CASE AUTH/3266/10/19 and AUTH/3279/11/19

HEALTH PROFESSIONAL v OTSUKA UK AND OTSUKA EUROPE

Alleged pre-licence promotion

A health professional complained about two online press releases about ASTX727, a fixed dose combination of oral cedazuridine and decitabine which was being studied for the possible treatment of myelodysplatic syndrome (MDS) including chronic myelomonocytic leukemia (CMML). Astex Pharmaceuticals Inc in the US, a wholly owned subsidiary of Otsuka Pharmaceuticals Co Ltd had issued one of the press releases and the second press release was issued jointly by Astex and Otsuka Pharmaceutical Co Ltd in Japan (OPCJ). The second press release was the subject of another complaint, Cases AUTH/3212/6/19 and AUTH/3262/6/19.

The matter was taken up with Otsuka Pharmaceuticals (UK) Limited and Otsuka Pharmaceuticals Europe Limited as UK based affiliates were responsible for the acts/omissions of overseas affiliates that came within the scope of the Code.

The detailed response from Otsuka UK and Otsuka Europe is given below.

The first press release the complainant drew attention to was headed 'Astex Pharmaceuticals Announces That Its Novel, Oral Hypomethylating Agent ASTX727 Has Been Granted Orphan Drug Designation for the Treatment of Myelodysplatic Syndrome (Including Chronic Myelomonocytic Leukemia) by the US FDA'. As the press release appeared on a UK website, the complainant considered that it must conform to the ABPI Code.

The complainant alleged that the press release was promotional and that it encouraged patients to request the treatment from their doctors (although not currently available in the UK). The complainant queried whether Astex/Otsuka would undertake to provide the medicine for UK based patients.

The complainant stated that the press release encouraged false hope for patients and queried whether 'novel' meant that ASTX727 had additional properties or benefits that no other current treatment had.

The first matter for the Panel to consider was whether the press releases were covered by the ABPI Code. The Panel noted that it appeared that the complainant had accessed the press release via uk.finance.yahoo.com. The Panel noted the submission from Otsuka Europe and Otsuka UK that the first press release was issued by Astex in the US. Otsuka Europe and Otsuka UK did not issue, approve for issue or authorize the press release. There was no mention of use of the medicine in the UK or Europe. The Panel also noted Otsuka Europe and Otsuka UK's submission that they did not review the press release as it was confirmed that it was not going to be issued in any country outside the US.

The Panel noted that the press release was circulated via third parties in the UK and Ireland as well as the US channel by Astex Pharmaceuticals Inc which was a wholly owned subsidiary of Otsuka Pharmaceuticals Co Ltd. The press release had been widely circulated to UK media organisations many of which were aimed at consumers.

The Panel considered therefore given the circulation to UK outlets , the press release was covered by the UK Code. The Panel noted the involvement of Otsuka Europe and Otsuka UK. However, it was a clearly established principle under the Code that the UK company was responsible for acts and omissions of its overseas affiliates that came within the scope of the Code.

The Panel noted Otsuka Europe and Otsuka UK's submission that ASTX727 did not have a marketing authorization in any country, the Panel considered therefore that it was not classified as a prescription only medicine. Relevant clauses of the Code regarding relations with the public only applied to prescription only medicines. On this very narrow technical point the Panel ruled no breach of the Code. However, the Panel considered that the press release issued to the public promoted an unlicensed medicine which meant that high standards had not been maintained. A breach of the Code was ruled.

With regard to the use of the word 'novel', the Panel noted the companies' submission that this was justified as it was an oral treatment and included an oral form of decitabine, which was currently only licensed as an IV treatment. Further it was a patented medicine. The Panel considered that the audience would understand novel to mean that the medicine, ASTX727 was new and unusual. The product had been granted orphan status. The Panel noted its comments and rulings above that ASTX727 was not a prescription only medicine. The Panel therefore ruled no breach of that clause with regard to the allegation that in using the word 'novel' to describe ASTX727 the press release would raise unfounded hopes of successful treatment. The Panel did not consider that the complainant had established that describing ASTX727 as novel was misleading and no breach of the Code was ruled.

