1. ABSTRACT

Title	Post-Authorisation Safety Study (PASS) of OZURDEX® (dexamethasone intravitreal implant): A Prospective Observational Study to Evaluate Long-Term Safety in Real-World Clinical Practice
Keywords	OZURDEX; retinal vein occlusion; non-infectious posterior segment uveitis; long-term safety; observational study
Rationale and background	Retinal vein occlusion (RVO) and non-infectious posterior segment uveitis (NIPSU) are prevalent sight-threatening conditions that can lead to macular oedema. OZURDEX, an intravitreal implant containing 700 mcg of dexamethasone, is indicated for the treatment of adult patients with macular oedema following RVO or inflammation of the posterior segment of the eye presenting as non-infectious uveitis. Development programme data demonstrated an acceptable benefit-risk profile for OZURDEX. However, due to the need to better understand the long-term safety profile and patterns of use of OZURDEX in patients with macular oedema secondary to RVO or NIPSU, as well as in patients who receive two or more repeat injections in the same eye due to deteriorating visual activity, the Marketing Authorisation Holder (MAH) conducted a post-authorisation safety study (PASS) of OZURDEX.
Research question and objectives	Primary • To evaluate the long-term safety of OZURDEX, including the identified and potential risks as listed in the Risk Management Plan (RMP), in patients with macular oedema following RVO or non-infectious posterior segment uveitis (NIPSU) who are treated with OZURDEX under conditions of routine medical practice Secondary • To describe treatment patterns for patients receiving OZURDEX for the treatment of macular oedema following RVO or NIPSU in real-world clinical practice
Study design	This was a multicentre, prospective, observational study to evaluate the long-term safety, and treatment patterns, for OZURDEX.
Setting	One hundred two ophthalmology clinics throughout Germany (N=25), France (N=13), the United Kingdom (N=41) and Spain (N=23) were included.
Subjects and study size	The study enrolled 800 patients receiving OZURDEX as part of routine clinical practice. Of these patients, 753 received on-study treatment and were included in the final analyses; 73.0% (n=550) of whom completed 24 months of follow-up.
Variables and data sources	Structured questionnaires, supplemented by medical record information, were used to elicit specific predetermined data elements for affected eyes at each visit. Study visits occurred at baseline (i.e. the first OZURDEX injection after study enrolment), and follow-up visits occurring at 6-month (±1 month) intervals. Serious adverse events (SAEs), adverse events of special interest (AESIs), and study discontinuations were reported in an ongoing manner during follow-up.
Results	The key results related to safety (primary objective) and treatment patterns (secondary objective) are presented here:

	Safety Non-ocular SAEs occurred in 8.9% of treated eyes during the 24 months study follow-up period. No notable differences in the incidence or type of non-ocular SAEs were identified when data were stratified by OZURDEX treatment experience, indication, or number of injections received. The incidence of serious ocular adverse events (OSAEs) was 3.4% (n=28) of the 819 treated eyes. Of note, 21 of the 28 OSAEs that occurred were suspected to be related to OZURDEX treatment. The type of treatment related OSAEs are consistent with the known safety profile of OZURDEX. No OSAEs occurred with a frequency greater than 2%, with cataract progression (1.6%) being the most common ocular SAE. OSAE rates were comparable across groups defined by indication, OZURDEX treatment experience, and number of injections received. The most commonly observed AESIs (i.e. >5%), across all strata, were increased intraocular pressure, cataract progression, and cataract formation. *Treatment Patterns* Overall, the number of injections per person-year on-study was 1.5 and a median of 27.14 weeks passed between subsequent injections. A median of 2.0 (range 1-10) on-study injections per patient and 2.0 (range 1-7) study injections per treated eye were administered. The number of on-study injections was comparable by demographic groups and based upon treatment experience and indication. The time between injections was also comparable by patient subgroups.
Discussion	The study results suggest that OZURDEX was well tolerated in patients with macular oedema due to RVO or NIPSU in the context of routine clinical practice and over a long period of follow-up. The safety profile in the current study is consistent with known safety profile of OZURDEX. No new safety concerns are identified in the long term safety study with repeated treatment in the same eye.
Marketing authorisation holder (MAH)	Allergan Pharmaceuticals Ireland, Ltd.
Name(s) and affiliation(s) of principal investigator(s)	[redacted]