Medicines & Healthcare products Regulatory Agency

MHRA Regulating Medicines and Medical Devices

Public Assessment Report

National Procedure

NEXPOVIO 20 mg film-coated tablets

(selinexor)

Product Licence Number: PLGB 44238/0001

Karyopharm Europe GmbH

LAY SUMMARY

NEXPOVIO 20 mg film-coated tablets

(selinexor)

This is a summary of the Public Assessment Report (PAR) for NEXPOVIO 20 mg film-coated tablets. It explains how this product was assessed and its authorisation recommended, as well as its conditions of use. It is not intended to provide practical advice on how to use this product.

This product will be referred to as NEXPOVIO in this lay summary for ease of reading.

For practical information about using NEXPOVIO, patients should read the Patient Information Leaflet (PIL) or contact their doctor or pharmacist.

What is NEXPOVIO and what is it used for?
This product has been authorised by MHRA for Great Britain (GB) (consisting of England, Scotland and Wales). This procedure relies on a European Commission (EC) decision on 26 March 2021 (EMEA/H/C/005127/0000), in accordance with the advice from the Committee for Medicinal Products for Human Use (CHMP). This is known as the EC Decision Reliance Procedure.

This application is a full-dossier application. This means that the results of pharmaceutical, non-clinical and clinical tests have been submitted to show that this medicine is suitable for treating the specified indications.

NEXPOVIO is used to treat adult patients with multiple myeloma (a cancer which affects a type of blood cell called the plasma cell) that has come back after treatment. Plasma cells, also called myeloma cells, can damage bones and kidneys and increase the risk of infection. Treatment with NEXPOVIO kills myeloma cells and reduces symptoms of the disease. NEXPOVIO is used together with dexamethasone in patients who have received at least four previous types of myeloma treatment and whose disease cannot be controlled with prior medicines used to treat multiple myeloma.

How does NEXPOVIO work?
NEXPOVIO contains the active substance called selinexor. Selinexor is a cancer medicine known as an XPO1 inhibitor. This means that selinexor blocks XPO1 that transports protein from the cell nucleus into the cell cytoplasm. Some cell protein must be in the nucleus in order to function property. By blocking XPO1 function, selinexor prevents the exit of certain proteins out of the nucleus, and interfering with the continued growth of cancer cells, and leading to the death of cancer cells.

How is NEXPOVIO used?
The pharmaceutical form of this medicine is a tablet and the route of administration is oral (by mouth). The tablets should be swallowed whole with a glass of water either with food or between meals. The patients should not chew, crush or break the tablets in order to prevent risk of skin irritation from the active substance.

Patients should take this medicine exactly as a doctor or pharmacist has told them. They should check with a doctor or a pharmacist if they are not sure.

The recommended dose is 80 mg (4 tablets) once daily, on days 1 and 3 of each week, or as directed by a doctor.

A doctor may alter the dose if side effects occur. It is important that patients should take this medicine as a doctor told them to avoid dosing errors.

A doctor will let patients know the duration of treatment based on how they are responding to treatment and side effects.

For further information on how NEXPOVIO is used, refer to the PIL and Summary of Product Characteristics (SmPC) available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

This medicine can only be obtained with a prescription.

The patient should always take the medicine exactly as their doctor/pharmacist has told them. The patient should check with their doctor or pharmacist if they are not sure.

What benefits of NEXPOVIO have been shown in studies?
A main study involving 83 patients with multiple myeloma showed that NEXPOVIO given together with low-dose dexamethasone was effective at reducing the cancer in patients whose disease had not improved after four previous treatment and had worsened after the last one. A quarter of patients (25.3%) had a reduction of their cancer with NEXPOVIO that lasted on average for 4 months.

What are the possible side effects of NEXPOVIO?
For the full list of all side effects reported with this medicine, see Section 4 of the PIL or the SmPC available on the MHRA website.

If a patient gets any side effects, they should talk to their doctor, pharmacist or nurse. This includes any possible side effects not listed in the product information or the PIL that comes with the medicine. Patients can also report suspected side effects themselves, or a report can be made on behalf of someone else they care for, directly via the Yellow Card scheme at www.mhra.gov.uk/yellowcard or search for 'MHRA Yellow Card' online. By reporting side effects, patients can help provide more information on the safety of this medicine.

Why was NEXPOVIO approved?
It was concluded that NEXPOVIO has been shown to be effective in the treatment of adult patients with multiple myeloma (a cancer which affects a type of blood cell called the plasma cell) that has come back after treatment. NEXPOVIO is used together with dexamethasone in patients who have received at least four previous types of myeloma treatment and whose disease cannot be controlled with prior medicines used to treat multiple myeloma. Furthermore, the side effects observed with use of this product is considered to be typical for this type of treatment. Therefore, the MHRA decided that the benefits are greater than the risks and recommended that this medicine can be approved for use.

