CASE AUTH/2888/11/16

NURSE v NAPP

Promoting a switch to Remsima

A hospital specialist nurse complained about a Remsima (infliximab) email from Napp Pharmaceuticals Limited. The subject of the email appeared in the email inbox as 'Why switch from Remicade to Remsima?' and was about switching from Remicade (infliximab, the originator product marketed by Merck Sharp & Dohme) to the biosimilar Remsima marketed by Napp. The body of the email, headed 'Don't get left behind – make the switch', informed the reader that 'Your colleagues from across the UK are switching from Remicade to Remsima and re-investing their savings to improve patient care' and that compared to Remicade, Remsima could offer highly similar clinical outcomes and that it was 'no different to what you're already used to with Remicade'. Remsima was indicated for, *inter alia*, rheumatoid arthritis (RA), Crohn's Disease and ulcerative colitis.

The complainant stated that he/she used this biosimilar; the hospital was considering a full scale switch but needed processes in place to ensure the safety and needs of its patients.

The complainant considered that Napp was pushing a switch with no consideration to patients' needs. Not all centres that had switched had been able to re-invest any cost savings into their services; the claim in this regard was wrong.

The complainant stated that the indications for use of this biosimilar and its efficacy should not be presented in the same advertisement to switch patients. In particular the complainant did not like the slogan 'Don't get left behind – make the switch'.

The detailed response from Napp is given below.

The Panel noted the complainant's concern that the email encouraged health professionals to switch from Remicade to Remsima with no consideration of patients' needs. In that regard the Panel further noted that readers could access four relevant case studies; each detailed, *inter alia*, stakeholder or clinical support, outcomes and benefits. Key learnings and advice included 'Before initiating the switch to an infliximab biosimilar, it is important to understand the safety, efficacy and economic arguments', 'Don't rush the switch process itself – give yourself time to resolve any technical issues and ensure that patient concerns have been addressed' and 'Engagement with all key-stakeholders is essential'. It seemed clear from the case studies that switches from Remicade to Remsima had taken place with due consideration of the patients' needs; in all cases the proposed switch was discussed with patients before their therapy was changed. The Panel considered that in referring to patients' needs and presenting a considered approach to switching, the email had encouraged the rational use of Remsima and in that regard it ruled no breach of the Code. In the Panel's view, the material was sufficiently complete to allow recipients to form their own opinion of the therapeutic value of Remsima. No breach of the Code was ruled.

The Panel considered that, contrary to Napp's submission, the unequivocal claim that 'Your colleagues from across the UK are switching from Remicade to Remsima and re-investing their savings to improve patient care' implied that every organisation that switched had savings to reinvest. The Panel further noted that in support of that claim, readers were provided with a link to the four case studies discussed above all of which were based in England. Given the small number of case studies offered and their limited geographical spread, the Panel considered that the claim was unequivocal and exaggerated and thereby misleading. A breach of the Code was ruled. The Panel considered that such a broad claim could not be substantiated; a breach of the Code was ruled.

In the Panel's view, the complainant's submission that the indications for Remsima and its efficacy should not be presented in an advertisement which promoted switching from Remicade appeared to run counter to his/her concern that the email encouraged health professionals to switch to Remsima with no consideration of patients' needs. The Panel did not consider that in referring to the clinical aspect of Remsima, the email was misleading or that claims could not be substantiated. No breaches of the Code were ruled. The Panel noted its ruling of no breach of the Code above in that it considered that the email had encouraged the rational use of Remsima.

The email was headed with the emboldened phrase, 'Don't get left behind – make the switch' which in the Panel's view, implied that if the reader did not switch patients from Remicade to Remsima, they and their clinical practice were in some ways out-dated. The Panel considered that the phrase did not recognise the professional standing of the audience and their ability to make their own decisions and was likely to cause offence. A breach of the Code was ruled.

The Panel noted its rulings above and considered that high standards had not been maintained. A breach of the Code was ruled.

