XALUPRINE®

(mercaptopurine) 20 mg/ml oral suspension

A fluid approach to acute lymphoblastic leukaemia

Mercaptopurine is part of the gold-standard maintenance regimen for ALL patients.[1]

Xaluprine® (mercaptopurine) 20 mg/ml oral suspension is the SMC and the AWMSG recommended treatment option for ALL patients.[2,3] It offers a flexible, accurate dosing alternative to mercaptopurine tablets.[4,5]

Palatable[6]

Natural raspberry taste with no artificial colours, flavours or added sugar[5]

Alcohol free[5]

Lactose free[5]

Accurate dosing to 2mg[5]

Easy to swallow & well tolerated[6,7]

Addresses the difficulty children have with swallowing tablets[6]

Xaluprine® is indicated for the treatment of ALL in adults, adolescents and children.[5] Mercaptopurine is the cornerstone of maintenance therapy for acute lymphoblastic leukaemia and proven to increase disease-free survival.[1,7]

A fluid approach to acute lymphoblastic leukaemia

Systemic exposure to mercaptopurine is critical for remissions in children with acute lymphoblastic leuk

**Xaluprine®
(mercaptopurine)
20 mg/ml oral suspension
offers a palatable
medication which is
acceptable to children
and will help support
adherence to
therapy[6]**

Maximising mercaptopurine adherence and maintaining steady thiopurine exposure minimises relapses in children with ALL.[11]

Non-adherence, or drug interruptions can result in relapse and emergence of resistance.[11]

Adherence to a medicine is related to many factors, but palatability and acceptability of formulations are considered key factors for children.[12]

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**59% of
relapses can
be attributed to
non-adherence[11]**

durable
kaemia (ALL)[11]

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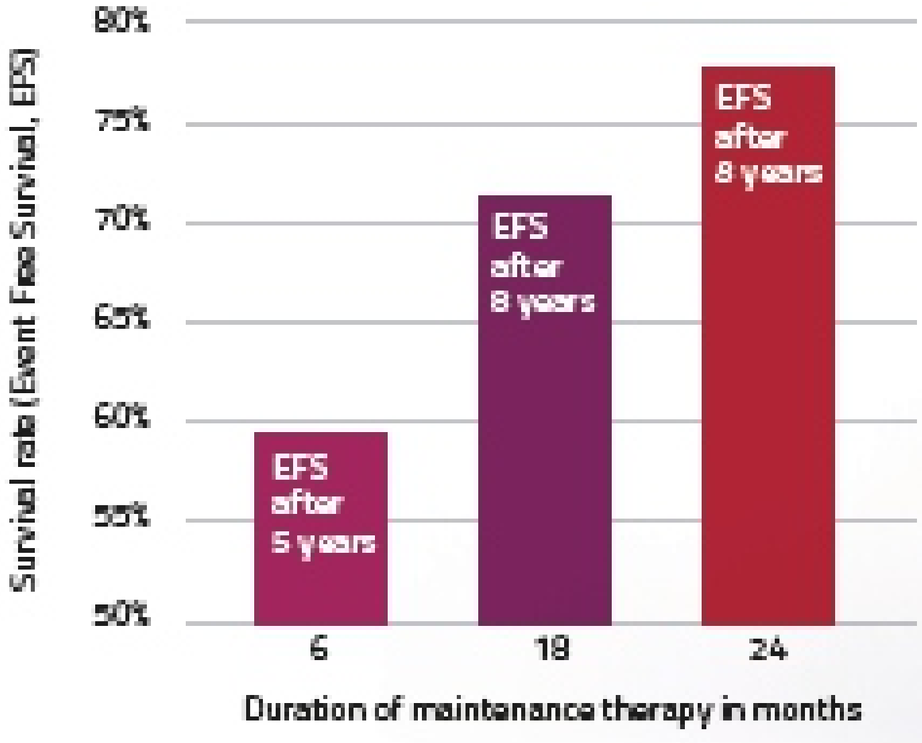
lapse[11]

Maintenance therapy with mercaptopurine is essential for patient survival[13,14]

Survival rates (event-free survival) increase with the duration of mercaptopurine administration in maintenance therapy.[13,14]



Schrappe, et al. 2000, Toyoda, et al. 2000

Accurate and convenient dosing

Mercaptopurine is an established treatment in the maintenance phase of ALL.[5] Xaluprine® (mercaptopurine) 20 mg/ml oral suspension provides accurate, flexible dosing for ALL patients.[6,7] Previously, the use of tablets has made administration difficult for parents and carers of children with ALL.[7,9]