NEXPOVIO has been authorised with a Conditional Marketing Authorisation (CMA). In general, CMAs are intended for medicinal products that address an unmet medical need, such as a lack of alternative therapy for a serious and life-threatening disease. CMAs may be granted where comprehensive clinical data is not yet complete, but it is judged that such data will become available soon.

What measures are being taken to ensure the safe and effective use of NEXPOVIO?
A Risk Management Plan (RMP) has been developed to ensure that NEXPOVIO is used as safely as possible. Based on this plan, safety information has been included in the SmPC and the PIL, including the appropriate precautions to be followed by healthcare professionals and patients.

Known side effects are continuously monitored. Furthermore, new safety signals reported by patients/healthcare professionals will be monitored and reviewed continuously.

Other information about NEXPOVIO
A Conditional Marketing Authorisation was granted in Great Britain (GB, consisting of England, Scotland and Wales) on 26 May 2021.

The full PAR for NEXPOVIO follows this summary.

This summary was last updated in July 2021.

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I INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare products Regulatory Agency (MHRA) considered that the application for NEXPOVIO 20 mg film-coated tablets (PLGB 44238/0001) could be approved.

The product is approved for the following indication:

- NEXPOVIO is indicated in combination with dexamethasone for the treatment of multiple myeloma in adult patients who have received at least four prior therapies and whose disease is refractory to at least two proteasome inhibitors, two immunomodulatory agents and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy.

NEXPOVIO contains the active substance selinexor which is a reversible covalent selective inhibitor of nuclear export (SINE) compound that specifically blocks exportin 1 (XPO1). XPO1 is the major mediator of the nuclear export of many cargo proteins including tumour suppressor proteins (TSPs), growth regulators and mRNAs of growth promoting (oncogenic) proteins. XPO1 inhibition by selinexor leads to marked accumulation of TSPs in the nucleus, cell cycle arrest, reductions in several oncoproteins such as c-Myc and cyclin D1, and apoptosis of cancer cells.

This application was approved under Regulation 50 of The Human Medicines Regulation 2012, as amended (previously Article 8(3) of Directive 2001/83/EC, as amended), a full-dossier application. All non-clinical data submitted were from studies conducted in accordance with Good Laboratory Practice (GLP). All clinical data submitted were from studies conducted in accordance with Good Clinical Practice (GCP).

For NEXPOVIO 20 mg film-coated tablets, in coming to its decision, MHRA has relied on a European Commission (EC) decision on 26 March 2021 (EMEA/H/C/005127/0000), in accordance with the advice from the Committee for Medicinal Products for Human Use (CHMP).

For the scientific discussion of the quality, non-clinical and clinical assessment conduct by the European Medicines Agency (EMA), please refer to the European Public Assessment Reports, available on the EMA website.

This product has been authorised as a Conditional Marketing Authorisation (CMA). In general, CMAs are granted in the interest of public health and are intended for medicinal products that fulfil an unmet medical need and the benefit of immediate availability outweighs the risk posed from less comprehensive data than normally required. Unmet medical needs include, for example, treatment or diagnosis of serious and life-threatening diseases where no satisfactory treatment methods are available. CMAs may be granted where comprehensive clinical data is not yet complete, but it is judged that such data will become available soon. Adequate evidence of safety and efficacy to enable the MHRA to conclude that the benefits are greater than the risks is required, and has been provided for, NEXPOVIO. The CMA for NEXPOVIO, including the provision of any new information, will be reviewed every year and this report will be updated as necessary.

In line with the legal requirements for children's medicines, the application included a licensing authority decision on the agreement of a full product specific waiver (Decision P/0384/2018).

The MHRA has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for this product at all sites responsible for the manufacture, assembly and batch release of this product.

A Risk Management Plan (RMP) and a summary of the pharmacovigilance system have been provided with this application and are satisfactory.

A national marketing authorisation was granted in Great Britain (GB, consisting of England, Scotland and Wales) on 26 May 2021

II. ASSESSOR'S COMMENTS ON THE PRODUCT INFORMATION SUMMARY OF PRODUCT CHARACTERITICS (SmPC)

The SmPC is in line with current guidelines and are satisfactory.

PATIENT INFORMATION LEAFLET (PIL)

The PIL is in line with current guidelines and is satisfactory.

