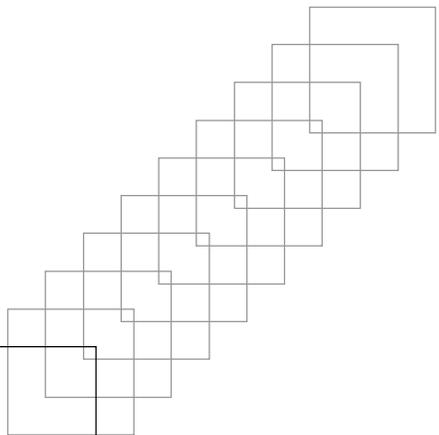




BRIDGING REPORT



**Bridging Study of the Package Information
Leaflet for:**

**[Product Name] Preservative free 40 micrograms/ml
eye drops solution, multi - dose container
Travoprost**

Date: 22/12/2014





Bridging Report for
[Product Name] Preservative free 40 micrograms/ml eye drops solution, multi - dose container
Travoprost

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1. Introduction

According to the directive Article 59(3) of Directive 2001/83/EC as amended by directive 2004/27/EC, **ELC Group** confirms that the Package Information Leaflet for **[Product Name] Preservative free 40 micrograms/ml eye drops solution, multi - dose container** (henceforth referred to as the Daughter PIL) contains the required statutory information. Furthermore, it is confirmed that the Daughter Package Information Leaflet is similar to the Package Information Leaflet for **[Travoprost] 40 micrograms/ml eye drops, solution** (henceforth referred to as the Parent PIL), and therefore requires no separate user testing.

The basis for this report and its evaluation comes from both the European Commission (Article 59(3) of Council Directive 2001/83/EC and also by Article 63(2) of Directive 2001/83/EC as amended), the European Commission document “Guideline on the readability of the labelling and package leaflet of medicinal products for human use” (2009), Recommendations for Bridging from CMDh (April 2009, revision 1) and MHRA guidance on bridging (Guidance for the Pharmaceutical Industry on the use of BRIDGING STUDIES to demonstrate compliance with article 59(3) of Council Directive 2001/83/EC [Consultation with Target Patient Groups]), as well as specific information and feedback obtained by ELC Group from the relevant authorities on the use of bridging in user testing schemes.

Differences between the Daughter PIL and the Parent PIL are presented with analysis and evidence which show that these differences have little material impact on readability. Results from the readability testing study of the Parent PIL should therefore be extrapolated to the Daughter PIL.

Name of the Daughter PIL:

[Product Name] Preservative free 40 micrograms/ml eye drops solution, multi - dose container

Name of the Parent PIL:

[Travoprost] 40 micrograms/ml eye drops, solution

Marketing Authorisation Holder/Applicant:

PharmaSwiss Česká republika s.r.o.
Jankovcova 1569/2c
170 00 Praha 7, Czech Republic

This report was prepared by:

Name:
Title: Life Sciences Project Manager

Company's address:



2. Product Descriptions

Daughter PIL

[Product Name] Preservative Free eye drops are used to treat high pressure in the eye. This pressure can lead to an illness called **glaucoma**.

High pressure in the eye. Your eyeballs contain a clear, watery liquid which feeds the inside of the eye. Liquid is always emptying out of the eye, and more liquid is always being produced. If the eye fills up faster than it empties, the pressure inside the eye builds up. If it gets too high, it can damage your sight.

[Product Name] Preservative Free is one of a group of medicines for glaucoma called prostaglandin analogues. It works by increasing the outflow of liquid, which lowers the pressure in the eye. It may be used on its own or with other drops e.g. beta-blockers, which also reduce pressure.

Parent PIL

[Travoprost] eye drops are used to treat high pressure in the eye. This pressure can lead to an illness called **glaucoma**.

High pressure in the eye. Your eyeballs contain a clear, watery liquid which feeds the inside of the eye. Liquid is always emptying out of the eye, and more liquid is always being produced. If the eye fills up faster than it empties, the pressure inside the eye builds up. If it gets too high, it can damage your sight.

[Travoprost] is one of a group of medicines for glaucoma called prostaglandin analogues. It works by increasing the outflow of liquid, which lowers the pressure in the eye. It may be used on its own or with other drops e.g. beta-blockers, which also reduce pressure.



