Court of Appeal upholds lawfulness of NHS Avastin choice policy for wet AMD patients

In a major judgment that will have widespread significance for the NHS and the pharmaceutical industry, the Court of Appeal (the Vice President Underhill LJ, Floyd and Rose LJJ) today dismissed an appeal by pharmaceutical companies Bayer and Novartis to challenge a policy adopted by 12 NHS clinical commissioning groups which recommending that NHS clinicians should offer patients a choice between 2 licensed medicines for the treatment of wet age-related macular degeneration (marketed by Bayer and Novartis) and a much cheaper drug, Avastin, which had an EU marketing authorisation as a cancer drug. The appeal was against the decision of Whipple J on 21 September 2018 who had dismissed the judicial review of the policy brought by the pharmaceutical companies: [2018] EWHC 2465 (Admin).

The CCGs wanted to adopt the policy because, according to NICE, all 3 drugs had equal clinical effectiveness and equal safety profiles but compounded Avastin was far cheaper. The CCGs estimated that, if significant numbers of patients agreed to be treated with Avastin, millions of pounds would become available for the CCGs to fund NHS treatment for other patients. Accordingly, giving wet AMD patients the choice between drugs would be both clinically effective and cost-effective and thus be of considerable overall benefit to the NHS.

The pharmaceutical companies which marketed the licenced drugs mounted a wide-ranging challenge to the CCG policy, based on a variety of both European and domestic law arguments. Their arguments relied heavily on alleged contraventions, in EU law, of Directive 2001/83/EC (the "Medicines Directive") and, in domestic law, of section 10 of the Medicines Act 1968 (the "1968 Act") as well as what were said to be the common law requirements relating to the lawful promulgation of policies.

However, in a 214-paragraph judgment, the pharmaceutical companies' arguments were comprehensively dismissed by the Court.

The breadth of the issues that the Court was required to address in order to reach its decision means the judgment will have far-reaching implications for the NHS. The main

judgment was given by the Vice President, Underhill LJ, with whom Floyd and Rose LJJ agreed. Rose LJ also gave short concurring judgment, with which Underhill LJ agreed. The Court began by an examination of the regulatory regime; then examined the legality of each of the 4 modes of operation of the Policy; and finally ruled on the individual grounds of appeal. In summary, the Court found as follows:

- After setting out a detailed analysis of the EU and domestic legislative regimes, the Court examined the CJEU case-law on compounded Avastin: §50-§118.

- Key amongst the CJEU cases for the purposes of the present case was Case C-535/11 *Novartis Pharma GmbH v. Apozyt GmbH* EU:C:2013:226. This case introduced a narrow judicially developed exemption from the requirements of the Medicines Directive and, in particular, from the requirement to obtain a Marketing Authorisation under the Directive for supplying compounded Avastin to clinicians and hospitals.

- The Court held that the *Apozyt* exemption was available were two conditions were satisfied: the medicinal product in question must not be modified by the relevant process (the "no modification requirement") and an individual prescription for its use had to be in existence prior to its compounding (the "prior prescription requirement"): see, for example, §141.

- Avastin was not to be treated as "modified" simply because of any risk of contamination or other changes to its substance as a consequence of poor quality control in the compounding process. What mattered was whether the compounding process introduced changes to the substance of the drug. There was no evidence that the process in the case of compounding of Avastin necessarily involved any such changes. As such, the "no modification" requirement could be satisfied: §142.

- As regards the prior prescriptions requirement, the Court said "*there is clearly no legal reason why a hospital could not apply a system under which CB was prepared only against individual prescriptions, as happens in Italy*": §143.

- The Court then analysed the legality of the 4 identified modes of application of the policy. Mode 1 involved "whole vial use", that is the extraction of a small quantity of Avastin from a whole vial with the remainder being discarded. This did not involve any compounding at all. Mode 2 involved the compounding process being undertaken by an NHS pharmacy in the hospital in which it was administered. Mode 3 involved supply to a hospital pharmacy of Avastin compounded by an NHS pharmacy in a different Trust. Mode 4 involved commercial compounding, by commercial non-NHS bodies.

- The Court started by analysing Mode 2, namely in-house compounding in a hospital's own pharmacy. It concluded that there was no practical reason why any of the Trusts in the CCGs' areas could not prepare their own compounded Avastin, although this was more likely for the 3 Trusts who claimed already to have the necessary facilities: §146. The Court rejected the suggestion that the terms of the Policy would not cover Mode 2. The Appellants had attempted to rely on evidence relating to the pricing of treatments which, they contended, were compatible with external supplies. The Court held that although the Policy originally contemplated external supply as the basis of its operation, the wording of the Policy was capable of extending to Mode 2: §147.

- As regards Mode 3, namely supply by an NHS pharmacy in one NHS Trust to an NHS hospital in another Trust, the Court concluded this fell within the *Apozyt* exemption at §141-§143 and so was potentially lawful.

- The Appellants had argued that, even if the CCGs were able to benefit from the *Apozyt* exemption, they would be in breach of domestic law because section 10 of the 1968 Act did not give full effect to the exemption. Further, in a new argument, they argued that regulation 18 of the Human Medicines Regulations 2012 (the "HMR"), implementing Article 77(1) of the Medicines Directive, required a wholesale dealer's licence to be in place: §151. The Court rejected the pharmaceutical

companies' arguments which sought to limited the extent of the activities covered by section 10 of the 1968 Act. The court decided that the language of section 10(1)(a) was capable of covering the production of compounded Avastin in bulk. Similarly, regulation 46 was capable of being construed to cover the supply of Avastin under Mode 3. If there were room for doubt on any of these points, the Court considered that it should adopt an interpretation that conformed with the approach taken by the CJEU to the Medicines Directive: §155-§156.