LABEL

The labelling is in line with current guidelines and is satisfactory.

III. QUALITY ASPECTS

MHRA considered that the quality data submitted for this application is satisfactory.

The grant of a Marketing Authorisation is recommended.

IV. NON-CLINICAL ASPECTS

MHRA considered that the non-clinical data submitted for this application is satisfactory.

The grant of a Marketing Authorisation is recommended.

V. CLINICAL ASPECTS

MHRA considered that the clinical data submitted for this application is satisfactory.

The grant of a Marketing Authorisation is recommended.

V. RISK MANAGEMENT PLAN (RMP)

The applicant has submitted an RMP, in accordance with the requirements of Regulation 182 of The Human Medicines Regulation 2012, as amended. The applicant proposes only routine pharmacovigilance and routine risk minimisation measures for all safety concerns. This is acceptable.

VII. USER CONSULTATION

A full colour mock-up of the Patient Information Leaflet (PIL) has been provided with the application in accordance with the requirements.

The PIL has been evaluated via a user consultation study in accordance with the legal requirements. The results show that the PIL meets the criteria for readability as set out in the Guideline on the readability of the label and package leaflet of medicinal products for human use.

VIII. OVERALL CONCLUSION, BENEFIT/RISK AND RECOMMENDATION

The quality of the product is acceptable, and no new non-clinical or clinical safety concerns have been identified. The benefit/risk balance is, therefore, considered to be positive.

For products granted a Conditional Marketing Authorisation.

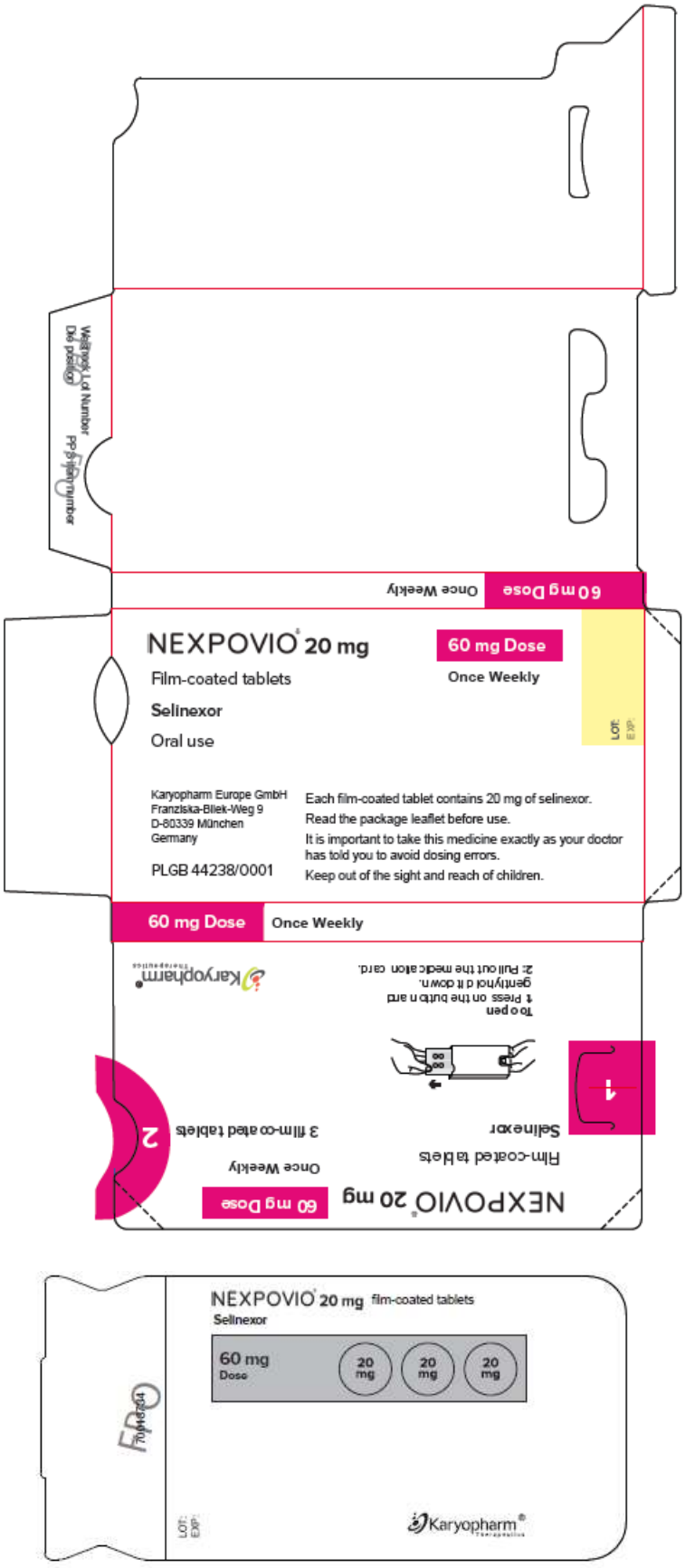
NEXPOVIO 20 mg film-coated tablets have been authorised with a Conditional Marketing Authorisation (CMA). The Marketing Authorisation Holder shall complete, within the stated timeframe, the following measures:

Description	Due date
In order to confirm the efficacy and safety of selinexor in combination with dexamethasone in the treatment of multiple myeloma in adult patients who have received at least four prior therapies and whose disease is refractory to at least two proteasome inhibitors, two immunomodulatory agents and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy, the MAH should submit the results of the phase 3, KCP-330-023/BOSTON study (data cut off February 2021), comparing the efficacy and safety of selinexor plus bortezomib plus low-dose dexamethasone versus bortezomib plus low dose dexamethasone in adult patients with relapsed/refractory multiple myeloma who have received 1 to 3 prior anti-MM regimens.	May 2021

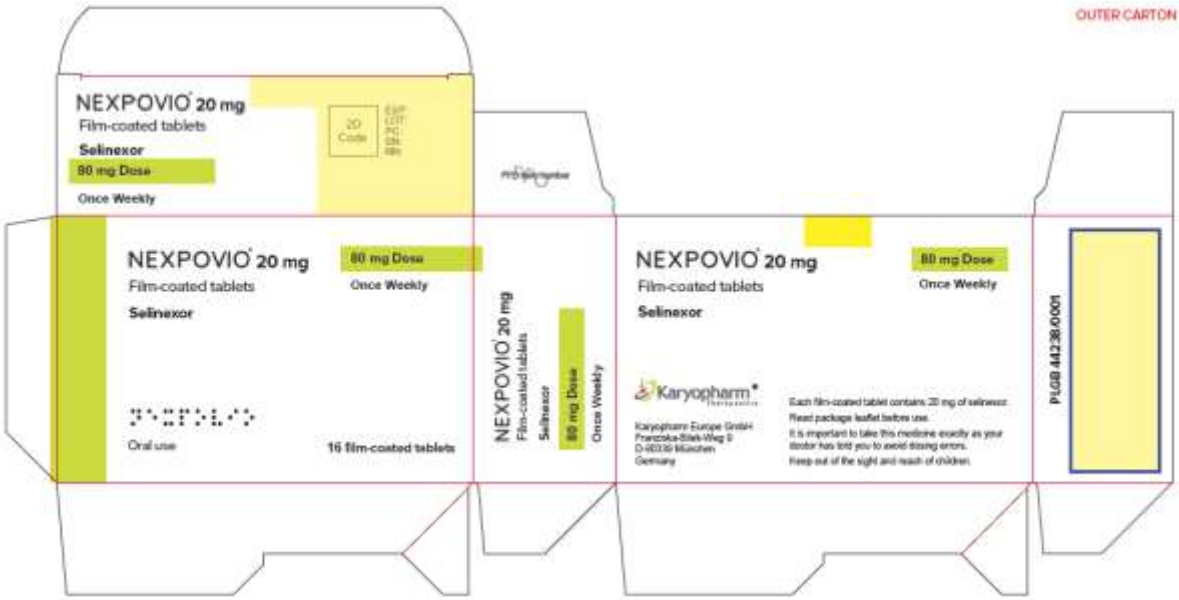
The Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and labelling are satisfactory.