3. Summary of the Bridging Process

Any differences between the two PILs in both the textual and visual presentations are outlined and analysed in this report. Once any and all differences have been acknowledged, addressed and discussed, it will be shown that the Daughter PIL requires no separate user testing due to its similarity to the already tested Parent PIL.

3.1 Aspects Investigated and Methodology Used

The Daughter PIL proposed for bridging and the Parent PIL were compared based on the following criteria:

- **Visual Presentation:** leaflet dimension, font, font size, coloring scheme, spacing, format, organization of sections and any graphics used in the PIL.
- **Contents:** key safety messages including indications, contraindications, side effects, ingredients, storage information, and any other relevant data.

3.2 Detailed Bridging Procedure

1. Readability testing was conducted on the Parent PIL.
2. Initial review and comparison of the Daughter and the Parent PIL based on the criteria above.
3. It was concluded that the Daughter PIL is similar to the Parent PIL.
4. A mock up was created for the Daughter PIL that is as similar as possible to the Parent PIL.
5. Differences between the Daughter PIL and the Parent PIL were analysed.
6. This final bridging report was created.

4. Timeline



5. Bridging Analysis Results

According to the guidance on the use of bridging studies, bridging is acceptable for Package Leaflets with minor differences. The content analysis to follow will look at the key differences and corresponding justifications so that each difference is deemed to be acceptable and/or of minimal significance.

5.1 Differences in Leaflet Content

This portion of the bridging study focuses on content present in the Daughter PIL and not present in the Parent PIL, since the contents of the Parent PIL have successfully completed readability testing. The following table highlights and discusses these differences.

Table 1. Differences by Package Leaflet Section

	Parent PIL	Daughter PIL
Top of leaflet	<p><u>[Travoprost]</u> 40 micrograms/ml eye drops, solution Travoprost</p>	<p><u>[Product Name] Preservative free</u> 40 micrograms/ml eye drops solution, <u>multi - dose container</u> Travoprost</p>
<i>Discussion</i>	<p>Although the active substance is identical in both medicines, the medicines' names are not the same. Additionally the Daughter PIL lists a different container. These minor differences will not affect the readability so no separate testing of the Daughter PIL should be required.</p> <p>Note: This point regarding name and packaging will not be highlighted or discussed again in this report.</p>	
Section #2	<p>[Travoprost] contains benzalkonium chloride If you wear soft contact lenses. Do not use the drops with your lenses in. Wait 15 minutes after using the drops before putting your lenses back in. There is a preservative in this medicine (benzalkonium chloride) that can discolour soft lenses.</p> <p>This preservative may cause also eye irritation or disruption to the surface of the eye.</p>	Not listed

	Parent PIL	Daughter PIL
<i>Discussion</i>	The Daughter PIL is for a preservative free medicinal product and therefore does not contain benzalkonium chloride which is the preservative used in the Parent PIL medicine. Because the Parent PIL is more complex in this case and it has successfully met the readability testing criteria, no separate testing should be required for the Daughter leaflet.	

Section #3

Instructions for use

- | | |
|---|--|
| <p><u>Immediately before using a bottle for the first time, tear-off the overwrap pouch (picture 1). Take out the bottle and [...]</u></p> <ul style="list-style-type: none"> • [...] • <u>Twist off</u> the cap.[...]
<ul style="list-style-type: none"> • Hold the bottle, pointing down, between your thumb and fingers [...]
<ul style="list-style-type: none"> • Close the <u>bottle</u> [...]. • [...] Do not open the <u>pouch</u> until you need to use the <u>bottle</u>. | <ul style="list-style-type: none"> • <u>Take the multi-dose container (picture 1a) out of the carton box. If the container is stored within an overwrap pouch, tear – off to open (picture 1b) and [...]</u> • [...] • <u>Remove the cap</u>. [...]
<ul style="list-style-type: none"> • Hold the bottle, <u>with the tip pointing down, between your thumb and fingers and press down on the bottom side (picture 3).</u> [...]
<ul style="list-style-type: none"> • Close the <u>multi-dose container</u> [...]. • [...] Do not open the <u>cap</u> until you need to use the <u>multi-dose container</u>. |
|---|--|

<i>Discussion</i>	The Daughter PIL is for a multi-dose container and not a bottle, therefore the wording for the method of use has changed slightly (see underlined). The supplementary wording reinforces the safe and effective use of the medicine and it is written using understandable language. Because the action taken by a patient is similar, these differences should not impact the readability of the Daughter PIL and no separate testing should be required.
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Section #3 Not listed



Image inserted

Parent PIL	Daughter PIL
------------	--------------



[...]
 image deleted

[...]



image inserted

[...]