A hospital gastroenterology specialist nurse complained about a Remsima (infliximab) email (Ref UK/REM-16038) from Napp Pharmaceuticals Limited. The subject of the email appeared in the email inbox as 'Why switch from Remicade to Remsima?' and was about switching from Remicade (infliximab, the originator product marketed by Merck Sharp & Dohme) to the biosimilar Remsima marketed by

Napp. The body of the email was headed 'Don't get left behind – make the switch'. The email stated that Remsima was infliximab, as 'proven by rigorous comparability testing vs Remicade (infliximab)' and informed the reader that 'Your colleagues from across the UK are switching from Remicade to Remsima and re-investing their savings to improve patient care'. The email stated that compared to Remicade, Remsima could offer highly similar clinical outcomes and that it was 'no different to what you're already used to with Remicade'.

Remsima was indicated for, *inter alia*, rheumatoid arthritis, Crohn's Disease and ulcerative colitis.

COMPLAINT

The complainant stated that he/she used this biosimilar but as yet had not switched for a number of reasons. The hospital was considering a full scale switch but needed processes in place to ensure the safety and needs of its patients.

The complainant did not like the content of the email and considered that Napp was pushing a switch with no consideration to patients' needs. Not all centres that had switched had been able to re-invest any cost savings into their services; the claim in this regard was wrong.

The complainant stated that the indications for use of this biosimilar and its efficacy should not be presented in the same advertisement to switch patients. In particular the complainant did not like the slogan 'Don't get left behind – make the switch'.

When writing to Napp the Authority asked it to respond in relation to Clauses 7.2, 7.4, 7.10, 9.1 and 9.2 of the Code.

RESPONSE

Napp stated that the email promoted switching from originator infliximab (Remicade) to biosimilar infliximab (Remsima) and focussed on the potential significant cost savings such a switch could provide and how these could be re-invested in service improvements. The email was sent to an identified list of 4,475 health professionals on 14 November 2016 who were appropriate to receive the information because they managed patients for whom infliximab was licensed and they had opted to receive promotional emails. It was sent to rheumatologists, rheumatology specialist nurses, gastroenterologists, gastroenterology specialist nurses and hospital pharmacists.

Napp identified four key points to the complaint:

1 Napp had pushed a switch with no consideration to patient needs
2 Napp had claimed that all UK centres were able to re-invest savings made by switching to services and the complainant considered that this was incorrect
3 That efficacy and therapeutic indications of a medicine should not be included in an advertisement which promoted a switch
4 The complainant disliked in particular the slogan 'Don't get left behind – make the switch'.

Napp strongly refuted the complaint and submitted that the Remsima email was not misleading, was capable of substantiation, promoted rational use of the medicine, did not cause offence and therefore did not breach Clauses 7.2, 7.4, 7.10 or 9.2.

Background

Napp explained that in the past 20 years biological medicines had brought significant therapeutic benefit to many patients but they accounted for a significant proportion of the annual NHS drug budget spend. For example, NHS expenditure on anti-TNF biological medicines in 2015 was £1.011 billion. Biosimilar medicines were being developed in line with rigorous EU requirements to provide therapeutic alternatives to their respective reference products at significantly reduced cost without jeopardising patient safety. NHS England defined a biosimilar medicine as:

> '….a biological medicine which is highly similar to another biological medicine already licensed for use. It is a biological medicine which has been shown not to have any clinically meaningful differences from the originator biological medicine in terms of quality, safety and efficacy.'

CT-P13 (Remsima or Inflectra) was the world's first biosimilar monoclonal antibody, and was granted a licence in Europe in 2013 for the same clinical indications as the originator, Remicade.

Napp submitted that switching from originator to biosimilar infliximab was both rational and responsible. Increasing clinical evidence confirmed that switching from the originator to CT-P13 was clinically safe and effective, a view supported by key authoritative professional bodies within the UK. For example, the British Society for Gastroenterology published guidance in March 2016 confirming that 'There is sufficient data from observational studies to show that safety and clinical efficacy of CT-P13 are comparable to the originator drug, with similar immunogenicity, and that switching from Remicade to CT-P13 was also safe and effective'. The recent Royal College of Physicians audit of biological therapies for inflammatory bowel disease stated 'all new starters should commence treatment on infliximab biosimilars. Consideration should be given whether to switch those patients currently established on Remicade to infliximab biosimilars'.