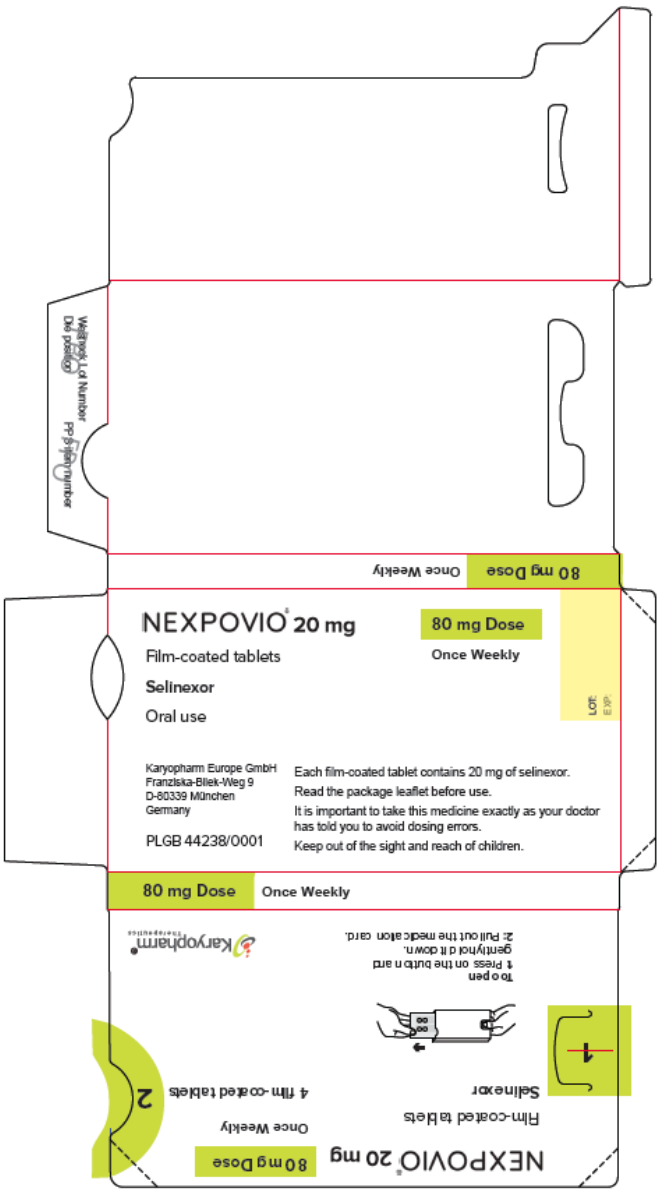
In accordance with legal requirements, the current approved GB versions of the SmPC and PIL for this product are available on the MHRA website.

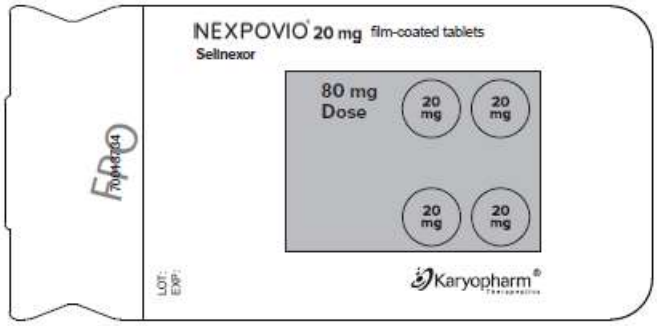
Representative copies of the labels at the time of GB licensing are provided below.


NEXPOVIO® 20 mg
Film-coated tablets
Selinexor
Oral use
60 mg Dose
Once Weekly
LOT:
EXP:
Karyopharm Europe GmbH
Franziska-Bilek-Weg 9
D-80339 München
Germany
PLGB 44238/0001
Each film-coated tablet contains 20 mg of selinexor.
Read the package leaflet before use.
It is important to take this medicine exactly as your doctor has told you to avoid dosing errors.
Keep out of the sight and reach of children.
60 mg Dose
Once Weekly
Karyopharm
1
2
NEXPOVIO® 20 mg
60 mg Dose
Once Weekly
Film-coated tablets
Selinexor
NEXPOVIO® 20 mg film-coated tablets
Selinexor
60 mg
Dose
20 mg
20 mg
20 mg
LOT:
EXP:
Karyopharm®