[...]

Discussion The images on how to use the medicine in the Daughter PIL were changed slightly. The additional images are of the multi-dose container and will enhance the understanding of how to use the specific container for the Daughter PIL. These additional images should not impact the readability or understanding of the Daughter PIL and no separate testing should be required.

Section#5

Do not use this medicine if you notice that the tamper evident seal has been broken [...]

Before opening, keep bottle in overwrap pouch in order to protect from moisture.
 [...]

You must throw away the bottle 4 weeks after you first opened it, to prevent infections, and use a new bottle.
 [...]

Do not use this medicine if you notice that the multi dose container has been broken [...].

Before opening, keep bottle in overwrap pouch (if available) in order to protect from moisture.
 [...]

You must throw away the bottle 4 weeks after you first opened it, to prevent infections. [...].

Discussion Minor wording changes were made to how to store the Daughter medicinal product. The supplement wording will reinforce how to safely store a multi-dose container and it is written using understandable language. These minor differences should not impact the readability of the Daughter PIL and therefore no separate testing should be required.

Section #6

What [Travoprost] contains
 [...]

- The other ingredients are benzalkonium chloride, macrogol glycerol hydroxy stearate 40, trometamol, disodium edetate, [...]

What [Product Name] Preservative Free contains
 [...]

- The other ingredients are macrogol glycerol hydroxy stearate 40, sodium chloride, propylene glycol, [...]



Bridging Report for
[Product Name] Preservative free 40 micrograms/ml eye drops solution, multi - dose container
Travoprost

Parent PIL

Daughter PIL

What Travoprost looks like and the contents of the pack

Travoprost is a clear, colourless solution supplied in packs containing translucent polypropylene 5ml bottle(s) with transparent low density polyethylene (LDPE) dropper and white high density polyethylene (HDPE) tamper-proof screw cap

packaged in overwrap pouch. Each bottle contains 2.5 ml solution.
[...]

DK/H/2189/001/DC: Cartons containing 1 or 3 bottles.

DK/H/2197/001/DC: Cartons containing 1, 3, 6, 9, 10 or 12 bottles.

DK/H/2198/001/DC: Cartons containing 1 or 3 bottles.

DK/H/2237/001/DC: Cartons containing 1 or 3 bottles.

DK/H/2287/001/DC: Cartons containing 1 or 3 bottles.

What [Product Name] Preservative Free looks like and the contents of the pack

[Product Name] Preservative Free is presented as a 2.5 ml clear, colorless aqueous solution, in a cardboard box containing

a 5 ml white plastic multi-dose container.

The multi – dose container can be available in an overwrap, inside the cardboard box.
[...]

Cartons containing [X] number of bottles.

Discussion

Both medicines list different excipients; additionally, they are using different types of packaging (see underlined). The information in the Daughter PIL is no more complicated than the Parent PIL; it was presented in a clear and organized manner. Additionally, the action a patient needs to take remains the same. Consequently, readability will not be affected so testing should not be required for the Daughter PIL.



5.2 Layout, Style and Language

Layout and style

	Parent PIL	Daughter PIL
Body Text		
Headings		
PIL Dimension	170 x 350 mm	170 x 350 mm
Colouring Scheme	White background with black body text and bold, black section headings	White background with black body text and bold, black section headings
Columns	Two columns	Two columns
Format	Double-sided	Double-sided
<i>Discussion</i>	The Daughter PIL and the Parent PIL are identical in both style and layout. The use of an index, numbered section headings and bold sub-headings were implemented consistently throughout both leaflets. Additionally, text is left-aligned and techniques to improve readability such as bullet-point lists, line spacing and bold font were applied in similar ways throughout both PILs.	

Language

Both PILs were written in English according to the QRD template. Except where indicated in Section 5.1, as well as where the Parent PIL serves as a more complex PIL, identical sentences were used for the information presented in both PILs.



6. Conclusion

In conclusion, this analysis is able to clearly establish that the leaflet text and mockup format for **[Product Name] Preservative free 40 micrograms/ml eye drops solution, multi - dose container** (Daughter PIL) is strongly similar to **[Travoprost] 40 micrograms/ml eye drops, solution** (Parent PIL). The results of this bridging study indicate that the leaflet for Daughter PIL is well structured and organized, easy to understand and written in a comprehensible manner and therefore requires no separate user testing.

