PROFESSIONAL INFORMATION

SCHEDULING STATUS

S4

1 NAME OF MEDICINE

Xofluza® 20 mg tablets

Xofluza® 40 mg tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient: baloxavir marboxil

20 mg film-coated tablets containing 20 mg baloxavir marboxil

40 mg film-coated tablets containing 40 mg baloxavir marboxil

Excipients with known effect: Lactose monohydrate.

Each 20 mg tablet contains 77, 9 mg of lactose monohydrate and 40 mg tablet contains 155,8 mg of lactose monohydrate (see section 4.4).

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Xofluza 20 mg tablets are white to light yellow, oblong shaped film-coated tablets debossed with " 772" on one side and "20" on the other side.

Xofluza 40 mg tablets are white to light yellow, oblong shaped film-coated tablets debossed on one side with "BXM40".

4 CLINICAL PARTICULARS

4.1 Therapeutic indication

Treatment of Influenza

Xofluza is indicated for the treatment of influenza in patients aged 12 and above who have been symptomatic for no more than 48 hours.

Xofluza is indicated for treatment of uncomplicated influenza in patients aged 12 years and above who have been symptomatic for no more than 48 hours, and are at high risk of developing influenza complications.

Post- exposure prophylaxis of Influenza

Xofluza is indicated for the post-exposure prophylaxis of influenza in individuals aged 12 and above.

4.2 Posology and method of administration

Method of Administration

Xofluza may be taken with or without food (see 5.1).

However, co-administration of Xofluza with dairy products and polyvalent cation containing laxatives or antacids, or oral supplements containing iron, zinc, selenium, calcium, magnesium should be avoided (see 4.5)

Treatment of Influenza.

A single dose of Xofluza should be taken within 48 hours of symptom onset.

Post-exposure prophylaxis of Influenza

A single dose of Xofluza should be taken as soon as possible within 48 hours following close contact with an individual known or suspected to have influenza.

The recommended dose of Xofluza depending on body weight is shown in

Table 1

Patient Body Weight (kg)	Recommended Single Oral Dose
40 kg to < 80 kg	40 mg
≥ 80 kg	80 mg

Dose Modifications

No dose reductions of Xofluza are recommended

Elderly use

No dosage adjustment is recommended (see section 5.2).

Renal Impairment

The safety and efficacy of Xofluza has not been studied in patients with renal impairment. A change in dose is not required for patients with renal impairment
(see section 5.2).

Hepatic Impairment

No dose adjustment is required in patients with mild (Child-Pugh class A) to moderate (Child-Pugh class B) hepatic impairment (see section 5.2).

Xofluza has not been studied in patients with severe hepatic impairment.

4.3 Contraindications

Xofluza is contraindicated in patients with a known hypersensitivity to baloxavir marboxil or any of the excipients in Xofluza.

4.4 Special warnings and precautions for use

General

No warnings and precautions based on the available data.

Sugar

Xofluza contains lactose. Patients with the rare hereditary conditions of galactose intolerance lactase deficiency, glucose-galactose malabsorption intolerance should not take Xofluza. Xofluza contains lactose which may have an effect on the glycaemic control of patients with diabetes mellitus.

4.5 Interaction with other medicines and other forms of interaction

No clinically significant interactions are anticipated between baloxavir marboxil or its active metabolite, baloxavir and substrates, inhibitors, or inducers of cytochrome P450 (CYP enzymes), substrates or inhibitors of UDP-glucuronosyltransferasHe (UGT) enzyme, or gut, renal, or hepatic transporters.

Polyvalent cation containing products may decrease plasma concentrations of baloxavir. Xofluza should not be taken with polyvalent cation containing laxatives or antacids, or oral supplements containing iron, zinc, selenium, calcium, magnesium.

Effects of Other medicines on Baloxavir Marboxil or its Active Metabolite Baloxavir

Itraconazole, an inhibitor of P-gp, increased the Cmax and AUC_{0-inf} of baloxavir 1.33 fold and 1.23 fold, respectively. These increases are not considered to be clinically meaningful.

Probenecid, an inhibitor of UGT enzyme, decreased the Cmax and AUC_{0-inf} of baloxavir by 21 % and 25 %, respectively. These decreases are not considered to be clinically meaningful.

Effects of Baloxavir Marboxil or its Active Metabolite Baloxavir on other medicines

In in vitro studies at clinically relevant concentrations, baloxavir marboxil and its active metabolite, baloxavir did not inhibit any of the following isozymes of CYP or UGT family: CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, CYP3A4, UGT1A1, UGT1A3, UGT1A4, UGT1A6, UGT1A9, UGT2B7, and UGT2B15 isozymes).

In in vitro studies at clinically relevant concentrations, baloxavir marboxil and baloxavir did not cause significant induction of CYP1A2, CYP2B6, and CYP3A4. In in vitro transporter studies at clinically relevant concentrations, baloxavir marboxil and baloxavir inhibited the efflux transporter (P-gp). Baloxavir but not baloxavir marboxil inhibited BCRP.

Based on in vitro transporter studies, despite a weak in vitro inhibitory potential, baloxavir is not expected to be an in vivo inhibitor of OATP1B1, OATP1B3, OCT1, OCT2, OAT1, OAT3, MATE1, or MATE2K, hence no relevant pharmacokinetic interaction is anticipated between baloxavir and medicines which are substrates of these transporters.

A single 40 mg dose of baloxavir marboxil did not affect the pharmacokinetics of midazolam, a substrate of CYP3A4, suggesting that baloxavir marboxil or baloxavir is not expected to affect the pharmacokinetics of co-administered medicines that are substrates of CYP3A.

A single 80 mg dose of baloxavir marboxil did not affect the pharmacokinetics of digoxin, a substrate of P-gp, suggesting that baloxavir marboxil or baloxavir is not expected to affect the pharmacokinetics of co-administered medicines that are substrates of P-gp.

A single 80 mg dose of baloxavir marboxil decreased Cmax and AUC0-inf of rosuvastatin, a substrate of BCRP, by 18 % and 17 %, respectively. These decreases are not considered to be clinically meaningful and indicate that baloxavir marboxil or baloxavir is not expected to affect the pharmacokinetics of co-administered drugs that are substrates of BCRP.

4.6 Fertility, pregnancy and lactation

Pregnancy

Xofluza should be avoided during pregnancy.The potential risk of Xofluza in pregnant women is unknown.