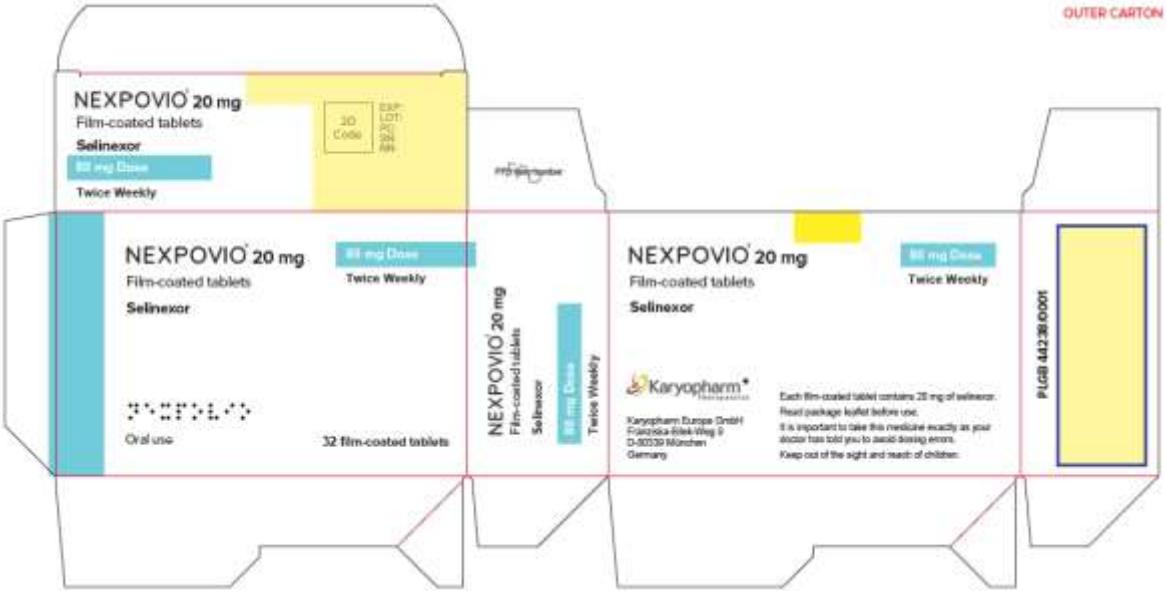
OUTER CARTON

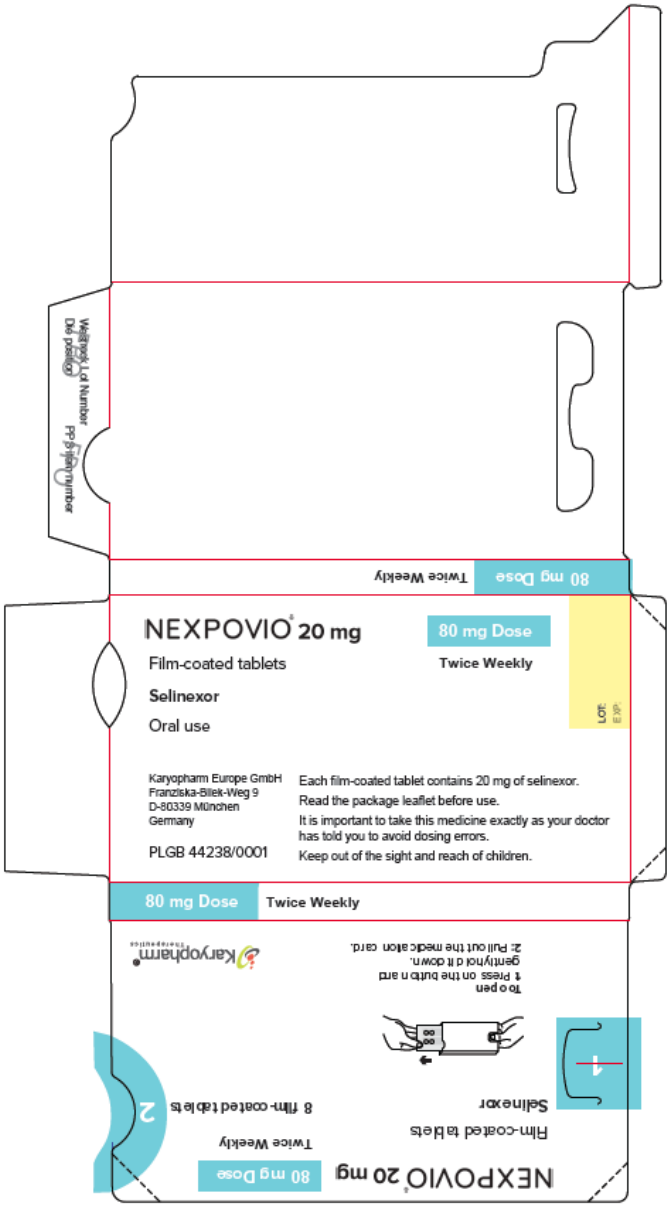


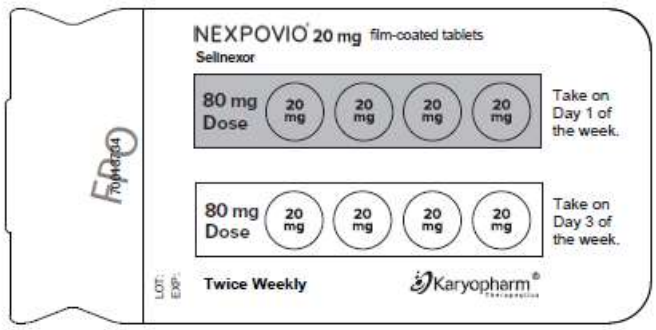


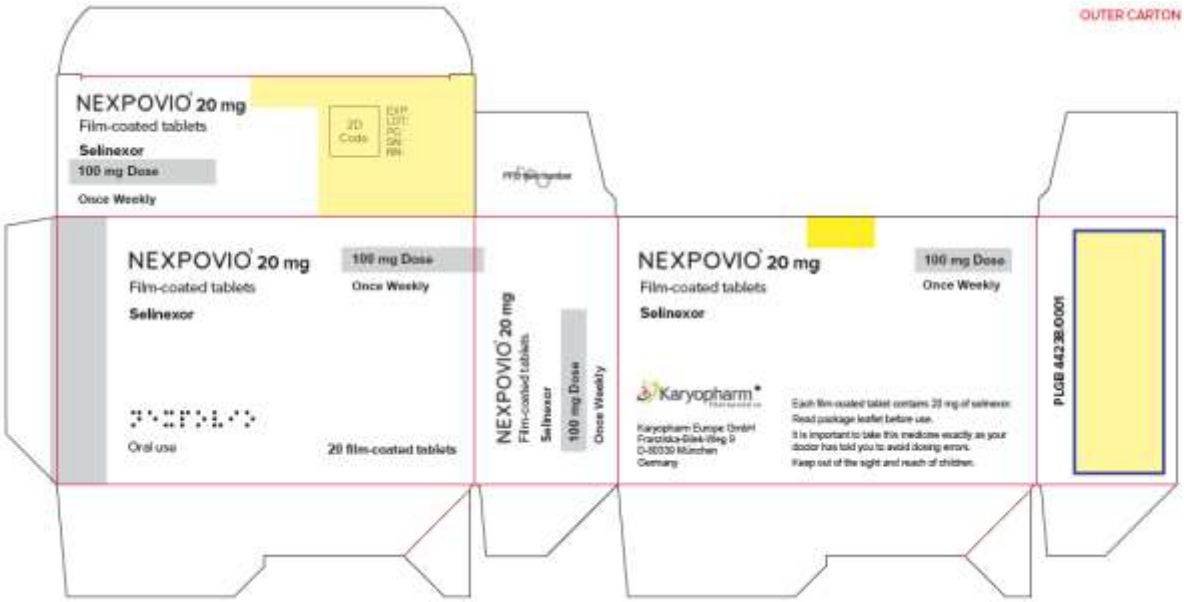


OUTER CARTON




NEXPOVIO 20 mg
Film-coated tablets
Selinexor
Oral use
80 mg Dose
Twice Weekly
LOT
EXP
Karyopharm Europe GmbH
Franziska-Bilek-Weg 9
D-80339 München
Germany
PLGB 44238/0001
Each film-coated tablet contains 20 mg of selinexor.
Read the package leaflet before use.
It is important to take this medicine exactly as your doctor has told you to avoid dosing errors.
Keep out of the sight and reach of children.
80 mg Dose
Twice Weekly
Karyopharm
To open
1: Press on the button and gently fold down.
2: Pull out the medication card.
2
8 film-coated tablets
Twice Weekly
80 mg Dose
NEXPOVIO 20 mg
Film-coated tablets
Selinexor


NEXPOVIO 20 mg film-coated tablets
Selinexor
80 mg Dose
20 mg
Take on Day 1 of the week.
80 mg Dose
Take on Day 3 of the week.
LOT
EXP
Twice Weekly
Karyopharm


OUTER CARTON
NEXPOVIO 20 mg
Film-coated tablets
Selinexor
100 mg Dose
Once Weekly
2D Code
NEXPOVIO 20 mg
Film-coated tablets
Selinexor
100 mg Dose
Once Weekly
Oral use
20 film-coated tablets
NEXPOVIO 20 mg
Film-coated tablets
Selinexor
100 mg Dose
Once Weekly
NEXPOVIO 20 mg
Film-coated tablets
Selinexor
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Keep out of the sight and reach of children.
PLGB 44238/0001