The Panel noted that a breach of Clause 2 was used as a sign of particular censure and was reserved for such use. The Panel considered that the circumstances did not amount to a breach of the Code and ruled accordingly.

The second press release the complainant drew attention to was headed 'Astex Pharmaceuticals and Otsuka announce results of latest study'. The study in question was the phase 3 ASCERTAIN Study with ASTX727.

The complainant alleged that the press release made outlandish claims, such as the safety and clinical profile of the medicine were similar in early trials but provided no additional data. It was clear from the press release that the medicine was not available in Europe but it encouraged patients to seek it out, given its positive results and the opportunity to participate in clinical trials. More concerning was some of the safety claims. 'The complainant alleged that the press release did not provide the reader with appropriate context (the data was from pharmacokinetic study).

The complainant would like to see the evidence to support the statement, '… the fixed dose combination of cedazuridine with decitabine enables successful oral delivery of

decitabine, alleviating the significant burden of five days monthly IV infusions for patients who may continue to benefit from the drug for several months or even years'. The complainant alleged that such claims were marketing claims and had no place in a press release. Such a statement did not do favours for evidence-based medicine.

The Panel noted that although the press release was issued by Astex in the US and Otsuka Japan and Otsuka Europe and Otsuka UK did not issue, approve for issue or authorize the material and there was no mention of use of the medicine in the UK or Europe it was howevera clearly established principle under the Code that the UK company was responsible for acts and omissions of its overseas affiliates that came within the scope of the Code.

The Panel noted that it appeared that the complainant had accessed the press release via cambridgenetwork.co.uk. The Panel noted that the press release was circulated via a third party by Astex Pharmaceuticals Inc which was a wholly owned subsidiary of Otsuka Pharmaceuticals Co Ltd. A list of the third party's circuits for press releases was provided by Otsuka which included circuits for the UK and Ireland. The Panel noted from emails provided by Otsuka Europe and Otsuka UK that both were aware that the press release was going to be issued in the UK and Ireland. From the detailed list provided in these cases the Panel noted that the press release had been widely circulated to UK media organisations many of which were aimed at consumers.

The Panel noted the companies' submission that Astex approached Otsuka Europe's communications team which liaised with Otsuka UK and a review of the press release using Zinc was initiated. The Panel queried why that review was not completed given that emails stated that 'we have to put joint Astex/Otsuka press releases through [Otuska UK] review if released in the UK'.

The Panel considered that given the circulation to UK outlets , the press release was covered by the UK Code. The Panel noted the involvement of Otsuka Europe and Otsuka UK.

The Panel also noted that Otsuka Europe and Otsuka UK had provided a further copy of their response to Cases AUTH/3212/6/19 and AUTH/3262/10/19 as their response to the allegations in this complaint. The complaints were similar but not the same.

The Panel noted that the press release referred to the safety and clinical activity of ASTX727 being similar to that observed in a previous study. It was stated in the press release that the outcome demonstrated that the fixed dose combination enabled '…successful oral delivery of decitabine alleviating the significant burden of five days of monthly IV infusions for patients who might continue to benefit from the drug for several months or even years'. It was further stated that ASTX727 could bring a new treatment option to patients with 'these deadly diseases'. The press release also stated that 'ASTX727 is an investigational compound and is not currently approved in any country'.

Given the circumstances the Panel did not consider that the distribution of the press release for an unlicensed medicine in itself meant that that medicine had been promoted. Nor did the Panel consider that the mention of other studies in the clinical programme necessarily promoted the medicine for those indications. It was not unreasonable to

give an overview. The Panel considered that some of the language within the press release was promotional as acknowledged by Otsuka Europe and Otsuka UK.