ELC also confirms the report conforms to the principles and success criteria featured in the European Commission's document "Consultation With Target Patient Groups - Meeting The Requirements Of Article 59(3) Without The Need For A Full Test - Recommendations For Bridging" (Revision 1, April 2009).

Based on the above mentioned facts the package leaflet can be qualified as ACCEPTABLE.

Life Sciences Project Manager



Bridging Report for
[Product Name] Preservative free 40 micrograms/ml eye drops solution, multi - dose container
Travoprost

7. Appendices



Bridging Report for
[Product Name] Preservative free 40 micrograms/ml eye drops solution, multi - dose container
Travoprost

Appendix 1 - The Package Leaflet for the Daughter PIL: [Product Name] Preservative free 40 micrograms/ml eye drops solution, multi - dose container

Package leaflet: Information for the user

[Product Name] Preservative free 40 micrograms/ml eye drops solution, multi-dose container Travoprost

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What [Product Name] Preservative Free is and what it is used for
2. What you need to know before you use [Product Name] Preservative Free
3. How to use [Product Name] Preservative Free
4. Possible side effects
5. How to store [Product Name] Preservative Free
6. Contents of the pack and other information

1. What [Product Name] Preservative Free is and what it is used for

[Product Name] Preservative Free eye drops are used to treat high pressure in the eye. This pressure can lead to an illness called **glaucoma**.

High pressure in the eye. Your eyeballs contain a clear, watery liquid which feeds the inside of the eye. Liquid is always emptying out of the eye, and more liquid is always being produced. If the eye fills up faster than it empties, the pressure inside the eye builds up. If it gets too high, it can damage your sight.

[Product Name] Preservative Free is one of a group of medicines for glaucoma called prostaglandin analogues. It works by increasing the outflow of liquid, which lowers the pressure in the eye. It may be used on its own or with other drops e.g. beta-blockers, which also reduce pressure.

2. What you need to know before you use [Product Name] Preservative Free

Do not use [Product Name] Preservative Free

- if you are allergic to travoprost or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions

- **If you are under 18.** [Product Name] Preservative Free is not to be used by people under 18 years of age.

[Product Name] Preservative Free may:

- increase the length, thickness, colour and/or number of your eyelashes and may cause unusual hair growth on your eyelids.
- change the colour of your iris (the coloured part of your eye). This change may be permanent.
- rarely cause breathlessness or wheezing or increase the symptoms of asthma. **If you are concerned about changes in your breathing pattern when using this medicine talk to your doctor as soon as possible.**
- be absorbed through the skin and therefore should not be used by women who are pregnant or are attempting to become pregnant. If any of the product comes into contact with the skin then it should be washed off straight away.

Children and adolescents

[Product Name] Preservative Free is not to be used by people under 18 years of age.

Other medicines and [Product Name] Preservative Free

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription.

Pregnancy and breast-feeding

Do not use [Product Name] Preservative Free if you are pregnant. If you think that you may be pregnant speak with your doctor right away. If you could become pregnant you must use adequate contraception whilst you use this medicine.

Do not use [Product Name] Preservative Free if you are breast feeding. This medicine may pass into your milk.

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking any medicine.

Driving and using machines

You may find that your vision is blurred for a time just after you use [Product Name] Preservative Free. Do not drive or use machines until this has worn off.

[Product Name] Preservative Free contains macrogol glycerol hydroxy stearate 40

This medicine contains macrogol glycerol hydroxy stearate 40, which may cause skin reactions.

3. How to use [Product Name] Preservative Free

Always use this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

Only use [Product Name] Preservative Free for dropping in your eyes.

The recommended dose

Adults: **1 drop in the eye or eyes, once a day** – in the evening. Only use [Product Name] Preservative Free in both eyes if your doctor told you to. Use this medicine for as long as your doctor told you to.

Instructions for use



1a



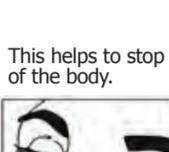
1b



2



3



4

- Take the multi-dose container (**picture 1a**) out of the carton box. If the container is stored within an overwrap pouch, tear – off to open (**picture 1b**) and write the date of opening on the label in the space provided.
- Get the medicine bottle and a mirror
- Wash your hands.
- Remove the cap.

- Hold the bottle, with the tip pointing down, between your thumb and fingers and press down on the bottom side (**picture 3**).
- Tilt your head back. Pull down your eyelid with a clean finger, until there is a 'pocket' between the eyelid and your eye. The drop will go in here (**picture 2**).