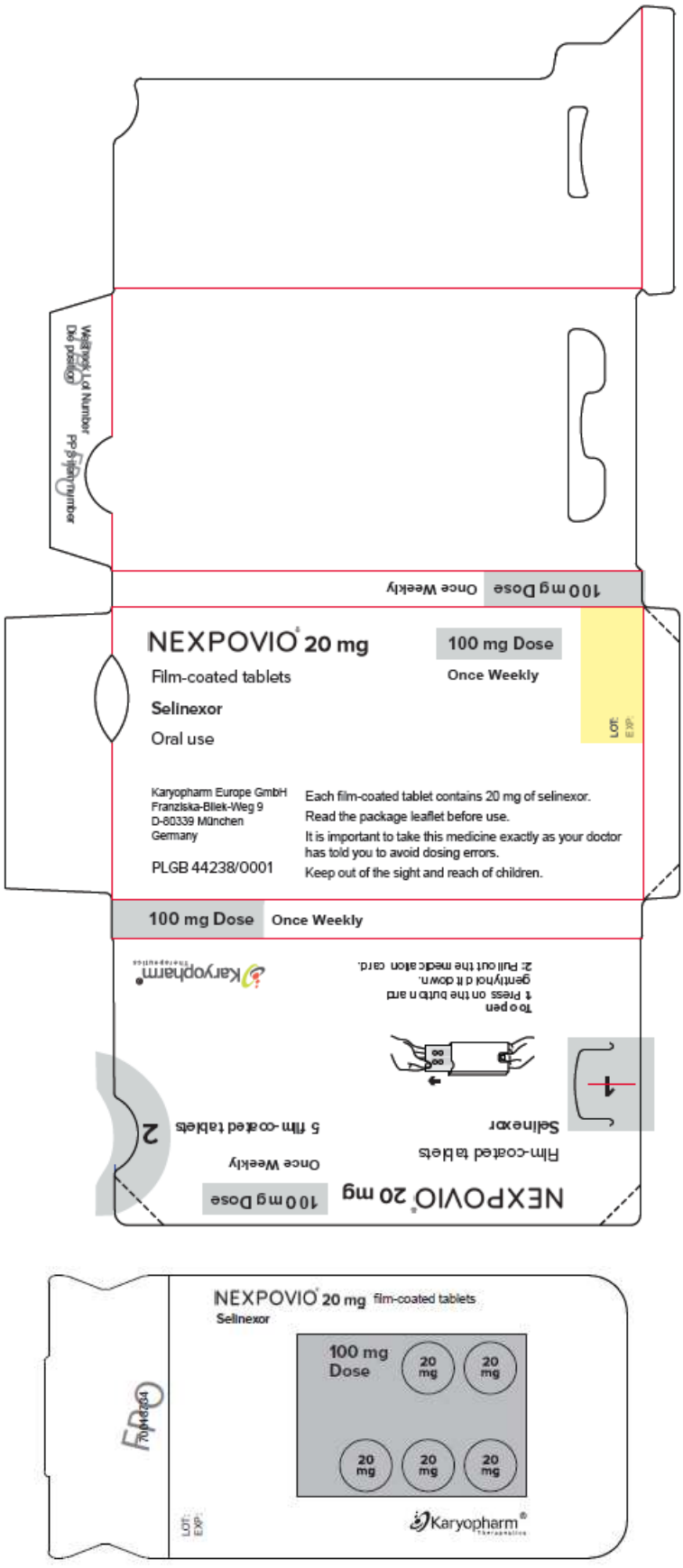
Batch/Lot Number
Do not use
PC
SN
Number
100 mg Dose
Once Weekly
NEXPOVIO® 20 mg
Film-coated tablets
Selinexor
Oral use
100 mg Dose
Once Weekly
Lot
EXP
Karyopharm Europe GmbH
Franziska-Bilek-Weg 9
D-80339 München
Germany
PLGB 44238/0001
Each film-coated tablet contains 20 mg of selinexor.
Read the package leaflet before use.
It is important to take this medicine exactly as your doctor has told you to avoid dosing errors.
Keep out of the sight and reach of children.
100 mg Dose
Once Weekly
Karyopharm
To open
1: Press on the button and gently hold it down.
2: Pull out the medication card.
1
Selinexor
Film-coated tablets
NEXPOVIO® 20 mg
100 mg Dose
Once Weekly
2
5 film-coated tablets
NEXPOVIO® 20 mg film-coated tablets
Selinexor
100 mg Dose
20 mg
20 mg
20 mg
20 mg
20 mg
Karyopharm
Lot
EXP

TABLE OF CONTENT OF THE PAR UPDATE

Steps taken after the initial procedure with an influence on the Public Assessment Report (non-safety variations of clinical significance).

Please note that only non-safety variations of clinical significance are recorded below and in the annexes to this PAR. The assessment of safety variations where significant changes are made are recorded on the MHRA website or European Medicines Agency (EMA) website. Minor changes to the marketing authorisation are recorded in the current SmPC and/or PIL available on the MHRA website.

Application type	**Scope**	**Product information affected**	**Date of grant**	**Outcome**	**Assessment report attached Y/N**