Furthermore, the issue of switching to biosimilar infliximab was addressed by the National Institute for Health and Care Excellence (NICE) in 'Introducing biosimilar versions of infliximab: Inflectra and Remsima' which concluded that this was a rational and responsible course of action.

In light of the above, Napp submitted that the focus of the email was designed to:

- Share the experiences of UK clinical centres which had switched to biosimilar infliximab

- Highlight the potential cost savings that switching to Remsima could provide should health professionals choose to switch and how these could be re-invested in services, focusing particularly on those in their own departments eg more specialist nurses
- Provide the clinical comparison between Remicade and Remsima, including efficacy, safety and administration.

The Code did not prohibit companies from promoting a simple switch from one medicine to another. Indeed, in Case AUTH/2795/9/15 about a Remsima switch leavepiece, the PMCPA stated 'it is not unacceptable under the Code for a company to promote a simple switch from one product to another; companies could not, however, assist a health professional in implementing a switch'. Napp was not found in breach of the Code.

Point 1

Napp disagreed that the email promoted a switch with no consideration for patient needs. The email presented comprehensive information, references and resources to health professionals, to potentially help the switch process in their centres, and the patient was considered in all of these. Firstly, health professionals were directed to four case studies on the Remsima website via a link highlighted in the email. Each clinical case study shared the experience of switching in different centres across the UK and was structured into five parts: i) stakeholder support; ii) gain-share; iii) the change process; iv) outcomes and benefits and v) key learnings and advice. In section iii (change process) of each case study, there was a focus on how the clinical centres involved had informed the patient about the switch process, including examples of how this was managed. The outcomes and benefits section (iv) also discussed how many patients were switched and if any adverse events occurred. Finally, the key learnings and advice section (v) included a comment recognising the importance of the patient in the process.

The email also provided health professionals with the relevant clinical evidence comparing Remsima with Remicade. Specific reference was made to the fact that the biosimilar Remsima had highly similar clinical outcomes in terms of efficacy, safety, quality and immunogenicity. These claims were fair, balanced, accurate and substantiated by references to the European Public Assessment Report (EPAR) and the pivotal clinical trials (PLANETAS (Park *et al* 2013) and PLANETRA (Yoo *et al* 2013)).

A highlighted link in the email directed the health professional to the resources page on the Remsima website via which he/she could download or request resources to support patients as part of the switch process. In particular the health professional could request patient support packs specific to each of the diseases for which Remsima was licensed. Napp thus refuted that it had promoted a switch to Remsima without regard to patients' needs, and the decision to switch to Remsima remained firmly in the hands of the health professional. Napp submitted that the email promoted the rational use of Remsima and it thus denied breaches of Clauses 7.2, 7.4 and 7.10.

Point 2

Napp submitted that the statement 'Your colleagues from across the UK are switching from Remicade to Remsima and re-investing their savings to improve patient care' did not state or infer that all colleagues who had switched to Remsima from Remicade had been able to re-invest savings in their departments. Instead Napp's intent was to share the experiences from four centres which had achieved gain-share agreements to the benefit of their clinical service such that other centres could learn from them and hopefully implement some of the learnings in their own centres should they decide to switch. The statement was immediately followed by a link to the case studies on the Remsima website.

Napp did not agree that the statement was misleading. It did not claim that all colleagues were switching nor that all were re-investing in patient care. Napp denied a breach of Clause 7.2. The statement could also be substantiated by the experiences provided in the four case studies. Napp thus refuted a breach of Clause 7.4.

Point 3

Napp disagreed with the complainant that therapeutic indications and efficacy data should not be included in an email which promoted a switch to Remsima. On the contrary, companies must present adequate information on the efficacy including indications and safety of a medicine in order for health professionals to make an informed clinical decision.

