

# Unlicensed medicines – legal and ethical issues

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## Agenda

- Introduction
- Unlicensed medicines vs 'off-label' prescribing
- Legislation
- Legal responsibility
- Professional guidance
- Risks and risk management
- Take-home points
- Questions

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## Groupwork - Scenario 1

- A patient brings a note to your practice from a paediatric cardiologist in which you are asked to take over the prescribing of a combination product containing hydrochlorothiazide and spironolactone for a child with a congenital heart malformation.
- Is this product licensed?
- Would you agree to take on prescribing responsibility for this patient?
- What would be consequences for you and the patient (and parents/guardians) if you:
  - Agreed?
  - Refused?

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## Groupwork - Scenario 2

- A consultant in child and adolescent mental health, to whom you have referred an 11-year-old child with an autism spectrum disorder who has been displaying violent and aggressive behaviour in school, contacts you to request that you would adopt shared care prescribing for her, now that her condition has been stabilised on treatment with psychosocial therapy and low-dose risperidone.
- Is this prescribing licensed?
- Would you agree to take on prescribing responsibility for this patient?
- What would be consequences for you and the patient (and parents/guardians) if you:
  - Agreed?
  - Refused?

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## Introduction

- Licensing procedures
- Licensed indications
- Prescribing outside a license
  - Unlicensed ('Off-label') use
  - Unlicensed medicines
- Medicines Act (1968) – determines licensing
- Consumer Protection Act (1987)

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## Off-label prescribing

- Where licensed indications
  - do not reflect established current knowledge
  - do not include well proven uses of a drug
  - are at variance e.g. one branded product has two licensed uses but another has only one
- Legal responsibility lies with person signing the prescription
- Manufacturer likely liable only if harm results from a defect in the product
- Absence of licensed indication doesn't imply absence of evidence e.g. spironolactone for heart failure, fluticasone for COPD
- May be helpful to recognise a spectrum of risk
  - From 'near-label' to speculative eccentricity
- Consider context – commonplace in children/elderly

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## What is the extent of the issue within UK General Practice?

McIntyre J et al. Arch Dis Child 2000;83:498-501

- Single practice study (Midlands, 1997)
  - 3347 prescription items, 160 drugs
  - 1175 children (65% <12s on practice list)
  - 84.5% licensed
  - 0.3% un-licensed
  - 10.5% 'off-label'
  - 4.7% insufficient information

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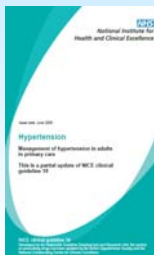
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## What does NICE say about treating elderly people

NICE Guideline 2006



- Patients over 80 years of age are poorly represented in clinical trials and the effectiveness of treatment is less certain.
- However, it is reasonable to assume that older patients will receive worthwhile benefits from drug treatment, particularly in terms of reduced risk of stroke.
- Offer patients over 80 years of age the same treatment as patients over the age of 55, taking account of co-morbidity and polypharmacy

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## What about in general practice?

Stewart C. Int J Pharm Pract 2003; 11: R81

- Audit of prescribing of atypicals to 374 patients in Ellesmere Port and Neston PCT (2003)
  - 48% olanzapine, 28% risperidone, 21% quetiapine, 2.6% amisulpride, clozapine 1%
- 53% initiated by specialists, 20% by GP led with advice from specialist, 28% led by GP
- 70% prescribed for off-label use
- 3% co-prescribed a typical agent
- Out of 188 patients who were switched from a typical to an atypical, 72% complied with NICE guidelines for the switch

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### Off-label prescribing – some common examples

Medicine	Unlicensed use(s)	Notes
Lisinopril	Heart failure	Well-supported by ATLAS study
Metoprolol	Heart failure	Well-supported by systematic reviews
Beclomethasone, fluticasone	COPD	Only Seretide licensed, only as Accuhaler
Atenolol, amitriptyline	Migraine	Efficacy consistently demonstrated (Prodigy)

14

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### Off label prescribing - antidepressants licensed for anxiety disorders

