PRESCRIBING INFORMATION – NORTHERN IRELAND

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 of the SmPC for how to report adverse reactions.

Paxlovid®▼ (nirmatrelvir/ritonavir) 150 mg + 100 mg film-coated tablets
Please refer to the Summary of Product Characteristics (SmPC) before prescribing Paxlovid.

Indications: Treatment of coronavirus disease 2019 (COVID-19) in adults who do not require supplemental oxygen and who are at increased risk for progression to severe COVID 19 (see section 5.1 of the SmPC). **Presentation:** Each pink film-coated tablet contains 150 mg of nirmatrelvir. Each white film-coated tablet contains 100 mg of ritonavir. **Dosage:** The recommended dosage is 300 mg nirmatrelvir (two 150 mg tablets) with 100 mg ritonavir (one 100 mg tablet) all taken together orally every 12 hours for 5 days. Paxlovid should be administered as soon as possible after a diagnosis of COVID-19 and within 5 days of symptom onset. Completion of the full 5-day treatment course is recommended even if the patient requires hospitalisation due to severe or critical COVID-19. In patients with moderate renal impairment, (eGFR ≥ 30 to < 60 mL/min) the dose of Paxlovid should be reduced to nirmatrelvir/ritonavir 150 mg/100 mg every 12 hours for 5 days. Paxlovid should not be used in patients with severe renal or severe (Child-Pugh Class C) hepatic impairment. **Contraindications:** Hypersensitivity to the active substances or to any of the excipients. Medicinal products listed below are a guide and not considered a comprehensive list of all possible medicinal products that are contraindicated with Paxlovid. Medicinal products that are highly dependent on CYP3A for clearance and for which elevated plasma concentrations are associated with serious and/or life-threatening reactions: ***Alpha1-adrenoreceptor antagonist:*** alfuzosin; ***Antianginal:*** ranolazine; ***Antiarrhythmics:*** amiodarone, dronedarone, flecainide, propafenone, quinidine; ***Antibiotics:*** fusidic acid; ***Anticancer drugs:*** neratinib, venetoclax; ***Anti-gout:*** colchicine; ***Antihistamines:*** terfenadine; ***Antipsychotics/Neuroleptics:*** clozapine, lurasidone, pimozide, quetiapine; ***Benign prostatic hyperplasia medicinal products:*** silodosin; ***Cardiovascular medicinal products:*** eplerenone, ivabradine; ***Ergot derivatives:*** dihydroergotamine, ergonovine, ergotamine, methylergonovine; ***GI motility agent:*** cisapride; ***Immunosuppressants:*** voclosporin; ***Lipid-modifying agents:*** lovastatin, simvastatin, lomitapide; ***Migraine medicinal products:*** eletriptan; ***PDE5 inhibitors:*** avanafil, sildenafil, tadalafil, vardenafil; ***Sedative/Hypnotics:*** clorazepate, diazepam, estazolam, flurazepam, oral midazolam, triazolam; ***Vasopressin receptor antagonists:*** tolvaptan. Medicinal products that are potent CYP3A inducers where significantly reduced nirmatrelvir/ritonavir plasma concentrations may be associated with the potential for loss of virologic response and possible resistance: ***Antibiotics:*** rifampicin; ***Anticancer drugs:*** apalutamide; ***Anticonvulsants:*** carbamazepine, phenobarbital, phenytoin; Herbal products: St. John's wort (***Hypericum perforatum***). Paxlovid cannot be started immediately after discontinuation of CYP3A4 inducers due to the delayed offset of the recently discontinued CYP3A4 inducer (see section 4.5 of the SmPC). In certain patients, a multi-disciplinary approach (e.g., involving physicians and specialists in clinical pharmacology) should be considered for management of DDIs especially if concomitant medications are withheld, their dosage is reduced, or if monitoring of side effects is necessary. **Warnings and Precautions:** ***Risk of serious adverse reactions due to interactions with other medicinal products:*** Due to effects on CYP3A metabolic pathways, potential for drug-drug interactions (DDIs) should be considered