As stated previously, companies were permitted under the Code to promote a simple switch from one medicine to another. However, materials which promoted a switch should also provide health professionals with all the information necessary such that they could form their own opinion of the therapeutic benefit of switching with regards to their patients. Napp submitted that the email provided health professionals with the appropriate information to allow them to make an informed decision about switching to Remsima. The email referenced the EPAR to reassure health professionals that 'Remsima is infliximab as proven by rigorous testing vs Remicade'. In addition, health professionals were directed to the pivotal clinical trials comparing Remicade with Remsima in terms of clinical efficacy, safety, quality and immunogenicity (Park *et al* and Yoo *et al*). Napp submitted that it was important to inform readers that Remsima was licensed for the same therapeutic indications as Remicade and had the same dosing, posology and infusion schedule. Taking the above into consideration, health professionals could then determine whether a switch was appropriate for their patients.

Napp submitted that the email promoted the rational use of the medicine and provided health professionals with accurate, balanced, fair information which was fully substantiated and hence did not contravene Clauses 7.2, 7.4 and 7.10.

Point 4

Napp stated that although the complainant had not specified exactly what he/she disliked about the

opening strapline 'Don't get left behind – make the switch', it explained the reasoning and intent behind its use.

It was clear from IMS commercial market share data in March 2016 (when the email was conceived) that there was a large disparity across the UK in the uptake and usage of biosimilar infliximab; it was as high as 82.3% usage of biosimilar infliximab CT-P13 (either Inflectra or Remsima) in some regions and as little as 3.2% in others. The email, with the subject title of 'Why switch from Remicade to Remsima' was meant to help address some of the reasons why a switch to Remsima had not occurred in some areas of the UK despite clinical and regulatory bodies considering switching to CT-P13 a rational use of the medicine.

Napp was aware that switching to a biosimilar and involvement in gain-share negotiations was new for many health professionals. The aim of the email was to:

- reassure that switching patients from Remicade to Remsima was a rational use of the medicine
- highlight the potential substantial cost savings to the NHS and how some of these savings could be re-invested in their services and finally
- provide health professionals with tools and information to help them understand the switch should they choose to do so.

The bold opening strapline 'Don't get left behind – make the switch' was used to draw the attention of readers to start to think about three things:

1 How to switch patients from Remicade to Remsima without jeopardising patient safety
2 Cost savings that switching to Remsima could generate
3 How the savings could be re-invested in patient services.

The strapline was a call to action for health professionals to consider the facts if it was right for them and their patients to make the switch, and Napp provided the literature resources for them to make an informed decision. Indeed, the strapline was in bold letters and in larger font than the rest of the text to gain the health professionals' attention, but never to offend. Napp's experience was that those units where clinicians/nurses/pharmacists were involved and took a lead in gain-share negotiations were more likely to see some of the savings re-invested in their departments rather than simply decreasing budget deficits within the NHS trust.

The strapline was immediately followed by evidence that many colleagues across the UK were switching. The statements 'Biosimilar infliximab volume market share in the South West of England was 82.3% for the month of March 2016' and 'Your colleagues from across the UK are switching from Remicade to Remsima and re-investing their savings to improve patient care', with a link to the four case studies described previously, were intended to re-assure readers that other centres in the UK were switching, that switching did not jeopardise clinical efficacy or patient safety and to give examples of how they implemented the switch.

As well as reading about the experiences of other centres, health professionals were provided with a link to the Remsima cost calculator to begin to realise what cost savings they could potentially achieve if they switched. The cost calculator allowed them to enter their own hospital data and their own vial acquisition prices (these would vary from hospital to hospital depending on local tenders) to simply calculate how much money their departments could potentially save from switching from Remicade to biosimilar Remsima. The calculator then gave an example of how this money might be re-invested in patient care by highlighting how many band 6 nurse salaries it could potentially fund.

As noted above, the email provided health professionals with the appropriate information to allow them to make a clinically informed decision about switching to Remsima. The email referenced the EPAR to reassure health professionals that 'Remsima is infliximab as proven by rigorous testing vs Remicade'.

