VALPROATE PRESCRIBING within MENTAL HEALTH & LEARNING DISABILITY SERVICES

VALPROATE PRESCRIBING REVIEW PROCESS

TARGET AUDIENCE	Prescribers within NHS Lanarkshire MHLD services
PATIENT GROUP	All new patients under the age of 55 where valproate is being considered, existing female patients under the age of 55 and male (new or existing) patients of any age prescribed valproate

Summary

- Regulatory changes have been announced by the MHRA to reduce the harms from valproate, including the significant risk of harm to the baby if taken during pregnancy, the risk of impaired fertility in males and potential association between valproate use by men around time of conception and an increased risk of neurodevelopmental disorders in their children.

- This document outlines the local processes for managing the prescribing of valproate:
  - to all new patients (male or female) under the age of 55
  - to existing female patients under the age of 55
  - to male (new or existing) patients of any age
  - for obtaining a local second opinion
  - for managing review of patients who do not attend/ are difficult to engage

Contents

Background and recent updates

From January 2024, the MHRA has introduced new restrictions on the prescribing of sodium valproate to ensure that:

- valproate is only used if other treatments are ineffective or not tolerated.
- any use of valproate in females of child-bearing potential who cannot be treated with other medicines is in accordance with a pregnancy prevention programme.
- these measures aim to reduce the initiation of valproate to only patients for whom no other therapeutic options are suitable.

The regulatory changes are;

A. **Valproate must not be started in new patients (male or female) younger than 55 years**, unless two specialists independently consider and document that there is no other effective or tolerated treatment, or there are compelling reasons that the reproductive risks do not apply.

B. At their next annual specialist review, **female patients of childbearing potential should be reviewed using a revised Valproate Risk Acknowledgement Form**, which will include the need for a second specialist signature if the patient is to continue with Valproate and subsequent annual reviews with one specialist unless the patient's situation changes.

In addition to January 2024 update, the MHRA made further recommendations in September 2024 that male patients of any age should be advised of the possible association between valproate use by men around the time of conception and increased risk of neurodevelopmental disorders in their children and advised to use effective contraception throughout valproate treatment.

Valproate new safety materials to support regulatory measures in men & women under 55

Valproate use in men: as a precaution, men and their partners should use effective contraception

Valproate advice for HCPs when discussing new recommendations for male patients

valproate.psychiatry@lanarkshire.scot.nhs.uk

Valproate prescribing in females

Prescribing valproate to a female of child-bearing potential without fulfilling the conditions of the pregnancy prevention programme is contraindicated and represents an unlicensed use of the drug.

The responsibility for initial completion of the risk acknowledgement form and for ongoing annual review lies with the specialist prescriber, therefore female patients of child-bearing potential on valproate must remain on psychiatrist caseloads.

A pregnancy prevention programme (consisting of the use effective contraception without interruption) must be in place **BEFORE** valproate is commenced in female patients of child-bearing potential.

At least one effective method of contraception, **preferably a highly effective user-independent form** such as an intra-uterine device, implant, female/ male sterilisation or 2 complementary forms of contraception including a barrier method should be used.

Sexual health services required a complete list of all currently prescribed medications included with referrals for contraceptive review due to potential interaction with enzyme-inducing medications.

Valproate risk acknowledgment forms

- All background information and risk materials including patient information, healthcare professional information, risk acknowledgement forms (separate forms for males and females) and any updates from the MHRA can be found here;
  Valproate new safety materials to support regulatory measures in men and women under 55 years

