CASE AUTH/2971/8/17

CLINICAL COMMISSIONING GROUP v THAME

Promotion of Thamicarb

Two members of staff from a clinical commissioning group (CCG) complained about a letter sent to a clinician by Thame Laboratories. The letter was about the prescription of Sodibic Oral Solution (sodium bicarbonate) as a food supplement instead of Thamicarb Oral Solution, marketed by Thame, which was the only licensed prescribed medicine form of sodium bicarbonate. The letter stated that sodium bicarbonate solution was a medicinal product and could not be presented as a food supplement or nutritional product. The letter drew attention to the Medicines and Healthcare Products Regulatory Agency's (MHRA's) position that products approved as food supplements should be avoided when licensed prescription products were available given that the latter had been tested for quality, safety and efficacy to ensure consumer safety. The letter urged the reader to comply with this guidance and stated that Thame Laboratories would 'vigorously prosecute' any non-compliance to the MHRA risk framework. A satisfactory response was requested within 15 days otherwise 'all such steps deemed necessary' would be taken.

The complainants alleged that the letter was bullying and threatening and listed a number of concerns including that:

- **it was inappropriate for a manufacturer to directly contact a clinician in order to request that he/she justify his/her clinical decision.**

- **The MHRA guidance on 'The supply of unlicensed medicinal products ("specials")' allowed a health professional to supply an unlicensed medicine where the licensed product could not meet an individual patient's needs. This was the case with Thamicarb where its short expiry once opened (3 days for the 100ml product and 7 days for the 500ml) made it impractical for the majority of patients to use safely. It was the responsibility of the health professional caring for the patient to make that decision.**

- **The letter stated that Thamicarb was 'the only licensed prescription medicinal form of Sodium Bicarbonate 1mmol/ml Oral Solution' but did not state that the licence was to treat hyperacidity, dyspepsia and symptomatic relief of heartburn and peptic ulceration in adults and children over 12 years old. The complainants alleged that the letter was misleading as it implied that Thamicarb was licensed for all of the indications that sodium bicarbonate oral solution might be used for rather than the restrictive licence it actually had.**

- **The complainants noted that the letter implied that the MHRA had commissioned Thame to identify practices prescribing food supplements and that the MHRA would take action against them. The CCG, did not believe the MHRA did this, it regulated medical products and devices.**

- **The CCG was not aware that the MHRA guidance was binding. A prescriber could prescribe an unlicensed product if he/she considered it was justified. The complainants alleged that Thame had misled the clinician.**

- **The complainants noted that the letter urged the recipient 'to ensure that Thamicarb Oral solution, the only licensed Rx medicinal Sodium Bicarbonate 1mmol/ml Oral Solution is being prescribed in your practice and also to refrain from prescribing the food supplement (Sodibic)'. The CCG found it difficult to understand how a pharmaceutical manufacture was able to recommend this based on prescribing data only and with no knowledge of the clinical circumstances in which it was prescribed. The health professional, not a pharmaceutical manufacturer, had the responsibility to decide if a switch to Thamicarb was clinically appropriate.**

The complainants noted that another practice had been sent a similar letter with regard to the prescribing of Syrsial (also a Thame product) which was a sodium chloride 1mmol/ml oral solution.

In an initial letter to the PMCPA one of the complainants stated that the cost of Thamicarb was extremely high when compared to other available products. The complainant further stated that the Specialist Pharmacy Service in October 2016 raised safety concerns about using Thamicarb due to the labelling of the product and the risk of dosing errors.

The detailed response from Thame Laboratories is given below.

The Panel disagreed with Thame's submission that the letter in question was non-promotional and that it was a communication which relayed regulatory guidance.

The Panel noted that the letter to the clinician urged him/her to refrain from prescribing Sodibic and ensure that Thamicarb Oral solution was being prescribed in his/her practice. The letter in question did not state Thamicarb's licensed indication such that it qualified the otherwise misleading implication that it was licensed for all indications and could be used with all patients that sodium bicarbonate oral solutions were prescribed for. The implication was misleading and was not capable of substantiation and a breach of the Code was ruled. Such promotion was inconsistent with the terms of Thamicarb's SPC. A breach of the Code was ruled.

The Panel considered that the letter implied that all patients on sodium bicarbonate oral solution could be switched to Thamicarb without any consideration of the patient's clinical circumstances as alleged and that was not so. The letter was misleading in this regard and a breach was ruled.

The Panel did not consider that the wording in the letter in question was specifically required by the MHRA and thus a breach was ruled. The Panel also considered that the phrase 'We have been advised by the MHRA to inform them of any findings where food supplements are being dispensed against prescriptions so they can take appropriate action' implied that the MHRA had formally requested Thame to identify practices prescribing food supplements and that was not so. The letter in question was misleading in this regard and a breach was ruled.