- Bring the bottle tip close to the eye. Use the mirror if it helps.

- **Do not touch your eye or eyelid, surrounding areas or other surfaces with the dropper.** It could infect the drops.
- Gently press down on the bottom side of the bottle to release one drop of medicine at a time (**picture 3**).
- After using the medicine, press a finger into the corner of your eye, by the nose (**picture 4**).

This helps to stop the medicine getting into the rest of the body.

- If you use drops in both eyes, repeat these same steps for your other eye.
- Close the multi-dose container cap firmly immediately after use.
- Only use one bottle of medicine at a time. Do not open the cap until you need to use the multi-dose container.

You must throw away the bottle 4 weeks after you first opened it, to prevent infections, and use a new bottle.

If a drop misses your eye, try again.

If you use more [Product Name] Preservative Free than you should

Rinse all medicine out of your eye with warm water. Do not put in any more drops until it is time for your next regular dose.

If you forget to use [Product Name] Preservative Free

Continue with the next dose as planned. Do not use a double dose to make up for a forgotten dose. The dose should not exceed one drop in the affected eye(s) daily.

If you stop using [Product Name] Preservative Free

Do not stop using this medicine without speaking to your doctor. This is because the pressure in your eye will not be controlled which could lead to loss of sight.

If you are using other eye drops

Leave at least 5 minutes between putting in [Product Name] Preservative Free and the other drops.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects although not everybody gets them.

If you experience side effects, you can usually carry on taking the drops, unless the effects are serious. If you are worried, talk to your doctor or pharmacist. Do not stop taking [Product Name] Preservative Free without speaking to your doctor.

Very common (may affect more than 1 in 10 people)

- Redness of the eye,
- Changes in the colour of the iris (coloured part of the eye).

Common (may affect up to 1 in 10 people)

- Effects in the eye:
- inflammation inside the eye
 - eye pain or swelling
 - eye irritation
 - eye discharge
 - sensitivity to light
 - blurred, reduced or abnormal vision
 - dry eye
 - itchy eye
 - increased tear production
 - abnormal or decreased eye sensation
 - eyelid abnormality, irritation, itching, redness, pain, swelling or crusting
 - discolouration of the eyelashes
 - increased or decreased growth or number of eyelashes

Effects in the body:

- headache
- skin darkening around the eyes.

Uncommon (may affect up to 1 in 100 people)

- Effects in the eye:
- inflammation or infection of the conjunctiva (thin membrane that covers the inner surface of the eyelid and the white part of the eyeball) or cornea
 - halo vision
 - corneal disorder
 - eye allergy
 - tired eyes
 - increase in pupil size

Effects in the body:

- asthma
- shortness of breath
- increased or decreased blood pressure
- irregular, increased, or decreased heart rate
- dizziness
- viral infection
- cough
- generalised weakness
- increased allergic symptoms
- throat irritation
- stuffy nose
- voice changes
- gastrointestinal discomfort or ulcer
- dry mouth
- constipation
- skin inflammation, redness or itching
- shoulder pain
- bad taste

Additional side effects that have been reported include:

Effects in the eye:

- inflammation of the back of the eye, sunken eyes.

Effects in the body:

- worsening of asthma
- ringing in ears
- increased prostate antigen (a protein produced by the prostate gland).

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V*. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store [Product Name] Preservative Free

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the bottle and the box after 'Exp'. The expiry date refers to the last day of the month.

Do not use this medicine if you notice that the multi dose container has been broken or damaged before you first open it.

Before opening, keep bottle in overwrap pouch (if available) in order to protect from moisture.

After first opening, this medicine does not require any special storage conditions.

You must throw away the bottle 4 weeks after you first opened it, to prevent infections. Write down the date you opened the bottle in the space on each bottle label and box.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What [Product Name] Preservative Free contains

- The active substance is travoprost. This medicine contains 40 micrograms/ml of travoprost.
- The other ingredients are macrogol glycerol hydroxy stearate 40, sodium chloride, propylene glycol, boric acid, mannitol, sodium hydroxide for pH adjustment and water for injection.

What [Product Name] Preservative free looks like and the contents of the pack
[Product Name] Preservative Free is presented as a 2.5 ml clear, colorless aqueous solution, in a cardboard box containing a 5 ml white plastic multi-dose container.

