

Prescribing and Clinical Effectiveness Bulletin

Volume 4; Number 16

October 2010

DISCONTINUATION OF MIXTARD 30 INSULIN PRODUCTS

Summary

- All Mixtard® 30 insulin presentations (Penfill®, InnoLet® and 10ml vials) are being discontinued from the 31st December 2010.
- All patients currently receiving Mixtard 30® will need to be reviewed and changed to an alternative product; the preferred option endorsed by PACEF is Humulin M3®. Alternatively Insuman Comb 25® should be considered.
- Published evidence shows that biphasic analogue insulins do not offer any advantage over conventional human biphasic insulins in terms of efficacy, long term outcomes or safety. As a result of this, biphasic analogue insulins, such as Novomix 30® and Humalog Mix25® should only be considered third line.
- This bulletin provides further information on the choices of M3 formulations available, general advice on switching insulin and details of suitable alternatives if Humulin M3® is not an appropriate choice.

Introduction

Mixtard® 30 insulin is human biphasic isophane insulin consisting of a mixture of 30% soluble and 70% isophane insulin. Novo-Nordisk has decided to withdraw the Mixtard® 30 formulations as a result of declining use over the last 6 years; declining market share is primarily due to the introduction and rise of insulin analogues.

All patients currently prescribed Mixtard® 30 in any presentation will need to be changed to an alternative preparation prior to the products being discontinued in December. Lincolnshire Prescribing and Clinical Effectiveness Forum (PACEF) have considered the possible alternatives to Mixtard® 30 and recommend the following options:

Option 1 (Preferred) :

If the patient has been using Mixtard® 30 for some time and is stable, consider a change to Humulin M3®. This is the most cost effective and straightforward switch.

Humulin M3® is a biphasic insulin nearly identical to Mixtard® 30 containing 30% soluble insulin and 70% isophane insulin. When switching from Mixtard® 30 to Humulin M3 no change in dose is required as it is dose equivalent. Like Mixtard® 30, Humulin M3® is administered about 30 minutes before meals. If there is a concern about hypoglycaemia occurring, then a 10% reduction in dose is advisable.

Humulin M3® is available as vials or cartridges. All patients currently receiving treatment with Human Mixtard® 30 via re-useable pens (Penfill) should be switched as soon as possible to Humulin M3® given using the HumaPen Luxura® device. For patients currently using the Mixtard® 30 pre-filled Innolet® device, a prefilled disposable injection device containing Humulin M3® known as KwikPen® was introduced during September 2010. This will replace the existing pre-filled device often referred to as the Humulin M3® pen, which is being discontinued by March 2011. Prescribers are reminded that to avoid confusion with the older pen device, they should prescribe the pre-filled Humulin M3 insulin pens by brand, as Humulin M3 Kwikpen®.

Option 2:

Where Humulin M3® has been considered and judged to be inappropriate Insuman Comb 25® can be considered as an alternative.

Insuman Comb 25® contains the same constituents as Mixtard® 30 and Humulin M3® but in a different ratio: 25% soluble insulin and 75% isophane insulin. Advice from the National Prescribing Centre (NPC) and the National Clinical Director for Diabetes states that this modest difference in ratio is unlikely to be clinically significant. Like Mixtard®30, Insuman Comb 25® is administered about 30 minutes before meals.

Option 3:

If neither Option 1 nor Option 2 is suitable, an alternative biphasic preparation containing an insulin analogue may be considered.

Insulin analogues whilst providing similar glycaemic control to human insulins have different pharmacokinetic properties and are more expensive. A recent review by the *Drug and Therapeutics Bulletin* concluded that: 'published evidence shows that biphasic analogue insulins do not offer any advantage over conventional human biphasic insulins in terms of efficacy, long term outcomes or safety' (*DTB* 2010; 48 (8): 85). Biphasic preparations that may be suitable alternatives to Mixtard®30 are Novomix 30® (containing insulin aspart) and Humalog Mix25® (containing insulin lispro). There is no direct dose conversion for patients switching from Mixtard®30 to a biphasic insulin analogue. An initial dose of 80-85% of the Mixtard®30 dose has been suggested, titrated upwards according to patient response. Insulin analogues have a faster onset of action than human insulin and should be administered shortly before meals; the timings of injections will need to be adjusted accordingly.