The Panel considered that the reference to criminal jurisdiction, by using the phrase 'vigorously prosecute' and the word 'non compliance' misleadingly implied that the activity was illegal as alleged and a breach was ruled. Further, the letter queried the health professional's decision to prescribe Sodibic without any knowledge of the clinical circumstances, stating that such a decision was inconsistent with MHRA Guidance and implied that serious consequences could ensue. In the Panel's view, the content and tone of the letter was such that it disparaged the professional opinion of the health professional at issue and a breach was ruled. Thame had failed to maintain high standards and a breach was ruled.

The Panel was very concerned about the content and tone of the letter and noted its comments and rulings above. The Panel noted that the misleading implication that patients could be switched without any consideration of their clinical circumstances might potentially prejudice patient safety. The Panel was particularly concerned about the misleading impression that the MHRA had formally requested that Thame identify and report practices prescribing food supplements and in this regard, noted the particular weight that would be attached by recipients to any reference to the MHRA. The Panel was also concerned about the implication of legal consequences if the letter was not adhered to including the reference to criminal jurisdiction by use of the phrase 'vigorously prosecute'. This impression was compounded by the fact that it was signed by the company's legal advisor. In the Panel's view, a health professional who had received the letter would be very concerned by the misleading implication that his/her prescribing decision was potentially illegal. The tone of the promotional letter could be seen as threatening and, in the Panel's view, brought discredit upon, and reduced confidence in, the pharmaceutical industry. A breach of Clause 2 was ruled.

Thame provided the requisite undertaking and assurance and as the case completed at Panel level the Appeal Board received the case report as set out in Paragraph 13.4 of the Constitution and Procedure.

The Appeal Board noted a letter sent to a clinician by Thame about Thamicarb Oral Solution (sodium bicarbonate) was misleading and disparaged the professional opinions of the reader. The Panel had considered that the tone of the promotional letter could be seen as threatening. The Appeal Board considered that this case raised serious issues. The Appeal Board was concerned that it appeared that further similar letters had been sent as referred to by the complainant. The Appeal Board was of the view that consideration should be given to the imposition of additional sanctions under Paragraph 11.1 of the Constitution and Procedure including possible recovery of the letter at issue. Thame should respond to these concerns in writing and it was invited to attend the Appeal Board when the matter was considered. Thame was provided with a copy of the papers.

The detailed response from Thame to the possibility of further sanctions being imposed is given below.

The Appeal Board noted that the company had apologised and agreed that the wording used in the letter at issue was totally unacceptable.

Whilst noting Thame's apology and remedial actions the Appeal Board was concerned to note that nearly 400 copies of the letter at issue had been sent. In addition, nearly 400 copies of a similar letter concerning Syrisal (sodium chloride, marketed by Thame) had also been sent.

Given the misleading content and threatening tone of the letter at issue the Appeal Board decided that in accordance with Paragraph 11.3 of the Constitution and Procedure, to require Thame to issue a corrective statement to all recipients of the letter at issue. Details of the proposed content and mode and timing of dissemination of the corrective statement must be provided to the Appeal Board for approval prior to use. The Appeal Board considered that the corrective statement should detail the Panel's comments. [The corrective statement, which was agreed by the Appeal Board prior to use, appears at the end of this report].

Two members of staff from a clinical commissioning group (CCG) complained about a letter sent to a clinician by Thame Laboratories Ltd. The letter dated 2 August 2017 was about the prescription of Sodibic Oral Solution (sodium bicarbonate) as a food supplement instead of Thamicarb Oral Solution, marketed by Thame, which was the only licensed prescribed medicine form of sodium bicarbonate. The letter stated that sodium bicarbonate solution was a medicinal product and could not be presented as a food supplement or nutritional product. The letter drew attention to the Medicines and Healthcare Products Regulatory Agency's (MHRA's) position that products approved as food supplements should be avoided when licensed prescription products were available given that the latter had been tested for quality, safety and efficacy to ensure consumer safety. The letter urged the reader to comply with this guidance and stated that Thame Laboratories would 'vigorously prosecute' any non-compliance to the MHRA risk framework. A satisfactory response was requested within 15 days otherwise 'all such steps deemed necessary' would be taken.

COMPLAINT

The complainants alleged that the letter was bullying and threatening and listed their concerns including that:

- it was inappropriate for a manufacturer to directly contact a clinician in order to request that he/she justify his/her clinical decision for an individual patient, it [Sodibic] was a niche product used 'off-label' as a diluent to make paediatric lansoprazole and GP practices were highly unlikely to have more than one patient taking it.

- Paragraph 2.2 in the MHRA guidance on 'The supply of unlicensed medicinal products ("specials")' allowed a health professional (doctor, dentist, pharmacist independent prescriber etc) to supply an unlicensed medicine in preference to a licensed medicine where the licensed product could not meet an individual patient's special needs. This was the case with Thamicarb where its short expiry once opened (3 days for the 100ml product and 7 days for the 500ml) made it impractical for the majority of patients to use safely. The MHRA also stated that it was the responsibility of the health professional caring for the patient to make that decision.