The Panel noted Otsuka's submission that although decitabine was licensed in the UK, the combination with cedazuridine (ASTX727) was not and that in the UK decitabine IV was licensed for newly diagnosed, de novo, or secondary acute myeloid leukaemia. The Panel also noted that the ASCERTAIN Study was a pharmacokinetic equivalence study and that safety and efficacy were secondary endpoints. The Panel agreed with Otsuka that statements about alleviating the burden of IV infusions, survival benefit, low level of gastrointestinal adverse events and the benefit of oral treatment were misleading and not capable of substantiation. The Panel ruled a breach of the Code as acknowledged by Otsuka UK and Otsuka Europe. There did not appear to be clinical evidence to support the claims for ASTX727 and gastro-intestinal side effects ; it was not clear from the outset that the study was a pharmacokinetic study and safety was a secondary endpoint. Thus, the Panel ruled a breach of the Code.

The Panel noted that ASTX727 was not classified as a prescription only medicine. Relevant clauses of the Code regarding relations with the public only applied to prescription only medicines. On this very narrow technical point the Panel ruled no breach of those clauses. However, the Panel considered that the press release issued to the public promoted an unlicensed medicine which meant that high standards had not been maintained and a breach of the Code was ruled.

The Panel considered that high standards had not been maintained with regard to the information about the study outcomes as ruled in breach of the Code above. The Panel therefore ruled a further breach of the Code.

The Panel noted that a breach of Clause 2 was used as a sign of particular censure and was reserved for such use. The Panel considered that the circumstances did not amount to a breach of the Code and ruled accordingly.

A health professional complained about two online press releases about ASTX727, a fixed dose combination of oral cedazuridine and decitabine which was being studied for the possible treatment of myelodysplatic syndrome (MDS) including chronic myelomonocytic leukemia (CMML). Astex Pharmaceuticals Inc in the US, a wholly owned subsidiary of Otsuka Pharmaceuticals Co Ltd had issued one of the press releases and the second press release was issued jointly by Astex and Otsuka Pharmaceutical Co Ltd in Japan (OPCJ). The second press release was the subject of another complaint, Cases AUTH/3212/6/19 and AUTH/3262/6/19.

The matter was taken up with Otsuka Pharmaceuticals (UK) Limited and Otsuka Pharmaceuticals Europe Limited as UK based affiliates were responsible for the acts/omissions of overseas affiliates that came within the scope of the Code.

1 Press release issued by Astex – announcement of orphan status designation by the FDA

COMPLAINT

The complainant drew attention to a press release on the uk.finance.yahoo.com website which was headed 'Astex Pharmaceuticals Announces That Its Novel, Oral Hypomethylating Agent ASTX727 Has Been Granted Orphan Drug Designation for the Treatment of Myelodysplatic Syndrome (Including Chronic Myelomonocytic Leukemia) by the US FDA'. As the press release appeared on a UK website, the complainant considered that it must conform to the ABPI Code.

The complainant alleged that the press release was promotional and that it encouraged patients to request the treatment from their doctors (although not currently available in the UK). This caused additional stress and strain for the NHS. The complainant queried whether Astex/Otsuka would undertake to provide the medicine for UK based patients.

The complainant stated that the press release encouraged false hope for patients and queried whether 'novel' meant that ASTX727 had additional properties or benefits that no other current treatment had.

When writing to Otsuka UK and Otsuka Europe, the Authority asked it to consider the requirements of Clauses 2, 9.1, 7.2, 26.1 and 26.2 of the Code.

RESPONSE

Otsuka UK and Otsuka Europe provided a joint response and stated that the press release was provided for awareness by Astex to Otsuka Europe on 28 August 2019 (copy provided). The planned distribution was a US healthcare audience targeted via a named third party. Otsuka UK and Otsuka Europe confirmed with Astex that given the release was being issued solely by Astex and with a US only target audience, it did not need to be reviewed by Otsuka UK and Otsuka Europe. It had since come to light that Astex released the press release to the same UK/Ireland channel as the press release in question in Cases AUTH/3212/6/19 and AUTH 3262/10/19 and in the second matter detailed below.

Otsuka UK and Otsuka Europe submitted that the press release and its appearance on ukfinance.yahoo.com fell outwith the scope of the Code. It was not issued by Otsuka UK or Otsuka Europe, nor was it approved or authorized for issue by either company; it was not available on either the Otsuka Europe or the Otsuka UK websites. Furthermore, the press release did not refer to the availability or use of the medicine in the UK.

