BRISTOL-MYERS SQUIBB and ASTRAZENECA v SANOFI

Promotion of Lyxumia

Bristol-Myers Squibb and AstraZeneca jointly complained about cost comparison claims in a Lyxumia (lixisenatide) leavepiece issued by Sanofi. Lyxumia was a glucagon-like peptide-1 (GLP-1) receptor agonist for use in the management of type 2 diabetes.

The complainants jointly marketed Byetta (exenatide) and Bydureon (exenatide prolonged release). Exenatide was also a GLP-1 receptor agonist for use in management of type 2 diabetes. Lyxumia, Byetta and Bydureon were all add-on therapies; if required Lyxumia and Byetta could be added to insulin therapy, Bydureon could not.

Bristol-Myers Squibb and AstraZeneca stated that the leavepiece at issue compared the cost of medicines but did not provide any appropriate data on clinical efficacy and safety. This was misleading and not in the best interests of patients; the leavepiece was not sufficiently complete to enable the recipients to form their own opinion of the therapeutic value of Lyxumia. Furthermore, the claim 'Lyxumia can lower your GLP-1 prescribing costs' did not account for differences in efficacy and safety between the treatments compared. Meaningful cost savings should not be based on acquisition price alone but should take into account comparative efficacy and safety in order for both short-term and long-term cost savings to be realised. The complainants alleged that the cost savings claims were not objective and were subject to multiple caveats, which were not explained or detailed in the leavepiece. In addition, comparisons were made between medicines which were not intended for add-on to basal insulin (the focus of the leavepiece), and the comparisons could not be substantiated.

Specifically, Lyxumia vs Bydureon was not a like for like comparison, and the representation of the costs and percentage saving quoted in the leavepiece were inaccurate, unfair, misleading and could not be substantiated because:

- **Bydureon was administered once weekly vs Lyxumia which was administered once a day. Bydureon was provided as four single weekly dose kits each of which contained a vial of exenatide, a syringe pre-filled with solvent, one vial connector, and two injection needles (one spare). The Lyxumia injection pen contained 14 doses but was not supplied with needles which had to be prescribed separately at an additional cost to the NHS (needle costs and dispensing charges). This was not reflected in the leavepiece.**

- **The recommended dose for Bydureon was 2mg exenatide once weekly with no dose titration required. Lyxumia was started at a dose of 10mcg for the first 14 days, and then increased to 20mcg at day 15. Thus within the first 28 days of Lyxumia treatment, two different strengths need to be prescribed thus incurring two dispensing charges (the two dispensing charges would still apply if one titration pack was prescribed).**

- **Bydureon was not licensed for add-on to insulin but Lyxumia was. It was thus inappropriate, misleading and unfair to compare the costs of Bydureon and Lyxumia in a leavepiece which clearly promoted the use of Lyxumia as add-on to basal insulin.**

The complainants further noted that guidance from the National Institute for Health and Care Excellence (NICE) stated that in order for continued treatment with GLP-1s to be justified there had to be an HbA1c reduction of 1% at 6 months. However, in the clinical trials cited in the Lyxumia summary of product characteristics (SPC), the efficacy of Lyxumia never reached a 1% reduction in HbA1c, conversely Bydureon had demonstrated >1% reduction from baseline. The leavepiece was alleged to be misleading as to the therapeutic value of Lyxumia vs the other medicines especially in the absence of any appropriate clinical efficacy data for Lyxumia.

Bristol-Myers Squibb and AstraZeneca noted that in studies in which Lyxumia was added to basal insulin, there was an increased incidence of hypoglycaemia in Lyxumia patients vs placebo. An increase in hypoglycaemia had direct cost implications in terms of increased use of blood glucose testing strips and/or hypoglycaemia rescue medicine. Conversely in a study of Byetta vs placebo when added to basal insulin, Byetta showed no increased risk of hypoglycaemia. Consequently the claim 'Lyxumia can lower your GLP-1 prescribing costs' was not objective and was indirectly misleading; choosing Lyxumia as an add-on to basal insulin would be associated with additional costs that were not reflected in the claim or the leavepiece. Bristol-Myers Squibb and AstraZeneca alleged that the claims about costs savings and reduction of prescribing costs were unfair, unbalanced, inaccurate and did not reflect the available evidence clearly. Furthermore, comparisons were made between medicines which were not intended for add-on to basal insulin (the focus of the leavepiece), and comparisons were made which could not be substantiated.