- The letter stated that Thamicarb was 'the only licensed prescription medicinal form of Sodium Bicarbonate 1mmol/ml Oral Solution' but did not state that the actual licence was '... to treat hyperacidity, dyspepsia and symptomatic relief of heartburn and peptic ulceration' in adults and children over 12 years old. The complainants noted that the CCG did not use it for the above indication, all use was 'off-label'. The complainants alleged that the letter was misleading as it implied that Thamicarb was licensed for all of the indications that sodium bicarbonate oral solutions might be used for rather than the restrictive licence it actually had. In addition, the majority of patients it would be used for across the CCG would be under 12 years old and so it would not be licensed for use in these patients.

- Where it was being used for the above indication, the CCG would ensure that Thamicarb was used in preference to other products.

- The complainants noted that the letter stated that 'we have been advised by the MHRA to inform them of any findings where food supplements are being dispensed against prescriptions so they can take appropriate action'. This implied that the MHRA had commissioned Thame to identify practices prescribing food supplements and that the MHRA would take action against the practices that prescribed food supplements although no documentation had been provided to confirm. Further, the CCG, did not believe the MHRA did this, it regulated medical products and devices. The complainants asked that Thame share the information from the MHRA requesting it did this.

- The complainants noted that Thame stated its intention to 'vigorously prosecute any aforementioned non-compliance to the MHRA risk framework'. It seemed that the company assumed that supplying sodium bicarbonate as a food supplement, in preference to the 'off-label' use of a licensed product, was illegal. The CCG was not aware that the MHRA guidance was binding and as guidance a prescriber could prescribe an unlicensed product (and in many case had no option but to) if he/she consider it was justified. The complainants did not believe the MHRA guidance was a legal mandate and in that regard they considered that Thame had misled the clinician.

- The complainants noted that the letter urged the recipient 'to ensure that Thamicarb Oral solution, the only licensed Rx medicinal Sodium Bicarbonate 1mmol/ml Oral Solution is being prescribed in your practice and also to refrain from prescribing the food supplement (Sodibic)'. The CCG found it difficult to understand how a pharmaceutical manufacture was able to recommend this based on prescribing data only and with no knowledge of the clinical indication for its use or the clinical circumstances in which it was prescribed. As noted above, this would not be practical for the majority of patients. The complainants repeated that the health professional looking after and prescribing for the patient, and not a pharmaceutical manufacturer, had the responsibility to decide if a switch to Thamicarb was clinically appropriate and whether 'off-label' prescribing of Thamicarb could meet the special needs and requirements of individual patients.

The complainants noted that another practice had been sent a similar letter with regard to the prescribing of Syrsial (also a Thame product) which was a sodium chloride 1mmol/ml oral solution.

In an initial letter to the PMCPA one of the complainants stated that the cost of Thamicarb was extremely high when compared to other available products. The complainant further stated that the Specialist Pharmacy Service in October 2016 raised safety concerns about using Thamicarb due to the labelling of the product and the risk of dosing errors.

When writing to Thame Laboratories, the Authority asked it to consider the requirements of Clauses 2, 3.2, 7.2, 7.4, 8.2, 9.1 and 9.5.

RESPONSE

Thame submitted that the letter at issue was not circulated in accordance with its standard operating procedure (SOP) for the review and approval of materials, due to a misunderstanding by individuals concerned. This had, in turn, identified a training need which would be addressed. The letter was intended to be non-promotional and a legal communication to bring the prescriber's attention to MHRA guidance (copy provided) which stated that unlicensed food supplements should not be used where a licensed product existed for a medical indication. This guidance was also consistent with guidance issued by the General Medical Council (GMC) and Medical Defence Union (MDU).
Thame stated that had the letter been circulated in the company approval procedure, it would not have been

approved or sent out. The company apologised for any offence that the tone of letter might have caused.

By way of background, Thame explained that in early 2017 it became aware that the unlicensed product Sodibic Oral Solution was being prescribed/promoted/supplied for the indication for which Thamicarb was licensed. Guidance was sought from the MHRA. Internally within the MHRA the matter was subsequently referred to the MHRA Inspectorate which telephoned the company. This conversation was not minuted.

Thame submitted that the letter did not seek to ask any doctor to justify his/her clinical decision for the medicines he/she might prescribe for an individual patient. A physician should prescribe the most appropriate treatment for the patient. The letter requested that doctors take into consideration and comply with MHRA guidance (of course Thame would expect this to be where appropriate) and stop prescribing a food supplement when prescribing for an indication where there was a licensed medicine. Thame reiterated that the letter was not promotional but a communication which relayed guidance.

Thame stated that whilst it had received medical information enquiries regarding the use of Thamicarb for the preparation of lansoprazole solutions it had consistently advised that it had no information on that use of product and could not recommend such use.

Thame noted that it did not promote Thamicarb for any unlicensed indication; it only sought to protect its product for the licensed indication.