In response to a request for comment on the detailed allegations regarding the content of the press release, the companies maintained their position that the press release fell outside the scope of the Code; it was issued by a company based outside the UK, made no reference to the availability or use of the medicines in the UK and was not issued with the authority of either Otsuka UK or Otsuka Europe. The companies, however, responded to the specific clauses raised.

The companies submitted that the intended UK audience appeared to have been very broad based on the media circuits to which the release was distributed. Details were provided and the companies submitted that on the whole the press release appeared to have been aimed at consumer media. The companies submitted that the content was suitable for readers of the website on which this press release appeared (uk.finance.yahoo.com) given that an announcement of orphan drug status in any country was an event that could impact on the share price of a pharmaceutical company. However, the content of the press release was not something that could reasonably be assumed to be of interest to the broad audience to which

the press release was targeted; with that in mind, the companies noted that the press release made reference to the name of the molecule and the intended indication.

With regard to whether this amounted to promotion to the public, or whether it encouraged members of the public to ask for a specific medicine, the companies noted that the requirements of Clauses 26.1 and 26.2 related to medicines which had a marketing authorization. Therefore, given that ASTX727 did not have a marketing authorization in any country, the companies submitted that there was no breach of these clauses, should the matter be deemed to fall within the scope of the Code. However, such a reference in a press release aimed at a broad public audience might amount to a failure to maintain high standards, contrary to the requirements of Clause 9.1.

In relation to the complainant's concern about use of the word 'novel', this legitimate description of ASTX727 stemmed from it being a combination of decitabine and cedazuridine. The incorporation of cedazuridine to decitabine inhibited cytidine deaminase which otherwise degraded decitabine when administered orally. Decitabine was at present only administered by IV injection and the additional property of oral administration was a benefit not currently available for the medicine. In addition, ASTX727 was a patented drug, which by definition required 'novelty'. With this in mind, the companies did not consider that describing ASTX727 as 'novel'was inaccurate or misleading, and denied a breach of Clause 7.2.

The companies submitted that their understanding was that the press release was not going to be issued in any countries outside of the US and for this reason Otsuka UK and Otsuka Europe did not review it, therefore they did not consider that any act or omission by either company amounted to bringing the industry into disrepute, or reducing confidence in it. The companies submitted that, if this press release fell within the scope of the Code, there had been no breach of Clause 2.

PANEL RULING

The first matter for the Panel to consider was whether the press releases were covered by the Code. The Panel noted that it appeared that the complainant had accessed the press release via uk.finance.yahoo.com. The Panel noted the submission from Otsuka Europe and Otsuka UK that the first press release was issued by Astex in the US. Otsuka Europe and Otsuka UK did not issue, approve for issue or authorize the press release. There was no mention of use of the medicine in the UK or Europe. The Panel also noted Otsuka Europe and Otsuka UK's submission did not review the press release as it was confirmed in email communication provided that it was not going to be issued in any country outside the US.

The Panel noted that the press release was circulated via a third party to a UK and Ireland channel as well as the US channel by Astex Pharmaceuticals Inc which was a wholly owned subsidiary of Otsuka Pharmaceuticals Co Ltd. From the detailed list provided in these cases the Panel noted that the press release had been widely circulated to UK media organisations many of which were aimed at consumers.

The Panel considered therefore given the circulation to UK outlets the press release was covered by the UK Code. The Panel noted the involvement of Otsuka Europe and Otsuka UK. However, it was a clearly established principle under the Code that the UK company was responsible for acts and omissions of its overseas affiliates that came within the scope of the

Code. If it were otherwise UK companies would be able to rely on such acts and omissions as a means of circumventing the Code.

The Panel noted that Clause 26.1 stated that prescription only medicines must not be advertised to the public. The Panel noted that Clause 26.2 stated that information about prescription only medicines which is made available to the public either directly or indirectly must be factual and presented in a balanced way. It must not raise unfounded hopes of successful treatment or be misleading with respect to the safety of the product. Statements must not be made for the purpose of encouraging members of the public to ask their health professional to prescribe a specific prescription only medicine.