Xaluprine® oral suspension	Mercaptopurine tablets
Dose is easy to calculate and administer[6]	Individualising doses for young children is extremely difficult as the dose needs to be adjusted according to body surface area[7,9]
Can be given accurately, down to a dose of 2mg (0.1ml), using the supplied 1ml (purple) or 5ml (white) oral syringe[6]	Tablet splitting is associated with potential exposure of parents/carers to cytotoxic contamination[7,9]

Dosing calculation chart

Age	BSA (m^2)†	Dose‡ (mg)	Volume (ml)
3 months	0.27 - 0.33	20 - 25	1.0 - 1.2
1 year	0.47 - 0.53	35 - 40	1.8 - 2.0
3 years	0.61 - 0.67	46 - 50	2.3 - 2.5
5 years	0.74 - 0.79	56 - 59	2.8 - 3.0
10 years	1.07 - 1.13	80 - 85	4.0 - 4.2
12 years	1.27 - 1.33	95 - 100	4.8 - 5.0
18 years	1.77 - 1.83	133 - 137	6.7 - 6.9

†Based on WHO growth charts for children (may not correspond to the BSA of individual patients)[19]
‡Based on a typical starting dose of 75mg/m^2 [19]

Abbreviated Prescribing Information for Xaluprine® (mercaptopurine) 20 mg/ml oral suspension:

Please refer to the full Summary of Product Characteristics and the treatment protocol when prescribing Xaluprine®.

Presentation: Oral suspension, each 1 ml contains: 20 mg mercaptopurine (as monohydrate), 3 mg aspartame, 1 mg methyl hydroxybenzoate (as the sodium salt), 0.5 mg ethyl hydroxybenzoate (as the sodium salt), 1 mg potassium sorbate and sucrose (trace). **Indications:** For the treatment of acute lymphoblastic leukaemia (ALL) in adults, adolescents and children. **Dose and administration:** The dose is governed by cautiously monitored haematotoxicity and should be carefully adjusted to suit the individual patient. Starting or target doses vary between 25 - 75mg/m2 body surface area per day, but should be lower in patients with reduced or absent TPMT and/or NUDT15 activity. *Elderly:* Monitor renal and hepatic function and if there is any impairment, consider reducing the dose. *Renal impairment:* Consider reduced starting doses. Monitor patients for dose related adverse reactions. *Hepatic impairment:* Consider reduced starting doses. Monitor patients for dose related adverse reactions. *Switching between tablet and oral suspension and vice versa:* The oral suspension and tablet are not bioequivalent. Intensified haematological monitoring is advised on switching formulations. *Administration:* Redisperse by shaking vigorously at least for 30 seconds. Xaluprine should be taken in the evening and may be taken with food or on an empty stomach. Standardise the method of administration. Xaluprine should not be taken with milk or dairy products but it should be taken at least 1 hour before or 2 hours after milk or dairy products. Water should be taken after each dose. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients. Concomitant use with yellow fever vaccine. **Special Warnings and precautions for Use:** *Cytotoxicity and haematological monitoring:* Monitor haematological parameters. Interrupt treatment immediately at the first sign of abnormally large fall in leucocyte and platelet counts. Bone marrow suppression is reversible if 6–mercaptopurine is withdrawn early. Patients with little or no inherited TPMT and / or NUDT15 activity are at increased risk for severe toxicity and require substantial dose reduction. TPMT / NUDT15 testing cannot substitute for haematological monitoring. *Immunosuppression:* Immunisations with live organism vaccines are not recommended. *Hepatotoxicity:* Monitor liver function weekly. More frequent monitoring may be advisable in those with pre-existing liver disease or receiving other potentially hepatotoxic therapy. Discontinue Xaluprine if jaundice becomes apparent. *Renal toxicity:* Monitor uric acid levels in blood and urine during remission induction. Hydration and urine alkalinisation may minimize potential renal complications. *Pancreatitis* is a common (frequency of ≥ 1/100 to < 1/10) adverse reaction in patients treated for the unlicensed indication inflammatory bowel disease. *Mutagenicity and carcinogenicity:* Increased risk of developing lymphoproliferative disorders and other malignancies, notably skin cancers (melanoma and non-melanoma), sarcomas (Kaposi's and non-Kaposi's) and uterine cervical cancer in situ. A combination of multiple immunosuppressants (including thiopurines), given concomitantly increases the risk of Epstein-Barr virus (EBV)-associated lymphoproliferative disorders. Hepatosplenic T-cell lymphoma has been reported in patients with inflammatory bowel disease (unlicensed indication) with or without concomitant treatment with anti-TNF alpha antibody. *Macrophage Activation Syndrome:* A life-threatening disorder that may develop in patients with autoimmune conditions, in particular with inflammatory bowel disease (unlicensed indication). *Infections:* Increased susceptibility to viral, fungal and bacterial infections, including severe or atypical infection, and viral reactivation. *Excipients:* Aspartame may be harmful for people with phenylketonuria. Sodium methyl parahydroxybenzoate and sodium ethyl parahydroxybenzoate may cause delayed allergic reaction. *Safe handling of the suspension:* Avoid Xaluprine contact with skin or mucous membrane. For contact with skin or mucosa, wash immediately and thoroughly with soap and water. **Interactions:** When allopurinol and 6–mercaptopurine are administered concomitantly only a quarter of the usual dose of 6– mercaptopurine must be given. Other xanthine oxidase inhibitors should be avoided. Reinforced monitoring of INR is recommended in patients co-administered anti-coagulants. Aminosalicylate derivatives inhibit TPMT enzyme and should be administered with caution. **Pregnancy and Lactation:** Do not use during pregnancy unless expected benefits outweigh any possible risk. Do not use whilst breast-feeding. **Contraception:** Sexually active men and women should use effective methods of contraception during treatment and for at least three months after receiving the last dose. **Undesirable effects:** **refer to the SPC for full list.** Bone marrow suppression leading to leucopenia and thrombocytopenia is the most common adverse reaction. Anaemia, anorexia, stomatitis, diarrhoea, vomiting, nausea, biliary stasis and hepatotoxicity are common adverse reactions. The following adverse reactions have also been reported from uncommonly to very rarely: infections and infestations, arthralgia, skin rash, drug fever, pancreatitis, oral ulceration, hepatic necrosis, facial oedema, hypoglycaemia, alopecia, photosensitivity, transient oligospermia, secondary leukaemia, myelodysplasia, hepatosplenic T-cell lymphoma and intestinal ulceration. **Overdose:** There is no antidote to Xaluprine. Monitor the blood picture and if necessary provide general supportive measures together with appropriate blood transfusion. Activated charcoal or gastric lavage can be undertaken within 60 minutes of ingestion. **Pack size:** 1 glass bottle containing 100 ml Xaluprine (mercaptopurine) 20mg/ml oral suspension. **Shelf-life/Storage:** 15 months; 56 days after first opening. Do not store above 25°C. **Legal category:** POM. **Marketing authorisation number:** EU/1/11/727/001. **Marketing authorisation holder:** Nova Laboratories Ireland Limited, 3rd Floor, Ulysses House, Foley Street, Dublin 1, D01 W2T2, Ireland. **Date of latest revision of brief prescribing information:** May 2019. **Further information including full prescribing information is available from:** Nova Laboratories Limited, Martin House, Gloucester Crescent, Wigston, Leicester, LE18 4YL, UK. Tel: +44 (0)116 223 0100.