General advice on switching insulins

- **Ensure the patient uses up existing stocks of Mixtard® 30 before issuing any prescriptions for the replacement insulin.**
- **When switching, ensure patients are supplied with a prescription for or a supply of the appropriate device to administer the new insulin.**
- **Consideration also needs to be given as to which pen device is most suitable for each patient. Commercial devices vary widely in terms of ease of use, the maximum/minimum dose which can be delivered and the personal preference of the patient and/or carer.**
- **Ensure all patients are counselled and monitored for compliance, blood sugar control and adverse effects.**

Cost impact of product withdrawal.

- Based on current prices, a switch from Mixtard® 30 cartridges to Humulin M3® cartridges is likely to be cost neutral.
- Switching from pre-filled pen devices to Humulin M3® using the KwikPen® device will increase the cost.
- It has been estimated that a direct switch from Mixtard® 30 to Novomix 30® will increase drug costs across England by £9M pa; in Lincolnshire this could be as much as £130,000pa, although the actual figure is hard to predict due to the necessity of individual patient review and dosage changes.

Cost comparison

Preferred option highlighted in bold.

Insulin	Product	Cost	Compatible device
Mixtard® 30	3ml pen fill	£19.08 (5 x 3ml)	Novopen® 4 £26.56
	3ml InnoLet® pre-filled pen	£19.87	
	10ml vial	£7.48	
Humulin M3®	3ml cartridge	£19.08 (5x3ml)	Autopen Classic ® £15.79 Or HumaPen Luxura ® £26.36
	3ml Humulin M3® pre-filled pen	£28.44 (5 x 3ml)	To be discontinued 31 st March 2011
	3ml KwikPen® pre-filled pen	£21.70 (5 x 3ml)	Launched September 2010
	10ml vial	£15.68	
Insuman Comb 25®	3ml cartridge	£17.50 (5 x 3ml)	Optipen® Pro £22.00 Autopen 24 £15.55 Both the Autopen 24 and Optipen are being discontinued from December 2010. Replacement device ClickSTAR® (£17.50) will be available from November 2010.
	3ml *Optiset® pre-filled	£17.50 (5 x 3ml)	This is being discontinued in December 2010
	3ml SoloSTAR® pre-filled	£19.80 (5 x 3ml)	Available from November 2010
	5ml vial	£5.61	
Novomix 30®	3ml pen fill	£29.43	Novopen® 4 £26.56
	3ml Flexpen®	£32.00	
Humalog Mix 25®	3ml cartridge	£29.46 (5 x 3ml)	HumaPen® £26.56 or Autopen Classic ®£15.79
	3ml KwikPen pre-filled	£30.98 (5 x 3ml)	
	10ml vial	£16.61	

Based on prices September 2010 MIMS .Although the price of all pen devices is quoted, refillable pen devices are often provided free of charge from manufacturers.

There have been a lot of recent changes in both the prices of insulin pen devices (re-useable and pre-filled) and the introduction of new pen devices. Please refer to either the most recent edition of MIMS or directly with the manufacturer for the latest information on price and product availability.

Acknowledgements

Many thanks to the Medicines Management Team at Nottingham County PCT for sharing their briefing letter on the discontinuation of Mixtard® 30 Insulin and Gill Kaylor, Prescribing Advisor, NHSL for her contributions to this bulletin.

C.M Johnson
Interface Lead Pharmacist
NHS Lincolnshire

October 2010

References

1. UKMI Midlands - Medicines management news Vol 1 issue 1 6th September.
2. UKMI medicines Q&As. UK Medicines Information. (Q&A 360.1) accessed from www.nelm.nhs.uk.
3. 'Mixtard 30 – going, going, gone?', *DTB* 2010; 48 (8): 85