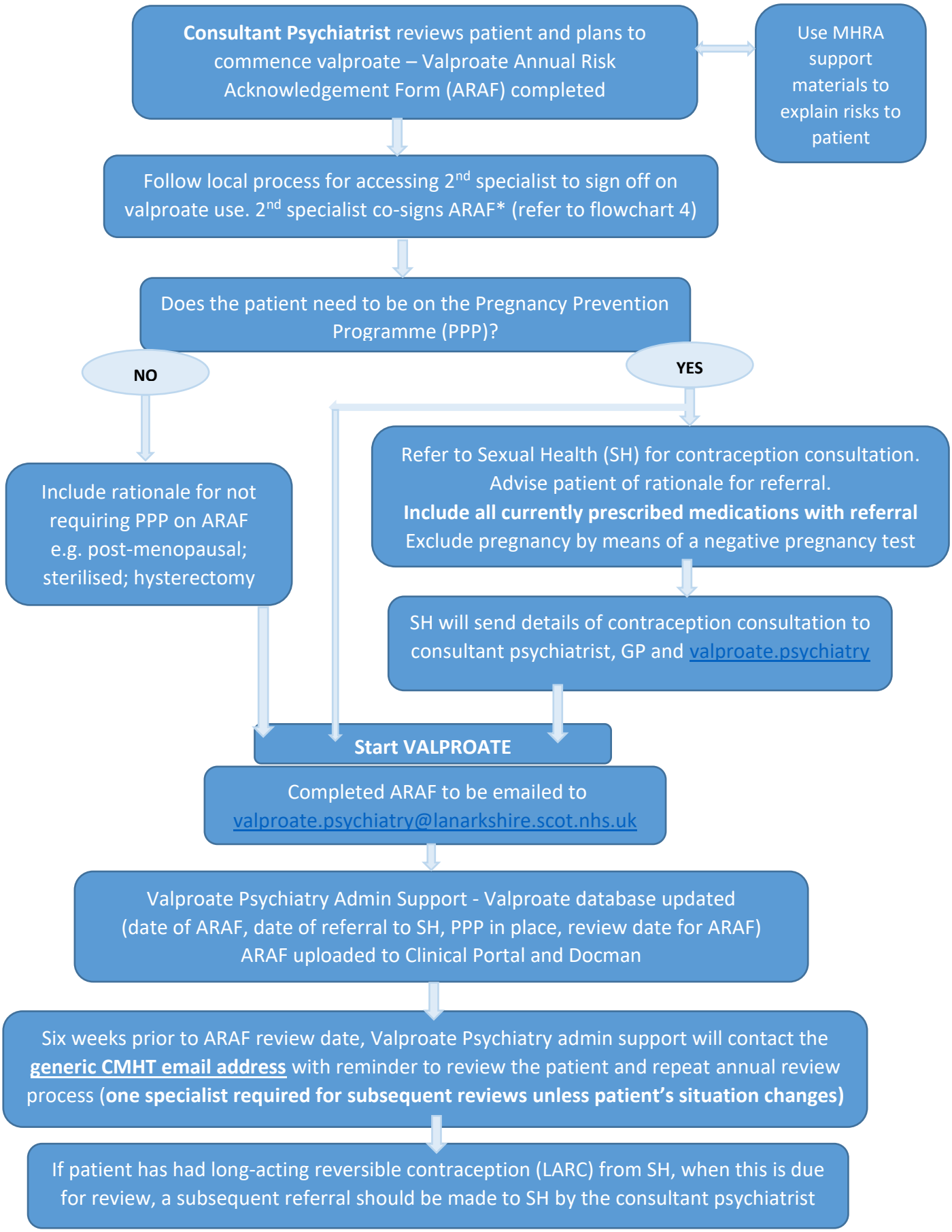
- The MHRA have recently confirmed that 'wet signatures' are not mandatory on the risk acknowledgement form as long as the contribution of the patient is noted, verbal consent is obtained and the patient receives written information and a copy of the risk acknowledgment form.

