Report Nexpovio® - Selinexor

Product & Mechanism of action	Authorized indications Licensing status	Essential therapeutic features	NHS impact
Substance: Selinexor **Brand Name:** -Xpovio™ (US)[1]; -Nexpovio (EU)[2]. **Originator/licensee:** Karyopharm Europe GmbH **Classification:** NI **ATC code:** L01XX66 **Orphan Status:** **Eu:** No **Us:** Yes **Mechanism of action:** Selinexor is a reversible covalent SINE compound that specifically blocks XPO1. XPO1 is the major mediator of the nuclear export of many cargo proteins including TSPs, growth regulators and mRNAs of growth promoting proteins. XPO1 inhibition by selinexor leads to marked accumulation of TSPs in the nucleus, cell cycle arrest, reductions in several oncoprotein and apoptosis of cancer cells [2].	**Authorized Indication:** **EMA and FDA:** Selinexor is indicated in combination with bortezomib and dexamethasone for the treatment of adult pts with MM who have received at least one prior therapy [1,2]. **Route of administration:** OS **Licensing status** **EU CHMP P.O. date:** 19/05/2022 **FDA M.A. date:** 18/12/2020 **EU Speed Approval Pathway:** No **FDA Speed Approval Pathway:** Yes ----- **ABBREVIATIONS:** AE: Adverse Event HR: Hazard Ratio MM: Multiple Myeloma PFS: Progression Free Survival Pts: Patients SC: Subcutaneous SAE: Serious Adverse Event SINE: Selective Inhibitor of Nuclear Export TEAE: Treatment-Emergent Adverse Event TSPs: Tumour Suppressor Proteins XPO1: Exportin 1	**Summary of clinical EFFICACY:** The BOSTON Trial (NCT03110562) is a randomized (1:1) open-label, multicenter, active comparator-controlled trial in pts ≥18 years old with MM who had previously received at least one and at most three prior therapies (n=402). Pts received once-weekly selinexor orally (100 mg) in combination with once-weekly sc bortezomib (1.3 mg/m^2) and dexamethasone (20 mg) twice-weekly orally (n=195) each 5-week cycle compared to the standard bortezomib (1.3 mg/m^2 twice per week for the first 24 weeks and once per week thereafter) plus dexamethasone (20 mg four times per week for the first 24 weeks and twice per week thereafter) (n=207) [3]. The primary endpoint was PFS, defined as time from randomisation until the first disease progression, assessed by an independent review committee, or until death from any cause in the intention-to-treat population. The estimated median PFS was 13.9 months (95% CI: 11.7, Not Estimable) for the selinexor arm and 9.5 months (95% CI: 8.1, 10.8) for the comparator arm (HR 0.70; 95% CI 0.53–0.93, p=0.0075) [3]. **Summary of clinical SAFETY:** The most common any grade TEAEs were thrombocytopenia (60% in the selinexor group vs 27% in the comparator group), nausea (50% vs 10%), fatigue (42% vs 18%), anaemia (36% vs 23%) and decreased appetite (35 % vs 5%). The most common grade 3–4 TEAEs were thrombocytopenia (39% vs 17%), anaemia (16% vs 10%), pneumonia (12% vs 10%), and fatigue (13% vs 1%). SAEs were reported in 52% of pts in the selinexor group and 38% in the comparator group. Pneumonia was the most frequent SAE, with the same incidence (12%) in both groups. 21% of pts in the selinexor group and 16% in the comparator group discontinued study treatment because of TEAEs. Deaths due to AEs were of similar frequency in the two groups (6% in the selinexor group vs 5% in the comparator group) [3]. **Ongoing studies:** ● ***For the same indication:*** NCT05028348, NCT04939142 ● ***For other indications:*** NCT03555422, NCT02606461, NCT04442022 **Discontinued studies (for the same indication):** NCT02389543, NCT05170789, NCT02628704 ----- **References:** 1. https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/212306s005lbl.pdf 2. https://www.ema.europa.eu/en/medicines/human/EPAR/nexpovio. 3. Grosicki S., Simonova M. et al.: Once-per week selinexor, bortezomib, and dexamethasone versus twice-per-week bortezomib and dexamethasone in patients with multiple myeloma (BOSTON): a randomised, open-label, phase 3 trial. Lancet 2020; 396: 1563–73. 4. https://www.drugs.com/price-guide/xpovio 5. https://www.annalsofoncology.org/action/showPdf?pii=S0923-7534%2820%2943169-2. 6. https://www.clinicaltrials.gov/ct2/results?term=selinexor&recrs=b&recrs=a&recrs=f&recrs=d&age_v=&gndr=&type=&rslt=&phase=2&Search=Apply	**Cost of therapy:** $22.977,50 for 12 tablets/pack (20 mg) – US [4]. **Epidemiology:** MM is a plasma cell neoplasm that accounts for 1%-1.8% of all cancers and is the second most common haematological malignancy with an estimated incidence in Europe of 4.5-6.0/100,000/year. Despite the significant improvement in patients' survival over the past 20 years, only 10%-15% of pts achieve or exceed expected survival compared with the matched general population [5]. ----- **POSSIBLE PLACE IN THERAPY** Second-line options for MM pts depend on the first-line therapies and on the sensitivity to lenalidomide or bortezomib. Treatment options include: ● carfilzomib or daratumumab or elotuzumab or ixazomib, in combination with lenalidomide+dexamethasone, ● pomalidomide or selinexor or daratumumab or venetoclax, in combination with bortezomib+dexamethasone, ● daratumumab or isatuximab, in combination with carfilzomib+dexamethasone, ● carfolzomib+dexamethasone [5]. **OTHER INDICATIONS IN DEVELOPMENT** Liposarcoma, Endometrial cancer, Diffuse Large B-cell Lymphoma [6]. **SAME INDICATION IN EARLIER LINE(S) OF TREATMENT:** First-line treatment of MM (NCT04717700, NCT04782687). **OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION**

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		7. https://www.clinicaltrials.gov/ct2/results?cond=relapsed+refractory+multiple+myeloma&recrs=b&recrs=a&recrs=f&recrs=d&age_v=&gndr=&type=&rslt=&phase=2&Search=Apply	Belantamab mafodotin, elranatamab [7]. *Service reorganization: No *Possible off label use: Yes