Weekend therapy in diabetes
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Abstract
This article introduces the concept of "weekend therapy", which has now become reality in diabetes. It briefly describes injectable and oral drugs which are currently available, or are in advanced stages of development, for use in once weekly administration. These include dulaglutide, exenatide QW, semaglutide, omarigliptin and trelagliptin.

Keywords: Dulaglutide, Exenatide QW, Glucagon-like peptide 1 receptor agonists (GLP1RA), Semaglutide, Oimarigliptin, Trelagliptin.

Introduction
Once weekly therapy is popular in many endocrine diseases, including osteoporosis, hyper prolactinaemia and hypothyroidism. The use of such treatment regimens is thought to promote adherence and facilitate optimal outcomes.1 Recent advances in pharmacotherapy have now made it possible for such regimes to be offered in type 2 diabetes as well. We suggest the term 'weekend therapy', similar to that used in acne management,2 for this form of management.

Classification
Weekend therapy can be oral or injectable (Table-1). The oral drugs being developed for use in diabetes care include the dipeptidyl peptidase 4 inhibitors (DPP4i) omarigliptin and trelagliptin.3,4 All injectables that can be used as weekend therapy belong to the class of glucagon-like peptide 1 receptor agonists (GLP1RA). While exenatide QW and dulaglutide are approved for use in many markets, semaglutide is in advanced stages of development.5-7

Clinical Pharmacology
Omarigliptin has been studied as a 25 mg weekly dose, while trelagliptin is used in 100 mg weekly doses. Dulaglutide is available as a ready to use, prefilled pen, in strengths of 0.75 mg and 1.5 mg. Exenatide QW needs to be reconstituted before use, and is marketed in 2mg doses.

All once-weekly therapies described in this article are backed by robust clinical development programmes. While dulaglutide has been studied in the AWARD trials, exenatide QW has been assessed in the DURATION trials. One must be aware of the contraindications of long-acting DPP4i and GLP1RA. These are similar to those of other members of these drug classes.

Strengths and Limitations
The strengths and limitations of using a once weekly therapy are listed in Table-2. Such treatment offers the advantages of lower pill/injection burden enhanced convenience and adherence, with minimal requirement of self-monitoring of blood glucose. Thus, it lends itself to use as 'directly observed therapy' (DOT) in situations where intermittent oversight by health care professionals is required, or is available.8 All the molecules available as once-weekly preparations have a low risk of hypoglycaemia as well.

At the same time, the weekend therapies require less frequent glucose monitoring, and obviate the need for

Table-1: Once weekly/weekend therapies in diabetes.

<table>
<thead>
<tr>
<th>Dipeptidyl peptidase (DPP) 4 inhibitors</th>
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<tr>
<td>Omarigliptin</td>
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<td>Trelagliptin</td>
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<tr>
<td>Glucagon-like peptide (GLP) 1 receptor agonists</td>
</tr>
<tr>
<td>Exenatide QW</td>
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<tr>
<td>Dulaglutide</td>
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<td>Semaglutide</td>
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Table-2: Strengths and limitations of weekend therapy in diabetes.

- Strengths
  - Less complexity
  - Low pill/injection burden
  - Low risk of hypoglycaemia
  - Less frequent glucose monitoring required
  - Better adherence

- Limitations
  - Less flexibility
  - Inability to withdraw dose in case of adverse event.
self-monitoring of blood glucose (SMBG). This allows use of such therapy in patients who are unable to, or unwilling to monitor blood glucose frequently. Similarly, the injectable weekend therapies may be useful in patients who need GLP1RA, but are either unable or unwilling to accept or take daily injections.

Limitations, however, relate to their prolonged half-life and duration of action. Once in the system an injected or ingested drug cannot be taken out. This implies that once an adverse event occurs, it will continue to exert its effects for the remainder of its duration of action. Flexibility is also limited in such a regime: one cannot titrate doses to change the effect required.

Conclusion
As diabetes care evolves and improves, the weekend therapies maybe helpful in a large subset of patients. They may especially be useful in primary and rural health settings as minimal counselling and monitoring is required to use them effectively.

References
2. Loesche C, Pernin C, Poncet M. Adapalene 0.1% and benzoyl peroxide 2.5% as a fixed-dose combination gel is as well tolerated as the individual components alone in terms of cumulative irritancy. Eur J Dermatol, 2008; 18: 524-526.