- On submission of completed risk acknowledgement form to the generic email address valproate.psychiatry@lanarkshire.scot.nhs.uk, the form will be uploaded to primary care system- *Docman* and to clinical portal, under 'assessments'; 'risk assessments'

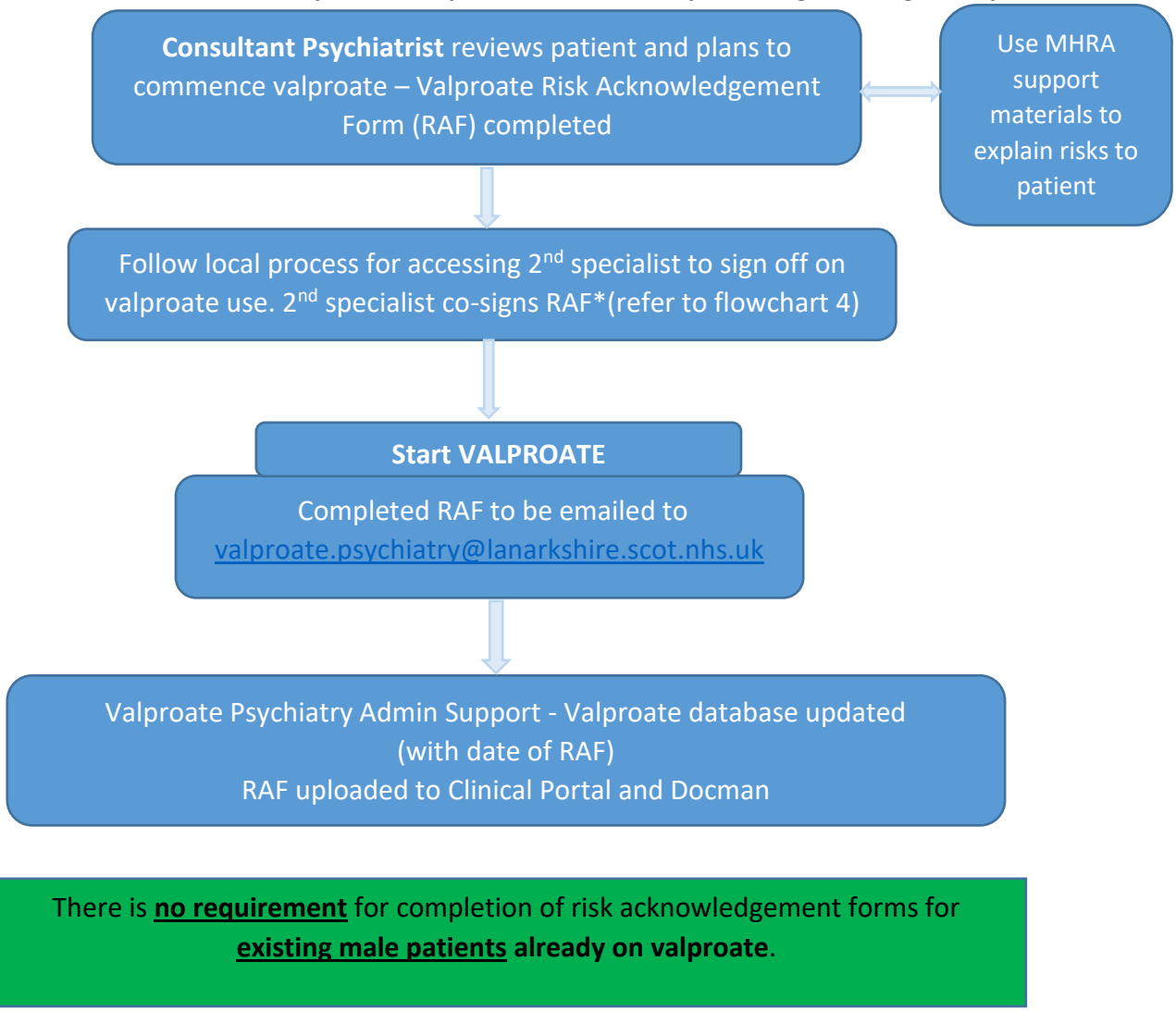
- The national advice regarding valproate is subject to ongoing review, with potential further changes to processes in the future.