Xofluza given to pregnant rabbits caused maternal toxicity resulting in miscarriages and an increase in the incidence of skeletal abnormalities.

Breastfeeding/Lactation

The safety of Xofluza during lactation has not been established. Use of Xofluza during lactation is not recommended. It is not known whether baloxavir marboxil and the active metabolite, baloxavir, are excreted in human breast milk. When dosed at 1 mg/kg, baloxavir marboxil or its metabolites are secreted in the milk of lactating rats.

Labour and Delivery

The safe use of Xofluza during labor and delivery has not been established.

Fertility

No effects on fertility were observed in animal studies performed with Xofluza.

4.7 Effects on ability to drive and use machines.

No studies on the effects on the ability to drive and to use machines have been performed.

4.8 Undesirable effects

Clinical Trials

The overall safety profile of Xofluza is based on data from 2 483 subjects in 18 clinical trials receiving Xofluza.

Treatment of influenza

No adverse drug reactions were observed on pooled data from 3 placebo controlled clinical studies (studies 1518T0821, 1601T0831and 1602T0832) in adult and adolescent patients, in which a total of 1 640 patients received Xofluza.

This included otherwise healthy adults, and adolescents and patients at high risk of developing complications associated with influenza,e.g. elderly patients and patients with chronic cardiac or respiratory disease.1 334 patients (81,3 %) were adults ≥ 18 years to ≤ 64 years, 209 patients (12,7 %) were adults ≥ 65 years and 97 patients (5,9 %) were adolescents (≥ 12 years to < 18 years). Of these, 1 440 patients received Xofluza at 40 mg and 80 mg doses and 100 patients each received 10 mg or 20 mg doses. The safety profile in patients at high risk was similar to that in otherwise healthy adults and adolescents

Post-exposure prophylaxis of Influenza

No adverse drug reactions have been identified based on a placebo-controlled clinical study (study 1719T0834), in which a total of 374 subjects received Xofluza. The safety profile of Xofluza administered for post-exposure prophylaxis of influenza is comparable to the safety profile established for the treatment of influenza

Table 2 Incidence of adverse events occurring in ≥ 1 % of subjects receiving Xofluza in the acute uncomplicated influenza trials

Adverse Event	**Xofluza (N- 710)**	**Placebo (N = 409)**
Diarrhoea	3 %	5 %
Bronchitis	2 %	4 %
Nausea	1 %	1 %
Nasopharyngitis	1 %	1 %
Headache	1 %	2 %

Post marketing experience

The following adverse drug reactions have been identified from postmarketing Experience with baloxavir marboxil (Table 3) based on spontaneous case reports and cases from non-interventional study programs. Adverse drug reactions are listed according to system organ classes in MedDRA and the corresponding frequency category estimation for each adverse drug reaction is based on the following convention.

Table 3 Adverse drug reactions from post marketing experience

Adverse reactions	**Frequency Category**
Anaphylaxis	Unknown[1]
Anaphylactic reactions	Unknown[1]
Hypersensitivity	Unknown[1]
Skin and subcutaneous disorders	
Urticaria	Uncommon[2]
Angioedema	Unknown[1]

[1] Not observed in clinical trials. As these events are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency.

[2] Calculated from frequency of events in completed clinical studies.

Hypersensitivity reactions have been observed in the postmarketing setting which include reports of anaphylaxis/anaphylactic reactions and less severe forms of hypersensitivity reactions including urticaria and angioedema.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare

professionals are asked to report any suspected adverse reactions to SAHPRA via he 6.04 Adverse Drug Reaction Report Form , found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

Clinical experience

Reports of overdoses with Xofluza have been received from clinical trials and during postmarketing experience. In the majority of cases reporting overdose, no adverse events were reported. Whilst a limited number of cases of overdose have been reported in association with adverse events, data are insufficient to determine what symptoms may be anticipated as a result of an overdose

Management:

No known specific antidote exists for Xofluza. In the event of overdose, standard supportive medical care should be initiated based on the patient's signs and symptoms. Xofluza is unlikely to be significantly removed by dialysis due to high serum protein binding.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antiviral agents, ATC Code: J05AX25

Mechanism of Action

Baloxavir marboxil is a prodrug that is converted by hydrolysis to, baloxavir, the active form that exerts anti-influenza activity. Baloxavir acts on the cap-dependent endonuclease (CEN), an influenza virus-specific enzyme in the polymerase acidic (PA) subunit of the viral RNA polymerase complex and thereby inhibits the transcription of influenza virus genomes resulting in inhibition of influenza virus replication. The 50% inhibition concentration (IC50) of baloxavir was 1.4 to 3.1

nmol/L for influenza A viruses and 4.5 to 8.9 nmol/L for influenza B viruses in an enzyme inhibition assay.

Nonclinical studies demonstrate potent antiviral activity of baloxavir against influenza A and B virus in vitro and in vivo. The antiviral activity of baloxavir against laboratory strains and clinical isolates of influenza A and B viruses was determined in the MDCK cell culture assay. The median 50 % effective concentration (EC50) values of baloxavir were 0,73 nmol/L (n=31; range: 0,20-1,85 nmol/) for subtype A/H1N1 strains, 0,83 nmol/L (n=33; range: 0,35-2,63 nmol/L) for subtype A/H3N2 strains, and 5,97 nmol/L (n=30; range: 2,67-14,23 nmol/L) for type B strains. In a MDCK cell-based virus titre reduction assay, the 90 % effective concentration (EC90) values of baloxavir were in the range of 0,46 to 0,98 nmol/L for subtype A/H1N1 and A/H3N2 viruses, 0,80 to 3,16 nmol/L for avian subtype A/H5N1 and A/H7N9 viruses, and 2,21 to 6,48 nmol/L for type B viruses.

Viruses bearing the PA/I38T/M/F/N/S mutation selected in vitro or in clinical studies show reduced susceptibility to baloxavir. Baloxavir is active against neuraminidase inhibitor resistant strains including H274Y in A/H1N1, E119V and R292K in A/H3N2, and R152K and D198E in type B virus, H274Y in A/H5N1, R292K in A/H7N9. The relationship between antiviral activity in cell culture and inhibition of influenza virus replication in humans has not been established. At twice the expected exposure from recommended dosing, Xofluza did not prolong the QTc interval.

