Part 4: The grounds of challenge and the lines of defence

This next part of the podcast series analyses the grounds upon which Bayer and Novartis sought to argue that the policy to offer NHS patients a choice between Avastin and the two licenced drugs for treating wet AMD patients was unlawful.

Whilst there were long and detailed statements of case on both sides and numerous bundles of documents produced in this case, the legal grounds can be summarised reasonably succinctly.

The first ground advanced by Bayer went to the heart of the case. Bayer alleged that the CCG choice policy was premised on error of law because there was no lawful basis upon which a Trust could secure a supply of compounded bevacizumab. Their case was that the compounding of Avastin into smaller vials created a new medicinal product which fell outside the marketing authorisation which had been granted for Avastin. They therefore argued that this new product – compounded bevacizumab or "CB" - was an unlicensed medicine. They then alleged that any supply of this type of unlicensed medicine was not permitted under the Medicines Directive or the Human Medicines Regulations 2012.

Secondly, Bayer alleged that a system of bulk supply of compounded bevacizumab undermined the objectives of the EU medicines directive and was therefore breach of the duty of sincere cooperation in article 4(3) of the Treaty of the European Union.

Thirdly, Bayer claimed that the process of offering patients access to a drug which did not have a NICE Technology Appraisal breached the legal requirement on the CCGs to provide access to NHS patients for products which had NICE TAG approval.

The case advanced by Novartis overlapped with that advanced by Bayer. Novartis also alleged that the CCG policy was premised on the basis that it was lawful to compound Avastin and that this was wrong in law. Novartis alleged that any compounding of Avastin would create a new medicinal product which would then be distributed without a marketing

authorisation, and that this supply would breach the terms of the Medicines Directive and the Human Medicines Regulations 2012.

Secondly, Novartis claimed that the bulk supply of CB breached the terms of the Medicines Act 1968, which were amended by the Human Medicines Regulations 2012. They alleged that the exemptions in section 10 of the Medicines Act 1968 did not extend to the preparation of large quantities of unlicensed medicines.

Thirdly, Novartis claimed that the only body that was entitled to reach judgements about the clinical effectiveness, safety and quality of medicinal products was the European Medicines Agency – the EMA - and that the policy was unlawful because it was premised on a decision by the CCGs concerning the clinical effectiveness, safety and quality of Avastin as a treatment for wet AMD patients. That, so Novartis claimed, was unlawful because that decision could only be made by the EMA.

Fourthly, Novartis claimed that the decision was unlawful because it effectively replaced the NICE TAGs system which was required to guide clinical decision-making concerning drugs which were within the scope of a NICE TAG.

Finally, Novartis claimed that the patient information leaflets provided by the CCGs for the Trusts and the Question and Answer document were misleading and were irrational.

It was also a theme of both cases that doctors who acted in accordance with the policy would be acting unlawfully because they would be acting in breach of the terms of the GMC Code of Good Medical Practice. It was also part of their case that, when making decisions about which drugs should be prescribed for patients or providing advice to patients about pro-choices, it was unlawful for doctors to make any reference to the cost to the NHS of the various drugs. The pharmaceutical companies argued that these decisions should be solely driven by considerations of the patient's best interests and that the cost of drugs could not form part of any advice provided to patients or a decision-making on the part of doctors.

The CCGs filed Summary Grounds and, once permission had been given, filed Detailed Grounds responding to each of these points. In summary the defence advanced by the CCGs was as follows:

1. The CCGs relied on a series of cases in the Court of Justice of the European Union – the CJEU - to argue that the compounding of Avastin and its subsequent supply to a doctor treating patients was not the "*placing on the market*" of a new medicinal product and therefore did not breach the terms of the Medicines Directive. The CCGs sought to rely on the "*Apozyt* exception" developed by the CJEU and repeated in a number of cases concerning the supply of compounded Avastin in order to argue that supplies of this type did not breach the medicines directive.

2. The CCGs then argued that a manufacturing and supply process which had been specifically approved by the CJEU could not breach the duty of sincere cooperation because it was an approved process which was plainly lawful.

3. The CCGs denied that the EMA was the only body that was entitled to express a view about the clinical effectiveness, safety or quality of a medicinal product. They relied upon a whole series of domestic and EU law judgements to show that the health services of member states were entitled to form their own views, independently of the EMA on these issues. They also relied on the fact that the EMA was only able to express a view on the clinical effectiveness, safety or quality of a medicinal product if a pharmaceutical company decided to make an application for marketing authorisation for a medicinal product for a particular proposed patient group. The absurdity of that argument was demonstrated by the present situation because the case advanced by the pharmaceutical companies was that nobody was entitled to form a view on the clinical effectiveness, safety or quality of the use of Avastin for wet AMD patients because the intellectual property rights holder for this drug, namely Roche, had decided not to make an application to the EMA for approval for the use of this drug for wet AMD patients. That limitation was characterised by the CCGs as being absurd because it placed all of the power in the hands of the

pharmaceutical companies - dependent on which drugs they chose to put through the EMA process.

4. The CCGs did not accept that offering patients the choice undermined the NICE TAG system. If patients chose Lucentis or Eylea, the CCGs argued that they would continue to fund the cost of those drugs for the patient as they were obliged to do. However, they argued that it was no part of the NICE TAG system to limit the choices available to patients to drugs which had NICE TAG approval.

5. The CCGs did not accept the doctors would act in breach of the GMC Code of Good Medical practice by prescribing Avastin, and relied upon the GMC's own statements - to that effect. They also did not accept that doctors were obliged to ignore the cost of medical treatment when providing advice to patients - whether individually or generally.

6. Finally, the CCGs did not accept that any of the patient information leaflets for Q & A forms were misleading. But, in any event, they said that these were only drafts and no decision had been made about the final form of any patient information leaflet says this was a matter for the trusts and not for the CCGs.

There was a subsidiary issue in the case as to whether the pharmaceutical companies were entitled to lead evidence which sought to undermine the conclusions reached by the CCGs that the 3 drugs - Avastin, Lucentis and Eylea - had equal clinical effectiveness and equal safety. There was no rationality challenge by the pharmaceutical companies to this conclusion but nonetheless detailed expert evidence was served - without permission having been obtained as required by CPR 35 - which sought to question whether this conclusion was open to the CCGs.

The CCGs took a twin track response to this evidence. First, their position was that expert evidence was not admissible without the permission of the court and that permission should be refused. Secondly, they served expert evidence to support the rationality of their

conclusions. That issue was, to some extent, overtaken by the publication of the definitive NICE Guidelines in January 2018 after the issue of proceedings. Those Guidelines reached the view that these three drugs were equally clinically effective and equally safe.

In broad terms, those were the technical legal arguments that were advanced before Whipple J in July 2018. The question as to whether, in order to take advantage of the *Apozyt* exemption, a system of individual prior prescriptions was needed emerged as a subsidiary issue before the first instance trial. The position of the pharmaceutical companies was that this was necessary and that the policy was unlawful because it did not provide but such a system needed to be set up.

The position of the CCGs was that a system of prior prescriptions was not necessary in order to take advantage of the *Apozyt* exemption but, if they were wrong on this point, they argued that this was a matter for the Trusts when they implemented the policy and that there was nothing in principle that would prevent such a system being set up.

Any summary of the arguments fails to capture the subtlety of the arguments on both sides of this complicated case but these were, in general terms, the lines advanced by both parties in the case before Mrs Justice Whipple and subsequently before the Court of Appeal.