Lead Author	**Lorna Templeton**	**Date approved**	**19th March 2025**
Version	**V4**	**Review Date**	**19th March 2028**

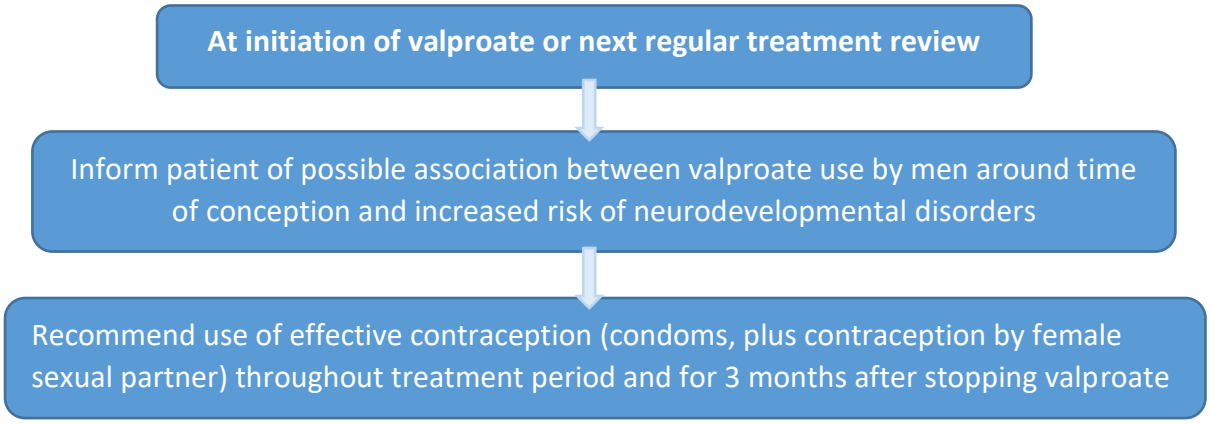
Flowchart 1: Process for any new female patients less than 55 years of age starting on valproate



Flowchart 2a: Process for any new male patients less than 55 years of age starting on valproate