5.2 Pharmacokinetic properties

After oral administration, baloxavir marboxil is extensively converted to its active metabolite, baloxavir, predominantly by arylacetamide deacetylase in the gastrointestinal lumen, intestinal epithelium, and liver.

The plasma concentration of baloxavir marboxil was very low or below the limit of quantitation (< 0,100 ng/mL).

The pharmacokinetic parameters of baloxavir in Japanese healthy adult subjects after a single oral administration of 40 mg baloxavir marboxil in the fasted and fed states are summarised in Table 4. The pharmacokinetic parameters of baloxavir in Caucasian healthy adult subjects after a single oral administration of 80 mg baloxavir marboxil in the fasted state are summarised in Table 5.

Table 4 Pharmacokinetic parameters of plasma baloxavir in Japanese healthy subjects after administration of a single oral dose of 40 mg baloxavir marboxil in the fasted and fed state.

Parameters	**Geometric Mean (CV %)**	
	Fasted	**Fed**
N	14	14
C_{max} (ng/m)	130 (24,1)	67,6 (40,0)
T_{max} [a] (hr)	4,00 (3,00, 5,00)	4,00 (0,50, 5,00)
$AUC_{0\text{-}las}$ (ng hr/m)	6 932 (19,2)	4 406 (38,8)
$AUC_{0\text{-}inf}$ (ng hr/m)	7 086 (19,6)	4 540 (39,1)
$t_{1/2,}$ (hr)	93,9 (21,6)	97,5 (22,8)
CL/F (/hr)	4,78 (19,6)	7,45 (39,1)
V_z /F ( )	647 (19,1)	1 050 (35,6)

a Median (Min, Max)

Table 5: Pharmacokinetic parameters of plasma baloxavir in Caucasian healthy subjects after administration of a single oral dose of 80 mg of baloxavir marboxil in the fasted state (Study 1612T081C)

Parameters	**Geometric Mean (CV %)**
N	12
Cmax (ng/mL)	145 (25,4)
$AUC_{0\text{-}las}$ (ng hr/mL)	6 305 (21,2)
$AUC_{0\text{-}inf}$ (ng hr/mL)	6 551 (22,5)

t1/2,z (hr)	79,1 (22,4)
CL/F (ℓ/hr)	10,3 (22,5)

Absorption

Following a single oral administration of 80 mg of baloxavir marboxil, peak plasma concentration (T_{max}) of baloxavir was reached at approximately 4 hours in the fasted state. The absolute bioavailability of baloxavir marboxil has not been established.

Food effect

A food-effect study involving administration of baloxavir marboxil to healthy volunteers under fasting conditions and with a meal (approximately 400 to 500 kcal including 150 kcal from fat) indicated that the C_{max} and AUC of baloxavir were decreased by 48 % and 36 %, respectively, under fed conditions. T_{max} was unchanged in the presence of food. In clinical studies with influenza patients where baloxavir marboxil was administered with or without food, no clinically relevant differences in efficacy were observed.

Distribution

In an in vitro study, the binding of baloxavir to human serum proteins, primarily albumin, is 92, 9 % to 93,9 %. The apparent volume of distribution of baloxavir following a single oral administration of 80 mg of baloxavir marboxil approximately 1 180 L in Caucasian patients and 647 L in Japanese subjects.

Metabolism

In vitro studies revealed that arylacetamide deacetylase in the gastrointestinal lumen, intestinal epithelium, and the liver mainly contributes to the conversion from baloxavir marboxil to baloxavir and baloxavir is primarily metabolised by UGT1A3 with minor contribution from CYP3A4.

In the human mass balance study, after administration of a single oral dose of 40mg of [14C]-labeled baloxavir marboxil, baloxavir accounted for 82,2 % of the plasma AUC for total radioactivity. Baloxavir glucuronide (16,4 % of the plasma AUC for total radioactivity) and (12aR,5R,11S) sulfoxide of baloxavir (1,5 % of the plasma AUC for total radioactivity) were also detected in plasma, confirming that the in vivo metabolism of baloxavir marboxil occurs via ester hydrolysis to form baloxavir with subsequent metabolism of baloxavir to form sulfoxides, and a glucuronide.

Excretion

Baloxavir marboxil and baloxavir were excreted mainly via the faecal route in humans. Following a single oral administration of 40 mg of [^{14}C]-labelled baloxavir marboxil, the proportion of total radioactivity excreted in faeces was 80,1 % of the administered dose and 14,7% was excreted in urine. The amount of baloxavir excreted in the urine was 3,3 % of the administered dose.

Elimination

The apparent terminal elimination half-life (t1/2,z) of baloxavir after a single oral administration of baloxavir marboxil is 79,1 hours in Caucasian patients, and 93,9 hours in Japanese subjects, see Tables 1 and 2.

Linearity/non-linearity

Following single oral administration of baloxavir marboxil, baloxavir exhibits linear pharmacokinetics in the fasted state within the dose range of 6 mg to 80 mg.

Pharmacokinetics in Special Populations

Body weight

Body weight is identified as the significant covariate based on the population pharmacokinetic analysis. The dose proposed in adults is 40 mg for patients with body weight 40 kg to < 80 kg, and 80 mg for patients with body weight ≥ 80 kg.

Gender

A population pharmacokinetic analysis did not identify a clinically meaningful effect of gender on the pharmacokinetics of baloxavir. No dose adjustment based on gender is required.

Race

Based on a population pharmacokinetic analysis, race is a covariate on CL-F of baloxavir in addition to body weight; however, no dose adjustment of baloxavir marboxil based on race is required.

Age

A population pharmacokinetic analysis using plasma baloxavir concentrations from clinical studies with baloxavir marboxil for subjects aged 12 to 64 years did not identify a clinically meaningful effect of age on the pharmacokinetics of baloxavir.

Paediatric Population

The pharmacokinetics of baloxavir in paediatric patients (< 12 years of age) has not been established.

Elderly Population

Pharmacokinetic data collected in patients ≥ 65 years show that exposure to baloxavir was similar to patients aged ≥ 12 to 64 years.

Renal impairment

The effects of renal impairment on the pharmacokinetics of baloxavir marboxil or baloxavir have not been evaluated. Renal impairment is not expected to alter the elimination of

baloxavir marboxil or baloxavir. Renal excretion represents a minor pathway of elimination for baloxavir marboxil or baloxavir. A population pharmacokinetic analysis did not identify a clinically meaningful effect of renal
function on the pharmacokinetics of baloxavir. No dose adjustment is required in patients with renal impairment. Baloxavir is unlikely to be significantly removed by dialysis.