The multi – dose container can be available in an overwrap, inside the cardboard box.

The product is available in the following pack sizes:

Cartons containing [X] number of bottles.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

<to be completed nationally>

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:
<to be completed nationally>

This leaflet was last revised in MM/YYYY.



Bridging Report for
[Product Name] Preservative free 40 micrograms/ml eye drops solution, multi - dose container
Travoprost

Appendix 2 - The Package Leaflet for the Parent PIL: [Travoprost] 40 micrograms/ml eye drops, solution

Package leaflet: Information for the user

[Travoprost] 40 micrograms/ml eye drops, solution Travoprost

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or your pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What [Travoprost] is and what it is used for
2. What you need to know before you use [Travoprost]
3. How to use [Travoprost]
4. Possible side effects
5. How to store [Travoprost]
6. Contents of the pack and other information

1. What [Travoprost] is and what it is used for

[Travoprost] eye drops are used to treat high pressure in the eye. This pressure can lead to an illness called **glaucoma**.

High pressure in the eye. Your eyeballs contain a clear, watery liquid which feeds the inside of the eye. Liquid is always emptying out of the eye, and more liquid is always being produced. If the eye fills up faster than it empties, the pressure inside the eye builds up. If it gets too high, it can damage your sight.

[Travoprost] is one of a group of medicines for glaucoma called prostaglandin analogues. It works by increasing the outflow of liquid, which lowers the pressure in the eye. It may be used on its own or with other drops e.g. beta-blockers, which also reduce pressure.

2. What you need to know before you use [Travoprost]

Do not use [Travoprost]

- if you are allergic to travoprost or any of the other ingredients of this medicine (listed in section 6)

Warnings and precautions

- **If you are under 18.** [Travoprost] is not to be used by people under 18 years of age.

[Travoprost] may:

- increase the length, thickness, colour and/or number of your eyelashes and may cause unusual hair growth on your eyelids.
- change the colour of your iris (the coloured part of your eye). This change may be permanent.
- rarely cause breathlessness or wheezing or increase the symptoms of asthma. **If you are concerned about changes in your breathing pattern when using this medicine talk to your doctor as soon as possible.**
- be absorbed through the skin and therefore should not be used by women who are pregnant or are attempting to become pregnant. If any of the product comes into contact with the skin then it should be washed off straight away.

Children and adolescents

[Travoprost] is not to be used by people under 18 years of age.

Other medicines and [Travoprost]

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription.

Pregnancy and breast-feeding

Do not use [Travoprost] if you are pregnant. If you think that you may be pregnant speak with your doctor right away. If you could become pregnant you must use adequate contraception whilst you use this medicine.

Do not use [Travoprost] if you are breast feeding. This medicine may pass into your milk. If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking any medicine.

Driving and using machines

You may find that your vision is blurred for a time just after you use [Travoprost]. Do not drive or use machines until this has worn off.

[Travoprost] contains benzalkonium chloride if you wear soft contact lenses. Do not use the drops with your lenses in. Wait 15 minutes after using the drops before putting your lenses back in. There is a preservative in this medicine (benzalkonium chloride) that can discolour soft lenses.

This preservative may cause also eye irritation or disruption to the surface of the eye.

[Travoprost] contains macrogol glycerol hydroxy stearate 40
This medicine contains macrogol glycerol hydroxy stearate 40, which may cause skin reactions.

3. How to use [Travoprost]

Always use this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

Only use [Travoprost] for dropping in your eyes.

The recommended dose

Adults: **1 drop in the eye or eyes**, once a day – in the evening. Only use [Travoprost] in both eyes if your doctor told you to. Use this medicine for as long as your doctor told you to.



1

- Immediately before using a bottle for the first time, tear-off the overwrap pouch (**picture 1**). Take out the bottle and write the date of opening on the label in the space provided.
- Get the medicine bottle and a mirror
- Wash your hands.
- Twist off the cap.



2

- Hold the bottle, pointing down, between your thumb and fingers.
- Tilt your head back. Pull down your eyelid with a clean finger, until there is a 'pocket' between the eyelid and your eye. The drop will go in here (**picture 2**).
- Bring the bottle tip close to the eye. Use the mirror if it helps.



3

- **Do not touch your eye or eyelid, surrounding areas or other surfaces with the dropper.** It could infect the drops.
- Gently squeeze the bottle to release one drop of medicine at a time (**picture 3**).
- After using the medicine, press a finger into the corner of your eye, by the nose (**picture 4**).