with other medicinal products prior to and during Paxlovid therapy; concomitant medicinal products should be reviewed during Paxlovid therapy and the patient should be monitored for the adverse reactions associated with the concomitant medicinal products. The risk of interactions with concomitant medications during the 5-day treatment period for Paxlovid should be weighed against the risk of not receiving Paxlovid; please refer to Table 1 in SmPC section 4.5. ***Coadministration with calcineurin inhibitors and mTOR inhibitors:*** Consultation of a multidisciplinary group (e.g., involving physicians, specialists in immunosuppressive therapy, and/or specialists in clinical pharmacology) is required to handle the complexity of this coadministration by closely and regularly monitoring immunosuppressant serum concentrations and adjusting the dose of the immunosuppressant in accordance with the latest guidelines (see SmPC section 4.5). ***Hypersensitivity reactions:*** If signs and symptoms of a clinically significant hypersensitivity reaction (including Toxic Epidermal Necrolysis and Stevens-Johnson syndrome) or anaphylaxis occur, immediately discontinue Paxlovid and initiate appropriate medications and/or supportive care. ***Severe renal impairment:*** Paxlovid should not be used in patients with severe renal impairment (eGFR < 30 mL/min, including patients with ESRD under haemodialysis). ***Severe hepatic impairment:*** Paxlovid should not be used in patients with severe (Child-Pugh Class C) hepatic impairment. ***Hepatotoxicity:*** Caution should be exercised when administering Paxlovid to patients with pre-existing liver diseases, liver enzyme abnormalities or hepatitis. ***HIV resistance:*** As nirmatrelvir is coadministered with ritonavir, there may be a risk of HIV-1 developing resistance to HIV protease inhibitors in individuals with uncontrolled or undiagnosed HIV-1 infection. ***Excipients:*** nirmatrelvir tablets contain lactose, patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine. Contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'. **Drug Interactions:** Nirmatrelvir and ritonavir are CYP3A substrates. Coadministration of Paxlovid with medicinal products that induce CYP3A may decrease nirmatrelvir and ritonavir plasma concentrations and reduce Paxlovid therapeutic effect. Coadministration of Paxlovid with medicinal product that inhibits CYP3A4 may increase nirmatrelvir and ritonavir plasma concentrations. Paxlovid (nirmatrelvir/ritonavir) is a strong inhibitor of CYP3A and increases plasma concentrations of medicinal products that are primarily metabolised by CYP3A. Ritonavir has a high affinity for several cytochrome P450 (CYP) isoforms and may inhibit oxidation with the following ranked order: CYP3A4 > CYP2D6. Coadministration of Paxlovid with drug substrates of CYP2D6 may increase the CYP2D6 substrate concentration. Paxlovid also has a high affinity for P glycoprotein (P-gp) and inhibits this transporter; caution should thus be exercised in case of concomitant treatment. Close drug monitoring for safety and efficacy should be performed, and dose reduction may be adjusted accordingly, or avoid concomitant use. Paxlovid may induce glucuronidation and oxidation by CYP1A2, CYP2C8, CYP2C9 and CYP2C19 thereby increasing the biotransformation of some medicinal products metabolised by these pathways. Based on ***in vitro*** studies there is a potential for nirmatrelvir to inhibit MDR1, MATE1, OCT1 and OATP1B1 at clinically relevant concentrations. Dedicated drug-drug interactions studies conducted with Paxlovid indicate that the drug interactions are primarily due to ritonavir. Hence, drug interactions pertaining to ritonavir are applicable for Paxlovid. Medicinal products listed here are a guide and not considered a comprehensive list of all possible medicinal products that may interact with nirmatrelvir/ritonavir: ***Amphetamine