Hepatic impairment

Geometric mean ratios (90 % confidence interval) of C_{max} and AUC of baloxavir in patients with moderate hepatic impairment (Child-Pugh class B) compared to healthy controls were 0,80 (0,50 - 1,28) and 1,12 (0,78 - 1,61), respectively.

Since no clinically meaningful differences in the pharmacokinetics of baloxavir were observed in patients with moderate hepatic impairment (Child-Pugh class B)
compared with healthy controls with normal hepatic function, no dose adjustment is required in patients with mild or moderate hepatic impairment. The pharmacokinetics in patients with severe hepatic impairment has not been evaluated.

Summary of clinical studies

Treatment of Influenza

Otherwise healthy patients

Study 1601T0831

Study 1601T0831 is a randomised, double-blind, multicentre, placebo- and active-controlled study designed to evaluate the efficacy and safety of single oral dose of baloxavir compared with placebo or oseltamivir in otherwise healthy adult and adolescent patients (aged ≥ 12 years to ≤ 64 years) with influenza.

A total of 1 436 patients were randomised to receive treatment in the 2016-2017 Northern Hemisphere influenza season. Patients were randomised to receive 40 mg or 80 mg of baloxavir according to weight (< 80 kg or 80 kg respectively), oseltamivir 75 mg twice daily for 5 days (if aged > 20 years) or placebo. The predominant influenza virus strain in this study was the A/H3 subtype (84,8 % to 88,1 %) followed by the B type (8,3 % to 9,0 %) and the A/H1N1pdm subtype (0,5 % to 3,0 %). The primary efficacy endpoint was time to alleviation of symptoms (cough, sore throat, headache, nasal congestion, feverishness or chills, muscle or joint pain, and fatigue). A
statistically significant and clinically meaningful improvement in the primary endpoint was seen for baloxavir when compared with placebo, see Table 6.

Table 6 Time alleviation of symptoms in otherwise healthy patients with influenza (baloxavir vs placebo)

Time to Alleviation of Symptoms (Median [hours])			
Baloxavir 40/80 mg (95 % CI) N=455	Placebo (95 % CI) N=230	Difference between Baloxavir and placebo (95 % CI for difference)	P-value
53,7 (49,5, 58,5)	80,2 (72,6, 87,1)	-26,5 (35,8, 17,8)	< 0,0001

When the baloxavir group was compared to the oseltamivir group, there was no statistically significant difference in time to alleviation of symptoms (53,5 h s 53,8 h respectively), see Table 7.

Table 7 Time to alleviation of symptoms in otherwise healthy patients with influenza (≥ 20 years of age), (Baloxavir vs Oseltamivir)

Time to Alleviation of Symptoms (Median [hours])			
Baloxavir 40/80 mg (95 % CI) N=375	Oseltamivir (95 % CI) N=377	Difference between Baloxavir and Oseltamivir (95 % CI for difference)	P-value
53,5 (48,0, 58,5)	53,8 (50,2, 56,4)	-0,3 (6,6, 6,6)	0,7560

CI: Confidence interval

Secondary endpoints included time to resolution of fever and culture-based assessment of time to cessation of viral shedding (by virus titre).

Resolution of fever

Following study medicine administration there was faster resolution of fever in the baloxavir group compared with the placebo group. The median time to resolution of fever in patients treated with baloxavir was 24,5 hours (95 % CI: 22,6, 26,6) compared with 42,0 hours (95 % CI: 37,4, 44,6) in those receiving placebo. No difference was noted in duration of fever in the baloxavir group compared with the oseltamivir group.

Antiviral Activity

Patients treated with baloxavir showed a rapid reduction in virus titre. The median time to cessation of viral shedding determined by virus titre was 24,0 hours (95 % CI: 24,0, 48,0) in the baloxavir group compared with 72 hours (95 % CI: 72,0, 96,0) in the oseltamivir group and 96,0 hours (95 %CI: 96,0, 96,0) in the placebo group.

Study 1518T0821

The phase 2 study was designed to evaluate the efficacy and safety of a single oral dose of baloxavir compared with placebo in otherwise healthy adult patients (aged ≥ 20 years to ≤ 64 years) with influenza. A total of 400 patients were randomised to one of three dose groups of baloxavir (10, 20 or 40 mg) or placebo in the 2015-2016 Northern Hemisphere influenza season in Japan. The predominant influenza virus strain as A/H1N1pdm subtype (61 % to 71 %) followed by B subtype (21 % to 24 %) and A/H3N2 subtype (5 % to 13 %). The median time to alleviation of symptoms was significantly shorter ($p < 0,05$) compared with placebo in all dose groups. At 40 mg the median time to alleviation of symptoms was 49,5 hours (95 % CI: 44,5, 64,4) in the baloxavir group versus 77,7 hours (96 % CI: 67,6, 88,7) in the placebo group.

Resolution of Fever

The median time to resolution of fever was significantly reduced in all dose groups compared with placebo. At 40 mg the median time was 28,9 hours (95 % CI: 24,5, 34,7) versus 45,3 hours (95 % CI: 35,6, 54,0) in the placebo group. Viral endpoint results were consistent with those in study 1601T0831.

Study 1602T0832

Study 1602T0832 is a randomised, double-blind, multicentre, placebo- and active controlled study designed to evaluate the efficacy and safety of single oral dose of baloxavir compared with placebo or oseltamivir in adult and adolescent patients (aged ≥ 12 years) with influenza at high risk of influenza complications (e.g. asthma or chronic lung disease, endocrine disorders, heart disease, age ≥ 65 years, metabolic disorders, morbid obesity).

A total of 2 184 patients were randomised to receive a single oral dose of 40 mg or 80 mg of baloxavir according to body weight 40 to < 80kg or ≥ 80kg respectively), oseltamivir 75 mg

twice daily for 5 days, or placebo. The predominant influenza viruses in this study were the A/H3 subtype (46,9 % to 48,8 %) and influenza B (38,3 % to 43,5 %).

The primary efficacy endpoint was time to improvement of influenza symptoms (cough, sore throat, headache, nasal congestion, feverishness or chills, muscle or joint pain, and fatigue). A statistically significant improvement in the primary endpoint was observed for baloxavir when compared with placebo, see Table 8.