- The Appellants argued that NHS supplies were unlawful due to fact that NHS hospitals did not have a wholesale dealer's licence. On this point, the Court accepted the CCGs' argument that the starting point was Article 77 of the Medicines Directive, which regulation 18 was intended to implement. Article 77 was concerned with wholesale distribution, a term which expressly excluded supply to the public. The rationale of the *Apozyt* exemption applied equally to the wholesale dealer's licence argument. There was no warrant for giving regulation 18 a wider reading than Article 77, and the Court rejected arguments to the contrary effect based on the *Oakley* principle: *Oakley Inc v. Animal Ltd* [2005] EWCA Civ 1191, [2006] Ch 337: §159-162.

- Finally on Mode 3, the court decided that it was not an unrealistic option merely because of the prior prescriptions requirement. The Appellants had failed to demonstrate that such a system could not be operated. Although a system based on prior prescriptions would be administratively more complex and more expensive that one without such a requirement, it would still be "*a price worth paying in view of the savings to be made*": §164.

- The court decided that the lawfulness of Mode 4, namely a commercial supply of compounded Avastin, was unclear. However, the Court reached no final conclusion on this because it did not need to do so and could not do so because the evidence was not before the court: §168. Underhill LJ was "*provisionally unpersuaded*" that the fact that there was an established market for commercially compounded Avastin

necessarily meant that any hospital pharmacies acquiring it from commercial bodies would be bound to be acting lawfully, but he reached no final view on the point: §169.

- The Appellants conceded that Mode 1, namely whole vial use, did not involve any breach of the Medicines Directive because it involved no compounding. For the same reason, that this was not what the Policy was concerned with: §172. However, the Court was clear that Mode 1 was "*plainly not unlawful*": §195.

- Against that background, the Court examined the individual grounds of appeal. As regards Ground 2 (whether prior prescriptions were required under the *Apozyt* exemption), the Court had ruled that they were, but it confirmed that this did not mean the policy was unlawful because such a system could, in fact, be adopted: §175. Provided the requirements of the *Apozt* exemption were satisfied, there would be no unlawfulness: §193.

- Ground 3 involved a number of sub-grounds: whether compounded Avastin was a "modification" of Avastin and so involved a new placing on the market (Ground 3A); whether Modes 2-4 in any event involved a placing on the market (Ground 3B); whether the Policy undermined the Directive (Ground 3D); whether the Policy was contrary to GMC Guidance (Ground 3E). Ground 3C (non-industrial preparation) was not pursued at the hearing after the CCGs accepted that the preparation of compounded Avastin involved the use of an industrial process.

- On Ground 3A, the Court agreed with Whipple J that the compounding process did not involve a modification of Avastin such as to take it outside the *Apozyt* exemption: §101. On Ground 3B, there was no placing on the market in any event and no wholesale dealer's licence was required: §162. Ground 3D was said to be "misconceived": §183. The exemption existed and the compounding of Avastin was capable of falling within it, so it made no sense to describe the compounding process as undermining the Medicines Directive: §183. On Ground 3E, the Court agreed with

Whipple J that it would not be a breach of the GMC Guidance for a clinician to prescribe Avastin on the grounds of cost when a licensed alternative was available, and even so that did not make the policy unlawful: §192.

- Ground 4, namely single-vial use of Avastin, was held to be lawful but single-vial use of Avastin was strictly irrelevant to the issue of the lawfulness of the Policy because the Policy was directed to the use of compounded Avastin. But it was "plainly not unlawful": §194-§195.

- Finally, Ground 1 concerned the test for reviewing the legality of the Policy. The basis for assessing this ground was that there were, broadly, two modes of implementation of the Policy. One (Modes 2 and 3) involved acquiring it from an NHS hospital pharmacy. This was lawful provided an individual prescription was in place. The other (Mode 4) involved acquisition from a commercial compounder. It was impossible to say whether Mode 4 was lawful. The Appellants contended the Policy was unlawful because it left open the possibility of implementation through Mode 4 which they presumed to be unlawful. It would, however, have been wrong to hold the Policy to be unlawful on that basis. This was not a case where a policy itself promoted a course which the court held to be unlawful. It left the means of implementation to the Trusts, who had their own legal advice. It did not lead to or encourage unlawfulness: §200. It did not make any difference that Mode 2 was probably not contemplated when the Policy was promulgated, or that Mode 3, while contemplated, required a prior prescription: §204 and §205. In short, it did not matter that one of the ways in which the Trusts might seek to implement the Policy might be unlawful: §206. Rose LJ provided further analysis on this point at §214.

- Underhill LJ concluded by expressly rejecting an argument that the judgment would open the door to widespread evasion of the requirements of the licensing system: "There is nothing inherently illegitimate in prescribing decisions being influenced by cost considerations where the evidence shows no differences in efficacy or safety": §211.

The judgment thus confirmed that the CCGs' Policy was lawful. At a time when there is increased focus on the availability and affordability of NHS services, the judgment is a welcome confirmation of the role that costs considerations are able to play in the formulation of policy in a state-funded healthcare system.

The CCGs were represented by David Lock QC and David Blundell QC, instructed by Dawn Brathwaite of Mills & Reeve. Further analysis of the judgment is provided in a series of podcasts to follow on the Landmark Website.