With regard to the complainants' comments about the MHRA guidance on 'specials', Thame noted that paragraphs 2.2 and 2.3 in the guidance stated:

> '2.2 An unlicensed medicinal product may only be supplied in order to meet the special needs of an individual patient. An unlicensed medicinal product should not be supplied where an equivalent licensed medicinal product can meet the special needs of the patient. Responsibility for deciding whether an individual patient has "special needs" which a licensed product cannot meet should be a matter for the doctor, dentist, nurse independent prescriber, pharmacist independent prescriber or supplementary prescriber responsible for the patient's care. Examples of "special needs" include an intolerance or allergy to a particular ingredient, or an inability to ingest solid oral dosage forms. These examples are not exhaustive.
>
> 2.3 The requirement for a "special need" relates to the special clinical needs of the individual patient. It does not include reasons of cost, convenience or operational needs (see Section 10 of this guide). Anyone supplying an unlicensed medicinal product, where an equivalent licensed medicinal product is available must be satisfied as to the existence of a special need for the unlicensed medicinal product. MHRA expects that documentary evidence of this special need should be obtained by manufacturers, importers or distributors and that this evidence should be made available on request of the Licensing Authority. This may take the form of a prescriber's letter, however an alternative fully documented audit trail through the supply chain confirming special need may be acceptable.'

Further, guidance from the General Medical Council (GMC) on the use of unlicensed medicines stated:

> '68. You should usually prescribe licensed medicines in accordance with the terms of their licence. However, you may prescribe unlicensed medicines where, on the basis of an assessment of the individual patient, you conclude, for medical reasons, that it is necessary to do so to meet the specific needs of the patient.
>
> 69. Prescribing unlicensed medicines may be necessary where:
>
> a. There is no suitably licensed medicine that will meet the patient's need. Examples include (but are not limited to), for example, where
>
> i. there is no licensed medicine applicable to the particular patient. For example, if the patient is a child and a medicine licensed only for adult patients would meet the needs of the child; or
>
> ii. a medicine licensed to treat a condition or symptom in children would nonetheless not meet the specific assessed needs of the particular child patient, but a medicine licensed for the same condition or symptom in adults would do so; or
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> iii. the dosage specified for a licensed medicine would not meet the patient's need; or
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> iv. the patient needs a medicine in a formulation that is not specified in an applicable licence.
>
> b. Or where a suitably licensed medicine that would meet the patient's need is not available. This may arise where, for example, there is a temporary shortage in supply; or
>
> c. The prescribing forms part of a properly approved research project.
>
> 70. When prescribing an unlicensed medicine you must:
>
> a. be satisfied that there is sufficient evidence or experience of using the medicine to demonstrate its safety and efficacy
>
> b. take responsibility for prescribing the medicine and for overseeing the patient's care, monitoring, and any follow up treatment, or ensure that arrangements are made for another suitable doctor to do so
> c. make a clear, accurate and legible record of all medicines prescribed and, where you are not following common practice, your reasons for prescribing an unlicensed medicine.'

Thame explained that Thamicarb was a licensed medicine; Sodibic was not and was thus not subject to the same controls in terms of quality, manufacture, safety and efficacy. There were sound scientific reasons why Thamicarb had a short in-use shelf life. Once the bottle was opened there was dissociation of the bicarbonate ion and the resultant release of carbon dioxide this meant that with the repeated opening and closing of the bottle the pH of the solution became more alkaline. The British Pharmacopeia (BP) stipulated that the sodium bicarbonate oral solution should have a pH of between 7.0 and 8.5. Studies which mimicked normal daily use had shown that the BP pH limits were exceeded on or after day 4 from the 100ml bottle and after day 8 from the 500ml bottle. Hence there was a product quality perspective to the guidance. Thame expected the same would occur with the unlicensed product and as far as it was aware, the unlicensed product did not provide information regarding shelf life. Thamicarb did not contain any preservatives.

With regard to the complainants' concern about the licensed indication not being stated in the letter, Thame noted that, as stated previously, the letter was to advise prescribers of guidance that existed, which advised them that when a licensed medicine existed it should be used for the indications licensed and not an unlicensed version made available in this case as a food supplement. Hence the letter was intended to be a legal announcement/communication. Thame agreed that it would have been helpful to include the indications and dosage, but the intent was non promotional. Inclusion of the indications could be regarded as a product claim and therefore the letter would be deemed promotional.

Thame had no comment with regard to the complainants' statement that where it was being used for the above indication, the complainants would ensure that Thamicarb was used in preference to other products.

Thame noted that the complainants referred to the statement that '**... we have been advised by the MHRA to inform them of any findings where food supplements are being dispensed against prescriptions so they can take appropriate action'**, which implied that the MHRA had commissioned Thame to identify practices prescribing food supplements and that the MHRA would act against practices identified as prescribing food supplements.

Thame stated that the wording in bold was unfortunate. As stated above, there was a telephone conversation with the MHRA Inspectorate which was not minuted during which the Inspectorate stated that if Thame became aware of the promotion/use of a sodium bicarbonate oral solution sold as a food supplement for a medicinal indication, it should be brought to its attention.

With regard to the complainants' comments about possible prosecution, Thame again referred to the relevant MHRA/GMC guidance to prescribers. The expectation was that guidance was followed whenever possible. Clearly when managing a patient there might be instances where following guidance for clinical (special need) reasons was not possible and the MHRA/GMC guidance addressed this. Thame stated that the wording 'intends to vigorously prosecute any aforementioned non-compliance to the MHRA risk framework' used in the letter was unfortunate and would not have been used had the letter gone through the copy approval procedure.

