PART V: RISK MINIMISATION MEASURES (INCLUDING EVALUATION OF THE EFFECTIVENESS OF RISK MINIMISATION ACTIVITIES)

V.1. Routine risk minimisation measures

Table 1: Description of routine risk minimisation measures by safety concern

Safety concern	**Routine risk minimisation activities**
Drug abuse and drug dependence	• Routine risk communication: Warning in Section 4.4 in SmPC: Potential for Abuse • Routine risk minimisation activities recommending specific clinical measures to address the risk: Not applicable • Other routine risk minimisation measures: Prescription only medicine classified as a controlled drug at national levels providing a restricted access complying with the schedule I of the United Nations Convention on Narcotic Drugs.

V.1.1. Evaluation of effectiveness of risk minimization measures

Effectiveness of risk minimization measures regarding drug abuse and dependence	
How effectiveness of risk minimization measures for the safety concern will be measured	**Labeling/Information supply**: Readability testing of the patient information leaflet (PIL) has been conducted using a readability study by structured face to face interviews. Subjects read mock-ups of the PIL and were asked questions designed to determine whether they could locate specific information in the PIL and understand and explain that information and how they should act upon it. As labeling is implemented at the time of launch, a baseline value without this measure is not available. Readability testing of the Patient Information Leaflet is seen as a surrogate parameter for the effectiveness of the measure. **Controlled access**: Process implementation is checked regarding the scheduling status prior to launching of the product in a particular country. The scheduling status will be applied for proactively by the marketing authorization holder (MAH) until a decision on international scheduling has been taken by the United Nation's Commission on Narcotic Drugs (UN CND). The international scheduling by the UN CND is supported by the MAH. **Routine Pharmacovigilance:** in addition to the above mentioned measures of effectiveness of risk minimisation measures, Grünenthal continuously monitors the topics of abuse and dependence via routine pharmacovigilance with the aim of identifying any changes in reporting rates adjusted for exposure or in the observed patterns of abuse associated with tapentadol.
Criteria for judging the success of the proposed risk minimization measures	**Labeling/Information supply**: Information presented in the PIL is deemed to have passed the readability test when 90% of subjects locate the information correctly and, of those, 90% understand the meaning of the information and explain correctly how they would act upon it. **Controlled access:** As no increased or changed risk profile has been seen

Effectiveness of risk minimization measures regarding drug abuse and dependence	
	during routine pharmacovigilance and data from RADARS in the USA (a country with a problem of high prescription drug abuse) provide low and stable rates for tapentadol abuse and diversion, no specific measures for judging the success of routine risk minimization measures have been implemented. Abuse levels should be in the range of drugs with comparable abuse liability and comparable risk minimization. **Routine Pharmacovigilance:** if there is no relevant increase to the exposure adjusted rates of abuse or change to the patterns of abuse that are observed for tapentadol.
Planned dates for assessment	**Labeling/Information supply**: Readability testing was performed prior to submission for authorization. A further assessment is not planned, but might be considered for major changes of the PIL. **Routine Pharmacovigilance:** the topics of abuse and dependence are monitored via routine signaling on an ongoing basis.
Results of effectiveness measurement	**Labeling/Information supply**: The PIL for the Palexia Film-coated 50 mg tablets (tested as example for all tablets strengths) and for Oral Solution 4mg/ml were considered, after two rounds of testing in 2 x 10 subjects, to meet the pass criteria for readability testing for all 16 and 17 questions posed, as set out in the Medicines and Healthcare products Regulatory Agency (MHRA) Guidance on the User Testing of Package leaflets (June 2005, updated march 2007) and the draft EC guideline on the readability of the Label and Package Label-leaflet of Medicinal Products for Human Use, September 2006. **Routine Pharmacovigilance:** no relevant changes in exposure adjusted reporting rates or the pattern of cases has been identified in routine signaling activities or in periodic and cumulative reviews in PSURs up to the DLP of the most recent PSUR (20 May 2024).
Impact of risk minimization	**Controlled access:** in certain countries, e.g., Mexico and other Latin American countries, the inappropriately stringent scheduling status might prevent patients in need to receive legitimate pain medication as pharmacies supplying the medication are sparse. According to the International Narcotics Control Board (**Error! Reference source not found.**) annual report of 2011 ‘the use of opioid analgesics for medical purposes remains low in Mexico’. Consequently the INCB encouraged to ‘take the necessary steps to ensure that adequate access to those narcotic drugs is provided for those in need of medical treatment’. A country by country evaluation might be necessary to find the right balance between the controlled access status (e.g., which schedule if several options exist) and the availability of the drug to the patients in need of treatment. **Routine Pharmacovigilance:** the existing risk minimisation measures applicable to the risks of abuse and dependence of tapentadol are considered adequate.

V.2 Additional Risk Minimisation Measures

Routine risk minimisation activities as described in Part V.1 are sufficient to manage the safety concerns of tapentadol.

V.3 Summary of risk minimisation measures

Table 2: Summary table of pharmacovigilance activities and risk minimisation activities by safety concern

Safety concern	Risk minimisation measures	Pharmacovigilance activities
Drug abuse, drug dependence	• Routine risk communication: Warning in Section 4.4 in SmPC: Potential for Abuse • Routine risk minimisation activities recommending specific clinical measures to address the risk: Not applicable • Other routine risk minimisation measures: Prescription only medicine classified as a controlled drug at national levels providing a restricted access complying with the schedule I of the United Nations Convention on Narcotic Drugs.	Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection: • Use of literature containing RADARS data, NAVIPPRO® system has not been further used for evaluation, considering consistent data between both sources in the past and thus sufficiency of RADARS reports for further abuse status monitoring.