Adverse events should be reported.
Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.
Adverse events should also be reported to Nova Laboratories Ltd, Martin House, Gloucester Crescent, Wigston, Leicester LE18 4YL

References: 1. UKALL 2019 Interim Guidelines v1.0 20-Feb-2019. 2. Scottish Medicines Consortium mercaptopurine 20mg/ml oral suspension (Xaluprine®). 3. All Wales Medicines Strategy Group, mercaptopurine (Xaluprine®) Ref No. 1252. 4. EMA 2011, Committee for Medicinal Products for Human Use assessment report: Mercaptopurine Nova Laboratories. 5. SMPC Nova Laboratories Ltd. Xaluprine 20 mg/ml oral suspension Summary of Product Characteristics. 6. Mulla H et al. Journ Onco Pharm Prac. 2015 Jun;22(3):387-95. 7. Mulla H et al. Journ Clin Pharm. 2012 Oct;52(10):1610-3. 8. Haute Autorité de Santé Xaluprine 20 mg/ml, oral suspension Transparency Committee Opinion. 9. Breitkreutz J & Boos J. Paed & Gerital Drug Delivery. 2007 Jan 1;4(1):37-45. 10. WHO, Child Growth Standards. 11. Bhatia S et al. JAMA oncol. 2015 Jun 1; 1(3):287-95. 12. Venables R et al. Internal Journ Pharma, 580(1-2), 55–62. doi:10.1016/j.ijpharm.2019.01.029. 13. Schrappe et al. Leukemia, 2000, 14, 2205–2222. 14. Toyoda et al. Journ Clin Oncol 2000 Apr; 18(7): 1508–1516.

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