The detailed response from Sanofi is given below.

The Panel noted that comparisons based on acquisition cost alone were not prohibited by the Code. All price comparisons must be accurate, fair

and must not mislead and valid comparisons could only be made where like was compared with like. Thus price comparisons should be made on the basis of the equivalent dosage requirement for the same indications.

The front cover of the leavepiece was headed 'When it's time to add to basal insulin' and featured the strapline 'A positive addition can make all the difference'. The comparison chart at issue was headed 'LYXUMIA can lower your GLP-1 prescribing costs' and listed the 28 day acquisition cost for Lyxumia 20mcg once daily (least expensive), Byetta 10mcg twice daily, Bydureon 2mg once weekly and Victoza 1.2mg and 1.8mg once-daily. The next column listed 'savings with Lyxumia' as 15%, 26%, 26% and 51% respectively. The third and final column showed by means of a tick that Lyxumia and Byetta were 'Licensed to add-on to basal insulin' whereas Bydureon and Victoza were not. The Panel considered that it was sufficiently clear that the costs of the five medicines cited in the table were acquisition costs only and not a cost-effectiveness analysis or similar. No breach of the Code was ruled.

The Panel noted that the 28 day acquisition cost of Lyxumia did not include the additional cost of needles whereas needles were provided with and included in the cost of Bydureon. The Panel considered that the comparison with Bydureon was misleading and unfair; breaches of the Code were ruled. Similarly the claim for a 26% cost saving with Lyxumia compared with Bydureon was misleading and not capable of substantiation. Breaches of the Code were ruled.

The Panel considered that it was clear that the 28 day acquisition cost of Lyxumia given in the table was based on a dose of 20mcg once-daily; the starting dose was 10mcg daily for 14 days with the fixed maintenance dose of 20mcg once daily starting on day 15. The Panel considered that it would have been helpful if the table had stated that maintenance doses were used. Nonetheless, given that the dose was clearly stated it did not consider that the failure to include the cost of the dose titration during the first 28 days was misleading as alleged and no breach of the Code was ruled.

The Panel noted that Lyxumia and Bydureon were indicated for the treatment of adults with type 2 diabetes in combination with oral glucose-lowering medicines when adequate glycaemic control could not be achieved. However, unlike Lyxumia, Bydureon was not licensed for use in combination with basal insulin as indicated in the third column of the cost comparison table. However the Panel noted that the primary message of the leavepiece was about the use of Lyxumia as an add-on to basal insulin and it noted several references in this regard. In the Panel's view, given the context of the leavepiece, the comparison with Bydureon in the table was misleading as Bydureon was not so indicated. A breach of the Code was ruled.

The Panel noted the allegation that the leavepiece as a whole was misleading, not in the best interests of patients and was not sufficiently complete to enable recipients to form their own opinion of the therapeutic value of Lyxumia because it compared the cost of medicines but did not include any appropriate safety or efficacy data. The Panel noted its comment above that comparisons based on acquisition cost alone were not prohibited by the Code. The Panel did not consider that the lack of clinical and safety data in that regard was misleading as alleged and thus ruled no breach of the Code.

Bristol-Myers Squibb Pharmaceuticals Limited and AstraZeneca UK Limited, jointly complained about cost comparison claims in a Lyxumia (lixisenatide) leavepiece (ref GBIE.LYX.13.04.14) issued by Sanofi. Lyxumia was a glucagon-like peptide-1 (GLP-1) receptor agonist for add-on use in adults with type 2 diabetes uncontrolled by oral antidiabetic medicines and/or basal insulin together with diet and exercise.

Bristol-Myers Squibb and AstraZeneca, jointly marketed Byetta (exenatide) and Bydureon (exenatide prolonged release). Exenatide was also a GLP-1 receptor agonist for add-on use in adults with type 2 diabetes who had not achieved adequate glycaemic control on maximally tolerated doses of certain oral antidiabetic medicines and had not achieved adequate glycaemic control with these agents. Bydureon, the prolonged release preparation was not indicated for add-on use with insulin.