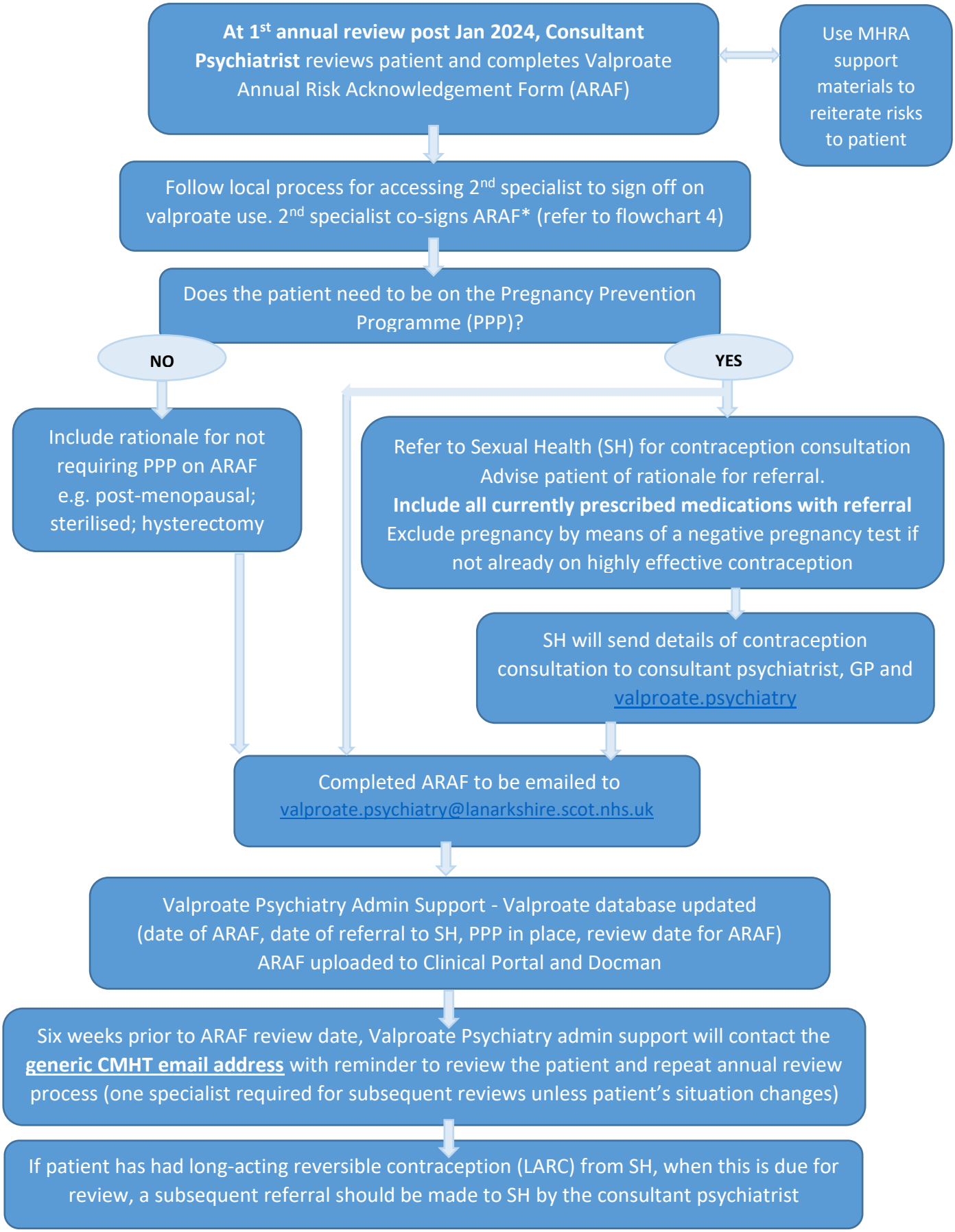


Flow chart 2b: Additional advice for any new or existing male patients of any age who may father children