The Panel noted Otsuka Europe and Otsuka UK's submission that ASTX727 did not have a marketing authorization in any country, the Panel considered therefore that it was not classified as a prescription only medicine. Clauses 26.1 and 26.2 only applied to prescription only medicines. On this very narrow technical point the Panel ruled no breach of Clauses 26.1 and 26.2 of the Code. However, the Panel considered that the press release issued to the public promoted an unlicensed medicine which meant that Otsuka had failed to maintain high standards and a breach of Clause 9.1 was ruled.

With regard to the use of the word 'novel', the Panel noted the submission from the companies that this was justified as it was an oral treatment and included an oral form of decitabine, which was currently only licensed as an IV treatment. Further it was a patented medicine. The Panel considered that the audience would understand novel to mean that the medicine, ASTX727 was new and unusual. The product had been granted orphan status. The Panel noted its comments and rulings above; Clause 26.2 did not apply to ASTX727 as it was not a prescription only medicine. The Panel therefore ruled no breach of that clause with regard to the allegation that in using the word 'novel' to describe ASTX727 the press release would raise unfounded hopes of successful treatment. The Panel did not consider that the complainant had established that describing ASTX727 as novel was misleading and no breach of Clause 7.2 was ruled.

The Panel noted that a breach of Clause 2 was used as a sign of particular censure and was reserved for such use. The Panel considered that the circumstances did not amount to a breach of Clause 2 and ruled accordingly.

2 Press release issued by Astex and Otsuka

COMPLAINT

The complainant drew attention to a press release on Cambridgenetwork.co.uk headed 'Astex Pharmaceuticals and Otsuka announce results of latest study'. The study in question was the phase 3 ASCERTAIN Study with ASTX727.

The complainant alleged that the press release made outlandish claims, such as the safety and clinical profile of the medicine were similar in early trials but provided no additional data. It was clear from the press release that the medicine was not available in Europe but it encouraged patients to seek it out, given its positive results and the opportunity to participate in clinical trials. More concerning was some of the safety claims, 'The drug's safety profile was similar to that of IV decitabine. Of particular note was the low level of gastrointestinal adverse events'. The complainant alleged that the press release did not provide the reader with appropriate context (the data was from pharmacokinetic study).

The complainant would like to see the evidence to support the statement, '… the fixed dose combination of cedazuridine with decitabine enables successful oral delivery of decitabine, alleviating the significant burden of five days monthly IV infusions for patients who may continue to benefit from the drug for several months or even years'. The complainant alleged that such claims were marketing claims and had no place in a press release. .

When writing to Otsuka UK and Otsuka Europe, the Authority asked it to consider the requirements of Clauses 2, 9.1, 7.2, 7.4, 7.9 and 26.2 of the Code.

RESPONSE

Otsuka UK and Otsuka Europe referred to its response to Case AUTH/3212/6/19 and Case AUTH/3262/10/19 as this related to the same press release. In those cases the companies submitted that the matter fell outside the scope of the Code. Specifically, the companies noted that Clause 28.2 stated that information or promotional material about medicines which was placed on the Internet outside the UK would be regarded as coming within the scope of the Code, if:

- it was placed there by a UK company/with a UK company's authority, or
- it was placed there by an affiliate of a UK company, or with the authority of such a company and it made specific reference to the availability or use of the medicine in the UK.

The press release in question was issued by Astex in the US and Otsuka in Japan. It was not issued by Otsuka Europe or Otsuka UK, nor was it approved for issue or authorized by either of those two companies. Furthermore, the press release did not refer to the availability or use of the medicine in the UK. There was no mention of use in the UK or European market or relevance of the information to a UK or European audience, in that it did not refer to any intention imminently or at all to seek a marketing authorization in Europe. The information about the diseases of relevance to the referenced application to the FDA focused upon US statistics and North American research sites.

Astex approached the Otsuka Europe communications team which then liaised with Otsuka in relation to the press release and whilst it was placed in Zinc for Otsuka UK examination, and a review initiated, that review was never completed and the press release was not approved by Otsuka UK, and it was not released 'with the authority' of Otsuka UK.