During the course of inter-company dialogue, Sanofi withdrew a journal advertisement (ref GBIE.LYX.13.02.11) and later withdrew a Lyxumia leavepiece (ref GBIE.LYX.13.01.14) which contained claims which stated that Lyxumia provided cost-saving opportunities and 20mcg could deliver a cost saving of 15% vs Byetta 10mcg twice-daily and 26% vs Bydureon 2mg once-daily. Bristol-Myers Squibb and AstraZeneca subsequently became aware of a revised Lyxumia leavepiece (ref GBIE.LYX.13.04.14) in use; this leavepiece focussed on the use of Lyxumia as an add-on to basal insulin.

COMPLAINT

Bristol-Myers Squibb and AstraZeneca stated that the revised leavepiece, compared the cost of medicines but did not provide any appropriate data on clinical efficacy and safety. Furthermore, the claims relating to saving with Lyxumia (in the cost comparison table) and 'Lyxumia can lower your GLP-1 prescribing costs' did not account for differences in efficacy and safety between the treatments compared and was not within the spirit of Code. True cost savings which were meaningful to health professionals and payers should not be based on acquisition price alone, but must instead take into account comparative efficacy and safety data in order for both short-term and long-term cost savings to be realised. As such, the claims about cost savings were not objective and were subject to multiple caveats, which were neither explained nor detailed in the leavepiece. In addition, comparisons were made between medicines which were not intended for add-on to basal insulin (the focus of

this leavepiece), and the comparisons could not be substantiated.

Specifically, the complainants alleged that the comparison with Bydureon was not valid, it did not compare like for like, and the representation of the costs and percentage saving quoted in the leavepiece for Lyxumia vs Bydureon were inaccurate, unfair, misleading and could not be substantiated because:

- Bydureon was a once-weekly GLP-1 receptor agonist compared with Lyxumia which was once a day. Bydureon was provided as four single weekly dose kits each of which contained one vial of 2mg exenatide, one pre-filled syringe of 0.65ml solvent, one vial connector, and two injection needles (one spare). Lyxumia was prescribed as an injection pen containing 14 doses; needles had to be prescribed separately. As a result, for Lyxumia, the NHS had to pay the needle acquisition and dispensing costs. This was not reflected in the leavepiece.

- The recommended dose for Bydureon was 2mg exenatide once-weekly – there was no dose titration required. Lyxumia must be started at a dose of 10mcg for the first 14 days, and then increased to 20mcg at day 15.

  In addition to the acquisition costs (including needles), there were additional prescription charges to the NHS that had not been factored into the 'cost saving' calculation promoted by Sanofi. Due to the requirement for dose titration within the first 28 days when initiating treatment with Lyxumia, two different strengths need to be prescribed each of which incurred a dispensing charge (the two dispensing charges to the NHS would still apply if one titration pack was prescribed).

- Bydureon was not licensed for add-on to insulin but Lyxumia was licensed for add-on to basal insulin. Bristol-Myers Squibb and AstraZeneca alleged it was wholly inappropriate to compare the costs of Bydureon and Lyxumia in a leavepiece clearly focussed on promoting the use of Lyxumia as add-on to basal insulin. The comparison was not on the basis of an equivalent dosage for the same indication which was misleading and unfair.

Furthermore, the complainants noted that National Institute for Health and Care Excellence (NICE) guidance stated that in order for continued treatment with GLP-1s to be justified there had to be an HbA1c reduction of 1% at 6 months. However, in the clinical trials published to date and cited in the Lyxumia summary of product characteristics (SPC), the efficacy of Lyxumia never reached a 1% reduction in HbA1c from baseline in the overall primary population studied. In contrast, Bydureon had demonstrated >1% reduction from baseline in all studies. The leavepiece was alleged to be misleading as to the therapeutic value of Lyxumia vs the other medicines especially in the absence of any appropriate clinical efficacy data for Lyxumia.

