Part 3: details of the policy adopted by the CCGs

In 2017, the 12 clinical commissioning groups in the North East of England worked together to develop a common policy for offering wet AMD patients a choice between the three drugs to treat that condition, namely Avastin, Lucentis and Eylea. The CCGs estimated that there were approximately 20,000 new wet AMD cases per year in England, of which about 1,400 arose in their area. They also noted that the number of cases of wet AMD was rising and, with an ageing population, was projected to continue to rise. The CCGs projected that they would save upwards of £9M per year if a policy in favour of promoting Avastin as the preferred option for NHS wet AMD patients was adopted by the Trusts which provided this treatment.

The extent of any financial savings that the NHS would achieve depended, of course, on the number of wet AMD patients who chose to be treated with Avastin rather than those who elected to be treated with the more expensive drugs, namely either Lucentis or Eylea. However, the CCGs decided to provide information to patients about the equal clinical efficacy and clinical safety of the three drugs and also to explain the wider benefits to the NHS that would arise if patients chose to be treated with the cheaper drug. On that basis, the CCGs considered that a significant proportion of patients were likely to choose Avastin, thus delivering multi-million pound savings to the CCGs which could then be recycled into funding of other medical treatment for other patients.

The policy proposed that Avastin would be offered to wet AMD patients as the "*preferred treatment option*" for new patients and for existing patients were being treated with either Lucentis or Eylea where there was an inadequate clinical response and treatments which has been considered.

The policy was expressed in extremely simple terms. It did not require the Trusts to implement the policy but was merely advisory. In particular, it did not explain how the Trusts were supposed to source supplies of Avastin in order to give patients a choice.

It also did not provide any details about the steps that the Trusts would have to follow in order to secure a lawful supply of Avastin so as to be able to implement the policy. These were all matters to be decided upon by the Trusts.

The CCGs noted that there was an established market for the supply of compounded Avastin in the UK and they assumed that Trusts would be able to take advantage of that market in securing supplies of compounded Avastin, just as private hospitals secured supplies of compounded Avastin in order to treat their wet AMD patients.

During the course of the litigation there was considerable debate about how a lawful supply of compounded Avastin could be secured by the Trusts. The pharmaceutical companies alleged that there was no method of lawfully supplying compounded Avastin for wet AMD patients and they also alleged that hospitals would not be able to create their own compounded Avastin in order to supply that drug to their own ophthalmologists. In the end, the pharmaceutical companies lost on both those points.

The final position was that there were four potential ways in which an ophthalmologist would be able to treat a wet AMD patient with Avastin. These were known as "modes" 1 to 4 and can be summarised as follows:

Mode 1: This mode was known as "whole vial use" and was discussed after the policy was originally adopted. It was thus not a mode that was envisaged at the time that the CCGs adopted the policy. In summary, in this mode the clinician takes a 4ml vial of Avastin - that is the full size vial used for cancer treatment which cost approximately £300 – and uses 0.1ml from the vial to inject into the eye of the wet AMD patient and discards the rest. Whilst this is wasteful, it is nonetheless significantly cheaper than purchasing either Lucentis or Eylea.

Mode 2: This mode was known as "in-house compounding". All major hospitals have pharmacies which carry out sophisticated manipulation of drugs in accordance with the requirements of the hospital's clinical teams. Accordingly, at least at some of the hospitals contracted to the CCGs the hospitals had the facilities needed to compound Avastin in

sterile conditions. It was, of course, each individual hospital to decide whether they wish to do so.

Mode 3: This mode was known as "NHS supply". It was envisaged that a hospitals which had industrial scale aseptic compounding facilities would undertake large-scale compounding of Avastin into vials appropriate for intravitreal use, and then sell the vials to the NHS hospital where they were due to be used. The evidence was that there are a number of NHS hospitals that had such facilities. They were used, for example, to supply compounded Avastin on a large scale for the clinical trials which were used in order to prove that this drug was clinically effective and safe for wet AMD patients.

Mode 4: This mode was known as "commercial supply". The precise identity of commercial suppliers of compounded Avastin was never clearly explained in the evidence since neither side chose to lead this evidence. It was thus unclear whether the commercial suppliers of compounded Avastin which operated in the present "mature market" (as Whipple J found to exist) to supply private hospitals in the United Kingdom were private pharmacies - which could potentially take advantage of the pharmacy exemption under article 40 of the Medicines Directive - or were commercial drug manufacturers which were not pharmacies. If the latter was the position, it was unclear how such organisations operated lawfully unless they purported to supply compounded Avastin as a "special" under article 5 of the Directive. However, it was difficult to see how the specials conditions could be satisfied for the treatment of wet AMD patients because there were commercially available alternative medicines that were equally clinically effective (albeit more expensive).

It is important to note that the adoption of the policy by the CCGs did not mandate any hospital trust in the north-east of England - or elsewhere - to offer wet AMD patients the choice of being treated with Avastin. The policy was purely advisory and it would have been entirely possible for NHS Trusts to have declined to implement the policy.

Equally, the policy did not attempt to explain whether, as part of any lawful supply arrangement, it was necessary for a clinician to have written up a patient for a prescription

of Avastin in advance of an order being placed for Avastin to be compounded. The "prior prescription" issue played relatively little part in the initial stages of this litigation but assumed a significant importance in the decision of the Court of Appeal, as we will see in later chapters of this podcast.

By September 2017, all of the Governing Bodies of the 12 CCGs in the North East had resolved to adopt a policy in favour of giving NHS wet AMD patients a choice of drugs which included treatment with Avastin as the preferred choice. Once that policy was implemented by the Trusts, it appeared inevitable that significant numbers of patients would choose to be treated with Avastin and thus the sales of Lucentis and Eylea would fall. It was therefore unsurprising that both Bayer and Novartis sent correspondence to both the CCGs and the Trusts alleging that the policy was unlawful for a variety of reasons.

The CCGs have already taken legal advice and defended their position. The next step was that Bayer and Novartis issued judicial review proceedings seeking an order from the court quashing the decisions to adopt the policy. The next chapter in this podcast will examine the grounds upon which Bayer and Novartis sought to rely in order to argue that this choice policy was unlawful and the grounds of defence relied on by the CCGs.