In light of the above, Otsuka Europe and Otsuka UK reiterated that their position that the press release fell outside the scope of the Code. The companies questioned whether it was procedurally fair to ask them to defend the contents of a press release that they neither prepared, issued or authorized and which focused on potential availability of a product in North America rather than Europe.

Whilst the companies maintained that the press release was outside the scope of the Code, they responded to the clauses raised in this case by providing a further copy of their response to Cases AUTH/3212/6/19 and AUTH/3262/10/19 . The allegations in the current cases (Cases AUTH/3266/10/19 and AUTH/3279/11/19) were similar but not the same in relation to this press release.

Otsuka Europe and Otsuka UK's response to Cases AUTH/3212/6/19 and AUTH/3262/10/19

Otsuka Europe and Otsuka UK noted that the press release detailed the results of the ASCERTAIN study, a phase III pharmacokinetic equivalence study of ASTX727 (oral cedazuridine and decitabine fixed-dose combination) versus IV decitabine in patients with myelodysplastic syndromes (MDS) and chronic myelomonocytic leukaemia (CMML). The primary end point for the study is total 5-day area under the curve (AUC) exposures of decitabine. There were a number of secondary endpoints, including number of patients with adverse events, the severity of adverse events, leukaemia-free survival and overall survival.

Based on the media circuits to which the release was distributed and the information on research results contained within it, the press release appeared to have been aimed at the public at large.

Statements about ASTX727

There were a number of statements in the press release about ASTX727, such as those in relation to the medicine alleviating the burden of IV infusions, survival benefit, the benefit of oral treatment and a low level of gastrointestinal adverse events. Given that the study in question was a pharmacokinetic equivalence study and safety and efficacy were secondary endpoints, Otsuka Europe and Otsuka UK submitted that they were misleading and could not be substantiated, contrary to the requirements of Clauses 7.2 and 7.4. Further, the statement in relation to side effects did not reflect the available evidence, contrary to the requirements of Clause 7.9.

With regard to encouraging members of the public to ask for a specific medicine, Otsuka Europe and Otsuka UK noted that the requirements of Clause 26.2 related to medicines that had a marketing authorization, therefore the companies did not consider that there was any breach of that clause, should the matter be deemed to fall within the scope of the Code. However, such statements about a medicine in a document aimed at the public amounted to a failure to maintain high standards, contrary to the requirements of Clause 9.1.

The complainant in Cases AUTH/3212/6/19 and AUTH/3262/10/19 noted that the press release was not clear that ASTX727 was an investigational compound. The bullet points at the beginning of the press release stated that a new drug application was planned for the end of 2019, it was noted in the body of the press release that ASTX727 was an investigational compound and the quotation referred to 'regulatory review and approvals'. Thus Otsuka Europe and Otsuka UK submitted that it was sufficiently clear that the medicine was not yet available for use.

Otsuka Europe and Otsuka UK stated that given the above, and if the Panel deemed that the press release fell within the scope of the Code, the content of the press release failed to maintain high standards, contrary to the requirements of Clause 9.1. The Panel might also consider that, given the misleading nature of the information within the press release and the broad target audience, it brought discredit upon, and reduced confidence in, the pharmaceutical industry, contrary to the requirements of Clause 2.

PANEL RULING

The Panel noted the submission from Otsuka Europe and Otsuka UK that the press release was issued by Astex in the US and Otsuka Japan. Otsuka Europe and Otsuka UK did not issue, approve for issue or authorize the press release and there was no mention of use of the medicine in the UK or Europe. However, it was a clearly established principle under the Code that the UK company was responsible for acts and omissions of its overseas affiliates that came within the scope of the Code. If it were otherwise UK companies would be able to rely on such acts and omissions as a means of circumventing the Code.

