Use according to any one of the preceding claims, wherein the preparation is to be taken once a day.

This Sheet Has Been Replaced



REPLACEMENT SHEET

21 JUL 1997

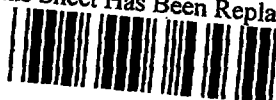
THIS SHEET HAS BEEN
REPLACED

NEW USE OF BAMBUTEROL

Abstract

Use of bambuterol or a pharmaceutically acceptable salt thereof for the manufacture of a pharmaceutical preparation with lipid lowering effect.

This Sheet Has Been Replaced



REPLACEMENT SHEET

21 JUL 1997

REPLACEMENT SHEET

- 2 -

levels and to lower S-LDL-cholesterol levels compared to placebo. This was accompanied by a significant decrease in both S-cholesterol and S-triglyceride levels. Cf Table 1.

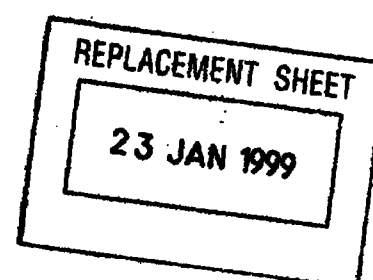
Table 1.

Effects of bambuterol on lipoprotein metabolism markers in 16 diabetes mellitus patients.				
N = 16	Before treatment	After 3 weeks	After 6 weeks	
<u>S-HDL-Cholesterol</u> (mmol/L)	1.06 ± 0.31	P: 1.12 ± 0.34 B: 1.29 ± 0.35	1.18 ± 0.33 1.26 ± 0.35	p=0.0001
<u>S-LDL-Cholesterol</u> (mmol/L)	4.04 ± 0.92	P: 4.11 ± 0.89 B: 3.85 ± 0.98	4.11 ± 0.93 3.90 ± 0.97	p=0.004
<u>S-Cholesterol</u> (mmol/L)	5.92 ± 1.08	P: 6.02 ± 0.93 B: 5.76 ± 1.14	6.00 ± 0.89 5.78 ± 1.05	p=0.029
<u>S-Triglyceride</u> (mmol/L)	1.86 ± 1.82	P: 1.69 ± 1.10 B: 1.38 ± 0.86	1.58 ± 0.98 1.36 ± 0.86	p=0.026
P = Placebo B = Bambuterol				

Conclusion

From the results given in Table 1, it can be concluded that bambuterol gives beneficial effects on the lipoprotein metabolism in patients with moderately impaired lipoprotein status. The effect of bambuterol is persistent and highly significant and of the same order as seen with other well known lipid lowering drugs. Bambuterol thus offers a new, convenient lipid lowering therapy, since bambuterol is dosed only once daily.

REPLACEMENT SHEETS SG	
☒ Description :	paged ...2... to paged ...
☒ Claim(s) :	paged ...3... to paged ...
☐ Drawing(s) :	paged to paged
☒ Abstract :	paged ...4... to paged ...
DATE OF RECEIPT ...23/1/99.....	



- 3 -

**Claims**

1. Use of bambuterol, or a pharmaceutically acceptable salt thereof, in the manufacture of a pharmaceutical preparation with lipid lowering effects.
2. Use according to claim 1, wherein bambuterol is in the form of its hydrochloride.
3. Use according to either claim 1 or claim 2, wherein the preparation contains between 5-30 mg of bambuterol.
4. Use according to claim 3, wherein the preparation contains 10-20 mg of bambuterol.
5. Use according to any one of the preceding claims, wherein the preparation is to be taken once a day.

REPLACEMENT SHEET

23 JAN 1999

- 4 -

NEW USE OF BAMBUTEROL

Abstract

Use of bambuterol or a pharmaceutically acceptable salt thereof for the manufacture of a pharmaceutical preparation with lipid lowering effect.