With regard to one of the complainant's comments about the high cost of Thamicarb, Thame referred to point 2.3 in the MHRA guidance on 'The supply of unlicensed medicinal products ("specials")' above. Thame also noted that the complainant stated that in October 2016 the Specialist Pharmacy Service was concerned about the safety of using Thamicarb due to the labelling of the product and risk of dosing errors. Thame submitted that the labelling of Thamicarb had been reviewed both during registration by the Medical and Quality (pharmaceutical) assessors at the MHRA and the Health Products Regulatory Agency (HPRA) in Ireland and subsequently during variation assessments. The company was in regular contact with the NHS Commercial Medicines Unit concerning this and its other products.

With regard to Clause 3.2, Thame noted that the letter's author intended the letter to be a legal announcement/communication to draw the prescriber's attention to the fact that when a licensed medicine existed for a particular indication, then an unlicensed medicine should not be prescribed (paragraph 2.2 of the MHRA guidance above). The letter was intended to be non promotional. Thame acknowledged that including the indications could have improved clarity but such could be regarded as a product claim and therefore the piece would be promotional. There was no intention to be inconsistent with the terms of the marketing authorisation.

With regard to Clause 7.2, Thame reiterated that the letter was intended to be a non promotional legal announcement /communication. The information was consistent with guidance provided to medical practitioners by the MHRA and the GMC. The information was accurate but could have been presented in a clearer and better manner.

Thame submitted that as per Clause 7.4, the information in the letter, with reference to guidelines, was capable of substantiation – other than details of the MHRA telephone conversation which was not minuted. The information was consistent with guidance provided to medical practitioners. As stated above, the letter could have been better presented.

Thame submitted that the letter did not disparage the clinical and scientific opinions of health professionals (Clause 8.2) but brought guidance to their attention.

Thame stated that as per Clause 9.1, it strove to consistently maintain high standards in all its activities. The in-house copy approval procedure strove to ensure that all promotional materials were of a high standard. The letter at issue could have been phrased differently which would have improved the standard of the communication and avoided this complaint.

Thame submitted that as the letter was intended to be non-promotional, the requirements of Clause 9.5 that promotional material should not refer to the MHRA etc was not applicable. As stated above, the letter's author intended to bring to the prescriber's attention the fact that there was guidance to health professions issued by the regulators (MHRA/GMC) that when a licensed medicine existed for a particular licensed indication then an unlicensed medicine should not be prescribed except in exceptional special need situations. In the case of Thamicarb, unlicensed products such as Sodibic, should not be prescribed for the indication for which Thamicarb was indicated (except in special need situations as described in the guidance).

Thame reiterated the non-promotional intent of the letter. The company knew, as stated earlier, that a preparation sold without any licence potentially as a food supplement might have been used as a medicine for the indications for which Thamicarb was licensed. As previously stated, the letter could have been presented more clearly and in a less legalistic tone. Thame stated that it had no desire to participate in any promotional activity which might bring discredit upon, or reduce confidence in, the industry in which it operated.

In summary, Thame noted that the complaint related to a non-promotional letter sent to a practice to bring to its attention regulatory authority guidance that existed regarding the prescribing of an unlicensed medicine where a licensed medicine existed for an indication and to bring to the practice's attention a specific issue regarding sodium bicarbonate oral solution. Thame accepted that the communication could have been presented more appropriately in a better manner and style. Neither the company nor the letter's author intended to contravene any clause of the Code.

PANEL RULING

The Panel disagreed with Thame's submission that the letter in question was non-promotional and that it was a communication which relayed regulatory guidance. The Panel noted that Clause 1.2 of the Code defined promotion as any activity undertaken by a pharmaceutical company or with its authority which promoted the administration, consumption, prescription, purchase, recommendation, sale, supply or use of its medicines. The letter stated '… we would urge you to ensure that Thamicarb Oral solution, the only licensed Sodium Bicarbonate 1mmol/ml Oral Solution is being prescribed in your practice and also to refrain from prescribing food supplements (Sodibic)'. In the Panel's view, noting the broad definition of promotion in the Code, the letter was promotional.

The Panel noted that the letter to the clinician urged him/her to refrain from prescribing Sodibic and ensure that Thamicarb Oral solution was being prescribed in his/her practice. The letter in question did not state Thamicarb's licensed indication such that it qualified the otherwise misleading implication that it was licensed for all indications and could be used with all patients that sodium bicarbonate oral solutions were prescribed for. According to material provided by Thame, Sodibic was licensed as a food supplement and was supplied as a special. Material provided by Thame referred to the use of Sodibic to treat acidic conditions of the blood and urine and as an antacid to balance excess stomach acidity. Thamicarb was indicated to treat hyperacidity, dyspepsia and symptomatic relief of heartburn and peptic ulceration. The SPC gave the dose for adults and children over 12 years and stated that it was not to be taken by children under 12 years old. The implication was misleading and was not capable of substantiation and a breach of Clauses 7.2 and 7.4 was ruled. In the Panel's view, this misleading implication also meant that Thamicarb had not been promoted in accordance with the terms of its marketing authorisation and such promotion was inconsistent with the terms of its SPC. A breach of Clause 3.2 was ruled.

