The basic medication law in our country is the Medication Act (19) which regulates within the framework of the national government competencies all issues related to manufacture, preparation, quality control, pricing, information, advertising, import & export, prescribing, authorizations, registries and all other matters related to medications. In addition, it regulates the procedures for taking drugs to market and the professionals who guarantee, control, prescribe or dispense drugs (art. 1). The sale of medications is only authorized in chemists/pharmacies together with the preparation, manufacture, import & export, distribution, marketing, prescription and dispensation of products or preparations presented as medications but are not legally recognized, or home-made remedies (art. 6).

Of special interest are the drugs currently utilized for treating ARMD, the requirements which must be followed for utilizing foreign medications legally distributed in other countries but not authorized in Spain (art. 37). In these cases a number of forms must be filled in (medical prescription in the corresponding prescription form and ophthalmologist report, including previous treatments and the essential nature of the prescription or, in the absence thereof, the Ministry authorization request forms A2 and A3, because the Health and Consumers Ministry is required to authorize the importation of each drug and, to do so, it must be crucial for treating or diagnosing specific pathologies.

In addition to said basic medications law, we believe it is also relevant to make reference to Royal Decree 223 dated Feb. 6, 2004 which regulates Clinical Tests with Medications (2) because this legal text, in addition to regulating said scientific research, attributes to the Spanish Medication and Health Products Agency the competence to authorize the use of medications which are not authorized for distribution, in individual cases and for therapeutic reasons, because on some occasions a patient may need a drug beyond the scope of general usage. This administration of drugs is defined in Article 28 of said decree under the term «Compassionate use of medications», understanding as such the use thereof in individual patients outside the scope of a clinical test of a drug being researched, as well as the prescription of pharmaceutical specialties for usage indications or conditions other than the authorized uses, when the doctor considers under his exclusive responsibility that said use is essential.

Said type of medication also requires filling in forms (ophthalmological report summarizing previous therapies and the absence of treatment alternatives, agreement of the hospital director, Informed Consent document and authorization of the Medications Agency) and can be requested by specialist hospital doctors through the Pharmacy services for admitted or outpatients. The compassionate use of medications is the legal tool which the specialist must use for the patients who are not inclu-
ded in clinical essays but need a treatment which is not authorized, because this provides legal coverage in case of complications or side effects leading to legal action for malpractice initiated by the patient or his/her relatives.

Finally, unauthorized medications can be utilized when in clinical research phase within the framework of clinical tests. Said Royal Decree states clearly in Art. 1 that «the administration of a drug under research to a single patient in the scope of usual medical practice with the sole purpose of obtaining a therapeutic benefit for the patient, will not be considered to be a clinical test. Said cases must be regulated by the Compassionate use principle», adding that «medical practice and professional freedom to prescribe shall not comprise in any case the execution of unauthorized clinical tests or the use of remedies which are secret or otherwise not declared to the health authorities».

Accordingly, there are only four ways to administer a drug to a patient: 1) as an authorized medication (registered pharmaceutical specialties), 2) a medication in the clinical research phase (defined as such by the administration and restricted to the framework of a specific and duly authorized clinical essay), 3) as a foreign drug (medications legally distributed in other countries and deemed to be essential, with authorization by the Ministry), and 4) as a compassionate use of medication when indicated by a hospital specialist for a patient who does not have (or has unsuccessfully received) therapeutic alternatives and the use thereof is regarded as indispensable.

Applying the above to the laws on the matter, the medications routinely utilized for treating wet ARMD fall under four conditions:

1) Photodynamic therapy (TFD): VISUDYNE® is utilized for treating small lesions of any angiographic type, and large lesions when mainly classical or concealed with recent progression and VA ≤ 0.4 (3); although the indications for which its use has been approved are classical subfoveal neovascular membranes or with evidence of recent progression of the disease and secondary to pathological myopia. If we consider the application of photodynamic therapy to a patient not fulfilling these conditions, we could still do it but invoking the compassionate use option because we will utilize a pharmaceutical specialty for a condition different to that for which it has been authorized. Therefore, we must fill in a number of documents stating that there are not alternative treatments or they have been exhausted without results and that, under the responsibility of the requesting hospital specialist, the photodynamic therapy is considered to be essential for the patient. In addition, we will have to wait until the Medications Agency issues the authorization.