derivatives:*** amphetamine; ***Analgesics:*** buprenorphine, fentanyl, methadone, morphine, pethidine, piroxicam; ***Antiarrhythmics:*** digoxin; ***Antiasthmatic:*** theophylline; ***Anticancer:*** abemaciclib, afatinib, ceritinib, dasatinib, nilotinib, vinblastine, vincristine, encorafenib, fostamatinib, ibrutinib, venetoclax (contraindicated in some circumstances); ***Anticoagulants:*** dabigatran, rivaroxaban, warfarin; ***Anticonvulsants:*** divalproex, lamotrigine; ***Anticorticosteroids:*** ketoconazole; ***Antidepressants:*** amitriptyline, fluoxetine, imipramine, nortriptyline, paroxetine, sertraline; ***Anti-HCV:*** glecaprevir/pibrentasvir; ***Antihistamines:*** fexofenadine, loratadine; ***Anti-HIV:*** efavirenz, maraviroc, raltegravir, zidovudine; ***Anti-infectives:*** atovaquone, bedaquiline, clarithromycin, delamanid, erythromycin, itraconazole, rifabutin, sulfamethoxazole/trimethoprim, voriconazole; ***Antipsychotics:*** haloperidol, risperidone, thioridazine; ***β2-agonist (long acting):*** salmeterol; ***Calcium channel antagonist:*** amlodipine, diltiazem, nifedipine, lercanidipine; ***Endothelin antagonists:*** bosentan, riociguat; ***HMG Co-A reductase:*** atorvastatin, fluvastatin, pravastatin, rosuvastatin; ***Hormonal contraceptive:*** ethinyl estradiol; ***Immunosuppressants:*** cyclosporine, tacrolimus, everolimus, sirolimus; ***Sedatives/Hypnotics:*** alprazolam, buspirone, parenteral midazolam; ***Sleeping agent:*** zolpidem; ***Smoke cessation:*** buproprion; ***Steroids:*** budesonide, inhaled, injectable or intranasal fluticasone propionate, triamcinolone, dexamethasone, prednisolone; ***Thyroid hormone replacement therapy:*** levothyroxine. Please refer to Table 1 in SmPC section 4.5 for additional information on interaction with medicinal products / other forms of interaction. **Fertility, pregnancy and lactation:** Women of childbearing potential should avoid becoming pregnant during treatment with Paxlovid and as a precautionary measure for 7 days after completing Paxlovid. Patients using combined hormonal contraceptives should be advised to use an effective alternative contraceptive method or an additional barrier method of contraception during treatment and until after one complete menstrual cycle after stopping Paxlovid. Paxlovid is not recommended during pregnancy and in women of childbearing potential not using contraception unless the clinical condition requires treatment with Paxlovid. Breast feeding should be discontinued during treatment with Paxlovid and as a precautionary measure for 7 days after completing Paxlovid. **Driving and operating machinery:** Paxlovid is expected to have no influence on the ability to drive and use machines. **Undesirable effects:** The safety profile of the product is based on adverse reactions reported in clinical trials and spontaneous reporting. Common (≥ 1/100 to < 1/10) adverse events reported were dysgeusia, headache, diarrhoea, vomiting and nausea. Uncommon ((≥ 1/1000 to < 1/100) adverse events reported were hypersensitivity including pruritus and rash. Rare (≥ 1/10,000 to < 1/1000) adverse events reported were anaphylaxis. See SmPC section 4.8 for full details.
Legal Category: POM. **Package Quantities:** 150 mg + 100 mg, 20 + 10 film coated tablets. **Marketing Authorisation Number:** EU/1/22/1625/001. **NHS price:** £829. **Marketing Authorisation Holder:** Pfizer Europe MA EEIG, Boulevard de la Plaine 17, 1050 Brussels, Belgium. Further Information is available on request from: Medical Information at Pfizer Limited, Walton Oaks, Dorking Road, Tadworth, Surrey, KT20 7NS, UK. Tel +44 (0)1304 616161

Adverse events should be reported. Reporting forms and information can be found at https://coronavirus-yellowcard.mhra.gov.uk or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Pfizer Medical Information on 01304 616161

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