The Panel noted that the CCG found it difficult to understand how a pharmaceutical manufacturer was able to recommend a switch based on prescribing data only and with no knowledge of the clinical indication for its use or the clinical circumstances in which it was prescribed, the letter took no account of whether a switch was clinically appropriate. The Panel noted Thamicarb's licensed indication and the Panel's comments and rulings in this regard as set out above. The Panel considered that the letter implied that all patients on sodium bicarbonate oral solution could be switched to Thamicarb without any consideration of the patient's clinical circumstances as alleged and that was not so. The letter was misleading in this regard and a breach of Clause 7.2 was ruled.

The Panel noted that Clause 9.5 stated that promotional material must not include any reference to, *inter alia*, the Medicines and Healthcare products Regulatory Agency, unless this was specifically required by the licensing authority. The exception mentioned in the relevant supplementary information in relation to factual safety information and the MHRA Drug Safety Update did not apply to the letter at issue. The Panel noted that the letter in question referred to the MHRA Guidance on the hierarchy for the use of unlicensed medicines which was an appendix to the MHRA's Guidance Note on the supply of unlicensed medicinal products (specials). The letter in question also stated that Thame had been advised by the MHRA to inform it of any findings where food supplements were being dispensed against prescriptions so they could take appropriate action. The Panel noted Thame's submission that it had an unminuted telephone conversation with the MHRA during which the Inspectorate stated that if Thame became aware of the promotion/use of a sodium bicarbonate oral solution sold as a food supplement for a medicinal indication, it should be brought to its attention. The Panel did not consider that Thame's account of the telephone conversation meant that the wording in the letter in question was specifically required by the MHRA as stated in Clause 9.5 and thus a breach of Clause 9.5 was ruled. The Panel also considered that the phrase 'We have been advised by the MHRA to inform them of any findings where food supplements are being dispensed against prescriptions so they can take appropriate action' implied that the MHRA

had formally requested Thame to identify practices prescribing food supplements and that was not so. The letter in question was misleading in this regard and a breach of Clause 7.2 was ruled.

The Panel noted the complainant's allegation that the phrase that the company 'intends to vigorously prosecute any aforementioned non-compliance to the MHRA risk framework' implied that supplying sodium bicarbonate as a food supplement in preference to the unlicensed use of a licensed product was illegal. The Panel noted the company's response that such guidance should be followed whenever possible but that there might be instances where following guidance was not possible for clinical reasons. The Panel also noted the company's submission that the phrase was unfortunate and would not have been used had the letter gone through the company copy approval procedure. The Panel considered that the reference to criminal jurisdiction, by using the phrase 'vigorously prosecute' and the word 'non compliance' misleadingly implied that the activity was illegal as alleged and a breach of Clause 7.2 was ruled.

The Panel noted the complainant's concern that it was inappropriate for a manufacturer to directly contact a clinician in order to request that he/she justify his/her clinical decision for an individual patient and the complainant's comments. The Panel noted that Clause 8.2 stated that health professions and the clinical and scientific opinions of health professionals must not be disparaged. According to the complainants, the clinician who had received the letter was at a practice that had only had one patient on Sodibic. Paragraph 2.2 of the MHRA guidance on 'The supply of unlicensed medicinal products ("specials")' allowed a health professional (doctor, dentist, pharmacist independent prescriber etc) to supply an unlicensed medicine in preference to a licensed medicine where the licensed product could not meet an individual patient's special needs. The Panel noted, however, that the majority of patients' for whom sodium bicarbonate would be used across the CCG would be under 12 years old and so Thamicarb would not be licensed for use in these patients and the MHRA guidance would not apply. The MHRA also stated that it was the responsibility of the health professional caring for the patient to make that decision. The Panel further noted that the complainants stated that where sodium bicarbonate was being used for Thamicarb's licensed indication, the CCG would ensure that Thamicarb was used in preference to other products. The Panel considered that the letter in question queried the health professional's decision to prescribe Sodibic without any knowledge of the clinical circumstances, stating that such a decision was inconsistent with MHRA Guidance and implied that serious consequences could ensue. In the Panel's view, the content and tone of the letter was such that it disparaged the professional opinion of the health professional at issue and a breach of Clause 8.2 was ruled.

Thame acknowledged that certain wording in the letter was unfortunate and would not have been approved or sent had it gone through the copy approval procedure in line with its SOP. The company also acknowledged that the information could have been presented in a better and clearer manner. In addition, the Panel noted its comments and rulings above and considered that Thame had failed to maintain high standards and a breach of Clause 9.1 was ruled.