2) The use of pegaptanib (MACUGEN®): at this time this drug is not authorized for distribution in Spain, although it will probably be so in the near future. As this drug is authorized in other countries (it was approved by the FDA in Dec. 2004 and very recently in Germany), we could utilize it as a foreign drug if considered to be essential, in the absence of alternative therapies (or unsuccessful treatments). This could be the case of patients with MNV who are not within the indications for applying photodynamic therapy or have done so without success, awaiting always the authorization of the Ministry.

3) The intraocular use of triamcinolone acetonide (TRIGON®) changing the vehicle by BSS should be administered invoking the compassionate use of medications (4) because we are utilizing a pharmaceutical specialty beyond the scope of the indications for which it was approved. At present, as this drug is authorized for intraocular administration in the USA, we can also apply it as a foreign drug provided we do so within the indications for which it has been authorized and we remember to have the patient sign an IC document because the intraocular injection of medication is an action of risk.

4) The use of bevacizumab (AVASTIN®), ranibizumab (LUCENTIS®,), anecortave acetate (REETANE®) and the like is more complicated, because it is not possible to invoke the foreign drug principle since it is not authorized in any country in the world for intraocular application for treating neovascular membranes. Neither could it be used via the compassionate use principle because there are alternative treatments available, such as photodynamic therapy or Macugen® (as a foreign drug). Only in the exceptional case that said treatments have been carried out without results the compassionate use could be considered. Therefore, at this time the use of these drugs is restricted to patients included in authorized clinical tests.

It is well known that retinologists are at risk of being sued by their patients. We have already proved that this subspecialty has one of the highest rates of claims within ophthalmology (5), and also saw that some authors attribute this to the fact that most of the pathologies treated by retinologists
entail the possibility of severe visual loss or even blindness, as this type of surgery is more complex than others (6). However, precisely for this reason it doesn’t make sense for them to assume an additional risk to that already involved in their usual practice and we are not referring to clearly illegal actions beyond the scope of action of any doctor such as buying drugs through the net or smuggle them into the country from a neighboring principality. We are referring to fellow ophthalmologists who, based on their good will and with the benefit of the patient in mind, encouraged by articles in journals or papers presented at meetings, apply with their patients medications in experimental stages beyond the scope of a duly authorized clinical test.

In nearly all retina meetings and in articles written by experts who have a deep knowledge of the issue (4) the issue of malpractice lawsuits is discussed in the context of the application of TRIGÓN® through a route for which it is not authorized, in addition to the inconveniences of changing the vehicle. Fortunately we already have this drug available as a foreign medication for said use and suppose that it will shortly be distributed in our country, thus providing a degree of calm to the daily practice of many colleagues who use it frequently.

Quite possibly we shall see the publication in the near future of the clinical tests being made with many antiangiogenic drugs we have mentioned, for the time being, are not authorized for use. The overwhelming price difference between some (7) will obviously constitute an important incentive for research besides probably obliging price adjustments so that a larger number of patients will benefit from these treatments. However, the price factor, which could be very important for hospital management, should not restrict the specialist’s prescriptions.

If we are unfortunate enough to be sued by a patient after suffering complications due to treatment with unauthorized drugs beyond the scope of legal stipulations, it is unlikely that our arguments will be sustained in court.

NOTE

Subsequently to the reception of this editorial, more specifically on June 30, 2006, the FDA (Food and Drug Administration) of the United States approved the use of Ranibizumab (Lucentis®) for treating wet ARMD.

REFERENCES

2. Real Decreto 223/2004 de 6 de febrero, por el que se regulan los ensayos clínicos con medicamentos. BOE n.º 33 de 27 de febrero de 2004; 325.