Bristol-Myers Squibb and AstraZeneca noted that in the Lyxumia add-on to basal insulin trials (Riddle *et al* 2013a and 2013b), there was an increased incidence of symptomatic documented hypoglycaemia (blood glucose <3.3mmol/L) in patients treated with Lyxumia vs those treated with placebo. This increase in hypoglycaemia had direct cost implications in terms of increased use of blood glucose testing strips and/or hypoglycaemia rescue medicine. In contrast, in a separate clinical study of Byetta compared with placebo when added to basal insulin, there was no increased risk in hypoglycaemia seen with Byetta vs placebo. Consequently the claim 'Lyxumia can lower your GLP-1 prescribing costs' was not objective and was indirectly misleading as the choice of Lyxumia over other appropriate therapies in the add-on to basal insulin clinical setting would be associated with additional treatment-related prescribing costs which had not been reflected.

Bristol-Myers Squibb and AstraZeneca alleged that the Sanofi leavepiece did not comply with either the spirit or the letter of the Code. Comparing costs without any consideration of clinical outcomes, the exclusion of appropriate clinical safety and efficacy data in this 'add-on to basal insulin' focussed leavepiece and aimed as prescribers was not in the best interests of patients and meant that the leavepiece was not sufficiently complete to allow clinicians to form their own opinion of the therapeutic value of Lyxumia. Bristol-Myers Squibb and AstraZeneca alleged that the claims about costs savings and reduced prescribing costs were unfair, unbalanced, inaccurate and did not reflect the available evidence clearly. They were therefore misleading and in breach of Clauses 7.2 and 7.3. Furthermore, comparisons were made between medicines which were not intended for add-on to basal insulin (the focus of the leavepiece), and comparisons were made which could not be substantiated. Bristol-Myers Squibb and AstraZeneca alleged breaches of Clauses 7.2, 7.3 and 7.4 of the Code.

Bristol-Myers Squibb and AstraZeneca knew that a similar cost comparison was ruled in breach of the Code in Case AUTH/2604/5/13, however, they considered that their concerns were wider than those at issue in that case.

RESPONSE

Sanofi explained that following the launch of Lyxumia in March 2013, it issued promotional material which included a cost comparison chart indicating the savings that could be achieved through use of Lyxumia compared with the three other GLP-1s available (exenatide, exenatide LAR and liraglutide). Although inter-company dialogue was initiated with Bristol-Myers Squibb and AstraZeneca about this table, the items were withdrawn in keeping with the undertakings given in Case AUTH/2604/5/13.

A new price comparison table was subsequently developed and included in the leavepiece ref GBIE. LYX.13.04.14 at issue in this case. For the sake of completeness, this item was also withdrawn on 28

June 2013, in part to affect changes committed to in inter-company dialogue, and replaced by item ref GBIE.LYX.13.07.12 in August 2013.

Sanofi's response was therefore centred on item ref GBIE.LYX.13.04.14, in accordance with the complaint, but with reference to the amendments made within item ref GBIE.LYX.13.07.12, where relevant. Copies of each leavepiece were provided.

Sanofi submitted that the essence of the complaint, and of the difference in opinion between the parties, centred on the comparison made of the prescribing costs (acquisition cost) of the GLP-1 agonists. The complainants maintained that a price comparison was inappropriate as the prescriber had insufficient information on which to assess the efficacy of the products. The complaints implied that comparison of price alone, as opposed to a wider assessment of additional costs, savings and clinical outcomes of efficacy and safety, was inappropriate and that only the latter, a detailed economic evaluation, was permissible.

Sanofi submitted that the Code clearly allowed both a comparison of acquisition costs alone and a more detailed economic evaluation extending to cost effectiveness - the wider savings realised taking into account the clinical benefits and differences in resource utilisation throughout the healthcare system. Both scenarios were clearly described in the supplementary information to Clause 7.2 along with prerequisites to their use. Sanofi maintained that the price comparison table at issue clearly demonstrated the savings that could be made in acquisition cost alone with Lyxumia compared with the three other GLP-1 agonists.

Sanofi's first reference to the difference in costs between the different GLP-1 agonists was made in the leavepiece ref GBIE.LYX.13.01.14. This contained a table containing similar cost savings claims that were ruled in breach of Clauses 7.2 and 7.3 (Case AUTH/2604/5/13) and the item was therefore withdrawn in June 2013. The claims were misleading as they extended beyond acquisition cost alone.