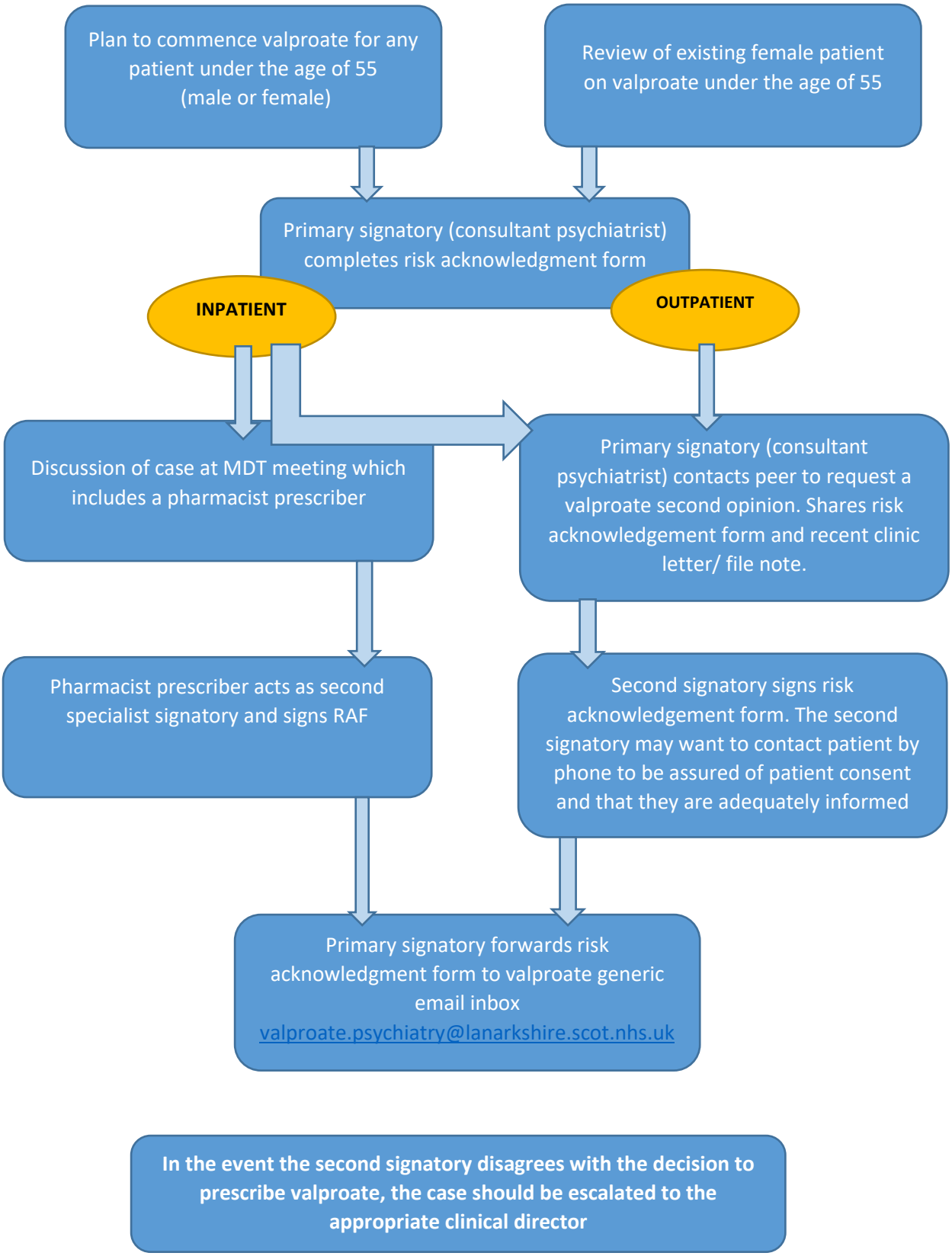


Valproate advice for HCPs when discussing new recommendations for male patients

Flowchart 3: Review process for existing female patients less than 55 years of age already prescribed valproate



Flowchart 4: Process for obtaining second opinions



Further information on accessing second opinions within NHS Lanarkshire's MHLD service

1. The responsibility for obtaining a second opinion lies with the patient's named consultant psychiatrist (the primary signatory of the risk acknowledgement form).

2. The primary signatory (consultant psychiatrist) must request a second opinion from another specialist prescriber.

3. The second opinion can be obtained from another consultant psychiatrist within the CMHT/ subspecialty or from a colleague from another locality who is not directly being supervised by the treating doctor. Consider peer group colleagues and/or informal peer or 'buddy' system.

4. Within NHS Lanarkshire MHLD services, a specialist prescriber may also include; mental health speciality doctors, mental health specialist nurses prescribers, mental health pharmacist prescriber (where the pharmacist is a named member of the MDT)

5. Discussion of cases at multidisciplinary team (MDT) meetings can substitute for the second signature, through a named representation of the MDT who should be a specialist prescriber.

6. The second signatory for initiation of valproate treatment and the decision to continue or switch valproate treatment should not be in direct line management of the primary signatory.

7. There is no expectation that the second signatory reviews the patient in person, however, they must have full access to all medical records and test results to be able to independently consider and document that there is no other effective or tolerated treatment.

8. The second signatory may want to contact the patient independently to ensure that they are adequately informed of risks and are consenting to treatment.

9. In the event the second signatory disagrees with the decision to prescribe valproate, the case should be escalated to the appropriate clinical director for further discussion.

10. From Mental Welfare Commission's December 2023 newsletter to Designated Medical Practitioners (DMPs)

MHRA VALPROATE REQUIREMENTS

If a Responsible Medical Officer (RMO) plans to use Valproate for those under 55 years old, the RMO will need to ask for a local second opinion. ***DMPs are not to be used as the second "independent specialist"****. If the local second opinion doctor agrees with the RMO's decision, then the RMO may ask for a DMP assessment (where applicable). When a DMP has the discussion with the RMO about the treatment plan, please ask the RMO if the MHRA requirements have been met. If the DMP chooses to authorise Valproate, then to please state on the T3B as a condition that* ***the MHRA requirements need to be met****.*

Managing review of patients who do not attend/ are difficult to engage

This is currently only relevant to female patients who are expected to have an annual review (includes existing patients and new female patients at subsequent annual reviews) as male patients under the age of 55 years of age should have risk acknowledgement forms completed (including second specialist signature) prior to commencing on valproate treatment and currently only require the risk acknowledgment form at the point of initiation.