The Panel was very concerned about the content and tone of the letter and noted its comments and rulings above. The Panel noted that the misleading implication that patients could be switched without any consideration of their clinical circumstances might potentially prejudice patient safety. The Panel was particularly concerned about the misleading impression that the MHRA had formally requested that Thame identify and report practices prescribing food supplements and in this regard, noted the particular weight that would be attached by recipients to any reference to the MHRA. The Panel was also concerned about the implication of legal consequences if the letter was not adhered to including the reference to criminal jurisdiction by use of the phrase 'vigorously prosecute'. This impression was compounded by the fact that it was signed by the company's legal advisor. In the Panel's view, a health professional who had received the letter would be very concerned by the misleading implication that his/her prescribing decision was potentially illegal. The tone of the promotional letter could be seen as threatening and, in the Panel's view, brought discredit upon, and reduced confidence in, the pharmaceutical industry. A breach of Clause 2 was ruled.

The Panel noted that the complainants' comment that another practice had received a similar letter with regard to the prescribing of Syrsial (also a Thame product) which was a sodium chloride 1mmol/ml oral solution. The Panel did not consider that this second letter was the subject of complaint. No further details were provided nor were particular clauses raised and the Panel made no rulings in this regard.

APPEAL BOARD CONSIDERATION OF CASE REPORT

Thame provided the requisite undertaking and assurance and as the case completed at Panel level the Appeal Board received the case report as set out in Paragraph 13.4 of the Constitution and Procedure.

The Appeal Board noted a letter sent to a clinician by Thame about Thamicarb Oral Solution (sodium bicarbonate) which was misleading and disparaged the professional opinions of the reader. The Panel had considered that the tone of the promotional letter could be seen as threatening. The Appeal Board considered that this case raised serious issues. The Appeal Board was concerned that it appeared that further similar letters had been sent as referred to by the complainant. The Appeal Board was of the view that consideration should be given to the imposition of additional sanctions under Paragraph 11.1 of the Constitution and Procedure including possible recovery of the letter at issue. Thame should respond to these concerns in writing and it was invited to attend the Appeal Board when this matter was considered. Thame was provided with a copy of the papers.

COMMENTS FROM THAME

Thame agreed and regarded the wording used in the letter at issue as totally unacceptable. The company deeply regretted any distress and annoyance that the letter might have caused. Thame had no desire to disparage the professional opinion of any health professionals or question their clinical judgement. The company was appalled that its communications appeared to threaten or bully any health professional and the company had no intention to threaten or bully anyone. The letter was an inappropriate and misguided attempt at bringing a particular point to the attention of health professionals regarding use of unlicensed food supplements where a licensed product was available. Had the letter been submitted through the company system for the review and approval of promotional material, it would have never been approved and sent out.

Background and actions taken to prevent a reoccurrence

Thame submitted that as stated in the response to the Panel, it became aware that the unlicensed product Sodibic Oral Solution was being prescribed/promoted/supplied for the indications where Thamicarb was licensed. The matter was referred to the MHRA and guidance sought which subsequently referred the matter to its inspectorate. A company legal advisor, who was involved in communicating to manufacturers of unlicensed medicines to advise them that Syri Limited held marketing authorisations for Thamicarb and Syrisal, through a misunderstanding together with a misinterpretation of the guidance that the MHRA gave the company, sent the communications in question to clinical commissioning groups and some GP surgeries which were known to use unlicensed Sodium Bicarbonate and Sodium Chloride Oral Solutions as unlicensed medicines between March and August 2017. The legal advisor considered the nature of the letter was a legal and commercial communication and not promotional. This was not questioned by the commercial team member involved. Thus, the letter was not submitted for review and approval of promotional material in accordance with company procedures.

Thame submitted that in September 2017 when notified of the complaint, with senior management becoming aware of the letter and its content, the company immediately instructed the commercial team and legal advisor to ensure that no further such letters were sent out for any of the two products concerned (Thamicarb/Syrisal). An assurance was provided by those concerned to this effect. The company confirmed that no such letters were sent since August 2017. The letter forming the complaint was one of the last letters sent.

Thame submitted that an internal review was conducted by the chief executive officer to establish how the letter managed to be sent without going through the company review and approval procedures which resulted in the following actions:

1 Retraining was conducted in December 2017 on the Code for all company staff who might be involved in contact with health professionals regarding promotional and non-promotional activities using all external consultants.

2 Following the above retraining on the Code the requirements of the company standard operating procedure (SOP) on the review and approval of promotional material (SOP/MI/001/v2 dated June 2017) was reiterated to all staff. All company staff were trained on procedures relating to their jobs using an electronic training matrix.

3 Further training would be provided when the 2018 Code update became available.

4 The company had ceased to seek advice on such matters from the legal adviser concerned in the occurrence.

5 The commercial team had been instructed that all communications considered to be of a non-promotional commercial nature to health professionals needed to be discussed with the Code of Practice signatories to confirm their nature.

Thame (Syri Limited) had held licences for medicinal products for 3 years. Currently the company approved about two to three promotional items per month predominantly mailings to clinical commissioning groups and health professionals through its approval system. The company had had no other complaints from any source including the PMCPA or the MHRA about any of its promotional items other than this letter.