Although never intended, Sanofi accepted the Panel's ruling and noted the Panel's opinion that it was not clear that the claims were only based on acquisition costs and not a cost-effectiveness analysis or similar.

A revised version of the table was therefore developed (leavepiece ref GBIE.LYX.13.04.14) with the express intent of leaving the reader in no doubt that the price comparison, and any savings to be made, was based on acquisition cost alone.

Sanofi submitted that the title ('Lyxumia can lower your GLP-1 prescribing costs') and table headings (including '28 day acquisition cost') made it sufficiently clear to the reader that it was a comparison of acquisition cost alone, not a wider analysis of cost savings. The title referred to GLP-1 prescribing costs, ie the direct cost to the NHS of the different medicines, and the first column referred specifically to 'acquisition cost' so as to reiterate this point and make it clear what cost was being referred to. Costs referred to were the NHS cost within MIMS (monthly index of medical specialities), adjusted to 28 days to allow for different pack sizes. In the case of Victoza, where two different maintenance doses might be used, both were presented for the sake of completeness.

Sanofi recognised that the supplementary information to Clause 7.2 provided specific advice on making comparisons on price alone, in that comparisons could only be made 'where like is compared with like, and on the equivalent dosage for the same indication'. The four GLP-1 agonists presented in the table were all indicated for the treatment of type 2 diabetes and the costs compared were those of the maintenance dose of each for 28 days - ie the equivalent dose for the same indication. Sanofi noted that the titration doses of Byetta and Lyxumia shared the same price as the maintenance dose, so no difference existed between the two with respect to the first 2-4 weeks of treatment.

Sanofi understood from the supplementary information for a price comparison that specific conditions had to be met - that although an economic evaluation required factors including efficacy to be taken into account, a simpler price comparison required just the price per dose, where indications matched. On the basis of the shared indication for all four GLP-1 agonists, Sanofi submitted that the requirements for a price comparison to be made were met and that to claim a lower price or acquisition cost, which of itself was an important factor in the choice of medicines, was appropriate.

Sanofi recognised that in comparing price alone, there must be no allusion to wider cost savings (for example through additional prescribing of needles, internal NHS charges, nursing time in administering injections) or to benefits such as differences in efficacy or safety, as suggested. Any such allusion would amount to an 'economic evaluation', for which the Code required full consideration of the additional costs and potential savings within the wider healthcare system. Sanofi had therefore deliberately not referred to any associated costs or savings beyond acquisition of the medicine alone so as to meet the requirements of the Code regarding price comparisons. It was by intent, not by omission, that reference to additional costs was excluded - it was clear that this was a 'price comparison' and not an 'economic evaluation'. Sanofi also recognised the direct parallels between this case and Case AUTH 224/6/09 [sic], in which a price comparison table was adjudged appropriate for reasons outlined matching those above.

In summary, Sanofi recognised the difference that the Code made in presenting an 'economic evaluation' and a 'price comparison'. Sanofi submitted that it had presented a genuine price comparison, in itself recognised as a relevant factor in the choice of medicines, and had done so in compliance with the Code, and that no breach of Clause 7.2 nor 7.3 had occurred. The prices referenced in the material were an accurate

representation of the indicative cost to the NHS, adjusted to the same time period where pack sizes differed. This was the only comparison to be made, and was substantiated by the cited data on file (copy provided). The requirements of Clause 7.4 had also been met and thus no breach had occurred.

Sanofi further noted that the complainants proposed that comparison with Bydureon (exenatide LAR) was inappropriate due to the different resource utilisation associated with the use of two products (the companies cited examples of differences in needle costs and dispensing fees), and implied that it was inappropriate to present a price comparison and that only an economic evaluation was appropriate.