For existing female patients and new female patients at subsequent annual reviews who are invited for an annual specialist review of valproate therapy in line with regulatory advice and who fail to attend, this should be managed in line with local standard non-attendance policy.

The patient and their GP should be written to advising that they will be discharged from the service if they fail to engage and explain that the clinical implications of this will mean that mental health services will no longer be able to recommend to their GP that valproate continues. If the patient wishes to continue on valproate, they must engage with the specialist review.

Reasonable attempts should be made to contact the patient taking into consideration information held within the CMHT about the patient's preferred method of communication and processes known to support their engagement.

References/Evidence

1. Valproate: organisations to prepare for new regulatory measures for oversight of prescribing to new patients and existing female patients. National Patient Safety Alert. MHRA Nov23 https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=103240

2. Valproate: review of safety data and expert advice on management of risks. Public Assessment Report MHRA Nov23 https://assets.publishing.service.gov.uk/media/65660310312f400013e5d508/Valproate-report-review-and-expert-advice.pdf

3. Drug Safety Update volume 17, issue 6: January 2024: 1 https://www.gov.uk/drug-safety-update/valproate-belvo-convulex-depakote-dyzantil-epilim-epilim-chrono-or-chronosphere-episenta-epival-and-syonellv-new-safety-and-educational-materials-to-support-regulatory-measures-in-men-and-women-under-55-years-of-age

4. Drug Safety Update volume 18, issue 2: September 2024: 1. Valproate use in men: as a precaution, men and their partners should use effective contraception - GOV.UK (www.gov.uk)

5. MHRA Safety Update volume 18, issue 7: February 2025: 1 https://www.gov.uk/drug-safety-update/valproate-belvo-convulex-depakote-dyzantil-epilim-epilim-chrono-or-chronosphere-episenta-epival-and-syonellv-review-by-two-specialists-is-required-for-initiating-valproate-but-not-for-male-patients-already-taking-valproate

6. Did Not Attend and No Access Visits Policy. NHS Lanarkshire Mental Health & Learning Disability Services. Jul 22 (under review - Apr 24)

Appendices

1. Governance information for Guidance document

Lead Author(s):	Lorna Templeton, Lead Pharmacist- MHLD
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Responsible Person (if different from lead author)	

CONSULTATION AND DISTRIBUTION RECORD	
Contributing Author/ Authors	Lorna Templeton; MHLD D&T
Consultation Process / Stakeholders:	Consultant Psychiatrists; MHLD CG; Members of NHS Lanarkshire's Valproate SLWG
Distribution	• All prescribers in MHLD services • MHLD service managers for dissemination to ward and community mental health teams. • MHLD D&T newsletter

CHANGE RECORD			
Date	**Lead Author**	**Change**	**Version No.**
Jul 22	S Leggate L Templeton	*New document to support local processes for management of women of child-bearing potential prescribed valproate*	1
Sep 23	L Templeton	*Updates from sexual health; definition of highly effective contraception; clarification regarding 'wet signatures' on RAFs*	2
Apr 24	L Templeton	*Significant update following regulatory changes from MHRA, including outlining processes for; new female patients less than 55 years of age starting on valproate; new male patients less than 55 years of age starting on valproate; existing female patients less than 55 years of age already prescribed valproate; obtaining second opinions; managing review of patients who do not attend/ are difficult to engage*	3
Feb 25	L Templeton	*Change of title to Valproate Prescribing Review Process Update to include recommendations from MHRA Sep24 and Feb25 alert around possible association between valproate use around time of conception and increased risk of neurodevelopmental disorders and their children*	4