Thame submitted that the occurence under review had been an isolated incident occurring between 8 and 13 months ago of which there had been no reoccurrence once brought to the company's attention and stopped. For the size of the company, the number of staff and the number of promotional items the company submitted it had a robust system in place for the approval of promotional materials.

The company intended at all times to be compliant with the Code and the MHRA Blue Guide and requested that the Appeal Board did not impose any additional sanctions on the first occurrence. The letters concerned were sent out 8-13 months ago and resulted from a misunderstanding and misinterpretation together with a company employee not questioning the opinion of a legal professional.

In response to a request to confirm the number of letters sent and to whom Thame confirmed that the number of letters sent were as follows:

Clinical commissioning groups:

Thamicarb 200 (one letter to each clinical commissioning group)

Syrisal 200 (one letter to each clinical commissioning group).

Thamicarb: one letter to each of 195 General Medical Practitioner Practices/Surgeries (not individual GPs) who had been identified using clinical commissioning group data as having prescribed unlicensed sodium bicarbonate oral solutions.

Syrisal: one letter to each of 196 General Medical Practioner Practices/Surgeries (not indivudal GPs) who had been identified using clinical commissioning group data as having prescribed unlicensed sodium chloride oral solutions.

APPEAL BOARD CONSIDERATION

The Appeal Board noted the Panel's rulings of breaches of Clauses 2, 3.2, 7.2, 7.4, 8.2, 9.1 and 9.5 of the Code. The Appeal Board noted that the company had apologised and agreed that the wording used in the letter at issue was totally unacceptable. The Appeal Board noted Thame's submission that it would now ensure that all non-promotional material of a commercial nature for health professionals would be discussed with its company signatories to confirm its nature.

The Appeal Board noted that the legal advisor who had sent the letter at issue had considered the nature of the letter was a legal and commercial communication and not promotional and that this was not questioned by the commercial team member involved. The Appeal Board considered that it should have been apparent that not only was the letter clearly promotional it was also unacceptable. The Appeal Board noted that the company had ceased to seek advice on such matters from the legal adviser. Staff had been retrained on the Code.

Whilst noting Thame's apology and remedial actions the Appeal Board was concerned to note that nearly 400 copies of the letter at issue had been sent. In addition, nearly 400 copies of a similar letter concerning Syrisal (marketed by Thame) had also been sent.

Given the misleading content and threatening tone of the letter at issue the Appeal Board decided that in accordance with Paragraph 11.3 of the Constitution and Procedure, to require Thame to issue a corrective statement to all recipients of the letter at issue. The Appeal Board considered that the corrective statement should detail the Panel's comments. [The corrective statement, which was agreed by the Appeal Board prior to use, appears at the end of this report].

Complaint received	**17 August 2017**
Undertaking received	**15 February 2018**
Appeal Board consideration	**22 March and 18 April 2017**
Corrective statement issued	**11 June 2018**

On 11 June 2018, Thame laboratories sent the following corrective statement to recipients of the letter at issue.

'Corrective statement

Between March and August 2017 Syri Ltd trading as Thame Laboratories sent a letter headed 'RE: Thamicarb, Sodium bicarbonate 1mmol/ml oral solution [PL 39307/0005]' about the prescription of Sodibic oral solution (sodium bicarbonate) as a food supplement instead of Thamicarb oral solution, marketed by Thame

You are being sent this corrective statement because you received this letter or a similar letter.

Following a complaint under the ABPI Code of Practice for the Pharmaceutical Industry, the Code of Practice Panel considered that the letter in question misleadingly stated that it was specifically required by the MHRA and that the MHRA had formally requested Thame to identify practices prescribing food supplements. The Panel noted the particular weight that would be attached by recipients to any reference to the MHRA.

The Panel considered that the letter implied that all patients on sodium bicarbonate oral solution could be switched to Thamicarb which was not so. The misleading implication that patients could be switched without any consideration of their clinical circumstances might potentially prejudice patient safety.

The letter did not state Thamicarb's licensed indication and that it could not be used with all patients that sodium bicarbonate oral solutions were prescribed for. The implication was misleading and was not capable of substantiation which also meant that the promotion of Thamicarb was inconsistent with the terms of its summary of product characteristics.

Use of the phrase 'vigorously prosecute' and the word 'non compliance' misleadingly implied that the use of a food supplement in preference to the unlicensed use of a licenced medicine was illegal. In addition the content of the letter disparaged the professional opinion of the health professionals who would be very concerned by the misleading implication that his/her prescribing decision was potentially illegal. The tone of the letter could be seen as threatening. Thame had failed to maintain high standards and it had brought discredit upon, and reduced confidence in, the pharmaceutical industry.

The Code of Practice Appeal Board required Thame Laboratories to issue this corrective statement and to circulate a copy of the published report for the case (Case AUTH/2971/8/17) which contains full details. This is enclosed.

Details of this case (Case AUTH/2971/8/17) are also available on the PMCPA website (www.pmcpa.org.uk).'