Sanofi agreed that were any comparison made beyond prescribing cost alone, or allusion to savings made beyond the acquisition cost, these factors would be relevant and would have to be included. However, as stated above, the comparison was clearly presented as one of price alone and savings on acquisition cost alone. The Code stipulated that both were acceptable, and Sanofi considered, as above, that as the products shared the same indication and each had a readily identifiable maintenance dose, then the conditions for presenting a price comparison were met. All four GLP-1 agonists were indicated for the treatment of type 2 diabetes (and only for the treatment of type 2 diabetes), and all, including Bydureon and Lyxumia had a clearly identifiable maintenance dose.

The choice of the usual maintenance dose (for a defined period of time) was made to represent the natural comparison that would be expected as representing equivalent dosage in the treatment of a long-term condition such as diabetes. Although in a full economic evaluation such comparison would need to take account of efficacy, the Code did not require this of a pure price comparison. Whilst it was true that for any comparison of two treatments a full economic evaluation would be likely to reveal differences in associated costs beyond the acquisition cost, to suggest that this was reason enough to prevent a comparison of cost alone was contrary to the supplementary information in the Code.

Finally, although not all GLP-1s were licensed for use with basal insulin, the fact that Lyxumia was but Bydureon was not, did not disqualify the fact that both were indicated for the treatment of type 2 diabetes. The complainants stated that reference to Bydureon in material focused on the use of Lyxumia in combination with basal insulin was unfair. Information on whether or not the product could be used with basal insulin was provided to ensure that readers were fully aware of the difference that might exist. Furthermore, no individual medicines were highlighted for specific comparison within the table - there was no invitation to draw attention to or make a comparison between any specific combinations of the listed medicines over another. Sanofi submitted that although the products might be used in different combinations (as was most often the case with this class of medicines), the shared indication meant that patients with type 2 diabetes, prior to the use of insulin could use any of the four medicines - and that a price comparison was therefore appropriate.

In summary, the leavepiece presented a price comparison of the four GLP-1 agonists available in the UK, not an economic evaluation. All were indicated for the treatment of type-2 diabetes, and a readily identifiable maintenance dose (or doses) existed for this indication. Sanofi thus considered that the price comparison met the requirements of Clause 7.2, as outlined within the relevant supplementary information, and that as these requirements were met, the price comparison was fair and appropriate. Sanofi denied any breach of Clauses 7.2, 7.3 or 7.4.

In response to a request for further information Sanofi submitted that a wide range of needles were suitable for use with Lyxumia. A copy of the October 2012 Drug Tariff detailing the price of all needles available to be used with pre-filled injector pens was provided. Sanofi stated that it was recommended that Lyxumia be used with a 4-5mm needle which many manufacturers provided; costs ranged from £1.67 to £3.55 for 28 days. 'Auto-shield' safety needles were not routinely used for self-administration so had not been considered. Where an auto-shield needle was required, additional cost would also need to be added to Bydureon as the needle provided was not an auto-shield type. Furthermore any comparison with Byetta would need to take into account an associated doubling of needle cost given its twice daily dosing.

PANEL RULING

The Panel noted that comparisons based on acquisition cost alone were not prohibited by the Code. The supplementary information to Clause 7.2 made it clear that, as with any comparison, price comparisons must be accurate, fair and must not mislead. Valid comparisons could only be made where like was compared with like. It followed therefore that a price comparison should be made on the basis of the equivalent dosage requirement for the same indications.

The Panel noted Bristol-Myers Squibb and AstraZeneca's allegation that comparisons in the table in question were not capable of substantiation and were made between medicines that were not intended to be added on to basal insulin. Further, it was alleged that the comparison of Lyxumia with Bydureon was not a valid comparison; it did not compare like with like and the representation of the costs and percentage saving quoted in the leavepiece were inaccurate, unfair, misleading and incapable of substantiation. It was also alleged that the omission of clinical and safety data in the leavepiece as a whole rendered it incomplete as clinicians could not form their own opinion of the therapeutic value of the medicine.