This helps to stop the medicine getting into the rest of the body.



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- If you use drops in both eyes, repeat these same steps for your other eye.
- Close the bottle cap firmly immediately after use.
- Only use one bottle of medicine at a time. Do not open the pouch until you need to use the bottle.

• **You must throw away the bottle 4 weeks after you first opened it**, to prevent infections, and use a new bottle.

If a drop misses your eye, try again.

If you use more [Travoprost] than you should
Rinse all medicine out of your eye with warm water. Do not put in any more drops until it is time for your next regular dose.

If you forget to use [Travoprost]

Continue with the next dose as planned. **Do not** use a double dose to make up for a forgotten dose. The dose should not exceed one drop in the affected eye(s) daily.

If you stop using [Travoprost]

Do not stop using this medicine without speaking to your doctor. This is because the pressure in your eye will not be controlled which could lead to loss of sight.

If you are using other eye drops

Leave at least 5 minutes between putting in [Travoprost] and the other drops.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects although not everybody gets them.

If you experience side effects, you can usually carry on taking the drops, unless the effects are serious. If you are worried, talk to your doctor or pharmacist. Do not stop taking [Travoprost] without speaking to your doctor.

Very common (may affect more than 1 in 10 people)

- Redness of the eye,
- Changes in the colour of the iris (coloured part of the eye).

Common (may affect up to 1 in 10 people)

Effects in the eye:

- inflammation inside the eye
- eye pain or swelling
- eye irritation
- eye discharge
- sensitivity to light
- blurred, reduced or abnormal vision
- dry eye
- itchy eye
- increased tear production
- abnormal or decreased eye sensation
- eyelid abnormality, irritation, itching, redness, pain, swelling or crusting
- discolouration of the eyelashes
- increased or decreased growth or number of eyelashes

Effects in the body:

- headache
- skin darkening around the eyes.

Uncommon (may affect up to 1 in 100 people)

Effects in the eye:

- inflammation or infection of the conjunctiva (thin membrane that covers the inner surface of the eyelid and the white part of the eyeball) or cornea
- halo vision
- corneal disorder
- eye allergy
- tired eyes.
- increase in pupil size

Effects in the body:

- asthma
- shortness of breath
- increased or decreased blood pressure
- irregular, increased, or decreased heart rate
- dizziness,
- viral infection
- cough
- generalised weakness
- increased allergic symptoms
- throat irritation
- stuffy nose
- voice changes
- gastrointestinal discomfort or ulcer
- dry mouth
- constipation
- skin inflammation, redness or itching
- shoulder pain
- bad taste.

Additional side effects that have been reported include:

Effects in the eye:

- inflammation of the back of the eye, sunken eyes.

Effects in the body:

- worsening of asthma
- ringing in ears
- increased prostate antigen (a protein produced by the prostate gland).

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V*. By reporting side effects you can help provide more information on the safety of this medicine.

- The other ingredients are macrogol glycerol hydroxy stearate 40, sodium chloride, propylene glycol, boric acid, mannitol, sodium hydroxide for pH adjustment and water for injection.

5. How to store [Travoprost]

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the bottle and the box after 'Exp'. The expiry date refers to the last day of the month.

Do not use this medicine if you notice that the tamper evident seal has been broken or damaged before you first open it.

Before opening, keep bottle in overwrap pouch in order to protect from moisture.

After first opening, this medicine does not require any special storage conditions.

You must throw away the bottle 4 weeks after you first opened it, to prevent infections, and use a new bottle. Write down the date you opened the bottle in the space on each bottle label and box.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What [Travoprost] contains

- The active substance is travoprost. This medicine contains 40 micrograms/ml of travoprost.
- The other ingredients are benzalkonium chloride, macrogol glycerol hydroxy stearate 40, trometamol, disodium edetate, boric acid, mannitol, sodium hydroxide for pH adjustment and water for injection.

What Travoprost looks like and the contents of the pack

Travoprost is a clear, colourless solution supplied in packs containing translucent polypropylene 5ml bottle(s) with transparent low density polyethylene (LDPE) dropper and white high density polyethylene (HDPE) tamper-proof screw cap packaged in overwrap pouch. Each bottle contains 2.5 ml solution.