Time to Improvement of Influenza Symptoms (Baloxavir vs Placebo)

Time to Improvement of Influenza Symptoms (Median [hours])			
Baloxavir 40/80 mg (95 % CI) N=385	***Placebo (95 % CI) N=385***	***Difference between Baloxavir and placebo (95 % CI for difference)***	***P-value***
73,2 (67,5, 85,1)	***102,3 (92,7, 113,1)***	***-29,1 (42,8, 14,6)***	***< 0,0001***

When the baloxavir group was compared to the oseltamivir group, there was no statistically significant difference in time to improvement of influenza symptoms (73,2 h vs 81,0 h respectively), see Table 9.

Table 9 Time to Improvement of Influenza Symptoms (Baloxavir vs Oseltamivir)

Time to Improvement of Influenza Symptoms (Median hours)			
Baloxavir 40/80 mg (95 % CI) N=385	Oseltamivir (95 % CI) N=388	Difference between Baloxavir and Oseltamivir (95 % CI for	P-value

		difference)	
73,2 (67,5, 85,1)	81,0 (69,4, 91,5)	-7,7 (−22,7, 7,9)	0.8347

Virus Subtype

For patients infected with type A/H3 virus (predominant strain), the median time to improvement of influenza symptoms was statistically significantly shorter in the baloxavir group compared with the placebo group but not compared with the oseltamivir group (see Table 9). In the subgroup of patients infected with type B virus, the median time to improvement of influenza symptoms was statistically significantly shorter in the baloxavir group compared with both the placebo and oseltamivir group.

Table 10 Time to Improvement of Symptoms by Influenza Virus Subtype

Time to Improvement of Symptoms (Hours) Median [95 % CI]			
Virus	Baloxavir	Placebo	Oseltamivir
A/H3	75,4 [62,4, 91,6] N= 180	100,4 [88,4, 113,4] N= 185	68,2 [53,9, 81,0] N= 190
B	74,6 [67,4, 90,2) N= 166	100,6 [82,8, 115,8] N= 167	101,6 [90,5, 114,9] N= 148

Resolution of Fever

The proportion of patients who had fever was reduced more rapidly in the baloxavir group than in the placebo group following study medicine administration. The median time to resolution of fever was 30,8 hours (95 % CI: 28,2, 35,4) in the baloxavir group compared with

50,7 hours (95 % CI: 44,6, 58,8) in the placebo group. No significant differences between the baloxavir group and the oseltamivir group were observed.

Incidence of Influenza-Related Complications

The overall incidence of influenza-related complications (death, hospitalisation, sinusitis, otitis media, bronchitis, and/or pneumonia) was 2,8 % (11/388 patients) in the baloxavir group compared with 10,4 % (40/386 patients) in the placebo group and 4,6 % (18/389 patients) in the oseltamivir group.

The lower overall incidence of influenza-related complications in the baloxavir marboxil group compared with the placebo group was mainly driven by lower incidences of bronchitis (1,8 % vs. 6,0 %, respectively) and sinusitis (0,3 % vs. 2,1 %,respectively).

The proportion of patients requiring systemic antibiotics for infections secondary to influenza infection was lower in the baloxavir group (3,4 %) compared with the placebo group (7,5 %), and the difference between these 2 groups was statistically significant
(p = 0,0112). The proportion of patients requiring systemic antibiotics in the baloxavir group was comparable with the proportion in the oseltamivir group (3,9 %).

Antiviral Activity

Patients at high risk of influenza complications, treated with baloxavir, showed a rapid reduction in virus titre and a significantly shortened time to cessation of viral shedding. The median time to cessation of viral shedding determined by virus titre was 48 hours in the baloxavir group compared with 96 hours in the placebo group and the oseltamivir group.

Post-exposure prophylaxis of influenza

Study 1719T0834

Study 1719T0834 was a phase 3, randomised, double-blind, multicenter, placebo-controlled

study designed to evaluate the efficacy of a single oral dose of Xofluza compared with placebo in the prevention of influenza in subjects who are household members of influenza-infected patients. Influenza-infected index patients were required to have onset of symptoms for ≤ 48 hours and subjects were required to have lived with the influenza-infected index patients for > 48 hours.

A total of 749 subjects were randomized and received a single oral dose of Xofluza, according to body weight and age, or placebo, on Day 1. Subjects 12 years of age and over received 40 mg or 80 mg of Xofluza according to weight (40 to < 80kg or ≥ 80kg respectively). Subjects under 12 years of age were dosed according to body weight.

The predominant influenza virus strains in the index patients of this study were the A/H3NX subtype (48.4% to 48.8%) and the A/H1N1pdm subtype (47.1% to 48.0%) followed by the B subtype (0.5% to 0.8%) according to household contact groups Xofluza and placebo, respectively. The primary efficacy endpoint was the proportion of household subjects who were infected with influenza virus and presented with fever and at least one respiratory symptom in the period from Day 1 to Day 10. Influenza virus positivity was assessed by reverse transcription polymerase chain reaction (RT-PCR), fever was defined as a body temperature (axillary) ≥ 37.5°C, and respiratory symptoms were defined as having a symptom of ‘cough’ or ‘nasal discharge/nasal congestion’ with a severity of ‘2, Moderate’ or ‘3, Severe’ as assessed in the subject diary.
There was a statistically significant reduction in the proportion of subjects with laboratory-confirmed clinical influenza from 13.6% in the placebo group to 1.9% in the baloxavir marboxil group (see Table 11)

Proportion of Subjects with Influenza Virus, Fever, and at least one Respiratory Symptom (%) mITT population			
Baloxavir marboxil (95% CI)	Placebo (95% CI)	Risk Ratio (95% CI for risk ratio)	P-value
N=374 1.9 (0.8, 3.8)	N=375 13.6 (10.3, 17.5)	0.14 (0.06, 0.30)	< 0.0001
Proportion of Subjects ≥ 12 years with Influenza Virus, Fever, and at least one Respiratory Symptom (%)			
N=303 1.3 (0.4, 3.3)	N=304 13.2 (9.6, 17.5)	0.10 (0.04, 0.28)	< 0.0001

The analysis for the secondary endpoint of proportion of subjects with influenza virus infection (RT-PCR positive regardless of clinical symptoms) in the period from Day 1 to Day 10 demonstrated results consistent with the primary endpoint. There was a reduction in the proportion of subjects with influenza virus infection from 30.4% (95% CI: 25.8, 35.3) in the placebo group to 13.1% (95% CI: 9.9, 16.9) in the baloxavir marboxil group.