Clomipramine	phobic and obsessional states
Trazodone	anxiety
Moclobemide	social phobia
Citalopram	panic disorder
Escitalopram	panic disorder
Fluoxetine	OCD
Fluvoxamine	OCD
Paroxetine	OCD, panic disorder, social phobia, PTSD, GAD
Sertraline	OCD, PTSD
Venlafaxine	GAD

15

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### Unlicensed medicines

- Products derived from licensed medicines
  - e.g. extemporaneously dispensed liquid formulation
- Products unrelated to any licensed medicine
- Products that no longer have a PL
  - e.g. pirenzepine
- Products being used in clinical trials
- Products licensed in another country
  - being imported and used on a named-patient basis
- Little prescribing of unlicensed medicines in mental health (c.f. paediatrics)

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### Legal responsibility

- Prescriber carries responsibility for patient's welfare
- May be called upon to justify actions in event of ADR
- Two main ways through which compensation may be sought
  - Negligence liability
  - Strict liability

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### Negligence liability

- Common law duty to take reasonable care
- Act in a way consistent with practice of responsible body of their peers of similar professional standing ('The Bolam Principle')
- Prescribers must understand the product and act responsibly with reasonable care and skill

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### Bolam principle

- Bolam judgement, 1957
- "A doctor is not guilty of negligence if he has acted in accordance with a practice accepted as proper by a responsible body of medical men skilled in that particular art"

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### Strict liability

- Product liability arising under the Consumer Protection Act (1987)
- Defective product which does not provide the safety that a person is entitled to expect
- Principally affects manufacturers of drugs

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### Professional Guidance - Children

Principles of unlicensed prescribing for children (Joint RCPCH/ NPPG)

- Prescribe on the basis of evidence of benefit (and risk), with due regard to cost
- Informed use whenever possible
- Prescribers should have access to good quality information
- Obtain consent whenever possible
- NHS organisations should support practice commended by a responsible body

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### Some sensible advice

General Medical Council

- Be satisfied that an alternative, licensed medicine would not meet the patient's needs
- Be satisfied that there is a sufficient evidence base and/or experience of using the medicine to demonstrate its safety and efficacy
- Take responsibility for prescribing the unlicensed or off-label medicine and for overseeing the patient's care, including monitoring and any follow up treatment
- Record the medicine prescribed and the reasons for choosing this medicine in the patient's notes.

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## Risks and risk management

Risk	Action
Prescriber is unaware of previous trials of licensed alternatives	Take comprehensive medication history – check for previous adequate trial of licensed alternative
Prescriber is unaware of balance of risk/benefit	Familiarise self with evidence of efficacy and safety for proposed prescribing
Prescribing outwith evidence base/expertise/common practice	Obtain advice of another specialist or specialist pharmacist
Patient is unaware of unlicensed status	Advise the patient of unlicensed status, esp where new/investigational medicine or serious risk of ADR
Patient has not given consent	Obtain consent wherever possible.
No record of consent being given	<ul style="list-style-type: none"> <li>Document consent where obtained</li> <li>Document where <b>not</b> obtained and why</li> </ul>
Avoidable ADR occurs	<ul style="list-style-type: none"> <li>Provide written information</li> <li>Monitor patient closely</li> <li>Document response &amp; tolerance</li> <li>Withdraw if ineffective</li> <li>Report ADRs/defective products to CSM/MHRA</li> </ul>

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<b>EFFECTIVE</b> <i>Beneficence</i>	<b>SAFE</b> <i>Non-maleficance</i>
<b>COST</b> <i>Justice</i>	<b>PATIENT FACTORS</b> <i>Patient autonomy</i>

From: What constitutes good prescribing?  
Barber N. BMJ 1995; 310: 923-925

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Hmmmm. What shall I do now? The same old evidence based procedure.....or an exciting but unproven risky alternative I've just thought of?



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### Take home points

- Unlicensed prescribing is commonplace in mental health settings
- Be aware of licensed indications but...
- Consider licensing issues in context of wider evidence base, patient preferences, and clinical judgement
- Obtain informed consent whenever possible and document
- Monitor closely, withdraw if ineffective
- Report ADRs to CSM

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