The Panel noted that it appeared that the complainant had accessed the press release via cambridgenetwork.co.uk. The Panel noted that the press release was circulated via a third party by Astex Pharmaceuticals Inc which was a wholly owned subsidiary of Otsuka Pharmaceuticals Co Ltd. A list of the third party circuits for press releases was provided by Otsuka which included circuits for the UK and Ireland. The Panel noted from the emails provided by Otsuka Europe and Otsuka UK that both were aware that the press release was going to be issued in the UK and Ireland. From the detailed list provided in these cases the Panel noted that the press release had been widely circulated to UK media organisations many of which were aimed at consumers.

The Panel noted the companies' submission that Astex approached Otsuka Europe's communications team which liaised with Otsuka UK and a review of the press release using Zinc was initiated. . The Panel queried why the review was not completed noting that the email communication stated that 'we have to put joint Astex/Otsuka press releases through [Otsuka UK]review if released in the UK'.

The Panel considered that given the circulation to UK outlets via the third party, the press release was covered by the Code. The Panel noted the involvement of Otsuka Europe and Otsuka UK.
The Panel also noted that Otsuka Europe and Otsuka UK had provided a further copy of their response to Cases AUTH/3212/6/19 and AUTH/3262/10/19 as their response to the allegations in this complaint. The complaints were similar but not the same.

The Panel noted that the press release referred to the safety and clinical activity of ASTX727 being similar to that observed in a previous study. It was stated in the press release that the outcome demonstrated that the fixed dose combination enabled '…successful oral delivery of decitabine alleviating the significant burden of five days of monthly IV infusions for patients who might continue to benefit from the drug for several months or even years'. It was further stated that ASTX727 could bring a new treatment option to patients with 'these deadly diseases'. The press release also stated that 'ASTX727 is an investigational compound and is not currently approved in any country'.

Given the circumstances the Panel did not consider that the distribution of the press release for an unlicensed medicine in itself meant that that medicine had been promoted. Nor did the Panel consider that the mention of other studies in the clinical programme necessarily promoted the medicine for those indications. It was not unreasonable to give an overview. The Panel considered that some of the language within the press release was promotional as acknowledged by Otsuka Europe and Otsuka UK.

The Panel noted Otsuka's submission that although decitabine was licensed in the UK, the combination with cedazuridine (ASTX727) was not and that in the UK decitabine IV was licensed for newly diagnosed, *de novo*, or secondary acute myeloid leukaemia. The Panel also

noted that the ASCERTAIN Study was a pharmacokinetic equivalence study and safety and efficacy were secondary endpoints. The Panel agreed with Otsuka that statements about alleviating the burden of IV infusions, survival benefit, low level of gastrointestinal adverse events and the benefit of oral treatment were misleading and not capable of substantiation. The Panel ruled a breach of Clauses 7.2 and 7.4 as acknowledged by Otsuka UK and Otsuka Europe. There did not appear to be clinical evidence to support the claims for ASTX727 and gastro-intestinal side effects as required by Clause 7.9; it was not clear from the outset that the study was a pharmacokinetic study and safety was a secondary endpoint. Thus, the Panel ruled a breach of Clause 7.9.

The Panel noted that Clause 26.1 stated that prescription only medicines must not be advertised to the public. Clause 26.2 stated that information about prescription only medicines which was made available to the public either directly or indirectly must be factual and presented in a balanced way. It must not raise unfounded hopes of successful treatment or be misleading with respect to the safety of the product. Statements must not be made for the purpose of encouraging members of the public to ask their health professional to prescribe a specific prescription only medicine.

The Panel noted that ASTX727 was not classified as a prescription only medicine. Clause 26.2 only applied to prescription only medicines. On this very narrow technical point the Panel ruled no breach of Clauses 26.2. However, the Panel considered that the press release issued to the public promoted an unlicensed medicine which meant that high standards had not been maintained and a breach of Clause 9.1 was ruled.

The Panel considered that high standards had not been maintained with regard to the information about the study outcomes as ruled in breach of the Code above. The Panel therefore ruled a breach of Clause 9.1.

The Panel noted that a breach of Clause 2 was used as a sign of particular censure and was reserved for such use. The Panel considered that the circumstances did not amount to a breach of Clause 2 and ruled accordingly.

Complaint received **26 September 2019**

Case completed **15 May 2020**