Resistance Monitoring during Clinical Development

Cell culture: Influenza A virus isolates with reduced susceptibility to baloxavir have been detected by serial passage of virus in cell culture in the presence of increasing concentrations of baloxavir. Reduced susceptibility of influenza A virus to baloxavir was observed in amino acid substitutions I38T (H1N1 and H3N2) and E199G (H3N2) in the polymerase acidic (PA) protein of the viral RNA polymerase complex. Influenza B virus isolates with reduced susceptibility to baloxavir have not been detected in cell culture.

Clinical studies: Influenza A virus isolates with treatment-emergent amino acid substitutions at position PA/I38T/F/M associated with > 10 fold reduced susceptibility to baloxavir were observed in clinical studies. The clinical impact of this reduced susceptibility is unknown.

No pre-treatment isolates, with amino acid substitutions associated with reduced susceptibility to baloxavir, were found in the clinical studies or in the National Centre for Biotechnology Information/Influenza virus resources database. Medical practitioners should consider available information from the National Institute for Communicable Diseases (NICD) on influenza virus susceptibility patterns and treatment effects when deciding whether to use baloxavir.

In the phase 3 study in otherwise healthy patients (1601T0831), PA/I38T/M were detected in 36 of 370 patients in the baloxavir treatment group. In the phase 3 study in high risk patients (1602T0832), PA/I38T/M/N were detected in 15 of 290 patients in the baloxavir treatment group.

Cross Resistance

No single amino acid substitution has been identified that could confer cross resistance between baloxavir and neuraminidase inhibitors (e.g., peramivir, oseltamivir, zanamivir). However, a virus may carry amino acid substitutions associated with reduced susceptibility to baloxavir in the PA protein and to neuraminidase inhibitors in the neuraminidase and may therefore exhibit reduced susceptibility to both classes of inhibitors. The clinical relevance of phenotypic cross resistance evaluations has not been established.

Immunogenicity

Immune Response

Interaction studies with influenza vaccines and baloxavir marboxil have not been conducted.

In studies of naturally acquired and experimental influenza, treatment with baloxavir did not impair normal humoral antibody response to infection.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Excipients - Core: croscarmellose sodium, lactose monohydrate, microcrystalline cellulose, povidone K25, and sodium stearyl fumarate.

Excipients Film coat: hypromellose, talc and titanium dioxide (E171).

Contains sugar (lactose monohydrate)

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store tablets at or below 30 °C

Store blister in outer carton until required for use, in order to protect from moisture and light.

Store out of reach of children.

Do not use after the expiry date (EXP) shown on the pack.

6.5 Nature and contents of container

20 mg tablets: Aluminium blister packs containing 2 or 4 tablets.

40 mg tablets: Aluminium blister packs containing 1 or 2 tablets.

Not all packs may be marketed.

6.6 Special precautions for disposal and other handling

Disposal of unused/expired medicines

The release of pharmaceuticals in the environment should be minimised. Medicines should not be disposed of via wastewater and disposal through household waste should be avoided. Use established collection systems, if available in your location.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Roche Products (Pty) Ltd

90 Bekker Road, Hertford Office Park,

Building E, Vorna Valley, Midrand,

Johannesburg, 1686

South Africa

Roche Ethical Assistance Line (REAL) toll-free: 0800 21 21 25

8. REGISTRATION NUMBER(S)

Xofluza 20 mg: 55/20.2.8/0333

Xofluza 40 mg: 55/20.2.8/0334

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Registration: 09 February 2021

10. DATE OF REVISION OF THE TEXT

Last revision: 05 May 2023

Approved Manufacturer(s):

Shionogi Pharma Co., Ltd., Settsu Plant

5-1, Mishima 2-chome

Settsu, Osaka 566-0022

Botswana:	NS2	BOT2103783/A BOT2103784/A

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS

S4

Xofluza® 20 mg Film-coated tablets

Xofluza® 40 mg Film-coated tablets

Baloxavir marboxil

Contains sugar (Each 20 mg tablet contains 77,9 mg of lactose monohydrate and 40 mg tablet contains 155,8 mg of lactose monohydrate)

Read all of this leaflet carefully before you start taking Xofluza

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist
- Xofluza has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What Xofluza is and what it is used for

- Xofluza is used for treatment of influenza (flu) 12 years of age or older, who have experienced flu symptoms for no more than 48 hours and/or you are at high risk of developing influenza complications.
- Xofluza is used to prevent influenza in individuals aged 12 years and older who have been in close contact with someone who is known or suspected to have influenza.

2. What you need to know before you use Xofluza

You should not take Xofluza:

- If you are hypersensitive (allergic) to baloxavir marboxil, or to any of the other ingredients of Xofluza.

Warnings and precautions

Take special care with Xofluza

Talk to your healthcare provider before you receive a live flu vaccine after you have taken Xofluza as no interaction studies with flu vaccines have been performed.

Children and adolescents

Do not take Xofluza if you are less than 12 years of age or weigh less than 40kg.

Other medicines and Xofluza

Taking other medicines with Xofluza

Always tell your healthcare professional if you are taking any other medicine. (This includes complementary or traditional medicines).

Taking Xofluza with food and drink

Xofluza can be taken with or without food.

Do not take Xofluza with calcium fortified beverages, laxatives, antacids or oral supplements containing iron, zinc, selenium, calcium or magnesium as they could interact with Xofluza and it will not work as well as it should.

Do not take Xofluza with dairy products or calcium fortified beverages, as it may not work so well. See “Taking other medicines with Xofluza” below.

Pregnancy and breastfeeding

Pregnancy

Tell your doctor If you are pregnant or plan to become pregnant. This is because it is not known if Xofluza can harm your inborn baby.

Breastfeeding

Tell your doctor if you are or are breastfeeding or plan to breastfeed your baby. This is because it is not known if Xofluza passes into your breast milk.

If you are pregnant or breastfeeding your baby, please consult your doctor pharmacist or other healthcare professional for advice before being taking Xofluza.

Driving and using machines

It is not known whether taking Xofluza will affect your ability to drive or use machines. However if you experience symptoms such as delirium or fever while you are taking Xofluza, do not drive or use machines until the symptoms disappear.

Important information about some of the ingredients of Xofluza

Xofluza contains lactose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking Xofluza.