The product is available in the following pack sizes:

- DK/H/2189/001/DC: Cartons containing 1 or 3 bottles.
- DK/H/2197/001/DC: Cartons containing 1, 3, 6, 9, 10 or 12 bottles.
- DK/H/2198/001/DC: Cartons containing 1 or 3 bottles.
- DK/H/2237/001/DC: Cartons containing 1 or 3 bottles.
- DK/H/2287/001/DC: Cartons containing 1 or 3 bottles.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

<to be completed nationally>

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:
<to be completed nationally>

This leaflet was last revised in 02/2014.



Appendix 3 - Protocol

PROTOCOL Bridging Study for the Package Information Leaflet (PIL)

[Product Name] Preservative free 40 micrograms/ml eye drops solution, multi - dose container

Project contractor:			
Project name:		Bridging Study	
Project Manager on behalf of ELC:			
Version Number:	1.0	Date:	18 th December 2014

Rationale:

The objectives of the bridging study of the Daughter PIL by ELC Group is to ensure that the PIL is compliant with the European Council Directive 2004/27/EC which states: "The package leaflet shall reflect the results of consultation with target patient groups to ensure that it is legible, clear and easy to use". In performing this study it will be demonstrated that the Daughter PIL is similar to the Package Information Leaflet for the Parent PIL, and therefore requires no further user testing.

The basis for the report and its evaluation will be based on both European Commission (Article 59(3) of Council Directive 2001/83/EC and also by Article 63(2) of Directive 2001/83/EC as amended), the European Commission document "Guideline on the readability of the labelling and package leaflet of medicinal products for human use" (2009), Recommendations for Bridging from CMDh (April 2009, Revision 1) and MHRA guidance on bridging (Guidance for the Pharmaceutical Industry on the use of BRIDGING STUDIES to demonstrate compliance with article 59(3) of Council Directive 2001/83/EC [Consultation with Target Patient Groups]), as well as specific information and feedback obtained by ELC Group from the relevant authorities on the use of bridging in user testing schemes.



Background:

Daughter PIL

[Product Name] Preservative Free eye drops are used to treat high pressure in the eye. This pressure can lead to an illness called **glaucoma**.

High pressure in the eye. Your eyeballs contain a clear, watery liquid which feeds the inside of the eye. Liquid is always emptying out of the eye, and more liquid is always being produced. If the eye fills up faster than it empties, the pressure inside the eye builds up. If it gets too high, it can damage your sight.

[Product Name] Preservative Free is one of a group of medicines for glaucoma called prostaglandin analogues. It works by increasing the outflow of liquid, which lowers the pressure in the eye. It may be used on its own or with other drops e.g. beta-blockers, which also reduce pressure.

Parent PIL

[Travoprost] eye drops are used to treat high pressure in the eye. This pressure can lead to an illness called **glaucoma**.

High pressure in the eye. Your eyeballs contain a clear, watery liquid which feeds the inside of the eye. Liquid is always emptying out of the eye, and more liquid is always being produced. If the eye fills up faster than it empties, the pressure inside the eye builds up. If it gets too high, it can damage your sight.

[Travoprost] is one of a group of medicines for glaucoma called prostaglandin analogues. It works by increasing the outflow of liquid, which lowers the pressure in the eye. It may be used on its own or with other drops e.g. beta-blockers, which also reduce pressure.

Study design:

The PIL proposed for bridging will be evaluated and compared to the previously approved PIL using the following criteria:

- **Layout and Style:** size, font, colors, and organization of sections.
- **Contents:** indications, contraindications, side effects, ingredients, storage information, and any other relevant data. Key safety messages of the Parent PIL have been successfully user tested; the key safety messages of the Daughter PIL are to be identical or very similar.

Once the PIL proposed for bridging is compared, differences between the PILs will be analyzed.



Responsibilities:

Sponsor

- Provide source documents

Contractor

- An assessment of PILs to determine if a bridging study is warranted.
- Comparison of the PIL proposed for bridging to the previously approved PIL.
- Analyses and reporting of differences.
- Delivery of the final report: a full report of testing ready for submission to regulatory authority in Europe, which shall include the results of the assessment carried out and PIL drafts annotated to show proposed amendments (if applicable).

Project Milestones:

Milestone
Receive source documents from client
Initial evaluation of Daughter PIL
Comparison of the Daughter PIL to the proposed Parent PIL
Preparation of a mock-up of the Daughter PIL, harmonised to the Parent PIL
Evaluation of differences between the Daughter and Parent PIL
Creation of the Final Report
Delivery of the final report and raw data to the sponsor