The front cover of the leavepiece (GBIE.LYX.13.04.14) was headed 'When it's time to add to basal insulin' followed by a photograph of a Lyxumia pen resting on a generic device labelled 'BASAL' to make a plus sign with the strapline 'A positive addition can make

all the difference'. Page 2 was headed 'Lyxumia is a positive addition with once-daily dosing'. The comparison chart at issue appeared on the bottom half of this page and was headed 'LYXUMIA can lower your GLP-1 prescribing costs'. The table listed the 28 day acquisition cost for Lyxumia 20mcg once-daily, Byetta 10mcg twice-daily, Bydureon 2mg once-weekly, Victoza 1.2mg once-daily and Victoza 1.8mg once-daily. Lyxumia cost £54.14 and Byetta 10mcg twice-daily cost £63.69. The other medicines increased in cost. The next column listed 'Savings with Lyxumia' as 15%, 26%, 26% and 51% respectively. The third and final column showed by means of a tick that Lyxumia 20mcg once-daily and Byetta 10mcg twice-daily were 'Licensed to add-on to basal insulin' whereas Bydureon 2mg once weekly and Victoza 1.2mg once-daily and 1.8mg once-daily were not. The Panel considered that it was sufficiently clear that the costs of the five medicines cited in the table were acquisition costs only and not a cost-effectiveness analysis or similar. The Panel ruled no breach of Clauses 7.2 and 7.3 in that regard.

The Panel noted that the 28 day acquisition cost of Lyxumia cited did not include the cost of needles which had to be purchased separately whereas the Bydureon dose kit included needles. The failure to include the cost of needles rendered the comparison with Bydureon misleading and unfair. A breach of Clauses 7.2 and 7.3 was ruled. The Panel thus considered that the claim for a 26% cost saving with Lyxumia compared with Bydureon was misleading. A breach of Clauses 7.2 and 7.3 was ruled. The cost saving of 26% was not capable of substantiation and a breach of Clause 7.4 was ruled.

The Panel considered that it was clear that the 28 day acquisition cost of Lyxumia given in the table was based on a dose of 20mcg once-daily. The Panel noted the dose titration in the Lyxumia SPC, the starting dose was 10mcg daily for 14 days with the fixed maintenance dose of 20mcg once-daily starting on day 15. The Panel considered that the comparison table was clear with regard to the doses used. The Panel considered that it would have been helpful if the table had stated that maintenance doses were used. Nonetheless, given that the 20mcg dose was clearly stated it did not consider the failure to include the cost of the dose titration during the first 28 days was misleading as alleged. The Panel ruled no breach of Clauses 7.2 or 7.3.

The Panel noted that both Lyxumia and Bydureon were indicated for the treatment of adults with type 2 diabetes in combination with oral glucose-lowering medicines when adequate glycaemic control could not be achieved. However, unlike Lyxumia, Bydureon was not licensed for use in combination with basal insulin. The Panel noted that this was indicated in the third column of the cost comparison table. However the Panel noted that the primary message of the leavepiece was about the use of Lyxumia as an add-on to basal insulin. The Panel noted the references to such use on the front cover of the leavepiece as set out above. Page 2 was headed 'Lyxumia is a positive addition with once-daily dosing'. Page 3 which faced the table in question was headed 'Luxumia is a positive addition which can make all the difference' followed by a photograph of a vertical generic device labelled 'BASAL INSULIN', a photograph of a horizontal Lyxumia pen and then a photograph of the Lyxumia pen resting on the generic device labelled 'BASAL INSULIN + LYXUMIA' to make a plus sign with the strapline 'A complementary approach to significantly reduce HbA1c'. Beneath, a bullet point read 'Strong evidence supporting the use of Lyxumia as add-on to basal insulin'. In the Panel's view, given the context of the leavepiece which promoted Lyxumia as an add-on to basal insulin, the comparison with Bydureon in the table was misleading as it was not so indicated. A breach of Clauses 7.2 and 7.3 was ruled.

The Panel noted Bristol-Myers Squibb and AstraZeneca's allegation that the leavepiece as a whole was misleading, not in the best interests of patients and was not sufficiently complete to enable recipients to form their own opinion of the therapeutic value of Lyxumia because it compared the cost of medicines but did not include any appropriate safety or efficacy data. The Panel noted its comment above that comparisons based on acquisition cost alone were not prohibited by the Code. The Panel did not consider that the lack of clinical and safety data in that regard was misleading as alleged and thus ruled no breach of Clause 7.2.

Complaint received **10 September 2013**

Case completed **8 November 2013**