Xofluza contains lactose which may have an effect on the control of your blood sugar if you have diabetes mellitus.

3. How to take Xofluza

Do not share medicines prescribed for you with any other person.

Always take Xofluza exactly as your doctor has instructed you. You should check with your doctor if you are unsure.

Your doctor will prescribe one dose of Xofluza and will tell you how many tablets to take depending on your weight. You can take Xofluza with or without food.

Your doctor will tell you how long your treatment with Xofluza will last. If you have the impression that the effect of Xofluza is too strong or too weak, tell your doctor or pharmacist.

If you take more Xofluza than you should:

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison control centre.

If you forget to take Xofluza:

As Xofluza is taken as a single dose, take the dose as soon as you remember. If it is more than 48 hours after you showed flu symptoms, contact your doctor for advice

If you stop taking Xofluza:

Xofluza is given as a single dose therefore no effects after stopping taking Xofluza are expected.

4. Possible side effects

Xofluza can have side effects

Not all side effects reported for Xofluza are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking Xofluza, please consult your doctor, pharmacist or healthcare professional for advice.

The most frequent side effects of Xofluza include:

- Diarrhoea
- Bronchitis
- Common cold symptoms (nasopharyngitis)
- Headache
- Nausea

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions to SAHPRA via the "6.04 Adverse Drug Reaction Report Form", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

5. How to store Xofluza

Store tablets at or below 30 C.

Store blister in outer carton until required for use, in order to protect from moisture and light.

Store all medicines out of reach of children.

Keep blister packs in outer container until required for use.

Do not use this medicine after the expiry date (EXP) stated on the outer carton.

Disposal of unused/expired medicine:

The release of pharmaceuticals in the environment should be minimised. Medicines should not be disposed of via wastewater and disposal through household waste should be avoided. Use established collection systems, if available in your location.

6. Contents of the pack and other information

What Xofluza contains

Each Xofluza 20 mg tablet contains 20 mg baloxavir marboxil.

Each Xofluza 40 mg tablet contains 40 mg baloxavir marboxil.

Excipients - Core: croscarmellose sodium, lactose monohydrate, microcrystalline cellulose, povidone K25 and sodium stearyl fumarate.

Excipients – Film coat: hypromellose, talc and titanium dioxide (E171). Contains sugar (77, 9 mg lactose monohydrate of the 20 mg and 155, 8 mg lactose monohydarte of the 40 mg)

What Xofluza looks like and contents of the pack

Xofluza 20 mg: White to light yellow, oblong shaped film-coated tablets debossed with “772” on the one side and “20” on the other side.

Xofluza 40 mg: White to light yellow, oblong shaped film-coated tablets debossed with “BXM40” on the one side.

20 mg tablets: Aluminium blister packs containing 2 or 4 tablets.

40 mg tablets: Aluminium blister packs containing 1 or 2 tablets.

Not all packs may be marketed.

7. Holder of Certificate of Registration

Roche Products (Pty) Ltd

Roche Products (Pty) Ltd

90 Bekker Road, Hertford Office Park,

Building E, Vorna Valley, Midrand,

Johannesburg, 1686

South Africa

Roche Ethical Assistance Line (REAL) toll-free: 0800 21 21 25

8. Registration number(s)

Xofluza 20 mg: 55/20.2.8/0333

Xofluza 40 mg: 55/20.2.8/0334

Last Revision: 05 May 2023

Botswana:	NS2	BOT2103783/A BOT2103784/A

PASIËNTINLIGTINGSBLAADJIE

SKEDULERINGSTATUS

S4

Xofluza® 20 mg Filmbedekte tablette

Xofluza® 40 mg Filmbedekte tablette

Baloxavir marboxil

Bevat suiker (Elke 20 mg tablet bevat 77,9 mg van laktose-monohidraat en 40 mg tablet bevat 155,8 mg van laktose-monohidraat)

Lees hierdie hele blaadjie noukeurig deur voor u begin om Xofluza te gebruik.

- Hou hierdie blaadjie. U sal dit dalk later weer moet lees.
- As u verdere vrae het, vra asseblief u dokter of u apteker.
- Xofluza is vir u persoonlik voorgeskryf en u moenie u medisyne met ander mense deel nie. Dit kan skadelik vir hulle wees, selfs al stem hulle simptome met u s'n ooreen.

Wat is in hierdie blaadjie

1. Wat Xofluza is en waarvoor dit gebruik word

- Xofluza word gebruik vir die behandeling van influensa (griep) in persone 12 jaar of ouer wat griepsimptome vir nie langer as 48 uur ervaar het nie en/of wat ’n hoë risiko loop om influensa-komplikasies te ontwikkel.
- Xofluza word gebruik om influensa te voorkom in individue 12 jaar en ouer wat in nabye kontak was met iemand wat influensa het of vermoedelik influensa het.

2. Wat u moet weet voor u Xofluza gebruik

U moet nie Xofluza neem nie:

- as u hipersensitief (allergies) is vir baloksavier marboksiel, of enige van die ander bestanddele van Xofluza.

Waarskuwings en voorsorgmaatreëls

Neem spesiale sorg met Xofluza

Praat met u gesondheidsorgverskaffer voordat u ’n lewende griepvaksien kry nadat u Xofluza geneem het, aangesien daar nog geen wisselwerkingstudies met griepvaksiene gedoen is nie.

Kinders en adolessente

Moenie Xofluza neem as jy jonger as 12 jaar is of minder as 40 kg weeg nie

Ander medisyne en Xofluza

Neem van ander medisyne saam met Xofluza

Vertel altyd u gesondheidsorgkundige as u enige ander medisyne neem. (Dit sluit aanvullende of tradisionele medisyne in).

Moenie Xofluza gebruik saam met kalsiumgefortifiseerde drankies, purgeermiddels, teensure of mondelikse aanvullings wat yster, sink, seleen, kalsium of magnesium bevat nie, aangesien dit op Xofluza kan reageer en nie so goed sal werk as wat dit moet nie.

Die neem van Xofluza met kos en drank

U kan Xofluza met of sonder voedsel neem.

Moenie Xofluza saam met suiwelprodukte of kalsiumgefortifiseerde drankies neem nie, aangesien dit dalk nie so goed sal werk nie. Sien “Neem van ander medisyne saam met Xofluza” hier onder.

Swangerskap en borsvoeding

Swangerskap

Vertel u dokter as u swanger is of beplan om swanger te raak. Die rede hiervoor is dat dit nie bekend is of Xofluza u ongebore baba kan benadeel nie.