In summary, the email provided appropriate clinical and financial information upon which health professionals could base a decision on whether to switch their patients to Remsima. The strapline was to gain attention and stimulate the health professionals' thinking and not to offend. It then went on to provide information and resources for clarity which would help health professionals make informed clinical decisions. Napp strongly believed the information provided was fair, balanced and accurate, capable of substantiation and promoted the rational use of Remsima and hence did not breach Clauses 7.2, 7.4 or 7.10. It also refuted that the email content, and in particular the strapline, caused offence and hence did not breach Clause 9.2.

Furthermore, Napp believed high standards had been maintained at all times by careful consideration of how to promote switching without jeopardising patient's safety or causing offence and hence it also refuted a breach of Clause 9.1.

PANEL RULING

Point 1 The Panel noted the complainant's concern that the email encouraged health professionals to switch from Remicade to Remsima with no consideration of patients' needs. In that regard the Panel further noted that readers could access four case studies about the switching of patients from Remicade to Remsima. Each of those case studies detailed, *inter alia*, stakeholder or clinical support, outcomes and benefits and key learnings and advice. Some of the key learnings and advice included 'Before initiating the switch to an infliximab biosimilar, it is important to understand the safety, efficacy and economic arguments', 'Don't rush the switch process itself – give yourself time to resolve any technical issues and ensure that patient concerns have been addressed' and 'Engagement with all key- stakeholders is essential'. It seemed clear from the case studies that switches from Remicade to Remsima had taken place with due

consideration of the patients' needs; in all cases the proposed switch was discussed with patients before their therapy was changed. The Panel considered that in referring to patients' needs and presenting a considered approach to switching, the email had encouraged the rational use of Remsima and in that regard it ruled no breach of Clause 7.10. In the Panel's view, the material was sufficiently complete to allow recipients to form their own opinion of the therapeutic value of Remsima. No breach of Clause 7.2 was ruled. The Panel did not consider that Clause 7.4 was relevant within the context of this matter and so it made no ruling in that regard.

Point 2 The Panel considered that, contrary to Napp's submission, the unequivocal claim that 'Your colleagues from across the UK are switching from Remicade to Remsima and re-investing their savings to improve patient care' implied that every organisation that switched had savings to reinvest. The Panel further noted that in support of that claim, readers were provided with a link to the four case studies discussed above at Point 1. None of those case studies, however, were based in Scotland, Wales or Northern Ireland. Given the small number of case studies offered and their limited geographical spread (England only), the Panel considered that the claim was unequivocal and exaggerated and thereby misleading. A breach of Clause 7.2 was ruled. The Panel considered that such a broad claim could not be substantiated; a breach of Clause 7.4 was ruled.

Point 3 The Panel noted that the supplementary information to Clause 19.1 stated that it was acceptable for companies to promote a simple switch from one product to another. In the Panel's view, the complainant's submission that the indications for Remsima and its efficacy should not be presented in an advertisement which promoted switching from Remicade appeared to run counter to his/her concern that the email encouraged health professionals to switch to Remsima with no consideration of patients' needs. The Panel did not consider that in referring to the clinical aspect of Remsima, the email was misleading or that claims could not be substantiated. No breach of Clauses 7.2 and 7.4 were ruled. The Panel noted its ruling of no breach of Clause 7.10 above in that it considered that the email had encouraged the rational use of Remsima.

Point 4 The Panel noted that the email was headed with the phrase, in emboldened text, 'Don't get left behind – make the switch'. In the Panel's view, the heading implied that if the reader did not switch patients from Remicade to Remsima, they and their clinical practice were in some ways out-dated. The Panel considered that the phrase did not recognise the professional standing of the audience and their ability to make their own decisions and was likely to cause offence. A breach of Clause 9.2 was ruled.

The Panel noted its rulings above and considered that high standards had not been maintained. A breach of Clause 9.1 was ruled.

Complaint received **17 November 2016**

Case completed **1 March 2017**