Borsvoeding

Vertel u dokter as u u baba borsvoed of beplan om te borsvoed. Die rede is dat dit nie bekend is of Xofluza in u borsmelk uitgeskei word nie.

As u swanger is of u baba borsvoed, raadpleeg asseblief u dokter, apteker of ander gesondheidsorgkundige vir raad voordat u Xofluza neem.

Motorbestuur en die gebruik van masjinerie

Dit is nie bekend of Xofluza u vermoë om te bestuur of met masjiene te werk sal affekteer nie. As u egter simptome soos delirium of koors ervaar terwyl u Xofluza neem, moenie bestuur of met masjiene werk totdat die simptome verdwyn nie.

Belangrike inligting oor ’n aantal bestanddele in Xofluza

Xofluza bevat laktose. Indien u dokter u vertel het dat u ’n intoleransie teenoor sekere suikers het, kontak u dokter voordat u Xofluza neem.

Xofluza bevat laktose wat ’n uitwerking op die beheer van u bloedsuiker kan hê as u diabetes mellitus het.

3. Hoe om Xofluza te gebruik

Moenie medisyne wat vir u voorgeskryf is, met enigiemand anders deel nie.

Neem Xofluza altyd presies volgens u dokter se aanwysings. U moet u dokter raadpleeg as u nie seker is nie.

U dokter sal een dosis Xofluza voorskryf en u vertel hoeveel tablette om te neem, afhangende van u gewig. U kan Xofluza met of sonder voedsel neem.

U dokter sal u sê hoe lank u behandeling met Xofluza sal duur. As u vermoed dat die effek van Xofluza te sterk of te swak is, praat met u dokter of apteker.

As u meer Xofluza neem as wat u moet:

In die geval van oordosering, raadpleeg u dokter of apteker. As nie een van hulle beskikbaar is nie, kontak die naaste hospitaal of gifsentrum.

As u vergeet om Xofluza te neem:

As Xofluza as ’n enkeldosis geneem word, neem die dosis sodra u onthou. As dit meer as 48 uur is nadat u griepsimptome getoon het, kontak u dokter vir advies.

As u ophou om Xofluza te neem:

Xofluza word as ’n enkeldosis gegee, dus word geen effekte verwag nadat opgehou word om Xofluza te neem nie.

4. Moontlike newe-effekte

Xofluza kan newe-effekte hê

Nie alle newe-effekte wat vir Xofluza aangemeld is, is in hierdie blaadjie ingesluit nie. As u algemene gesondheid vererger of as u enige ongunstige effekte ondervind terwyl u Xofluza neem, raadpleeg asseblief u dokter, apteker of gesondheidsorgkundige vir advies.

Die algemeenste newe-effekte van Xofluza sluit in:

- Diarree
- Brongitis
- Simptome van gewone verkoue (nasofaringitis)
- Hoofpyn
- Naarheid

Xofluza is nie effektief vir die behandeling of voorkoming van ander infeksies as influensa nie.

Indien u enige newe-effekte opmerk wat nie in hierdie blaadjie genoem word nie, stel asseblief u dokter of apteker in kennis.

Aanmelding van newe-effekte

Dit is belangrik om vermoedelik ongunstige reaksies ná magtiging van die medisyne aan te meld. Dit laat voortgesette monitering van die voordele/risiko-balans van die medisyne toe. Gesondheidsorgkundiges word gevra om enige vermoedelik ongunstige reaksies by SAHPRA aan te meld deur middel van die “6.04 Drug Reaction Report Form” wat aanlyn onder SAHPRA se publikasies gevind kan word: https://www.sahpra.org.za/Publications/Index/8

5. Hoe om Xofluza te bewaar

Bewaar tablette by of onder 30 °C.

‘Bewaar stulp in buitenste karton totdat dit vir gebruik nodig is ten einde dit teen vog en lig te beskerm’.

Bêre alle medisyne buite die bereik van kinders

Hou stulppakke in buitenste houer totdat dit vir gebruik nodig is.

Moenie hierdie medisyne gebruik na die vervaldatum (EXP) wat op die buitenste karton aangegee word nie.

Weggooi van ongebruikte medisyne/medisyne wat verval het:

Die vrystelling van farmaseutiese middels in die omgewing moet geminimaliseer word. Medisyne moenie met rioolwater of huishoudelike afval weggegooi word nie. Gebruik gevestigde insamelingstelsels indien in u gebied beskikbaar.

6. Inhoud van die pakkie en ander inligting

Wat Xofluza bevat

Elke 20 mg Xofluza-tablet bevat 20 mg baloksavier marboksiel.

Elke 40 mg Xofluza-tablet bevat 40 mg baloksavier marboksiel.

Geneesmiddeltoevoegings - Kern: kroskarmellose natrium, laktose-monohidraat, mikrokristallyn-sellulose, povidoon K25 en natrium stearielfumaraat.

Geneesmiddeltoevoegings - Filmbedekking: hipromellose, talk en titaandioksied (E171). Bevat suiker (77, 9 mg laktose-monohidraat van die 20 mg en 155,8 mg laktose-monohidraat van die 40 mg)

Hoe Xofluza lyk en die inhoud van die verpakking

Xofluza 20 mg: Wit tot liggeel, langwerpig-gevormde filmbedekte tablette, gedebosseleer met “772” op die een kant en “20” op die ander kant.

Xofluza 40 mg: Wit tot liggeel, langwerpig-gevormde filmbedekte tablette, gedebosseleer met “BXM40” op die een kant.

20 mg tablette: Aluminiumstulppakke bevat 2 of 4 tablette.

40 mg tablette: Aluminiumstulppakke bevat 1 of 2 tablette.

Dit is moontlik dat nie alle pakgroottes dalk bemark word nie.

7. Houer van registrasiesertifikaat

Roche Products (Pty) Ltd

Bekkerweg 90, Hertford Office Park

Gebou E, Vorna Vallei, Midrand,

Johannesburg,1686

Suid-Afrika

Roche etiekhulplyn (REAL), tolvry: 0800 21 21 25

8. Registrasienommer(s)

Xofluza 20 mg: 55/20.2.8/0333

Xofluza 40 mg: 55/20.2.8/0334

Vorige hersiening: 05 Mei 2023

Botswana:	NS2	BOT2103783/A BOT2103784/A